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## A hybrid method calculating linear energy transfer for intensity modulated proton therapy

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Intensity modulated proton therapy (IMPT) is an advanced form of radiation therapy in which the trajectory and energy of a focused beam of protons is precisely controlled so as to irradiate a tumor spot-by-spot and layer-by-layer with proton beamlets [1,2]. While the radiobiological effects of IMPT depend primarily on the physical dose distribution, studies have shown that linear energy transfer (LET) plays an important role as well [3]. LET can be used as indicator for radiobiological outcome at the microscopic level, which would justify the use of LET-based objectives in treatment plan optimization [4]. We developed a method using a hybrid approach to calculate proton LET for IMPT based on LET data pre-computed by Geant4 Monte Carlo (MC) simulations in a water phantom. The hybrid method was incorporated into our in-house treatment planning system (TPS) as an extension to calculate LET in voxelized patient geometries. First, we commissioned the Geant4 MC code to model three proton treatment nozzles in clinical use at our institution: one with no range shifter (VAC machine), a second with a range shifter 42.5 cm away from isocenter (RS machine), and a third with a range shifter 30 cm away from isocenter (ERS machine). The code was used to generate pencil beam LET kernels for all 97 proton energies used clinically. Second, the LET kernels were incorporated into the TPS using a ray-casting algorithm. Inhomogeneities were taken into account using water-equivalent thickness (WET). Since the LET kernels were pre-calculated, the time required to compute LET distributions in patient geometries was greatly reduced. It was found that the LET distributions calculated by our hybrid method agreed well with those found using a full MC calculation developed at Mayo Clinic in Rochester, Minnesota [5]. These LET distributions computed using our hybrid method were used to evaluate potential clinical benefits and toxicities for various tumor sites including lung, head and neck, esophagus, and brain. The LET calculation code has also been used in IMPT treatment planning, allowing for radiobiological optimization by including LET-weighted constraints in the inverse treatment planning process.

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