

EDITORIAL

A Hard Target Needs a Sharper DaRT

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We read with great interest a prospective trial by Popotvzer et al using a novel alpha-emitting brachytherapy source in the treatment of recurrent/unresectable squamous cell carcinoma of the skin and head/neck. This is a very challenging patient population, and we congratulate the investigators for developing this novel approach.

Interstitial brachytherapy in the head and neck, in the hands of skilled operators, is an indispensable component of local dose escalation for an otherwise devastating disease process.¹ This is particularly true for patients with prior radiation or for whom a morbid resection is impossible or cosmetically disfiguring.²

This first in-human approach used radium-224, which by virtue of its higher linear energy transfer and relative biologic effect may conquer the intrinsic radioresistant nature of hypoxic, clinically recurrent disease. The authors demonstrate a unique approach for alpha particle therapy delivery that they call diffusing alpha-emitting radiation therapy (DaRT). DaRT is a fundamentally innovative technique that cleverly overcomes the obstacle of the limited range of alpha particles in tissue. The mechanism for this effect is saturation of the tumor microenvironment with the initial decay product, a short-lived radon-220 radioisotope. This noble gas diffuses both within and around tumor cells and represents the starting point for a series of alpha decay cascades, ultimately resulting in tumor kill over a 2 to 3 mm distance around each seed. The authors delivered this therapy with a custom-designed applicator and threaded radionuclide seeds.

Despite a limited accrual of 28 evaluable patients, the authors should be applauded for their execution of an effective trial demonstrating 3 important facets:

1. Safe and well-tolerated therapy even in elderly and previously irradiated/resected patients, as acute toxicity predominantly resolved by 1 month after treatment. Postimplant radioactivity measurements indicated a minimal risk to radiosensitive tissues, and no acute grade 3 toxicities or any late toxicities were noted, which compares favorably to historical series.^{3,4} This attribute of DaRT is particularly important because so many patients with recurrent disease are not medically suitable for aggressive treatment.
2. Demonstration of therapeutic effect in all patients, with nearly 80% achieving complete eradication of clinically evident tumor. The remainder had at least a partial response. Unsurprisingly, radiation-naïve disease responded most vigorously; however, even among previously irradiated patients, a majority were able to achieve a complete response.
3. Translation of preclinical findings to tangible benefit in the clinic and innovation in our field. This is the first demonstration of alpha particle-based brachytherapy with a defined dose (10 Gy) that is capable of inducing vigorous clinical responses. It raises the question as to whether this approach could have value as an alternative to the more toxic and aggressive treatments that are currently offered.

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One aspect unexplored by these authors is the overall cost of the therapy and how widely available this treatment might be to patients around the world. However, we feel that this preliminary experience warrants additional studies and should spark interest in the multidisciplinary head and neck community.

References

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