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4	Excellent Acute Toxicity Outcomes with Proton Therapy for Partial Breast Irradiation in Early Stage Breast Cancer: Initial Results of a Multi-institutional Phase II Trial
<p>BACKGROUND AND PURPOSE: Partial breast irradiation (PBI) with proton therapy after lumpectomy for early stage invasive breast cancer is an area of active investigation. To date, multiple single-institutional studies have reported conflicting results on the acute toxicity of PBI. This prospective phase II trial investigates the feasibility, safety, and efficacy of delivering PBI with proton therapy in a multi-institutional setting. METHODS: Patients over the age of 50 years with ER positive nonlobular invasive breast cancer or ductal carcinoma in situ ≤ 3 cm in size who had undergone lumpectomy with at least 2 mm negative surgical margins were treated with proton therapy to a dose of 40 Gy delivered over 10 daily fractions. In this initial analysis, we assess early toxicity and treatment efficacy of proton PBI. Patients were followed 4 weeks post-treatment and annually thereafter, along with annual mammograms. Patient-reported quality of life and physician-reported cosmesis assessments including photographs were obtained at 1 and 3 years post-treatment. RESULTS: Of 40 enrolled patients, 38 were evaluable. At a median follow-up of 17.8 months (range 2-36 months), all patients had overall breast cosmesis that was scored "good" or "excellent". Of 6 grade 2 acute adverse events that occurred, only 1 was radiation dermatitis, with others including lymphedema, hot flashes, and fatigue. One grade 3 acute toxicity occurred 3 weeks after radiation completion in the form of vascular disease requiring stent placement, highly unlikely to be attributable to radiation effects. Patient-reported quality of life outcomes were recorded using the standardized Breast Cancer Treatment Outcome Scale (BCTOS) scored from 1-4 (1: none; 2: mild; 3: moderate; 4: large). Patients assigned a score of 4 for change in nipple appearance (n=2), breast shape (n=2), and scar tissue formation (n=2). To date, local, locoregional, and distant disease control are 100%, although one patient has developed a new hormone receptor negative invasive ductal carcinoma of the contralateral breast. CONCLUSION: Proton PBI provides excellent early cancer control with acceptable cosmetic outcomes and minimal adverse effects as per patient- and physician-reported assessments. On continued follow-up, late toxicity and cosmesis, as well as long-term disease control outcomes, will be assessed.</p>	
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24	Insurance Coverage and Related Referral Delays in Children Irradiated with Proton Therapy in the Pediatric Proton Consortium Registry
<p>BACKGROUND/OBJECTIVES: Third-party payer denial of proton radiotherapy can delay or prevent children from receiving toxicity-sparing treatment. We report the prevalence and type of insurance coverage and related treatment delays in children irradiated with proton therapy in the Pediatric Proton Consortium Registry. DESIGN/METHODS: A multi-institutional registry of integrated demographic, clinical, dosimetric, radiographic, and patient-reported data for childhood cancer patients undergoing proton radiation therapy was conceived in May 2010 and opened to enrollment in summer 2012. Data was frozen for analysis on February 3, 2017. RESULTS: Of 1,578 children enrolled from 49 states and 20 foreign countries, 1,438 (91%) had available insurance records. A total of 1,350 (86%) were covered by private, public, or foreign insurance (79% fully covered) while 88 (6%) were uninsured and were either charity sponsored or self paid. Principle insurers included employer-based or private companies (48%), foreign entities (18%), Medicaid (17%), and the military (2%). Ninety (6%) children experienced a delay in proton therapy while awaiting insurance approval, 51 (57%) and 32 (35%) of whom were insured privately and publicly by Medicaid, respectively. The</p>	

frequency of treatment delay due to insurance approval was 51/1029 (5%) for private/foreign insurance compared to 32/275 (12%) among Medicaid patients ($p < 0.001$). CONCLUSION: Proton therapy delay from the insurance approval process occurs in six percent of children and the rate is twice as high in Medicaid patients. Proton therapy remains more common in privately-insured children and less delayed. High-quality late effects research is needed to justify further expansion of timely access to toxicity-sparing proton therapy for all American children.

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34 Proton therapy is associated with superior survival and decreased risk of complications compared to IMRT for intermediate risk prostate cancer: A Medicare/SEER database study

RATIONALE: For patients treated with external radiotherapy for prostate cancer, there is a significantly higher integral dose given with IMRT compared to protons. This difference could increase the risk of complications or second malignancies with IMRT. METHODS: The SEER/Medicare database was used to evaluate patients with prostate cancer, with initial treatment from 2006-2012, treated with complete course of either protons or intensity modulated radiation therapy (IMRT). There were 29,554 IMRT patients and 1018 proton patients, with complete records available on 28,102 IMRT patients and 851 proton patients. The proton patients were matched to IMRT patients in a 1:5 matching process, using these parameters: comorbidity index, cancer stage, tumor grade, adjuvant chemo/hormone therapy, age, zip code and ethnicity. Medicare billing codes were evaluated for GI, GU, erectile dysfunction, bone/hip fracture, endocrine dysfunction and "other" complications. RESULTS: For the entire cohort of unmatched prostate cancer patients the 5 year overall survival was 93.4% for PBT vs 85.25% for IMRT ($p = 0.00001$). A total of 3867 IMRT patients were matched to 788 PBT patients. Using the matched patient cohort, the 5-yr overall survival for PBT was 93.25% vs 88.43% for IMRT ($p = 0.045$). The matched patient group of intermediate risk patients included 736 PBT and 3591 IMRT patients, with 5 year overall survival of 93.65% vs 88.27% ($p = 0.022$). There was no significant difference in erectile or bone/hip complications, but significantly more patients with GI, GU, endocrine, or "other" complications with IMRT compared to protons. In addition, there were greater numbers of patients with secondary malignancies with IMRT, with the curves beginning to separate after 3 years from treatment (10.5% for IMRT vs 6.1% for PBT at 5 years, $p = 0.09$). CONCLUSIONS: Proton therapy for prostate cancer is associated with fewer long term complications and a trend toward a lower risk of second malignancies. There is a difference in overall survival at 5 years; further work is necessary to determine if this difference is due to complications, second malignancies or prostate cancer recurrence.

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UFPTI

38 Potential Improved Outcomes with Proton Therapy in Prostate Cancer: A Comparison of IMRT and Proton Cohorts

BACKGROUND: The ProtecT trial underscores the importance of definitive treatment in prostate cancer patients with life expectancies > 10 years and the validity of radiation therapy (RT). To shed light on the controversy of whether Proton Therapy (PT) may offer advantages over photon based intensity modulated RT (IMRT), clinical outcomes of PT and IMRT cohorts from two institutions were directly compared. METHODS: The first comprised 1,214 men treated with image-guided PT using implanted fiducials from 2006 to 2010 to a dose of 78 Gy(RBE) in 39 fractions. The second comprised 301 men treated with image-guided IMRT using transabdominal ultrasound from 2000 to 2005 to a dose of 75.6 Gy in 42 fractions. Median age and follow-up were 66 yrs and 5.6 yrs for PT and 74 yrs

and 7.2 yrs for IMRT. Hormone therapy (ADT) was used with PT and IMRT, respectively, in 7% and 3% of low-risk, 9.9% and 25% of intermediate-risk, and 57.8% and 91% of high-risk patients. Comparative endpoints were GR \geq 3 gastrointestinal (GI) and urologic (GU) toxicity, and 5 Y freedom from biochemical progression (FFBP). RESULTS: The prevalence of GR \geq 3 toxicity at last follow-up for the PT and IMRT cohorts were 0.1% vs 1.3% (p=0.0065) for GI toxicity and 0.1% vs 4.3% (p<0.0001) for GU toxicity. FFBP rates for PT and IMRT for low-risk were 98.9% and 92.2% (p<0.0001), for intermediate-risk patients, 94.5% and 87.3% (p=0.0226), and for high-risk patients, 74.4% and 80.3% (P=0.5154). CONCLUSIONS: In this retrospective comparison of outcomes of men treated with IMRT and PT for prostate cancer, FFBP rates were better with PT for men with low- and intermediate-risk disease and similar in men with high-risk disease, despite longer and more frequent use of ADT in the IMRT cohort. It is notable that toxicity was less in the PT cohort despite the use of a higher median dose. While this study identified difficulties in comparing retrospective series (differences in age, RT dose and fraction size, and ADT use between cohorts), the magnitude of improvement with PT is intriguing and warrants prospective testing.

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43 A multi-institutional analysis of radiation modality for elderly patients with esophagus cancer

Purpose: The therapeutic gains of neoadjuvant chemoradiotherapy followed by esophagectomy may be offset by morbidity and mortality in elderly patients. Advanced radiation modalities may reduce collateral dose to the heart and lungs and possibly improve outcomes. We evaluated the impact of radiation modality on outcomes of trimodality therapy for elderly patients with esophagus cancer. Methods and Materials: We evaluated 571 patients treated with trimodality therapy at 3 high-volume tertiary U.S. cancer centers from 2007 to 2013. 202 of 571 (35%) patients were 65 years or older at diagnosis and were classified as elderly. 87 (43%) elderly patients received 3-D conformal radiation (3DRT), 73 (36%) received intensity-modulated radiation (IMRT), and 42 (21%) received passive scatter proton beam therapy (PBT). Outcomes were analyzed by radiation treatment modality and compared using univariable (UVA) and multivariable (MVA) logistic analyses. Results: Elderly patients had a higher risk for postoperative cardiac (UVA: OR 2.2, p<0.001; MVA: OR 2.07, p=0.004) and pulmonary toxicities (UVA: OR 2.0, p<0.001; MVA: OR 2.03, p<0.001), and a higher 90-day postoperative mortality (5.4 vs 2.2%, p=0.049) than younger patients. Elderly patients treated with PBT had a lower rate of 90-day postoperative mortality than patients treated with IMRT or 3DRT (0 vs 6.9%). Use of IMRT or PBT was associated with significantly lower cardiac complications in elderly patients compared to 3-D conformal radiotherapy (Table 1). Use of PBT was associated with significantly lower pulmonary complications than IMRT and 3DRT (Table 1). 8.1% of the elderly treated with 3DRT or IMRT experienced acute respiratory distress syndrome (ARDS) compared to 2.4% of those treated with PBT (p=0.307). Significantly more elderly patients treated with PBT were discharged within 7 days of surgery (23.8 vs 6.3%, p=0.002). Rates of pathologic complete response (28.6 vs 30.0%, p=1.000), relapse (42.9 vs 45%, p=0.863), and 3-year survival (63.2 vs 54.4%, p=0.237) for patients treated with PBT compared to those treated with 3DRT or IMRT. Conclusions: Proton beam therapy was associated with lower rates of 90-day postoperative mortality, postoperative pulmonary complications particularly ARDS, postoperative cardiac toxicity, and a shorter time to discharge when compared with 3DRT and IMRT.

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44 Comparative toxicities and costs of preoperative chemoradiotherapy of IMRT and Proton Beam Therapy for esophageal cancer

Background: To better understand the value of proton beam therapy (PBT), we conducted a comparative toxicity and cost analysis of PBT versus Intensity Modulated Radiation Therapy (IMRT) in patients treated with neoadjuvant CRT for esophageal cancer at a single, high volume center. Materials and Methods: Consecutive patients (N=237, IMRT=156 and PBT=81) from 2006 to 2013 who had at least 41.4 Gy, ≥30 days post-CRT followup, and Ivor-Lewis esophagectomy were analyzed. Cost analysis was based on aggregate health care claims from initial consultation to time of hospital discharge. Charges were discounted to the level of 1st quarter 2007. Differences in charges were examined by using generalized linear model (GLM), and multivariable generalized linear regression models assessed the independent association of patient characteristics and treatment costs. Results: The two groups were well balanced in patient, tumor, treatment characteristics, and underlying comorbid illnesses. In the postoperative period, rates of complications were slightly more for IMRT in pulmonary (19% vs 13%, p=NS) and GI (15% vs. 14%, p=NS), but higher in cardiac complications (10% vs 2.5%, p<0.05). As expected, the average cost of neoadjuvant CRT is greater for PBT (\$128,427 ± 15,800) than IMRT (\$71,108 ± 14,858) (p<0.0001). Conversely, the costs postoperatively were significantly higher for IMRT than PBT (\$109,807 vs. \$92,512). Age had a significant influence on this cost differential: patients <65 years, IMRT was more costly per patient by \$5,935, but for 65-74 and ≥75 years old, IMRT exceeds PBT by \$20,292 and \$67,876, respectively. The cost of hospitalization remains unchanged for PBT regardless of age group, but rises significantly for IMRT patients older than 65. This is largely due to greater number of procedures and supportive care used for IMRT patients, as well as the length of hospitalization (+2 days for 65-74 years and +7.11 days for ≥75 years old). Conclusions: Despite higher initial costs, the overall cost differential of PBT and IMRT may in fact be smaller than expected due to reduced postoperative complications for PBT. This is particularly significant for elderly patients > 65 years old. These results may help determine the optimal utilization of PBT in esophageal cancer.