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Hydrogel Spacing for Radiotherapy of Prostate Cancer: A Review of the Literature

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Abstract

Introduction: The rectum is particularly sensitive to radiation and it represents the dose limiting structure during radiation therapy for prostate cancer. Transperineally inserted rectal hydrogel spacers were proposed as a technique to limit the rectal radiation dose and rectal toxicity during prostate radiation therapy.

Methods: Different spacing materials, including hyaluronic acid, polyethylene glycol and human collagen, have been tested as potential rectal spacing agents to reduce radiation exposure to the rectum and limit rectal toxicity.

Results: Early results from studies in which 1 to 48 patients received rectal spacers demonstrate that rectal spacers during prostate radiation therapy appear to be feasible and tolerable, and are not associated with significant side effects. The published literature shows a median or mean space achieved between the rectum and prostate that typically ranges from 1.0 to 2.0 cm, significant reductions in rectal radiation dose, a low rate of acute gastrointestinal toxicity and short-term quality of life benefits when comparing men who receive rectal spacers during prostate radiation therapy to those who do not.

Conclusions: Rectal spacers could potentially allow for greater dose escalation and hypofractionation while reducing rectal toxicity or protecting against increased rectal toxicity. This could theoretically lead to better tumor control, decreased toxicity and health care costs, and improved patient and provider satisfaction. Although short-term results based on the small cohort studies summarized in this review are encouraging, longer followup and larger, randomized trials are needed to determine the impact of rectal spacers on tumor control and late rectal toxicity.

Key Words: prostate, prostatic neoplasms, radiotherapy, rectum, iatrogenic disease

Abbreviations and Acronyms

EBRT = external beam RT

EPIC = Expanded Prostate Cancer Index

HA = hyaluronic acid

HDR = high dose rate

IMRT = intensity modulated RT

LDR = low dose rate

MRI = magnetic resonance imaging

PEG = polyethylene glycol

QOL = quality of life

RT = radiation therapy

V = volume receiving percent of dose or greater

In 2014 there will be approximately 233,000 newly diagnosed cases of prostate cancer and 29,480 deaths from prostate cancer in the United States alone.[1] For localized prostate cancer radiotherapy (EBRT and/or brachytherapy) is an established potentially curative treatment option as outlined by the well-defined guidelines provided by the NCCN (National Comprehensive Cancer Network®).[2,3] Higher RT doses improve disease-free survival and margins up to 8 to 10 mm around the prostate are sometimes used to account for prostatic motion to ensure that the gland receives the full dose.[4–7] Due to the proximity of the sensitive rectal mucosa to the prostate the rectum is particularly sensitive to prostate RT and so rectal toxicity is a dose limiting factor during RT for prostate cancer.[8,9]

To address dose limiting rectal toxicity anorectal sparing devices were proposed for prostate RT to spare anorectal structures and limit rectal injury.[10] Anorectal sparing devices

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include endorectal balloons and transperineally inserted hydrogel spacers. Endorectal balloons predominantly help spare the lateral and posterior anorectal walls[11,12] while transperineally inserted hydrogel spacers increase the space between the prostate and rectum and, thus, tend to spare the anterior wall.[13,14]

In this review we describe the clinical usefulness of transperineally inserted hydrogel spacers. We summarize the published literature on the feasibility, dose impact and rectal toxicity associated with hydrogel spacers for RT for prostate cancer.

Procedure

Several similar approaches to placing rectal spacers have been described in the literature.[15–18] One of the most widely accepted techniques involves transperineal placement of the spacer using hydrodissection to facilitate the process.[15,18,19] Although hydrodissection is optional, it was proposed by Hatiboglu et al as a method to create space between Denonvilliers fascia and the anterior rectal wall to facilitate placement of the rectal spacer.[15] In this technique the patient is placed in the lithotomy position. Under transrectal ultrasound guidance an 18 gauge needle is inserted transperineally and cautiously directed toward the potential space between Denonvilliers [F1] fascia and the anterior rectal wall (fig. 1). After the needle is advanced into the proposed position the potential space is hydrodissected using up to 10 to 25 ml injectable saline [F2] (fig. 2).[15,18,19] If hydrodissection is not achieved, placement of the rectal spacer is aborted. However, if hydrodissection is accomplished, the rectal spacer can be placed by attaching the syringe/apparatus containing the spacer material and injecting [F3] the contents into the created space (fig. 3).

Investigators have studied various materials for rectal spacer devices for prostate RT with most of the literature focusing on HA, PEG and human collagen.[13,20–23] There are pros and cons inherent to each spacer material related to degradation, distribution and/or viscosity properties.[15] Early studies of rectal spacer use in prostate RT focused on HA.[13,23–25] However, the recent literature demonstrated that PEG or hydrogel products are less viscous, less susceptible to radiation degradation and better able to distribute uniformly between the prostate and rectum than HA.[20,21] Thus, PEG based materials, which are absorbable, nontoxic, water soluble, nonimmunogenic and persistent up to 3 months before hydrolysis, have become the most widely used materials for rectal spacers for prostate RT.[15,16,18,21,22,26]

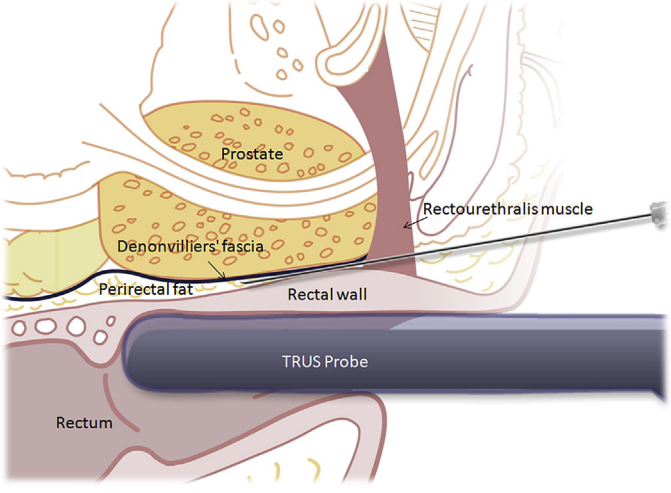

Figure 1. Under transrectal ultrasound (*TRUS*) guidance 18 gauge injection needle is inserted perineally and cautiously directed toward potential space between Denonvilliers fascia and anterior rectal wall.

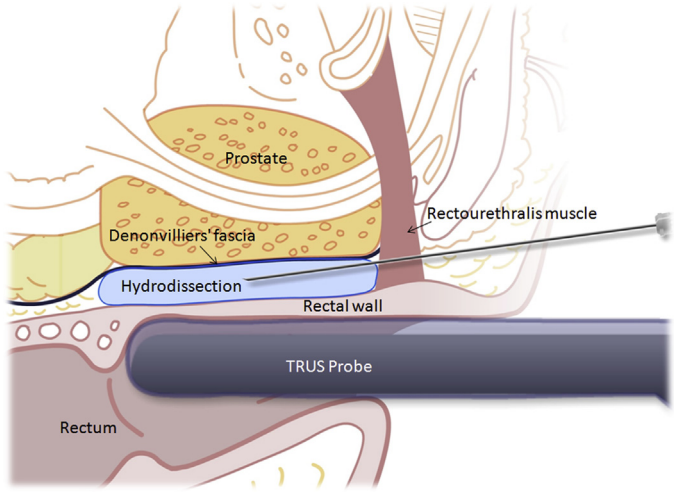

Figure 2. Needle is advanced into space, which is hydrodissected using up to 25 ml injectable saline. *TRUS*, transrectal ultrasound.

Clinical Usefulness

Feasibility of Rectal Spacer Placement

A strong, growing body of literature shows that space can be safely created between the prostate and rectum using absorbable biomaterials as rectal spacers during prostate RT. The median or mean space achieved between the rectum and prostate typically ranges from 1.0 to 2.0 cm in published spacer

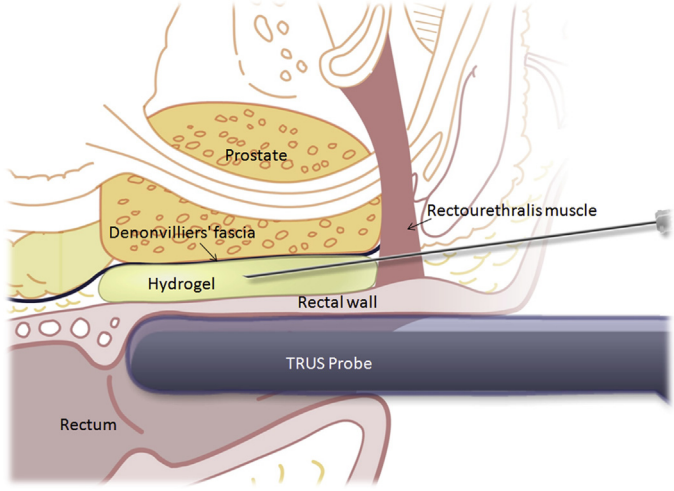

Figure 3. If hydrodissection is safely accomplished, rectal spacer is placed in space created. *TRUS*, transrectal ultrasound.