Three-Dimensional Treatment Planning for Transrectal Ultrasound-Guided Cytolytic Adenoviral Gene Therapy Part I

The primary technical challenge in an interstitial cytolytic adenoviral gene therapy program is the delivery of the virus to the tumor in a safe, efficient, and practical way. A technique similar to the implant of radioactive sources by transrectal ultrasound-guided approach is used but the “dosimetric” considerations include viral diffusion, viral replication, and cell lysis. Ideally, the planning system must also consider the treatment side effects resulting from uptake of virus by other normal tissues. Based on our initial clinic data, we have implemented a simple diffusion dosimetric model into the treatment planning system. Conceptually different from the standard drug or radiation doses, the first-generation virus concentration is defined as the dose in the planning system. The dose distribution following diffusion from a single injection will be used for calculation of the total viral dose distribution from multiple injections. By measuring the first generation dose and the tumor response, we can predict the therapeutic outcome resulting from a uniform gene distribution with no requirement for the monitoring of viral replication. This technique has been applied to our FDA approved protocol, “A Phase I Dose Escalation Trial of the Intraprostatic Injection of CN706, a Prostate-Specific Antigen Gene-Regulated Cytolytic Adenovirus, in Patients with Locally Recurrent Prostate Cancer Following Definitive Radiotherapy.”