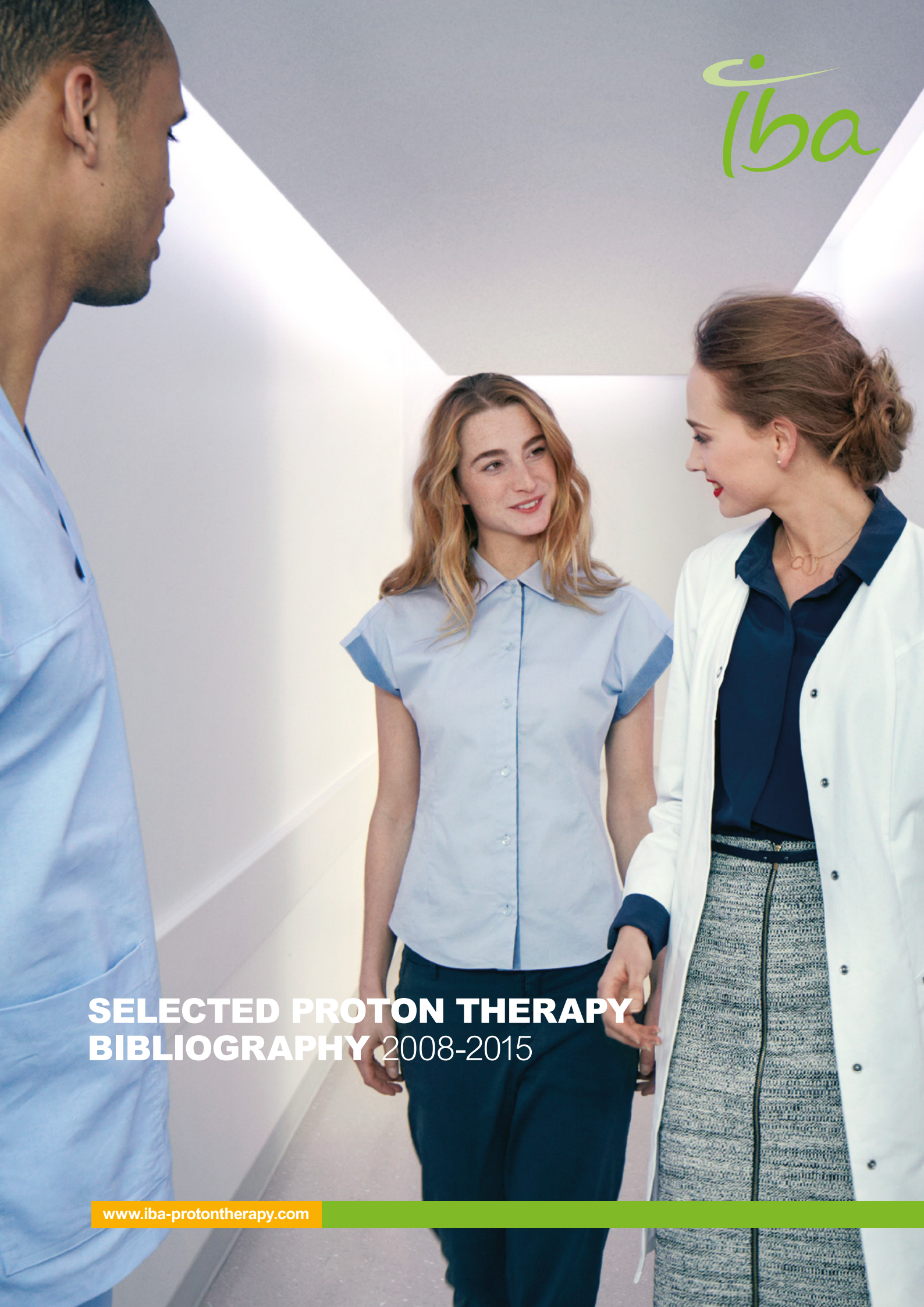


SELECTED PROTON THERAPY BIBLIOGRAPHY 2008-2015

www.iba-protontherapy.com

CONTENTS[1]

→ **REFERENCE BOOKS** **02**
→ **GENERAL ARTICLES** **03**
→ **CLINICAL INDICATIONS** **03**
– Central Nervous System Malignancies 04
– Ocular Malignancies and Benign Conditions 04
– Lymphomas 05
– Head and Neck Malignancies 07
– Lung Cancer and Thoracic Malignancies 07
– Breast Malignancies 08
– Liver Malignancies 09
– Pancreatic Malignancies 10
– Gastrointestinal Malignancies 10
– Cervical Malignancies 11
– Prostate Malignancies 11
– Sarcomas 11
– Pediatric Malignancies 12
→ **WEB REFERENCES** **14**

CONTACT US

AMERICAS
Toll-free: 1 877 IBA 4 PBT
T +1 904 491 6080

EUROPE, MIDDLE EAST AND AFRICA
T +32 10 203 342
F +32 10 475 923

RUSSIA & CIS
T/F +7 495 648 69 00
E-mail: info@iba-russia.ru

ASIA PACIFIC
T +86 10 8080 9186

E-mail: info-pt@iba-group.com
Visit us online at:
www.iba-proteusone.com

1. This literary review is a selection of articles about proton therapy and is not intended to be an exhaustive bibliography.

REFERENCE WORKS

→ Charlie Ma C.M. and Lomax T., "Proton and Carbon Ion Therapy", 2012, CRC Press.

This user guide for proton and carbon ion therapy in modern cancer treatment covers the physics and radiobiology of proton and ion beams, dosimetry methods, radiation measurements, treatment delivery systems, patient setup, target localization and treatment planning for clinical proton and carbon ion therapy. Detailed reports are also given on the treatment of pediatric cancers, lymphomas, and various other cancers.

→ Metz J.M. and Thomas R.T. Jr., "Proton Therapy", 2010, Radiation Medicine Rounds, Volume 1, Issue 3.

This work provides a comprehensive review for practitioners on the current status of PT, its scientific basis and current clinical applications, reviews of the available clinical evidence, discussions of costs and technology development, issues in establishing a PT center, and the future development of PT as a tool in clinical practice.

→ Paganetti H., "Proton Therapy Physics", 2012, Series in Medical Physics and Biomedical Engineering, Massachusetts General Hospital and Harvard Medical School, Boston, USA.

"Proton Therapy Physics" covers delivery methods of PT (including beam scanning and passive scattering) and clinical aspects (treatment planning and quality assurance), explores research topics such as biological treatment planning, and offers insight on the past, present, and future of PT from a physics perspective.

→ Yajnik S., "Proton Beam Therapy: How Protons Are Revolutionizing Cancer Treatment", 2012, Springer.

Here are discussed which conditions are suitable for treatment with PT, how the treatment is delivered, and the current data supporting its use.

GENERAL ARTICLES

→ Chung C.S. et al., "Comparative analysis of second malignancy risk in patients treated with Proton Therapy versus conventional Photon Therapy", Red Journal S0360-3016(08)01001-8, International Journal of Radiation Oncology, Biology, 2008 September 1.

Preliminary results here indicate that the use of PT is associated with a significantly lower risk of secondary malignancies compared to RT, even if additional analyses are required given the prolonged latency period for the development of radiation-induced cancers.

→ Dvorak T., Wazer D.E., "Evaluation of potential proton therapy utilization in a market-based environment", PubMed 20630388, Journal of the American College of Radiology, 2010, 7(7): 522-8.

Existing utilization patterns of highly conformal RT were used to estimate that about 1/3 of a patients irradiated annually at the institution could be potentially treated with PT, with an incremental cost of 20% across the entire treated patient population.

→ Grutters J. et al., "When to wait for more evidence? Real options analysis in proton therapy", The Oncologist, 2011, 16(12):1752-61.

As it is often unclear whether to adopt a new technology for cancer treatment or to wait for more evidence, a technique originating from financial economics called "real options analysis" can help make this trade-off. Regarding proton therapy, adopt and trial was found to be the preferred option.

→ Paganetti H. et al., "Assessment of radiation-induced second risks in proton therapy and IMRT for organs inside the primary radiation field", PubMed 22968191, Physics in medicine and biology, 2012, 57(19):6047-61.

Second malignancies in radiation therapy occur mainly within the beam path. Compared to traditional radiotherapy, PT can significantly reduce the risk of developing an in-field second malignancy, depending on treatment planning parameters.

→ Yoon M. et al., "Radiation-induced cancers from modern radiotherapy techniques: intensity-modulated radiotherapy versus proton therapy", PubMed 19879701, International Journal of Radiation Oncology, Biology, Physics, 2010, 77(5):1477-85.

Comparisons of organ-specific equivalent dose were made to assess the risk of secondary cancer after IMRT and PT in patients with prostate and head-and-neck cancer. The results showed the risk was either significantly lower with PT or, at least, did not exceed the risk induced by conventional IMRT.

CLINICAL INDICATIONS

CENTRAL NERVOUS SYSTEM MALIGNANCIES

→ Ares C. et al., "Effectiveness and safety of spot scanning proton radiation therapy for chordomas and chondrosarcomas of the skull base: first long-term report", PubMed 19386442, International Journal of Radiation Oncology, Biology, Physics, 2009 November 15, 75(4):1111-8.

Spot-scanning based PT for skull-base chordomas and chondrosarcomas appears to be effective and safe. With target definition, dose prescription and normal organ tolerance levels similar to passive-scattering PT, complication-free, tumor control and survival rates are comparable.

→ Brown A.P. et al., "Proton beam craniospinal irradiation reduces acute toxicity for adults with medulloblastoma", PubMed 23433794, International Journal of Radiation Oncology, Biology, Physics, 2013 June 1, 86(2):277-84.

This report is the first analysis of clinical outcomes for adult medulloblastoma patients treated with proton CSI. Patients treated with PT experienced less treatment-related morbidity than patients treated with conventional RT, including fewer acute gastrointestinal and hematologic toxicities.

→ Chen Y.L. et al. "Definitive high-dose photon/proton radiotherapy for unresected mobile spine and sacral chordomas", PubMed 23609202, Spine Journal, 2013 July 1, 38(15):E930-6.

The purpose of this study is to report the results of high-dose proton based definitive radiotherapy for unresected spinal chordomas. The results support the use of high-dose definitive radiotherapy for patients with medically inoperable or otherwise unresected, mobile spine or sacrococcygeal chordomas.

→ Delaney T.F. et al., "Phase II study of high-dose photon/proton radiotherapy in the management of spine sarcomas", PubMed 19095372, International Journal of Radiation Oncology, Biology, Physics, 2009, 74 (3):732-9.

Radiotherapy for spine sarcomas is constrained by spinal cord, nerve, and viscera tolerance. Negative surgical margins are uncommon, hence low doses are recommended. A Phase II clinical trial evaluated high-dose photon/proton XRT for spine sarcomas: local control appears high in patients radiated at the time of primary presentation.

→ Delaney T.F., "Long-term results of Phase II study of high dose photon/proton radiotherapy in the management of spine chordomas, chondrosarcomas and other sarcomas", PubMed 24752878, Journal of Surgical Oncology, 2014 August, 110(2):115-22.

Negative surgical margins are uncommon for spine sarcomas, hence adjuvant radiotherapy may be recommended. However, the dose to the tumor may be constrained by the spinal cord, nerves, and visceral tolerance. This study shows that local control with high dose photon/proton RT is high in patients with primary tumors, and late morbidity appears to be acceptable.

→ Deraniyagala R.L. et al., "Proton therapy for skull base chordomas: an outcome study from the university of Florida proton therapy institute", PubMed 24498590, Journal of Neurological Surgery, 2014 February, 75(1):53-7.

Skull base chordoma is a rare, locally aggressive tumor located adjacent to critical structures. Gross total resection is difficult to achieve, and PT has the conformal advantage of delivering a high postoperative dose to the tumor bed. The results obtained in this study are promising in terms of tumor control, and the toxicity profile is acceptable.

→ Grosshans D.R. et al., "Spot scanning proton therapy for malignancies of the base of skull: treatment planning, acute toxicities, and preliminary clinical outcomes", PubMed 25304948, International Journal of Radiation Oncology, Biology, Physics, 2014 November 1, 90(3):540-6.

This study describes treatment planning techniques and early clinical outcomes in patients treated with spot scanning PT for chordoma or chondrosarcoma of the skull base. In comparison to passive scattering, treatment plans for spot scanning PT displayed improved high-dose conformality. Clinically, treatment was well tolerated and disease control rates and toxicity profiles were favorable.

→ Hill-Kayser C. and Kirk M., "Brainstem-sparing craniospinal irradiation delivered with pencil beam scanning proton therapy", PubMed 25557901, Pediatric Blood Cancer, 2015 April, 62(4):718-20.

Delivery of craniospinal irradiation (CSI) is a curative approach to recurrent ependymoma but is associated with risks from reirradiation, particularly of the brainstem. PBS PT allows delivery of CSI with sparing of normal tissue and compares favorably to previously described methods using X-rays.

→ McDonald M.W. et al., "Proton therapy for atypical meningiomas", PubMed 25859843, Journal of Neuro-oncology, 2015 May, 123(1):123-8.

This paper reports clinical outcomes of PT in patients with World Health Organization grade 2 (atypical) meningiomas. Fractionated PT was associated with favorable tumor control rates.

→ Mizumoto M. et al., "Reirradiation for recurrent malignant brain tumor with radiotherapy or proton beam therapy. Technical considerations based on experience at a single institution", PubMed 23824106, Strahlentherapie und Onkologie, 2013 August, 189(8):656-63.

Radiotherapy for recurrent malignant brain tumors is usually limited because of the dose tolerance of the normal brain tissue. This study shows that reirradiation for recurrent malignant brain tumor using conventional RT, stereotactic RT or PT was feasible and effective in selected cases.

→ Shih H.A. et al., "Proton therapy for low-grade gliomas: Results from a prospective trial", PubMed 25585890, Cancer Cytopathology, 2015 May 15, 121(10):1712-9.

This prospective study evaluates the potential treatment toxicity and progression-free survival in patients with low-grade glioma who received treatment with PT. Patients tolerate PT well and only a subset develops neuroendocrine deficiencies.

→ Wattson D.A. et al., “Outcomes of proton therapy for patients with functional pituitary adenomas”, PubMed 25194666, International Journal of Radiation Oncology, Biology, Physics, 2014 November 1, 90(3):532-9.

This study evaluates the efficacy and toxicity of PT for functional pituitary adenomas (FPAs). Proton irradiation is an effective treatment for FPAs, with hypopituitarism remaining the primary adverse effect.

→ Weber D.C. et al.,“Spot-scanning based Proton Therapy for Intracranial Meningioma: Long-term Results from the Paul Scherrer Institute”, PubMed 22138457, International Journal of Radiation Oncology, Biology, Physics, 2012, 83(3):865-71.

In this study about the long-term clinical results of spot scanning PT for intracranial meningiomas, PT was proved to be a safe and effective treatment modality for patients with untreated, recurrent, or incompletely resected tumors.

OCULAR MALIGNANCIES AND BENIGN CONDITIONS

→ Kamran S.C. et al., “Outcomes of proton therapy for the treatment of uveal metastases”, PubMed 25442038, International Journal of Radiation Oncology, Biology, Physics, 2014 December 1, 90(5):1044-50.

Radiation therapy can be used to treat uveal metastases with the goal of local control and improvement of quality of life. PT is an effective and efficient means of treating uveal metastases, with minor acute adverse effects.

→ Mouw K.W. et al., “Proton radiation therapy for the treatment of retinoblastoma”, PubMed 25227498, International Journal of Radiation Oncology, Biology, Physics, 2014 November 15, 90(4):863-9.

This study investigates long-term disease and toxicity outcomes for pediatric retinoblastoma patients treated with PT. Long-term follow-up of retinoblastoma patients treated with PT demonstrates that it can achieve high local control rates, even in advanced cases, with many patients retaining useful vision in the treated eye.

→ Rahmi A. et al., “Proton beam therapy for presumed and confirmed iris melanomas: a review of 36 cases”, PubMed 25038910, Graefe’s Archive for Clinical and Experimental Ophthalmology, 2014 September, 252(9):1515-21.

This paper reports the clinical features and outcomes of iris melanomas treated by PT. PT appears to be the treatment of choice for the conservative treatment of iris melanomas with excellent tumor control and an acceptable complication rate.

→ Schönfeld S. et al., “Proton beam therapy leads to excellent local control rates in choroidal melanoma in the intermediate fundus zone”, PubMed 25128597, American Journal of Ophthalmology, 2014 December, 158(6):1184-91.

This study evaluates long-term outcomes of PT in the treatment of choroidal melanoma of the intermediate zone of the fundus and demonstrates the effectiveness of PT in tumor control and preservation of the globe in the analyzed patients.

→ Seibel I. et al., “Local recurrence after primary proton beam therapy in uveal melanoma: Risk factors, retreatment approaches and outcome”, PubMed 26133249, American Journal of Ophthalmology, 2015 June 29, pii: S0002-9394(15)00372-4.

This study evaluates the risk factors, recurrence rates, re-treatments, and long-term patient outcomes following PT for uveal melanoma. It is shown that each globe retaining re-treatment approach can result in satisfying local tumor control. In case of early detection of local recurrence, preservation of the globe can be warranted.

→ Wang Z. et al., “Charged particle radiation therapy for uveal melanoma: a systematic review and meta-analysis”, PubMed 23040219, International Journal of Radiation Oncology, Biology, Physics, 2013, 86(1):18-26.

The present analysis evaluates the efficacy and adverse effects of charged particle therapy (protons, helium ions, or carbon ions) for uveal melanoma. CPT was associated with lower retinopathy and cataract formation rates. Better outcomes may also be possible in terms of local recurrence, retinopathy, and cataract formation rates.

LYMPHOMAS

→ Rutenberg M.S., Flampouri S., Hoppe B.S., “Proton therapy for Hodgkin lymphoma”, PubMed 24842407, Current Hematologic Malignancy Reports, 2014 May 20.

This paper reviews the outcomes of Hodgkin lymphoma treated with PT and discusses the ability of protons to reduce radiation dose to OARs and the impact on the most significant late complications related to the treatment.

→ Sachsman S. et al., “Proton therapy in the management of non-Hodgkin lymphoma”, PubMed 25669925, Leukemia & Lymphoma, 2015 May, 18:1-5.

This study reviews a single institution’s experience managing patients with non-Hodgkin lymphoma (NHL) treated with PT. PT proved to be a feasible and effective treatment for NHL, with favorable early outcomes.

HEAD AND NECK MALIGNANCIES

- Chan A. and Liebsch N., "Proton radiation therapy for head and neck cancer", PubMed 18493920, Journal of surgical oncology, 2008, 97(8):697-700.

  Conventional RT can be associated with significant acute and long-term treatment-related toxicities in the treatment of head & neck tumors. Superior dose localization properties of proton radiation therapy allow smaller volumes of normal tissue to be irradiated than is feasible with any photon technique, and initial clinical experience with PT appears promising.

- Frank S.J. et al., "Gastrostomy Tubes Decrease by Over 50% With Intensity Modulated Proton Therapy (IMPT) During the Treatment of Oropharyngeal Cancer Patients: A Case–Control Study", International Journal of Radiation Oncology, Biology, Physics, 2013 October 1, Vol. 87, Issue 2, S144.

  A potential advantage of IMPT over IMRT in the treatment of oropharyngeal carcinoma (OPC) is a decrease in toxicity. This study quantifies the incidence of gastrostomy tube use in OPC patients treated with IMPT and compares it to gastrostomy use in patients treated with IMRT. Preliminary data suggest that IMPT has a lower rate of grade 3 dysphagia.

- Fuji H. et al., "High-dose proton beam therapy for sinonasal mucosal malignant melanoma", PubMed 25056641, Radiation Oncology, 2014 July 23, 9:162.

  The significance of definitive radiotherapy for sinonasal mucosal melanoma (SMM) is still controversial. This study evaluates the role of high-dose PT in patients with SMM. Findings suggest that high-dose PT is an effective local treatment that is less invasive than surgery but with comparable outcomes.

- Gunn G.B. and Frank S.J., "Advances in radiation oncology for the management of oropharyngeal tumors", PubMed 23910474, Otolaryngologic Clinics of North America, 2013, 46(4):629-43.

  The major benefits of modern radiation therapy in the treatment of oropharyngeal cancer are reduced xerostomia and better quality of life. Treatment-related toxicities must be kept in mind, particularly because most patients are expected to have a high probability of long-term survival after treatment. In this context, IMPT seems to provide additional advantages over IMRT by reducing radiation beam-path toxicities.

- Holliday E.B., Frank S.J., "Proton radiation therapy for head and neck cancer: a review of the clinical experience to date", PubMed 24837890, International Journal of Radiation Oncology, Biology, Physics, 2014 June 1, 89(2):292-302.

  PT has been used for cancer treatment since the 1950s, and both the number of patients and the variety of tumors treated have increased since then. Great interest has been expressed in evaluating whether PT can improve outcomes, especially early and late toxicity, when used in the treatment of head and neck malignancies. This review summarizes the progress made to date in addressing this question.

- Linton O.R. et al., "Proton therapy for head and neck adenoid cystic carcinoma: initial clinical outcomes", PubMed 25646551, Head & Neck, 2015 January, 37(1):117-24.

  The purpose of this study is to report outcomes of PT in head and neck adenoid cystic carcinoma. Initial outcomes are encouraging.

- Liu W. et al., "Effectiveness of robust optimization in intensity-modulated proton therapy planning for head and neck cancers", PubMed 23635259, Medical Physics, 2013, 40(5):051711.

  IMPT is highly sensitive to uncertainties in beam range and patient setup, which are conventionally addressed using geometrically expanded planning target volume (PTV). This paper evaluates IMPT for head & neck cancer and shows that robust optimization based on clinical target volume (CTV) provides significantly more robust dose distributions to targets and organs than PTV-based conventional optimization.

- Lukens J.N., Lin A. and Hahn S.M., "Proton therapy for head and neck cancer", PubMed 25811343, Current Opinion in Oncology, 2015 May, 27(3):165-71.

  PT for head and neck cancer is an area of active research, and the subject of heightened scrutiny due to the significant associated cost. This article highlights recent research into proton dosimetry, its clinical benefit relative to other advanced radiotherapy modalities, key safety and cost considerations.

- Ramaekers B., "Protons in head-and-neck cancer: bridging the gap of evidence", PubMed 23273998, International Journal of Radiation Oncology, Biology, Physics, 2013, 85(5):1282-8.

  Cost-effectiveness analysis based on normal tissue complication probability models and planning studies proved feasible and informative and enables the analysis of individualized strategies. The increased effectiveness of IMPT does not seem to outweigh the higher costs for all head-and-neck cancer patients. However, when assuming equal survival among both modalities, there seems to be value in identifying those patients for whom IMPT is cost-effective.

- Ramaekers B. et al., "Systematic review and meta-analysis of radiotherapy in various head and neck cancers: comparing photons, carbon-ions and protons", PubMed 20817407, Cancer Treatment Reviews, 2011, 37(3):185-201.

  This study synthesizes and compares available evidence considering the effectiveness of carbon-ion, proton and photon radiotherapy for head and neck cancer.

- Van de Water T. et al., "The potential benefit of radiotherapy with protons in head and neck cancer with respect to normal tissue sparing: a systematic review of literature", PubMed 21349950, The Oncologist, 2011, 16(3):366-77.

  Protons have the potential for a significantly lower normal tissue dose, while keeping similar or better target coverage. Scanned IMPT probably offers the most advantage and will allow for a substantially lower probability of radiation-induced side effects.

LUNG CANCER AND THORACIC MALIGNANCIES

- Berman A.T., James S.S. and Rengan R., "Proton Beam Therapy for Non-Small Cell Lung Cancer: Current Clinical Evidence and Future Directions, PubMed 26147335, Cancers, 2015 July 2, 7(3):1178-90.

  Lung cancer is the leading cancer cause of death in the US. Radiotherapy is an essential component of the definitive treatment of early-stage and locally-advanced lung cancer, and the palliative treatment of metastatic lung cancer. PT has the potential to decrease the toxicity of radiotherapy and subsequently to improve the therapeutic ratio.

- Bush D.A. et al., "High-dose hypofractionated proton beam radiation therapy is safe and effective for central and peripheral early-stage non-small cell lung cancer: results of a 12-year experience at Loma Linda University Medical Center", PubMed 23845845, International Journal of Radiation Oncology, Biology, Physics, 2013 August 1, 86(5):964-8.

  High-dose hypofractionated PT achieves excellent outcomes for central or peripheral lung carcinomas. The 70-Gy regimen has been adopted as standard therapy for T1 tumors at Loma Linda. Larger T2 tumors show improved outcomes with higher doses, suggesting that better results could be seen with intensified treatment.

- Chang J. et al., "Phase 2 study of high-dose proton therapy with concurrent chemotherapy for unresectable stage III nonsmall cell lung cancer", PubMed 21437893, The Oncologist, 2011, 117(20):4707-13.

  In this study, authors show that using PT to escalate the radiation dose to the tumor could improve the toxicity of conventional concurrent chemoradiation therapy for stage III non-small cell lung cancer.

- Chang J.Y. et al., "Clinical implementation of intensity modulated proton therapy for thoracic malignancies", PubMed 25260491, International Journal of Radiation Oncology, Biology, Physics, 2014 November 15, 90(4):809-18.

  This paper reports early experience with IMPT for thoracic malignancies in terms of motion analysis and management, plan optimization and robustness, and quality assurance. IMPT using 4D CT-based planning, motion management, and optimization was implemented successfully and met quality assurance parameters for treating challenging thoracic cancers.

- Colaco R.J. et al., "Dosimetric rationale and early experience at UFPTI of thoracic proton therapy and chemotherapy in limited-stage small cell lung cancer", PubMed 23438357, Acta Oncologica, 2013 February 26, 52(3):506-13.

  Concurrent chemoradiotherapy is the standard of care in patients with limited-stage SCLC. While treatment with conventional RT is associated with high toxicity rates (particularly acute esophagitis and pneumonitis), this study shows that PT with radical intent was well tolerated, with no cases of acute toxicities and better sparing of lung and esophagus.

- Gomez D.R., Chang J.Y., "Accelerated dose escalation with proton beam therapy for non-small cell lung cancer", PubMed 24688779, Journal of Thoracic Disease, 2014 April, 6(4):348-55.

  Local tumor control remains challenging in many cases of NSCLC, large or centrally located tumors. Concurrent chemotherapy and radiation can maximize tumor control and survival but a large proportion of patients cannot tolerate this therapy. The energy distribution of protons can be exploited to reduce involuntary irradiation of normal tissue and the resulting side effects.

- Hoppe B.S. et al., "Proton therapy with concurrent chemotherapy for non-small-cell lung cancer: technique and early results", PubMed 22264659, Clinical Lung Cancer, 2012 September, 13(5):352-8.

  PT can deliver a more conformal dose distribution than RT and may allow safe dose escalation in stage III lung cancer. Early outcomes are presented here for patients who received mediastinal PT with concurrent chemotherapy for NSCLC, which was associated with acceptable toxicity.

- Koay E.J. et al., "Adaptive/Nonadaptive Proton Radiation Planning and Outcomes in a Phase II Trial for Locally Advanced Non-small Cell Lung Cancer", PubMed 22543217, International Journal of Radiation Oncology, Biology, Physics, 2012, 84(5):1093-100.

  Adaptive planning can reduce normal tissue doses and prevent target misses, particularly for patients with large tumors that shrink substantially during therapy. Adaptive plans seem to have acceptable toxicity and achieve same local, regional, and distant control and overall survival as non-adaptive plans, even in patients with larger tumors.

- McAvoy S.A. et al., "Feasibility of proton beam therapy for reirradiation of locoregionally recurrent non-small cell lung cancer", PubMed 24016675, Radiotherapy and Oncology, 2013 October, 109(1):38-44.

  Options are limited for patients with intrathoracic recurrence of NSCLC who previously received radiation. This paper reports 5-year experience with the toxicity and efficacy of PT for reirradiation and shows that PT is an option for treating recurrent NSCLC.

- McAvoy S.A. et al., "Definitive reirradiation for locoregionally recurrent non-small cell lung cancer with proton beam therapy or intensity modulated radiation therapy: predictors of high-grade toxicity and survival outcomes", PubMed 25220718, International Journal of Radiation Oncology, Biology, Physics, 2014 November 15, 90(4):819-27.

  Intrathoracic recurrence of NSCLC after initial treatment remains a dominant cause of death. IMRT and PT are options for treating recurrent NSCLC, but rates of locoregional recurrence and distant metastasis are high, and patients should be selected carefully to maximize the benefit of additional aggressive local therapy while minimizing the risk of adverse side effects.

- Makita C. et al., "High-dose proton beam therapy for stage I non-small cell lung cancer: Clinical outcomes and prognostic factors", PubMed 25291076, Acta Oncologica, 2015 March, 54(3):307-14.

  Evidence has suggested that RT with a lower dose per fraction may be a reasonable option for the treatment of centrally located NSCLC. The aim of this study was to evaluate the safety and efficacy of two PT protocols for stage I NSCLC and to determine prognostic factors. Both high-dose PT protocols achieved high local control rates with tolerable toxicities.

- Ohno T. et al., “Comparison of dose-volume histograms between proton beam and X-ray conformal radiotherapy for locally advanced non-small-cell lung cancer”, PubMed 25368341, Journal of Radiation Research, 2015 January, 56(1):128-33.

  The purpose of this study was to compare the parameters of the dose-volume histogram between PT and conformal RT for locally advanced NSCLC. The number of inadequate X-ray plans increased in cases with advanced nodal stage. This study indicated that some patients who cannot receive RT may be able to be treated using PT.

- Oshiro Y. et al., “High-dose concurrent chemo-proton therapy for Stage III NSCLC: preliminary results of a Phase II study”, PubMed 24864278, Journal of Radiation Research, 2014 May 25.

  High-dose PT with concurrent chemotherapy is safe to use in the treatment of unresectable stage III NSCLC.

- Oshiro Y. et al., “Results of proton beam therapy without concurrent chemotherapy for patients with unresectable stage III non-small cell lung cancer”, PubMed 22157368, Journal of Thoracic Oncology, 2012 February, 7(2):370-5.

  This study was performed retrospectively to evaluate the outcomes of patients with stage III NSCLC after PT alone. The prognosis of patients with unresectable stage III NSCLC is poor without chemotherapy. Our data suggest that high-dose PT is beneficial and tolerable for these patients.

- Pan H.Y. et al., “Early experience with intensity modulated proton therapy for lung-intact mesothelioma: A case series”, PubMed 25572666, Practical Radiation Oncology, 2015 July-August, 5(4):e345-53.

  The purpose of this study was to describe our experience implementing IMPT for lung-intact malignant pleural mesothelioma, including patient selection, treatment planning, dose verification, and process optimization. Results showed that IMPT is feasible.

- Schild S.E. et al., “Proton beam therapy for locally advanced lung cancer: A review”, PubMed 25302161, World Journal of Clinical Oncology, 2014 October, 10;5(4):568-75.

  This review examines PT as a component of a combined modality program for locally advanced lung cancers. It is specifically written for non-radiation oncologists who desire greater understanding of this newer treatment modality, and shows that newer forms of radiotherapy such as PT should positively impact the care of lung cancer patients.

- Sejpal S. “Early findings on toxicity of proton beam therapy with concurrent chemotherapy for nonsmall cell lung cancer”, PubMed 21264827, Cancer, 2011, 1; 117(13):3004-13.

  Concurrent chemoradiation therapy, the standard of care for locally advanced NSCLC, can cause life-threatening pneumonitis and esophagitis. Whereas RT often cannot be given at tumoricidal doses without toxicity to proximal normal tissue, higher doses of proton radiation can be delivered with a lower risk of esophagitis and pneumonitis.

- Westover K.D. et al., “Proton SBRT for medically inoperable stage I NSCLC”, PubMed 22551902, Journal of Thoracic Oncology, 2012, 7(6):1021-5.

  The physical properties of proton beam radiation may offer advantages for treating patients with NSCLC. This study also shows its utility for the treatment of medically inoperable stage I NSCLC patients with stereotactic body radiation therapy (SBRT).

BREAST MALIGNANCIES

- Ares C. et al., “Postoperative proton radiotherapy for localized and locoregional breast cancer: potential for clinically relevant improvements?”, PubMed 19615828, International Journal of Radiation Oncology, Biology, Physics, 2010, 76(3):685-97.

  When complex-target irradiation is needed, 3D conformal RT often compromises the target coverage and increases the dose to OARs, and IMRT increases the integral dose. On the other hand, IMPT improves target coverage and reduction of low doses to OARs, potentially reducing the risk of late-toxicity.

- Bush D.A. et al., “Partial breast radiation therapy with proton beam: 5-year results with cosmetic outcomes”, PubMed 25084608, International Journal of Radiation Oncology, Biology, Physics, 2014 November 1, 90(3):501-5.

  This paper is an update of a previous report of a phase 2 trial using PT for partial breast irradiation in patients with early stage breast cancer. PT produces excellent ipsilateral breast recurrence-free survival with minimal toxicity and excellent cosmetic results. The treatment proves to be adaptable to all breast sizes and lumpectomy cavity configurations.

- Chang J. et al., “Phase II trial of proton beam accelerated partial breast irradiation in breast cancer”, PubMed 23891102, Radiotherapy and oncology: Journal of the European society for therapeutic radiology and oncology, 2013, S0167-8140(13)00284-3.

  Proton beam accelerated partial breast irradiation (PB-APBI) can be delivered with excellent disease control and tolerable skin toxicity to properly selected patients with early-stage breast cancer. Multiple-field PB-APBI may achieve a high rate of good-to-excellent cosmetic outcomes.

- Cuaron J.J. et al., “Early toxicity in patients treated with postoperative proton therapy for locally advanced breast cancer”, PubMed 25754632, International Journal of Radiation Oncology, Biology, Physics, 2015 June 1, 92(2):284-91.

  Postoperative PT for patients with breast cancer is well tolerated, with acceptable rates of skin toxicity. PT favorably spares normal tissue without compromising target coverage.

- Jimenez R. et al., “Intensity modulated proton therapy for post mastectomy radiation of bilateral implant reconstructed breasts: a treatment planning study”, PubMed 23647751, Radiotherapy and oncology: Journal of the European society for therapeutic radiology and oncology, 2013, 107(2):213-7.

  Delivery of post-mastectomy radiation (PMRT) in women with bilateral implants represents a technical challenge, particularly when attempting to cover regional lymph nodes. IMPT provides improved homogeneity to the chest wall and regional lymphatics with improved sparing of surrounding normal structures. It may also enable women with mastectomy to undergo radiation therapy without the need for delay in breast reconstruction.

- Lin L.L. et al., “Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer”, PubMed 25789715, Acta Oncologica, 2015 July, 54(7):1032-9.

  The purpose of this study was to compare the dose to the heart, left anterior descending (LAD) artery and lung between PT and RT for left-sided early stage breast cancer. PT was associated with lower dose to the LAD, which is the critical structure for late radiation therapy effects, compared to even the most optimized photon beam plan with deep inspiration breath hold and IMRT.

- MacDonald S.M. et al., “Proton therapy for breast cancer after mastectomy: early outcomes of a prospective clinical trial”, PubMed 23523326, International Journal of Radiation Oncology, Biology, Physics, 2013 July 1, 86(3):484-90.

  Dosimetric planning studies have described potential benefits for the use of PT for locally advanced breast cancer. This study shows that PT for postmastectomy radiotherapy is feasible and well tolerated. This treatment may be warranted for selected patients with unfavorable cardiac anatomy, immediate reconstruction, or both that otherwise limits optimal radiotherapy delivery using standard methods.

- MacDonald S.M. et al., “Proton radiotherapy for chest wall and regional lymphatic radiation; dose comparisons and treatment delivery”, PubMed 23521809, Radiation Oncology, 2013 March 24, 8(71).

  The delivery of post-mastectomy radiation therapy can be challenging for patients with left-sided breast cancer that have undergone mastectomy. Proton RT enables delivery of radiation to the chest wall and regional lymphatics, including the internal mammary nodes, without compromise of coverage and with improved sparing of surrounding normal structures.

- Mast M.E. et al., “Whole breast proton irradiation for maximal reduction of heart dose in breast cancer patients”, PubMed 25266130, Breast Cancer Research and Treatment, 2014 November, 148(1):33-9.

  IMPT could significantly decrease the dose to the heart and the region of the left anterior descending coronary artery compared to tangential IMRT with breath-hold, and could be particularly useful for patients at high risk for major coronary events.

- Xu N. et al., “Can Proton Therapy Improve the Therapeutic Ratio in Breast Cancer Patients at Risk for Nodal Disease?”, PubMed 23466577, American Journal of Clinical Oncology, 2014 December, 37(6):568-74.

  Regional node irradiation in patients with invasive breast cancer often results in increased radiation exposure to organs at risk. This study shows that regional node target coverage is inferior with 3D conformal RT compared with either IMRT or 3D conformal RT+PT, with which OARs were exposed to less radiation. PT offers both improved coverage of the regional lymph nodes and decreased dose to the heart, lung, and contralateral normal tissue.

LIVER MALIGNANCIES

- Bush D.A. et al., “The safety and efficacy of high-dose proton beam radiotherapy for hepatocellular carcinoma: a phase 2 prospective trial”, PubMed 21264826, Cancer, 2011, 117 (13): 3053-9.

  PT may provide useful local-regional treatment for hepatocellular carcinoma (HCC). In this study, PT was found to be a safe and effective local-regional therapy for inoperable HCC. A randomized controlled trial to compare its efficacy to a standard therapy has been initiated.

- Dionisi F., Widesott L., Lorentini S., Amichetti M., “Is there a role for proton therapy in the treatment of hepatocellular carcinoma? A systematic review”, PubMed 24560761, Radiotherapy and Oncology, 2014 April, 111(1):1-10.

  This paper reviews the literature concerning the systematic use of PT in the treatment of HCC, focusing on clinical results and technical issues. The literature search was conducted according to a specific protocol in the Medline and Scopus databases by two independent researchers covering the period of 1990-2012.

- Dionisi F. and Ben-Josef E., “The use of proton therapy in the treatment of gastrointestinal cancers: liver”, PubMed 25415681, Cancer Journal, 2014 November-December, 20(6):371-7.

  This article reviews the role of PT in the treatment of primary liver cancer focusing on hepatocellular carcinoma (HCC). The dose-sparing physical properties of protons are of great advantage in the treatment of HCC.

- Kim T.H. et al., “Phase I dose-escalation study of proton beam therapy for inoperable hepatocellular carcinoma”, PubMed 25381830, Cancer Research and Treatment, 2015 January, 47(1):34-45.

  The purpose of this study is to determine the optimal dose of PT in hepatocellular carcinoma patients (HCC). PT is safe and effective in patients with inoperable HCC, with at least 78 GyE10 of EQD2 needed to achieve sufficient local tumor control.

- Lee S.U. et al., “Effectiveness and safety of proton beam therapy for advanced hepatocellular carcinoma with portal vein tumor thrombosis”, PubMed 24589917, Strahlentherapie und Onkologie, 2014 Mar 4.

  This study evaluates the clinical effectiveness and safety of PT in advanced HCC patients with portal vein tumor thrombosis (PVTT). It suggests that PT could improve local progression-free survival, relapse-free survival, and overall survival in advanced HCC patients with PVTT, and that it is feasible and safe for these patients.

- Ling T.C. et al., “Proton therapy for hepatocellular carcinoma”, PubMed 23359779 Chinese Journal of Cancer Research, 2012 December, 24(4): 361–367.

  PT has seen an increasing role in the treatment of hepatocellular carcinoma (HCC). This review discusses the physical attributes and rationale for PT in HCC. It also reviews recent literature regarding clinical outcomes of using PT for the treatment of HCC.

- Masato A., “A phase I study on combined therapy with proton-beam radiotherapy and in situ tumor vaccination for locally advanced recurrent hepatocellular carcinoma” PubMed 24131485, Radiation Oncology, 2013, 8(239).

  This study reports on a prospective phase I study of ‘in situ’ tumor vaccination using CaITUMP, a newly developed immunoadjuvant, following local PT for HCC to prevent the cancer recurrence. The treatment was feasible and safe in patients with heavily pre-treated HCC.

→ Ohkawa A. et al., “Proton beam therapy for unresectable intrahepatic cholangiocarcinoma”, PubMed 25376272, Journal of Gastroenterology and Hepatology, 2015 May, 30(5):957-63.

Treatment for unresectable intrahepatic cholangiocarcinoma (ICC) has not been established. The aim of this study is to evaluate the outcomes of PT for patients with unresectable ICC. The results suggest that long-term survival can be achieved for patients without distant metastasis.

→ Petersen J. et al., “Normal liver tissue sparing by intensity-modulated proton stereotactic body radiotherapy for solitary liver tumours”, PubMed 21767180, Acta Oncologica (Stockholm, Sweden), 2011, 5 0(6):823-8.

Stereotactic body radiotherapy (SBRT) is often the preferred treatment for advanced liver tumors that are out of range of surgical resection or radiofrequency ablation. However, only a minority of patients may be candidates because of the limited radiation tolerance of normal liver and intestine. Due to the favorable depth-dose characteristics of protons, a considerable sparing of normal tissue can be obtained using proton-based SBRT for solitary liver tumors.

→ Sugahara S. et al. “Proton-beam therapy for hepatocellular carcinoma associated with portal vein tumor thrombosis”, PubMed 20013087, Strahlentherapie und Onkologie, 2009 December, 185(12):782-8.

The prognosis of patients with advanced hepatocellular carcinoma with portal vein tumor thrombosis is extremely poor, as effective treatment options are limited. This paper shows that PT improves local control and significantly prolongs survival in these patients.

→ Taddei P.J. et al., “Risk of second malignant neoplasm following proton versus intensity-modulated photon radiotherapies for hepatocellular carcinoma.” PubMed 21076199, Physics in medicine and biology, 2010, 7;55(23):7055-65.

Hepatocellular carcinoma (HCC) is the sixth most common cancer in the world, but radiotherapy remains uncommon because of the likelihood of radiation-induced liver disease. This study suggests that PT may reduce the risk of second malignant neoplasms compared to RT for some HCC patients.

PANCREATIC MALIGNANCIES

→ Hong T.S. et al., “Phase I study of preoperative short-course chemoradiation with proton beam therapy and capecitabine for resectable pancreatic ductal adenocarcinoma of the head”, PubMed 20421151, International Journal of Radiation Oncology, Biology, Physics, 2011, 79 (1): 151-7.

This study shows the safety and feasibility of 1 week of chemoradiation with PT and capecitabine followed by early surgery.

→ Nichols R.C. Jr et al., “Protons Offer Reduced Normal-Tissue Exposure for Patients Receiving Postoperative Radiotherapy for Resected Pancreatic Head Cancer”, PubMed 22245197, International Journal of Radiation Oncology, Biology, Physics, 2012, 83(1):158-63.

The potential role for adjuvant PT for resected pancreatic head cancer was assessed in this study. By reducing small bowel and stomach exposure, protons have the potential to reduce the acute and late toxicities of postoperative chemoradiation.

→ Nichols R.C. Jr. et al., “Proton therapy with concomitant capecitabine for pancreatic and ampullary cancers is associated with a low incidence of gastrointestinal toxicity”, PubMed 23477361, Acta Oncologica, 2013 April, 52(3):498-505.

PT may allow for significant sparing of the small bowel and stomach and is associated with a low rate of gastrointestinal toxicity. The favorable toxicity profile associated with PT may allow for radiotherapy dose escalation, chemotherapy intensification, and possibly increased acceptance of preoperative radiotherapy.

→ Thompson R.F. et al., “A dosimetric comparison of proton and photon therapy in unresectable cancers of the head of pancreas”, PubMed 25086521, Medical Physics, 2014 August, 41(8):081711.

Uncontrolled local growth is the cause of death in ~ 30% of patients with unresectable pancreatic cancers. In this study, the authors investigate the potential use of double scattering and PBS PT in limiting dose to critical OARs. If PT does not appear to reduce OAR volumes receiving high dose, it is however able to reduce the treated volume receiving low-intermediate doses.

GASTROINTESTINAL MALIGNANCIES

→ Colaco R.J. et al., “Protons offer reduced bone marrow, small bowel, and urinary bladder exposure for patients receiving neoadjuvant radiotherapy for resectable rectal cancer”, PubMed 24490037, Journal of Gastrointestinal Oncology, 2014 February, 5(1):3-8.

This study compares 3D conformal RT, IMRT and PT plans in patients undergoing neoadjuvant chemoradiation for resectable rectal cancer. By reducing bone marrow exposure, PT may reduce the acute hematologic toxicity of neoadjuvant chemoradiation.

→ Makishima H. et al., “Comparison of adverse effects of proton and X-ray chemoradiotherapy for esophageal cancer using an adaptive dose-volume histogram analysis”, PubMed 25755255, Journal of Radiation Research, 2015 May, 56(3):568-76.

Cardiopulmonary late toxicity is of concern in concurrent chemoradiotherapy (CCRT) for esophageal cancer. The aim of this study was to examine the benefit of PT using clinical data and adaptive dose-volume histogram analysis. Irradiation dose, volume and adverse effects on the heart and lung can be reduced using protons; hence PT is a promising treatment modality for the management of esophageal cancer.

→ Ojerholm E. et al., “Pencil-beam scanning proton therapy for anal cancer: a dosimetric comparison with intensity-modulated radiotherapy”, PubMed 25734796, Acta Oncologica, 2015 Mar 3:1-9.

Concurrent chemoradiotherapy cures most patients with anal squamous cell carcinoma at the cost of significant treatment-related toxicities. If IMRT reduces side effects compared to older techniques, PT offers additional advantages by reducing low dose radiation to important organs at risk.

→ Plastaras J.P., Dionisi F. and Wo J.Y., "Gastrointestinal cancer: non-liver proton therapy for gastrointestinal cancers", PubMed 25415682, Cancer Journal, 2014 November-December, 20(6):378-86.

Multimodality therapy for gastrointestinal cancers carries considerable risk for toxicity, as they inherently occur amid visceral organs particularly sensitive to radiotherapy. In many sites, local recurrences after chemoradiation pose a particular challenge, and reirradiation in these sites may be done successfully with PT.

CERVICAL MALIGNANCIES

→ Clivio A. et al., "Intensity modulated proton beam radiation for brachytherapy in patients with cervical carcinoma", PubMed 24119834, International Journal of Radiation Oncology, Biology, Physics, 2013 December 1, 87(5):897-903.

In patients who are not eligible for brachytherapy, IMPT as a boost technique additionally to external beam radiation therapy provides good target coverage and conformity and superior dose-volume parameters, compared with recommendations to MRI-guided brachytherapy. For selected patients, IMPT might be a valid alternative to brachytherapy and also superior to reference VMAT plans.

PROSTATE MALIGNANCIES

→ Hoppe B.S. et al., "Erectile function, incontinence, and other quality of life outcomes following proton therapy for prostate cancer in men 60 years old and younger", PubMed 22253020, Cancer, 2012, 15;118(18):4619-26.

Young men (≤ 60 years old) undergoing PT for treatment of prostate cancer have excellent outcomes with respect to erectile dysfunction, urinary incontinence, and other health-related quality of life parameters during the first 2 years after treatment.

→ Mendenhall N.P. et al., "Early outcomes from three prospective trials of image-guided proton therapy for prostate cancer", PubMed 21093164, International Journal of Radiation Oncology, Biology, Physics, 2012, 1; 82(1):213-21.

Early outcomes with image-guided PT for prostate cancer suggest high efficacy and minimal toxicity, with only 1.9% grade III genito-urinary symptoms and less than 0.5% grade III gastro-intestinal toxicities.

→ Mendenhall N.P., "Five-year outcomes from 3 prospective trials of image-guided proton therapy for prostate cancer", PubMed 24521677, International Journal of Radiation Oncology, Biology, Physics, 2014 March 1, 88(3):596-602.

Five-year clinical outcomes with image-guided PT for prostate cancer included extremely high efficacy, minimal physician-assessed toxicity, and excellent patient-reported outcomes.

→ Nihei K. et al., "Multi-institutional Phase II study of proton beam therapy for organ-confined prostate cancer focusing on the incidence of late rectal toxicities", PubMed 20832180, International Journal of Radiation Oncology, Biology, Physics, 2011, 81 (2):390-6.

PT is theoretically an excellent modality for external beam radiotherapy, providing an ideal dose distribution. However, it is not clear whether PT for prostate cancer can clinically control toxicities. This prospective study has revealed that PT for localized prostate cancer can achieve a low incidence of late grade II or greater rectal toxicities.

→ Wisenbaugh E.S. et al., "Proton beam therapy for localized prostate cancer 101: basics, controversies, and facts", PubMed 25009446, Reviews in Urology, 2014, 16(2):67-75.

PT for prostate cancer has become a source of controversy in the urologic community, and the rapid dissemination and marketing of this technology has led to many patients inquiring about this therapy. This article reviews the basic science of the proton beam and examines the literature so that every urologist is able to comfortably discuss this option with inquiring patients.

→ Zietman A.L. et al., "Randomized trial comparing conventional-dose with high-dose conformal radiation therapy in early-stage adenocarcinoma of the prostate: long-term results from proton radiation oncology group/american college of radiology 95-09", PubMed 20124169, Journal of Clinical Oncology (ASCO), 2010, 28 (7):1106-11.

This randomized controlled trial aimed at testing the hypothesis that increasing radiation dose delivered to men with early-stage prostate cancer improves clinical outcomes. The results showed superior long-term cancer control compared to conventional-dose radiation. This was achieved without an increase in grade III late urinary or rectal morbidity.

SARCOMAS

→ Ciernik I.F. et al., "Proton-based radiotherapy for unresectable or incompletely resected osteosarcoma", PubMed 21448934, Cancer, 2011, 117(19):4522-30.

A study was undertaken to assess clinical outcomes and the role of PT for local control of osteosarcoma. It was shown that PT to deliver high radiotherapy doses allows locally curative treatment for some patients with unresectable or incompletely resected osteosarcoma.

PEDIATRIC MALIGNANCIES

→ Armstrong F.D., Holtz Children's Hospital, "Proton-Beam Radiation Therapy and Health-Related Quality of Life in Children With CNS Tumors", JCO 2012 42 1248, Journal of Clinical Oncology (ASCO), 2012, Vol. 30, as 10.1200/JCO.2012.42.1248.

Children treated for CNS tumors with conventional RT or cranial radiation therapy (CRT) are at high risk of neurocognitive impairment or dysfunction. Delaying or reducing CRT and using chemotherapy as primary therapy have improved survival and the neurocognitive trajectory. Similarly, the use of PT may now offer the next step with respect to both survival and long-term neurocognitive functioning.

→ Amsbaugh M.J. et al., "Proton therapy for spinal ependymomas: planning, acute toxicities, and preliminary outcomes", PubMed 22245209, International Journal of Radiation Oncology, Biology, Physics, 2012 August 1, 83(5):1419-24.

PT offers a powerful treatment option in the pediatric population, where adverse events related to radiation exposure are of concern. This study reports acute toxicities and preliminary outcomes for pediatric patients with ependymomas of the spine treated with PT at the MD Anderson Cancer Center.

→ Bishop A.J. et al, "Proton beam therapy versus conformal photon radiation therapy for childhood craniopharyngioma: multi-institutional analysis of outcomes, cyst dynamics, and toxicity", PubMed 25052561, International Journal of Radiation Oncology, Biology, Physics, 2014 October 1, 90(2):354-61.

This paper compares PT with IMRT for pediatric craniopharyngioma in terms of disease control, cyst dynamics and toxicity.

→ Cotter S.E. et al., "Proton radiotherapy for solid tumors of childhood", PubMed 22417062, Technology in cancer research and treatment, 2012, 11(3):267-78.

The increasing efficacy of pediatric cancer therapy has produced many long-term survivors who now struggle with serious morbidities mostly related to radiation therapy. PT holds great promise to drastically reduce these treatment-related late effects in long term survivors by reducing dose to normal tissue.

→ Cotter S.E. et al. "Proton radiotherapy for pediatric bladder/prostate rhabdomyosarcoma: clinical outcomes and dosimetry compared to intensity modulated radiation therapy", PubMed 20934266, International Journal of Radiation Oncology, Biology, Physics, 2011 December 1, 81(5):1367-73.

This paper reports the clinical outcomes of 7 children with bladder/prostate rhabdomyosarcoma treated with PT and compares PT plans with matched IMRT plans, with an emphasis on dose savings to reproductive and skeletal structures. PT provides significant dose savings to normal structures compared to IMRT and is well tolerated in this patient population.

→ Greenberger B.A. et al., "Clinical outcomes and late endocrine, neurocognitive, and visual profiles of proton radiation for pediatric low-grade gliomas", PubMed 25035209, International Journal of Radiation Oncology, Biology, Physics, 2014 August 1, 89(5):1060-8.

Primary low-grade gliomas are common brain tumors of childhood, and many of them require radiation therapy as definitive treatment. Increased conformality could decrease the incidence and severity of late effects. PT appears to be associated with good clinical outcomes, especially when the tumor location allows for increased sparing of the left temporal lobe, hippocampus, and hypothalamic-pituitary axis.

→ Habrand J.L. et al., "Proton therapy in pediatric skull base and cervical canal low-grade bone malignancies", PubMed 18440726, International Journal of Radiation Oncology, Biology, Physics, 2008 July 1, 71(3):672-5.

This paper evaluates outcomes and tolerance of high-dose RT and PT in the management of skull base and cervical canal primary bony malignancies in children. High-dose combined fractionated photon-proton therapy is well tolerated in children and allows excellent local control with minimal long-term toxicity.

→ Hoppe B.S., "Involved-node proton therapy in combined modality therapy for hodgkin lymphoma: results of a phase 2 study", PubMed 24928256, International Journal of Radiation Oncology, Biology, Physics, 2014 August 1, 89(5):1053-9.

This study describes the early clinical outcomes of a prospective phase 2 study of consolidative involved-node PT as a component of combined-mode therapy in patients with stages I to III Hodgkin lymphoma with mediastinal involvement.

→ Indelicato D.J. et al., "Incidence and dosimetric parameters of pediatric brainstem toxicity following proton therapy", PubMed 25279957, Acta Oncologica, 2014 October, 53(10):1298-304.

PT offers superior low and intermediate radiation dose distribution compared with photon RT for brain and skull base tumors. This article investigates the tolerance of the pediatric brainstem to PT and shows that the utilization of current national brainstem dose guidelines is associated with a low risk of brainstem toxicity in pediatric patients.

→ Jimenez R. et al., "Proton radiation therapy for pediatric medulloblastoma and supratentorial primitive neuroectodermal tumors: outcomes for very young children treated with upfront chemotherapy", PubMed 23790826, International Journal of Radiation Oncology, Biology, Physics, 2013, 87(1):120-6.

Upfront chemotherapy followed by 3D PT presents good disease early outcomes for very young children with medulloblastoma or supratentorial primitive neuroectodermal tumor.

→ Kumar R.J. et al., "Breast cancer screening for childhood cancer survivors after craniospinal irradiation with protons versus x-rays: a dosimetric analysis and review of the literature", PubMed 23892352, Journal of Pediatric Hematology/Oncology, 2013, 35(6):462-7.

Early screening for breast cancer may be unnecessary after craniospinal irradiation with PT, whereas it should be considered with X-ray therapy, given doses to the breast that approach the Children's Oncology Group-recommended threshold.

→ Ladra M.M. and Yock T.I. "Proton radiotherapy for pediatric sarcoma", PubMed PMC3980591, Cancers, 2014 March, 6(1): 112–127.

Radiotherapy plays an integral role in the local control of pediatric sarcomas, which often arise adjacent to critical structures and growing organs. PT shows either equivalent or improved outcomes, and lower toxicity for soft tissue sarcoma compared to RT. For bone and cartilaginous sarcomas, a clearer advantage exists for PT due to its ability to increase total dose while respecting adjacent structures.

→ Lucas J.T. Jr. et al., “Proton therapy for pediatric and adolescent esthesioneuroblastoma”, PubMed 25820437, Pediatric Blood Cancer, 2015 March 27.

Esthesioneuroblastoma of the paranasal sinus comprises less than 3% of tumors in pediatric and adolescent patients. The collective adult literature indicates a critical role for radiotherapy in attaining cure, yet pediatric outcome data is limited. This study shows that PT provides excellent locoregional disease control even in patients with locally advanced disease and intracranial extension.

→ MacDonald S.M. et al., “Proton radiotherapy for childhood ependymoma: initial clinical outcomes and dose comparisons”, PubMed 18325681, International Journal of Radiation Oncology, Biology, Physics, 2008, 15; 71(4):979-86.

This study reports on clinical outcomes for pediatric patients treated with PT for intracranial ependymoma and compares the dose distributions of IMRT, 3D conformal PT and IMPT.

→ MacDonald S.M. et al., “Proton radiotherapy for pediatric central nervous system germ call tumors: early clinical outcomes”, PubMed 20452141, International Journal of Radiation Oncology, Biology, Physics, 2011, 79:121-129.

This paper reports early clinical outcomes for children with CNS germ cell tumors treated with PT and compares dose distributions for IMRT, 3D-CPT and IMPT with PBS for whole-ventricular irradiation with and without an involved-field boost. Preliminary disease control with PT compares favorably to the literature and dosimetric comparisons demonstrate the advantage of PT over IMRT for whole-ventricle radiation, with superior dose distributions and fewer beam angles.

→ MacDonald S.M., et al., “Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients”, PubMed 24101739, Neuro Oncology, 2013 November, 15(11):1552-9.

Ependymoma is treated with maximal surgical resection and localized radiotherapy. Minimizing unnecessary exposure to radiation is of paramount importance for young children. PT spares healthy tissue outside the target region, and outcomes for children treated with PT compare favorably with the literature.

→ McGovern S.L. et al., “Outcomes and acute toxicities of proton therapy for pediatric atypical teratoid/rhabdoid tumor of the central nervous system”, PubMed 25311260, International Journal of Radiation Oncology, Biology, Physics, 2014 December 1, 90(5):1143-52.

Atypical teratoid/rhabdoid tumor (AT/RT) of the CNS is a rare cancer primarily affecting children younger than 5 years old. This paper is the largest report of children with AT/RT treated with PT, and preliminary survival outcomes in this young pediatric population are encouraging compared to historic results.

→ Mailhot Vega R. et al., “Cost effectiveness of proton versus photon radiation therapy with respect to the risk of growth hormone deficiency in children”, PubMed 25641407, Cancer Cytopathology, 2015 May 15, 121(10):1694-702.

This study provides the first evidence-based guide for identifying children with brain tumors who may benefit the most from PT with respect to endocrine dysfunction. Indeed, PT may be more cost effective when the radiation dose to the hypothalamus can be spared, but not when tumors are involving or directly adjacent to the hypothalamus.

→ Mizumoto M. et al., “Proton beam therapy for pediatric ependymoma”, PubMed 25754294, Pediatrics International, 2015 March 6.

The aim of this study is to evaluate the efficacy of PT for pediatric patients with ependymoma. Proton beam therapy for pediatric ependymoma is safe, does not have specific toxicities, and can reduce irradiation of normal brain tissue.

→ Moteabbed M. et al., “The risk of radiation-induced second cancers in the high to medium dose region: a comparison between passive and scanned proton therapy, IMRT and VMAT for pediatric patients with brain tumors”, PubMed 24828559, Physics in Medicine and Biology, 2014 June 21, 59(12):2883-99.

The incidence of second malignant tumors is a clinically observed adverse late effect of radiation therapy. This study aims to evaluate the risk of second cancer incidence for pediatric patients with brain/head and neck tumors and compare passive scattering and pencil beam scanning PT, IMRT and VMAT.

→ Petrovic A. et al., “Proton therapy for uveal melanoma in 43 juvenile patients: long-term results”, PubMed 24405742, Ophthalmology, 2014 April, 121(4):898-904.

This study examines the metastatic and survival rates, eye retention probability and visual outcomes of juvenile patients after PT for uveal melanoma. It is shown that metastatic and survival rates are significantly better for juvenile than for adult patients.

→ Rombi B. et al., “Spot-scanning proton radiation therapy for pediatric chordoma and chondrosarcoma: clinical outcome of 26 patients treated at paul scherrer institute”, PubMed 23582853, International Journal of Radiation Oncology, Biology, Physics, 2013, 86(3):578-84.

Spot-scanning PT shows excellent clinical outcomes with acceptable rates of late toxicity in pediatric patients with chordoma or chondrosarcoma of the skull base or axial skeleton.

→ Rombi B. et al., “Proton radiotherapy for pediatric Ewing’s sarcoma: initial clinical outcomes”, PubMed 21856094, International Journal of Radiation Oncology, Biology, Physics, 2013, 82(3):1142-8.

This study presents preliminary clinical outcomes including late effects on pediatric Ewing’s sarcoma patients treated with PT. This treatment modality was well tolerated with few adverse events.

→ Rombi B. et al., “Proton radiotherapy for pediatric tumors: review of first clinical results”, PubMed 25260976, Italian Journal of Pediatrics, 2014 September 26, 40:74.

PT has been used safely and effectively for medulloblastoma, primitive neuro-ectodermal tumors, craniopharyngioma, ependymoma, germ cell intracranial tumors, low-grade glioma, retinoblastoma, rhabdomyosarcoma and other soft tissue sarcomas, Ewing’s sarcoma and other bone sarcomas. Other possible applications are emerging. The main advantage of PT is the sparing of intermediate-to-low-dose to healthy tissue.

→ Song S., “Proton beam therapy reduces the incidence of acute haematological and gastrointestinal toxicities associated with craniospinal irradiation in pediatric brain tumors”, PubMed 24913151, Acta Oncologica, 2014 March, 10:1-7.

This study shows that the acute toxicity of proton beam craniospinal irradiation (CSI) was lower compared to that of conventional photon beam CSI in children with brain tumors.

→ Song S. et al., “Proton beam therapy reduces the incidence of acute haematological and gastrointestinal toxicities associated with craniospinal irradiation in pediatric brain tumors”, PubMed 24913151, Acta Oncologica, 2014 September, 53(9):1158-64.

This paper compares the acute toxicity of PT craniospinal irradiation (CSI) to that of conventional RT CSI in children with brain tumors: the incidence rates of thrombocytopenia and diarrhoea were lower with PT than with RT, and one month after treatment, the recovery from leukopenia and thrombocytopenia was better in patients treated with PT.

→ Suneja G. et al., “Acute toxicity of proton beam radiation for pediatric central nervous system malignancies”, PubMed 23610011, Pediatric Blood & Cancer, 2013, 60(9):1431-6.

PT appears to be well tolerated in pediatric patients with CNS malignancies. Acute toxicity can be managed with supportive care.

→ Weber D.C. et al., “Tumor control and QoL outcomes of very young children with atypical teratoid/rhabdoid tumor treated with focal only chemo-radiation therapy using pencil beam scanning proton therapy”, PubMed 25362544, Journal of Neuro-oncology, 2015 January, 121(2):389-97.

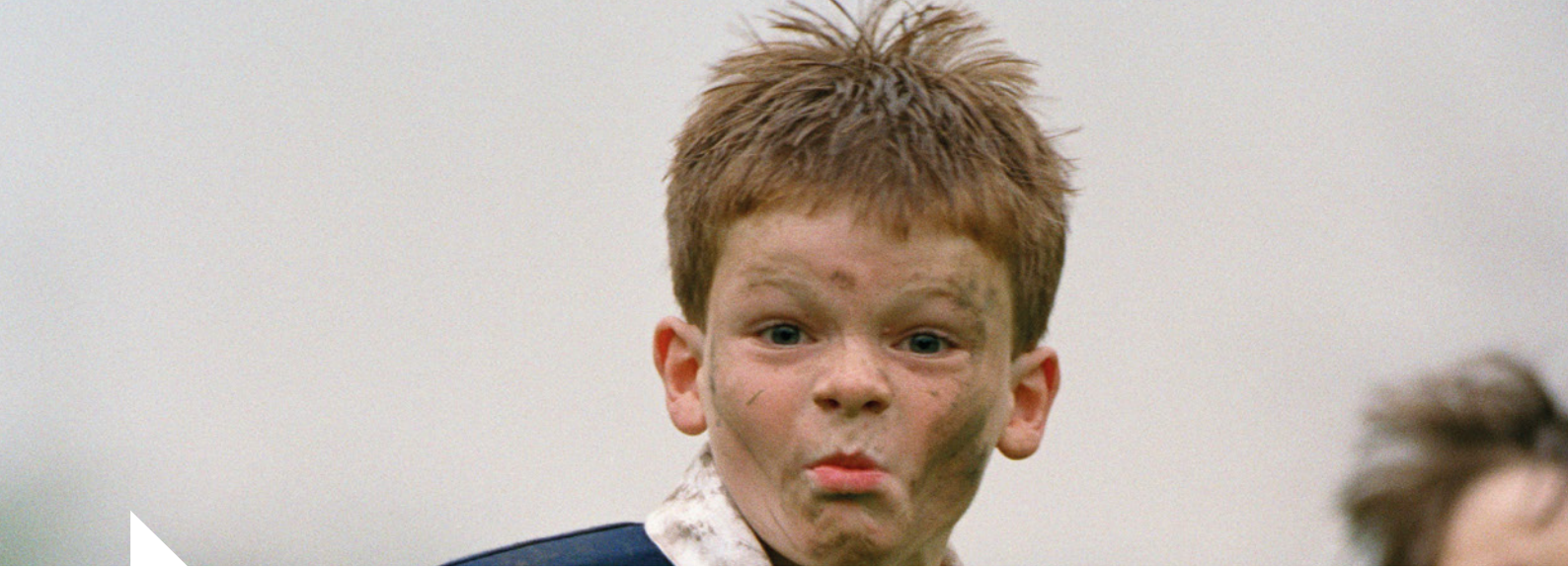
The aim of this analysis is to assess the early clinical results of PBS PT in the treatment of young children with non-metastatic atypical teratoid/rhabdoid tumor of the central nervous system. PBS PT is proven to be an effective treatment for those patients, with manageable acute toxicity.

→ Zhang R. et al., “Comparison of risk of radiogenic second cancer following photon and proton craniospinal irradiation for a pediatric medulloblastoma patient”, PubMed 23322160, Physics in Medicine and Biology, 2013, 58(4):807-23.

Pediatric patients who received radiation therapy are at risk of developing side effects such as radiogenic second cancer. PT confers lower predicted risk of second cancer than RT for pediatric medulloblastoma patients receiving craniospinal irradiation.

WEB REFERENCES

- National Association for Proton Therapy: www.proton-therapy.org
- OncoLink: www.oncolink.org
- Pediatric Proton Foundation: www.pediatricprotonfoundation.org
- Proton Therapy Today: www.protontherapytoday.com
- PubMed: http://www.ncbi.nlm.nih.gov/pubmed
- Particle Therapy Co-Operative Group: http://www.ptcog.ch/



Proton Therapy in your community ?

So Easy

With *Proteus*®**ONE***, you bring proton therapy to your local community and enhance your cancer patients' lives.

Proteus®**ONE*** is the compact and affordable IMPT* solution from IBA. The most advanced Proton Therapy solution, available for your clinic.

*IMPT : Intensity Modulated Proton Therapy

Proteus®**ONE*** is the only Intensity Modulated Proton Therapy (IMPT) solution integrating Pencil Beam Scanning (PBS) and 3D Cone Beam Computed Tomography (3D CBCT)

www.IBA-ProteusONE.com

Protect, enhance and save lives

iba

Proteus*®ONE*** is the brand name of a configuration of the Proteus 235.

IBA Group | IBAL01/5029 | Selected proton therapy bibliography 2008-2015

IBA, THE HIGH WAY TO PROTON THERAPY

In proton therapy, the development of practical and patient-centered solutions is only possible through constant collaboration, open engagement and shared research objectives. With 30 years of experience designing and developing proton therapy systems across the globe, IBA has grown a strong and vital community of proton therapy professionals. Together, this unprecedented community - of clinical leaders and distinguished technological experts - is advancing proton beam technology and clinical innovations.

By entering the IBA Proteus community:

- ***Your clinicians and researchers** will leverage the latest outcomedriven practices being advanced on a common technological platform. Sharing with a community of experienced clinical proton beam users will give them the capacity of your team to be trained with the utmost care and the highest standards of quality.*
- ***Your project management team** will be able to collaborate with the world's most experienced team of proton therapy experts (600+), cutting-edge technology and robust processes in system installation and operation.*
- ***Your executive team** will leverage the know-how and clinical understanding built on 30+ projects and 30,000+ patients treated to secure the institutions' investment.*

Together with our people, by sharing our passion for innovation and patient care, you can take comfortably the highway to the future of cancer care.

The IBA Proteus Community includes among others Massachusetts General Hospital Burr Proton Therapy Center, ProCure Proton Therapy Centers, University of Florida Proton Therapy Institute, University of Pennsylvania Health System Roberts Proton Therapy Center… in North America; or Centre de Protonthérapie Orsay de l'Institut Curie, Universitätsklinikum Carl Gustav Carus …in Europe; and Korean National Cancer Center, Appolo Health Group… in Asia.

VISIT US ONLINE AT:

www.iba-protontherapy.com

Protect, enhance and save lives

iba