Rectal Hydrogel Spacers and Prostate Radiotherapy

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Prostate cancer (PCa) is the second most commonly diagnosed male malignancy in the Western world.[1] Radical prostatectomy and radiotherapy (RT), in their various modalities, are currently recommended as definitive treatment options, alone or in combination, in men with organ-confined, locally advanced, and oligometastatic disease.

The literature has shown that higher doses given to the prostate improve biochemical disease-free survival, with acceptable acute and long-term toxicities,[2] but the increase in dose can also affect the rectum, which may increase the risk of long-term toxicity.

Three large randomized, non-inferiority trials evaluated the equivalence of hypofractionation (hRT) with standard fraction treatments. The Conventional or Hypofractionated High-dose Intensity-modulated Radiotherapy in Prostate cancer (CHHiP)[3] trial compared if hRT (60 Gy in 20 fractions) was non-inferior to conventional fractionation using 74 Gy in 37 fractions. The Radiation Therapy Oncology Group (RTOG) 0415 compared 73.8 Gy in 41 fractions given in 8.2 weeks to 70 Gy in 28 fractions over 5.6 weeks, also concluding that higher doses of hRT increase rectal complications given the small rectal volume.[4] Finally, the PROFIT[5] juxtaposed 70 Gy given in 28 fractions with conventional fractionation. The use of moderate hypofractionation and stereotactic body radiotherapy (SBRT) regimens for definitive PCa treatment has increased from 2004 to 2020, which implies that a higher dose could be given to the rectum but respecting defined constraints.[6]

All the above-mentioned studies included patients in different risk groups for biochemical failure as well as with different hormonal blockage profiles; however, they achieved similar results in terms of biochemical control. Conversely, late toxicity outcomes were slightly different: RTOG 0415 and CHHiP reported no difference in late toxicity, while PROFIT reported a lower rate of late toxicity with hRT.

To reduce the incidence of acute and late rectal toxicity, the insertion of a polyethylene glycol-based spacer between the rectum and the prostate, which is already approved in the USA, Europe, and Asia, is routinely performed. Last year, it had the clearance of the Brazilian Health Regulatory Agency (Agência Nacional de Vigilância Sanitária – ANVISA, in Portuguese). The support to the use of the hydrogel spacer is its allocation between the prostate and the rectum, splitting these two structures and thus reducing the dose of radiation received by the rectum. After a variable period of 3 to 4 months, the gel is reabsorbed.

A systematic review by Babar et al.[7] verified that SpaceOAR (Augmenix, Inc., Bedford, MA, USA) can reduce the radiation dose received by the rectum, resulting in decreased acute, grade-1 diarrhea and late grade-2 and above rectal toxicities. Recently, Applewhite et al.[8] published that these gel spacers may be an option for patients undergoing temporary or permanent brachytherapy, as well as for those who had failure to previous prostate cryoablation and were referred to salvage radiotherapy.

Centers that work with this technology have reported very few major complications. Scarce descriptions of prostatic or perineal abscess, rectal wall erosion, and recto-urethral fistula have been found in the literature. Anaphylaxis and acute pulmonary embolism, despite their rarity, may also occur. There were 22 reports discussing toxicity in 25 patients in the Manufacturer and User Facility Device Experience (MAUDE) database from January 2015 to March 2019. Unique major complications including acute pulmonary embolism, severe anaphylaxis, prostatic abscess and sepsis, purulent perineal drainage, rectal wall erosion, and recto-urethral fistula have been reported.[9]

The gains in rectal dosimetric parameters are clear if the gel is well positioned and should be a recommendation for all patients with previous rectal interventions or preexisting disease, and for those at risk of developing late severe rectal

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toxicity, such as patients with pelvic chronic disease or radiation history, ulcerative colitis, Crohn's disease, previous history of fistula, or nonspecific rectitis.

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Clinical Trials

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Conflict of Interests

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