

23 Early GI And GU Toxicity In 3 Prospective Trials Of Proton Therapy For Prostate Cancer
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Purpose/Objective(s): To report early GR 2 or higher gastrointestinal (GI) and urologic (GU) toxicity (CTCAE v.3) on 3 trials of proton therapy for prostate cancer.

Materials/Methods: From August 2006 to October 2007, 212 prostate cancer patients accrued to prospective IRB-approved trials of 78 CGE in 39 fractions for low risk, dose escalation from 78 CGE to 82 CGE for intermediate risk, and 78 CGE with concomitant taxotere followed by androgen deprivation for high risk disease. All patients have a minimum potential 1 y follow-up. Maximum GI and GU toxicity scores for each patient were recorded. Factors studied for potential association with toxicities included: pretreatment IPSS score, prostate size, age, smoking history, anti-coagulants, co-morbidities (DM, CD, HTN, COPD), prior rectal disease, prior GU symptoms requiring medical or surgical management, target volumes, and dosimetry parameters.

Results: GU toxicities comprised 47 GR 2 and 1 GR 3 at 6 months and 48 GR 2 and 1 GR 3 at 12 months. Retentive symptoms requiring alpha-blocking agents accounted for 98% of GR 2 GU toxicities, and included those present prior to proton therapy. On MVA, GR 2+ GU toxicities at 6 m were correlated with pretreatment prostatitis ($p = 0.0118$) and baseline IPSS ($p = 0.0192$), and at 12 m with age ($p = 0.0210$) and pretreatment GU symptom management ($p = 0.0001$) suggesting the predominant predictors of early GU toxicity were pretreatment clinical factors.

GI toxicities comprised only 1 GR 2 and no GR 3 or higher toxicities at 6 m and 8 GR 2 and 1 GR 3 at 12 m; 2 GR 2 GI toxicities occurred on both the low-risk and high-risk protocols, with the remaining occurring on the dose-escalation intermediate-risk protocol. UVA of the low-risk and intermediate-risk trials (no chemotherapy) showed a significant correlation between GR 2 or higher GI toxicity and the percentage of rectal wall receiving doses ranging from 25 to 80 CGE. Of the 10 patients developing GR 2 or higher GI symptoms at 6 or 12 months, 5 originally had GR 1 that progressed to GR 2 or 3 after a colonoscopic intervention. In a subset of 35 patients judged appropriate for brachytherapy (low risk, prostate size < 60 cc, IPSS < 15, and no prior GU symptom management), the 6 and 12 m rates of GR 2 GU toxicities were 17% and 9%, respectively; there were no GR 3 GU toxicities and no GR 2 or higher GI toxicities.

Conclusions: Early GU and GI toxicity on prospective trials of proton therapy has been minimal with GR 3 GU and GI toxicities at <1% and <0.5%, respectively. Early GU symptoms were associated with pretreatment conditions. Early GI toxicity was associated with the % of rectal wall receiving a range of doses from 25 CGE to 80 CGE, but was also significantly impacted by post-treatment colonoscopy interventions.

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