

# A Landmark Study Compares Proton Beam Therapy with Standard Radiation Therapy

## What is the value of proton beam therapy?

Massachusetts General Hospital, along with the University of Pennsylvania and several other proton centers, is leading a trial that may help settle a long-standing debate: Is proton beam therapy (PBT) more effective than intensity-modulated radiotherapy (IMRT) for prostate cancer?

The trial, Prostate Advanced Radiation Technologies Investigating Quality of Life (PARTIQoL),<sup>1</sup> is the first large Phase III randomized clinical trial to directly compare PBT with IMRT in prostate cancer. The five-year multicenter study, which opened in July 2012, is sponsored by Mass General and the National Cancer Institute and is still accruing patients.

In recent years, the Agency for Healthcare Research and Quality, Institute of Medicine, Centers for Medicare & Medicaid Services, other federal agencies, policymakers, clinicians, researchers and the media have called for a rigorous comparative evaluation of these two treatments prior to PBT's wider adoption. The study's principal investigator, Jason A. Efstathiou, MD, DPhil, says that the results will help prostate cancer patients and their physicians make better informed decisions regarding the most effective therapy with the least burdensome quality-of-life (QOL) issues, while also contributing to the larger debate about the investment in and impact of innovative technologies.

## TWO INNOVATIVE TECHNOLOGIES

Of the some 200,000 men who are diagnosed with prostate cancer annually, many will suffer lifelong morbidities resulting from treatment. PBT and IMRT are both targeted advanced radiation technologies that are capable of delivering higher doses of radiation more directly to the prostate than do older techniques, leading to higher cure rates. By sparing surrounding tissue and organs, these

technologies are meant to decrease toxicity and perhaps reduce the rare risk of developing a second cancer.

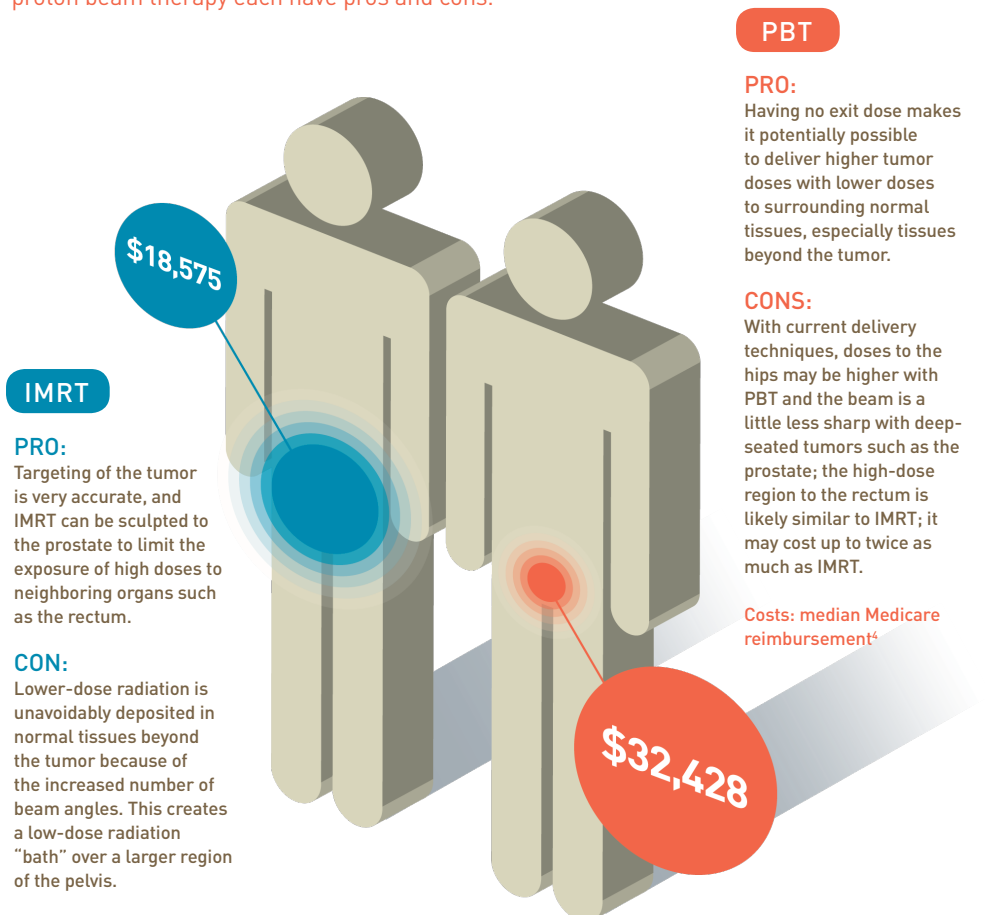
Unlike IMRT, PBT delivers radiation by using a more focused beam to the targeted tumor, with less of a low-dose bath for the pelvis and no "exit" dose irradiating tissue beyond the tumor. Theoretically, PBT may thus cause fewer side effects than IMRT.<sup>2</sup>

## SCANT EVIDENCE OF PBT'S BENEFIT IN PROSTATE CANCER

The theoretical advantage of PBT seemed particularly relevant to the prostate, which lies close to the bowel, bladder and rectum, which all may be affected by scattered radiation. But it is also possible that protons are not as sharp at the depth of deep-seated tumors like the prostate, and there are other potential *(continued on page 2)*

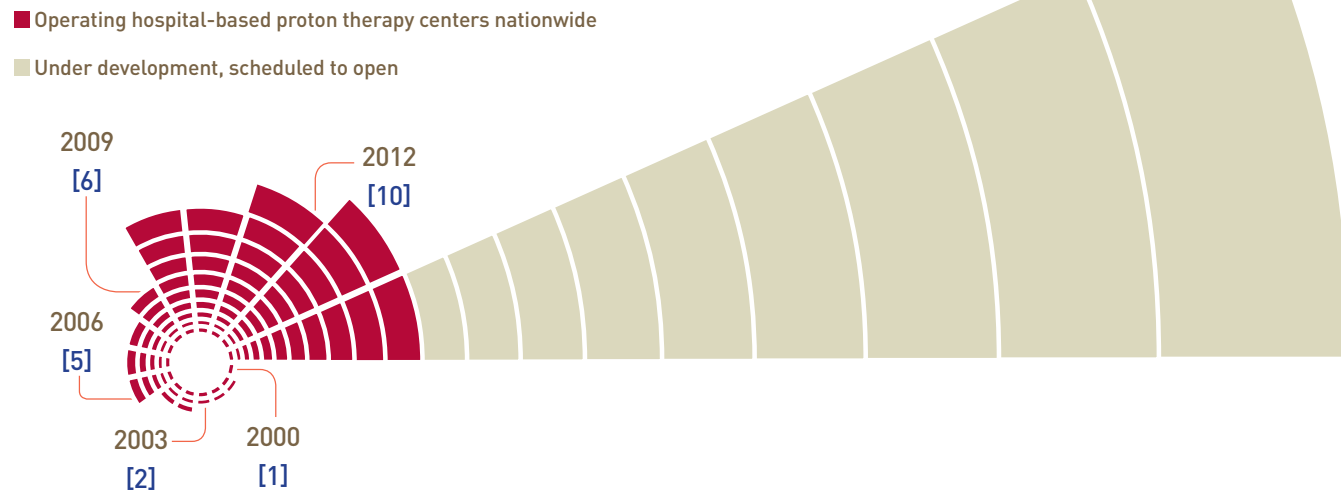
## Standard Radiotherapy vs. Proton Beam Therapy

For prostate cancer, intensity-modulated radiotherapy and proton beam therapy each have pros and cons.



## The Proton Therapy Boom

Prostate cancer has been a major driving force behind the establishment of new proton beam facilities.



(continued from page 2) advantages to IMRT.

The few studies comparing PBT with IMRT in prostate cancer have been retrospective, uncontrolled and conflicting. A 2012 study in *JAMA*<sup>3</sup> found that patients treated with IMRT had decreased bowel toxicity compared with those treated with PBT, while a 2012 study in the *Journal of the National Cancer Institute (JNCI)*<sup>4</sup> found that patients treated with PBT had improved urinary function in the short term. However, both studies relied on data from physician billing codes rather than patient reports. In *Cancer* this year, Dr. Efstathiou and colleagues described patient-reported outcomes following PBT, IMRT or 3-D conformal radiotherapy. PBT initially caused fewer

gastrointestinal and urinary problems, but after two years QOL outcomes were similar to IMRT.

### THE CONTROVERSY

According to the 2012 *JNCI* study, median Medicare reimbursement for PBT is \$32,428, compared with \$18,575 for IMRT. Despite the lack of well-designed prospective comparative studies to date and the higher cost, many men choose PBT over IMRT because of the assumption that it reduces long-term side effects. Prostate cancer has been a driving force behind the establishment of new proton beam facilities, which may double in three years and whose patient load in some cases may include up to 75 percent prostate patients.

point is bowel function because it is the most specific long-term side effect. The study will also:

- Develop predictive models of the association between radiation dose distribution and patient-reported bowel, urinary and erectile functions
- Identify and evaluate biomarkers, including circulating tumor cells, for the response to PBT and IMRT to guide future personalized medicine decisionmaking
- Assess longer-term survival rates and late effects
- Compare cost-effectiveness at current and future pricing schemes

### THE AIMS OF PARTIQOL

The PARTIQoL trial is looking at patient-reported QOL outcomes and other end points. The primary QOL end

“Despite a clear benefit in some cancers, such as pediatric malignancies, the rapid adoption of PBT may be happening before its effectiveness and comparative value has been rigorously evaluated in all disease sites,” noted Dr. Efstathiou. He hopes PARTIQoL will serve as a model for evaluating costly yet promising medical technologies. ■

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For more information on the PARTIQoL trial, please call 617-726-5866.

<sup>1</sup> <http://clinicaltrials.gov/ct2/show/NCT01617161>

<sup>2</sup> Efstathiou, J.A., P.J. Gray and A.L. Zietman. “Proton Beam Therapy and Localized Prostate Cancer: Current Status and Controversies.” *British Journal of Cancer* 108, no. 6 (April 2, 2013): 1225–1230.

<sup>3</sup> Sheets, N.C. et al. “Intensity-Modulated Radiation Therapy, Proton Therapy, or Conformal Radiation Therapy and Morbidity and Disease Control in Localized Prostate Cancer.” *JAMA* 2012; 307(15): 1611–1620.

<sup>4</sup> Yu, J.B. et al. “Proton Versus Intensity-Modulated Radiotherapy for Prostate Cancer: Patterns of Care and Early Toxicity.” *Journal of the National Cancer Institute*, 2013 Jan 2; 105(1): 25–32.