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Intratumoral Gene Therapy Injections with a Multi-pronged, Multi-side Hole Needle for Rectal Carcinoma

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Interventional radiologists can deliver therapeutics directly to a tumor via needle injection. One of the major limitations of directly injected gene therapies is limited delivery, penetration, and transfection efficiency of the genetic vector, which in many cases directly limits the therapeutic effect. Numerous preclinical oncology models exist which rely upon direct injection of DNA plasmid or vector through an end-hole needle and into a tumor. Selection of a physically more efficient device with more needles and more side holes could improve distribution of the therapeutic agent.[1] Small hepatocellular carcinomas have been effectively treated with alcohol injections via a multi-pronged, multi-side hole needle. [2]

TNferade (GenVec, Gaithersburg, MD) is an attenuated adenovirus vector whose cargo is the gene encoding for tumor necrosis factor-alpha (TNF α), a potent cytokine that can be tumorocidal and also makes nearby tumor cells more sensitive to chemotherapy and to radiation therapy. TNferade is turned on by a promoter that is turned on by radiation. [3] TNferade also causes a “bystander effect” whereby affected cells do not necessarily need to be transfected with virus, but can respond to the TNF α product programmed by the gene. Despite the bystander effect, injectable therapeutics may suffer from lack of exposure to tumor tissue or a limited distribution in target tumor. Optimizing the physical distribution of such a therapeutic agent should be a goal of the interventional radiologist performing direct gene therapy injections. 5 patients with T3, T4, or N+ rectal cancer were treated as part of a clinical trial with weekly transrectal ultrasound (TRUS) guided injections, monitored under direct TRUS visualization [fig 1]. Patients received injections via a Quadrafuse needle (Rex Medical, Conshohocken, PA & Alliance Medical, Austin, TX) [fig 1] with three prongs, each with three side holes, or a custom Bernardino needle (Cook Medical, Bloomington, IN) with three side holes. Five weekly injections of 4×10^{10} particle units TNF-erade were combined with 50.4 Gy of external beam radiation, chemotherapy with capecitabine, and surgical resection. No complications were seen from the 25 injection procedures in 5 patients. [3]

Direct injection of gene therapy is highly inefficient, which may limit transfection and theoretically limit therapeutic efficacy. Interventional radiologists should consider the speculative benefits of multi-pronged and multi-side hole needles when directly injecting gene therapies.

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Fig 1. Multi-prong, multi-side hole needle in rectal cancer monitoring gene therapy injection with ultrasound. Ultrasound shows central cannula (open arrow) has deployed prong (closed arrow) with side holes, to better distribute therapeutic agent.