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INVITED RESEARCH HIGHLIGHT

Prostate Cancer

How nerve-sparing technique has been applied to radiotherapy?

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The introduction of nerve-sparing technique is one of the most significant advances in the surgical treatment of prostate cancer and heralded a shift from a curing cancer at all-cost model to a curing cancer and preserving quality of life model.[1,2] In a recent article published in *Lancet Oncology* in May, Lee *et al.*[3] reviewed the concept of vessel-sparing and functional anatomy-based radiotherapy as well as outcomes with respect to erectile dysfunction, bringing to light a conceptual shift in the management of localized prostate cancer with radiotherapy, which parallels the shift in the surgical management of prostate cancer with the introduction of nerve-sparing technique. The hypothesis is that utilization of vessel-sparing and functional anatomy-based radiotherapy may result in a more personalized approach to this modality based on a patient's specific anatomy, therefore improving patient outcomes.

The concept of vessel-sparing and functional anatomy-based radiotherapy is grounded in two advantages of MRI-based planning: first, MRI can map the anatomic variation that exists among men which either allows for or prevents more targeted use of radiotherapy, and second, MRI-based planning can improve delineation of the prostate, neurovascular bundles, and vasculature compared to CT-based planning.[3,4] Historically, it has been understood that radiotherapy has direct arterial effects which contribute to erectile function in addition to its direct effects on nerves. Therefore, limiting radiation to these structures should improve outcomes with respect to erectile function in theory.

The review by Lee *et al.*[3] highlights some of the key anatomic structures that can be identified with MRI-based planning and potentially spared. The neurovascular bundles, though classically described as located in the posterolateral position, display some anatomic variation, with the majority of the neurovascular elements located within 1 cm of the prostate.[5] This distance is critical as variation may allow for nerve sparing in selected cases, and millimeter differences can affect radiation dose to these structures. The neurovascular bundles continue on to form the terminal branches of the cavernosal nerves, and although they cannot be visualized due to small caliber of these nerves, the radiation dose to the external sphincter has been investigated as a surrogate for the radiation dose to these nerves. The average distance of the sphincter (measured as the distance from the apex to the penile bulb) varies considerably among men, with an average length of 1.45 cm and range of 0.7–2.1 cm.[6] Radiation dose to the penile bulb can also be a surrogate for radiation to the cavernosal nerves, as well as to the internal pudendal artery and the corpora cavernosa, and radiation to the penile bulb correlates with erectile dysfunction 2 years after treatment.[7] Finally, the internal pudendal artery demonstrates an average distance of 2.2 cm measured by MRI compared to 0.92 cm measured by CT, and accessory pudendal arteries may prevent vessel-sparing radiation.[6]

To spare the functional anatomy and vessels, Lee *et al.* highlight their own work, in which they compare vessel-sparing radiotherapy with combination vessel-sparing radiotherapy and brachytherapy. The rationale is that by utilizing radiotherapy to treat the under dosed areas only, one can limit the amount of radiation to the sensitive structures listed previously. The main outcome was sexual function, measured by the International Index of Erectile Function (IIEF) and the Q3 assessment. While the authors noted an improvement in Q3 from 78.6% in the radiotherapy alone group to 91.8% in the combination therapy group, they did note that a third of men with ED were unresponsive to medications according to the IIEF.[8,9] Combination vessel-sparing radiotherapy and brachytherapy resulted in lower doses to the penile bulb, corpora cavernosa, and internal pudendal artery, and resulted in higher doses to the neurovascular bundles.[8] Yet, they did not observe any correlation between erectile dysfunction and dose to a specific structure.[8]

Lee *et al.*[3] have provided us with a thorough compilation of data regarding variation in anatomic structures that may contribute to erectile dysfunction after radiotherapy, as well as the clinical studies related to vessel-sparing and functional anatomy-based radiotherapy, as it pertains to erectile dysfunction outcomes. However, there are limitations to our understanding of how radiation doses to specific structures affect erectile dysfunction outcomes. Although touted as potentially game-changing, we have yet to see drastic changes in outcomes based on more targeted radiotherapy techniques, in contrast to the effect of nerve-sparing technique on radical prostatectomy.[10] As the authors allude to, sparing radiation to specific structures does not directly translate into improved outcomes as one might expect. Rather, further prospective study of anatomic relationships and variants might allow for a more personalized approach to counseling

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patients on the risk of erectile dysfunction after treatment. Lee *et al*.[3] focus on erectile function outcomes in their review, yet oncologic outcomes, which are just as important, should be also addressed. Perhaps, it is still early in its conception, and over time, enough patients will have been accrued that we will be able to address the question if equivalent cancer control can be achieved with vessel-sparing and functional anatomy-sparing techniques. A one-size-fits-all approach certainly does not apply to the surgical management of localized prostate cancer; therefore, a more targeted approach may not always be feasible with radiotherapy depending on the presence of adverse clinical or radiologic features.

Prospective evaluation of how radiation to specific structures surrounding the prostate as well as further understanding of determinants of radiation sensitivity will improve the way in which we counsel patients on the treatment options available for localized prostate cancer. Rather than providing patients with general statistics of outcomes, we may be able to personalize outcomes based on one's anatomy. Vessel-sparing and functional anatomy-based radiotherapy are other examples on how advances in prostate MRI are changing our approach to treating localized prostate cancer, yet much work is needed to translate this into improved patient outcomes.

COMPETING INTERESTS

The authors declared no competing interests.

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