Concurrent Pencil Beam Scanning Proton Therapy and Hyperthermia: Initial Clinical Experience

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Background: The addition of hyperthermia (HT) to conventional, photon radiotherapy courses is known to increase efficacy through multiple mechanisms including radiosensitization of hypoxic cell populations and inhibition of DNA repair. HT reduces the oxygen enhancement ratio of “low” linear energy transfer (LET) radiation (e.g. photon and proton) and increases radiobiologic effect (RBE), potentially mimicking high LET particle therapy (e.g. ¹²C ion) [Datta et al. 2014]. Naturally, both enthusiasm for improved outcomes and concerns regarding increased toxicity have arisen for this approach, yet exceedingly limited data exists to date as institutions with the capacity to deliver both proton therapy and hyperthermia are rare.

Methods: At the Maryland Proton Treatment Center, over 200 patients have been treated with pencil beam scanning proton therapy (PBSPT) since the facility’s activation in early 2016. The University of Maryland Medical Center has treated 87 patients with external (ETT) or interstitial thermal therapy in the last 4 years. All treatments have been delivered on the BSD-500 microwave hyperthermia platform with the target tumor temperature of 40-42°C. Three patients have been treated with concurrent PBSPT and ETT: 2 patients postoperatively, for myxofibrosarcoma, and one, for inguinal recurrence from vulvar squamous cell carcinoma (SCC). Treatment courses were as follows: inguinal SCC (reirradiation 45Gy(RBE), 9 twice-weekly-ETT, bolus 39°C-60 min), high grade chest wall myxofibrosarcoma (reirradiation 60Gy(RBE), 5 weekly-ETT, bolus 40°C-45 min), intermediate grade shoulder myxofibrosarcoma (de novo 66Gy(RBE), 4 weekly-ETT, bolus 40°C-45 min).

Results: All patients completed their courses of proton and hyperthermia treatment without substantial acute complication or interruption. The patient treated in the de novo setting for shoulder myxofibrosarcoma experienced only grade 1 radiation dermatitis, hyperpigmentation, fatigue, and pain under treatment; post-treatment, no significant complications (follow-up 6 mo). The patient reirradiated for recurrent chest wall myxofibrosarcoma experienced grade 2 radiation dermatitis and grade 1 fatigue and hyperpigmentation under treatment; post-treatment, grade 1 joint range of motion limitation (follow-up 3 mo). The patient reirradiated for inguinal vulvar SCC recurrence experienced grade 2 radiation dermatitis and grade 1 fatigue, pain, and hyperpigmentation under treatment; post-treatment, grade 3 soft tissue necrosis requiring aggressive wound care (follow-up 6 mo). The patients with myxofibrosarcoma have currently no evidence of disease; the patient with inguinal SCC has persistent disease outside of the reirradiation field, with tumoral response in-field.

Conclusion: Concurrent PBSPT and ETT appears safe, effective, and promising. Further investigation and expansion of clinical experience is warranted amongst institutions with technical capabilities.