PROSTATE CANCER VIRAL GENE THERAPY CAN IMPROVE IMRT

In men with newly diagnosed intermediate-risk prostate cancer, Freytag *et al.* evaluated whether intensity-modulated radiotherapy (IMRT) can be augmented using oncolytic adenovirus-mediated cytotoxic gene therapy (OAMCGT). In addition to the oncolytic effect of viral infection, the virus used was designed to sensitize cancer cells to IMRT through expression of cytosine deaminase and thymidine kinase, which are involved in activation of the prodrugs 5-fluorocytosine and valganciclovir, respectively.

In 21 patients, the adenoviral particles were injected into all sextants of the prostate in a skewed manner, with cancer harbouring regions receiving higher doses, followed by a 2-week course of the oral prodrugs. In addition, these men and 23 patients in a control group, received 40 × 2 Gy fractions of IMRT.

“Men who received OAMCGT plus IMRT had a 42% reduction in positive biopsies at 2 years relative to men who received IMRT only (33% versus 58%), and the results were even better (60% relative reduction) in men who had a low tumour burden (<50% positive biopsy cores at baseline),” states Freytag. Importantly, the authors highlight that the benefit of OAMCGT was similar to that previously attributed to 4 months of androgen-deprivation therapy used in a comparable setting. “These promising results were achieved without markedly increasing toxicity or diminishing the patients’ quality of life,” adds Freytag.

Of note, no such relative reduction was seen in patients with a high tumour burden (≥50% positive baseline biopsies), with a 60% frequency of positive 2-year biopsies in both groups. This finding might reflect skewing of the relative viral doses injected: men with a high tumour burden received 60% fewer viral particles per positive core than those with a low disease burden. Thus, the authors suggest that higher viral loads might be required for higher tumour burdens, and have previously shown that safely escalating the viral dose is feasible.

“We believe that biological approaches similar to ours may someday prove to be an effective alternative to surgery (and possibly radiation) for select patients,” Freytag opines. “However, we will have to make further improvements before this possibility becomes reality.”

David Killock

Original article Freytag, S. O. *et al.* Prospective randomized phase 2 trial of intensity modulated radiation therapy with or without oncolytic adenovirus-mediated cytotoxic gene therapy in intermediate-risk prostate cancer. *Int. J. Radiat. Oncol. Biol. Phys.* **89**, 268–276 (2014)