**Post-Mastectomy Radiotherapy using Proton Beam Therapy: Prospective Multi-Institutional PCG Registry Analysis**

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**Purpose/Objective(s):** To evaluate adverse events (AEs) and disease outcomes after post-mastectomy radiotherapy (PMRT) using proton beam therapy (PBT).

**Materials/Methods:** From 2011 to 2016, 125 patients with 129 treated chest walls (4 bilateral) were identified in the prospective multi-institutional Proton Collaborative Group (PCG) registry. AEs were prospectively recorded using CTCAE version 4.0. Acute AEs occurred within 6 months after start of PBT. Late AEs occurred or persisted beyond 6 months after start of PBT. Luminal A was defined as ER or PR-positive, HER2-normal, Ki-67 < 14%. Luminal B was defined as ER or PR-positive, HER2-normal, Ki-67 ≥ 14%. Luminal NOS was defined as ER or PR-positive, HER2-normal, Ki-67 not reported. Associations were assessed using Fisher’s exact and Wilcoxon tests. Statistical analysis was performed using a data management and decision management software.

**Results:** Median follow-up was 12 months (range 0-39). Median age at time of PBT was 52 (range 21-86). Median body mass index (BMI) was 27 (range 16-54). Histologic subtypes included: Luminal A or NOS 43%, Luminal B 26%, HER2-amplified 21%, and triple negative 10%. Most common clinical stage was cT2 40%, cN+ 67%, cM0 100%. All patients had mastectomy (20% bilateral) with 73% axillary lymph node dissection and 27% sentinel lymph node biopsy. Invasive margins were negative in 95%. Ductal carcinoma in situ (DCIS) margins were ≥ 2 mm in 86%. Systemic therapy was delivered in 94% with 84% receiving cyclophosphamide, 80% taxanes, 66% anthracyclines, 22% HER2-directed, and 16% platinum agents. Predominant regimen was doxorubicin, cyclophosphamide, and taxane (52%). Adjuvant endocrine therapy was used in 84%. Including chest wall boost, median total RT dose was 55.0 Gy Relative Biological Effectiveness (RBE) (range 43.2-70.4) in 1.8-2.0 Gy RBE fractions. RT fields included: chest wall 100%, axillary 96%, supraclavicular 99%, internal mammary 92%, chest wall boost 68%, and nodal boost 7%. Only 2% of patients did not complete the prescribed course due to pain/dermatitis, each reaching ≥ 50.4 Gy RBE before terminating RT during the chest wall boost. Maximum AE was grade 3 in 13% including acute grade 3 pain 8% and acute grade 3 dermatitis 8%. No patient had late AE > grade 2. Positive invasive margins and DCIS margins < 2 mm were associated with grade 3 pain (p=0.02, p=0.05). The patients with grade 3 pain who had positive invasive margins or DCIS margins < 2 mm all received chest wall boost and had median dose 60.4 Gy RBE. Patients with grade 3 dermatitis had higher median dose (60.4 Gy RBE vs 55.0 Gy RBE, p=0.10). At last follow-up, local recurrence was 2%, distant metastasis 6%, and breast cancer death 3%.

**Conclusion:** To our knowledge, this is the largest reported prospective cohort of PMRT using PBT. PMRT with comprehensive regional nodal irradiation using PBT was well-tolerated, with 13% acute grade 3 toxicities and no late grade 3 toxicities.