

# Proton Therapy Facts

Proton therapy is a medically necessary, FDA-cleared treatment for cancer patients. In the early days of proton therapy, because of technological limitations, the therapy was used for a limited number of conditions and demonstrated considerable value for pediatric populations, patients with tumors affecting the brain and skull-base, paranasal sinuses, eye tumors and arteriovenous malformations. With technological advances, the data show considerable promise and improvement in side effects of patients with cancers of the breast, esophagus, liver, lung and head and neck.

For many cancer patients, proton therapy is prescribed by their physician and is the optimal and most effective treatment option. Studies have shown that proton therapy can help increase survival, reduce the risk of secondary cancers, result in fewer acute and long-term conditions as well as debilitating short-term side effects and improve quality of life for individuals undergoing cancer treatment.

Outlined below are key research findings that underscore the many benefits of proton therapy for certain cancer patients:

## **SECONDARY CANCERS:**

- When compared with photon radiation, proton therapy allows for an increased dose of radiation to a cancerous tumor while decreasing the dose to adjacent critical structures. The use of proton radiation therapy has *not* been associated with an increased risk of secondary malignancies compared with photon therapy.<sup>1</sup>
- Compared with intensity-modulated radiation therapy (IMRT), proton therapy can reduce the risk of a patient developing a secondary cancer by 26 to 39 percent.<sup>2</sup>

## **HEAD AND NECK CANCERS (CANCERS OF THE OROPHARYNX NASOPHARYNX & SKULL-BASE CHORDOMAS):**

- With proton therapy, unnecessary radiation doses can be avoided in head and neck cancer patients, resulting in significant improvement in quality of life during and after treatment.<sup>3</sup>
- Patients with cancers of the oropharynx and nasopharynx had less swallowing dysfunction following proton therapy, and were approximately 60 percent less likely to need a feeding tube.<sup>4</sup>
- Proton therapy reduces the rates of feeding tube dependency and severe weight loss for patients with oropharyngeal cancers and improves survival for patients with paranasal and nasal cavity malignancies.<sup>5</sup>
- Proton beam therapy is “an effective treatment modality for skull base chordomas.”<sup>6</sup>
- Compared with historical photon therapy data, proton therapy results in better local control and overall survival treatments for patients with chordomas and chondrosarcomas of the spine.<sup>7</sup>

<sup>1</sup> Chung C S, Yock T I, et al. Incidence of Second Malignancies Among Patients Treated With Proton Versus Photon Radiation. *Int J Radiat Oncol Biol Phys*. Vol. 87, No. 1, pp. 46e52, 2013

<sup>2</sup> Fontenot JD, Lee AK, Newhauser WD. Risk of secondary malignant neoplasms from proton therapy and intensity-modulated x-ray therapy for early-stage prostate cancer. *Int J Radiat Oncol Biol Phys* 2009;74:616-22

<sup>3</sup> Blanchard P, et al. Intensity-modulated proton beam therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for patients with oropharynx cancer - A case matched analysis. *Radiother Oncol*. 2016;120(1):48-55.

<sup>4</sup> Blanchard P, et al. “Intensity modulated proton beam therapy (IMPT) versus intensity modulated photon therapy (IMRT) for oropharynx cancer patients – a case matched analysis” *Radiother Oncol*; 2016; 120:48-55

<sup>5</sup> Patel SH, et al. *Lancet Oncol*. 2014;15(9):1027-38

<sup>6</sup> 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. *Int J Radiat Oncol Biol Phys*. 2009;75(4):1111-8.

<sup>7</sup> Indelicato DJ, Rotondo RL, Begosh-Mayne D, et al. “A prospective outcomes study of proton therapy for chordomas and chondrosarcomas of the spine.” *Int J Radiat Oncol Biol Phys* 2016;95:297-303.

#### **BREAST CANCER:**

- Proton therapy after mastectomy or breast-conserving surgery significantly reduces cardiac exposure to radiation<sup>8</sup> and improves target coverage for the internal mammary nodes, which may positively impact long-term survival in breast cancer patients.<sup>9</sup>

#### **NON-SMALL CELL LUNG CANCER (NSCLC):**

- Virtual clinical studies have shown that, compared with photon-based radiation therapy, proton therapy can spare critical structures of excess radiation, particularly the heart, lungs, esophagus and spinal cord.<sup>10</sup>
- One study found that among NSCLC patients, those who received proton therapy reported less severe patient-reported symptoms such as fatigue, pain, drowsiness and lack of appetite than those receiving IMRT or 3D Conformal Radiation Therapy (3DCRT).<sup>11</sup>
- Other studies of proton therapy patients have demonstrated promising clinical outcomes in reducing toxic effects compared to IMRT.<sup>12</sup> Another study found that patients with locally advanced NSCLC also demonstrated an “excellent overall survival rate with tolerable toxicity” after undergoing proton therapy treatment with lower rates of toxicity than would be expected with photon therapy treatment.<sup>13</sup>

#### **PEDIATRIC CANCER:**

- Data show pediatric cancer patients benefit from reduced integral dose with protons compared with photons. Patients with tumors in the central nervous system, head and neck and some abdominal locations have a reduction of radiation dosage to normal tissues and potentially fewer late toxicities if treated with protons compared with photons.<sup>14</sup>

#### **ESOPHAGEAL CANCER:**

- In a study of nearly 450 patients with esophageal cancer, those who received proton therapy had fewer gastrointestinal and pulmonary toxicities than those receiving photon therapy.”<sup>15</sup>
- In patients with locally advanced esophageal cancer, proton therapy has been shown to be associated with improved survival rates compared to modulated radiation therapy.<sup>16</sup>
- Another study found that patients with esophageal cancer who underwent proton beam therapy treatment had significantly fewer postoperative complications and spent fewer days in the hospital compared to patients who underwent other types of radiation therapy.<sup>17</sup>

#### **LIVER CANCER:**

- In liver cancer, contemporary data for proton therapy are highly promising. In a recent phase II trial including a large number of patients with advanced liver disease, median progression-free survival was 36 months, with a 60 percent three-year progression-free survival rate for patients.<sup>18</sup>
- In a randomized trial of transarterial chemoembolization (TACE) versus proton therapy, proton therapy was superior on multiple metrics. For example, the total hospitalization days within 30 days of the procedures for the entire cohort was 166 versus 24, in favor of protons.<sup>19</sup>

<sup>8</sup> Lin LL, et al. Proton beam versus photon beam dose to the heart and left anterior descending artery for left-sided breast cancer. *Acta Oncol.* 2015;54(7):1032-9.

<sup>9</sup> Bradley J A, Dagan D, et al. Initial Report of a Prospective Dosimetric and Clinical Feasibility Trial Demonstrates the Potential of Protons to Increase the Therapeutic Ratio in Breast Cancer Compared With Photons. *Int J Radiation Oncol Biol Phys.* Vol. 95, No. 1, pp. 411e421, 2016

<sup>10</sup> Chang J Y, Jabbour S K, et al. Consensus Statement on Proton Therapy in Early-Stage and Locally Advanced Non Small Cell Lung Cancer. *Int J Radiation Oncol Biol Phys.* Vol. 95, No. 1, pp. 505-516, 2016

<sup>11</sup> Wang XS, Shi Q, Williams LA, et al. Prospective study of patient-reported symptom burden in patients with non-small-cell lung cancer undergoing proton or photon chemoradiation therapy. *J Pain Symptom Manage* 2016;51:832-838.

<sup>12</sup> Chang, Joe Y. “Proton beam radiotherapy and concurrent chemotherapy for unresectable stage III non-small-cell lung cancer: final results of a phase 2 study.” *Journal of the American Medical Association.* 2017.

<sup>13</sup> Nguyen QN, Ly NB, Komaki R, et al. “Long-term outcomes after proton therapy, with concurrent chemotherapy, for stage II-III inoperable non-small cell lung cancer” *Radiother Oncol* 2015;115:367-372.

<sup>14</sup> Ladra MM, et al. Preliminary results of a phase II trial of proton radiotherapy for pediatric rhabdomyosarcoma. *J Clin Oncol.* 2014;32(33):3762-70.

<sup>15</sup> Wang J, et al. *Int J Radiat Oncol Biol Phys.* 2013;86(5):885-91

<sup>16</sup> Mian, Xi. “Comparative outcomes after definitive chemoradiotherapy using proton beam therapy versus intensity modulated radiation therapy for esophageal cancer: a retrospective, single-institutional analysis.” *Int J Radiation Oncol Biol Phys.* 2017

<sup>17</sup> Lin SH, Merrell K W, Shen J, et al. “Multi-institutional analysis of radiation modality use and postoperative outcomes of neoadjuvant chemoradiation of esophageal cancer.” *Radiother Oncol* 2017;123:376-381.

<sup>18</sup> Bush, D. A., Kayali, Z., Grove, R. & Slater, J. D. The safety and efficacy of high-dose proton beam radiotherapy for hepatocellular carcinoma: a phase 2 prospective trial. *Cancer* 117, 3053(safety and ef

<sup>19</sup> Bush DA, Smith JC, Slater JD, Volk ML, Reeves ME, Cheng J: Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis, *Int J Radiat Oncol Biol Phys.* 95(1):477-482, 2016