

# Side effects of modern radiotherapy/IMRT to the prostate +/- pelvic nodes

2004 RBWH GP Preceptorship

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# Case

- 75 y.o. man
- PSA 6 ng/ml; G.S. 4+4=8; T2b
- Multi-parametric MRI- No extra-prostatic extension, no seminal vesicle involvement. PIRADs 4 mid-gland peripheral zone.
- PSMA-PET: prostate confined, no regional or distant metastases
- Treatment options:
  - Robot assisted radical prostatectomy +/- pelvic LN dissection
  - Definitive external beam radiotherapy + long course androgen deprivation therapy
    - Prostate +/- pelvic nodal irradiation
    - Probability of nodal involvement based on Roach formula 24%

# RT toxicities- prostate only RT

1. Gastrointestinal (GI)
2. Genitourinary (GU)
3. Bleeding (GI/GU) in anticoagulated patients
3. Erectile dysfunction
4. Fatigue
5. Insufficiency fractures
6. Secondary malignancies

***Acute:*** events occurred during and within 3 months from completing RT

***Late:*** events occurred >3 months after completing RT

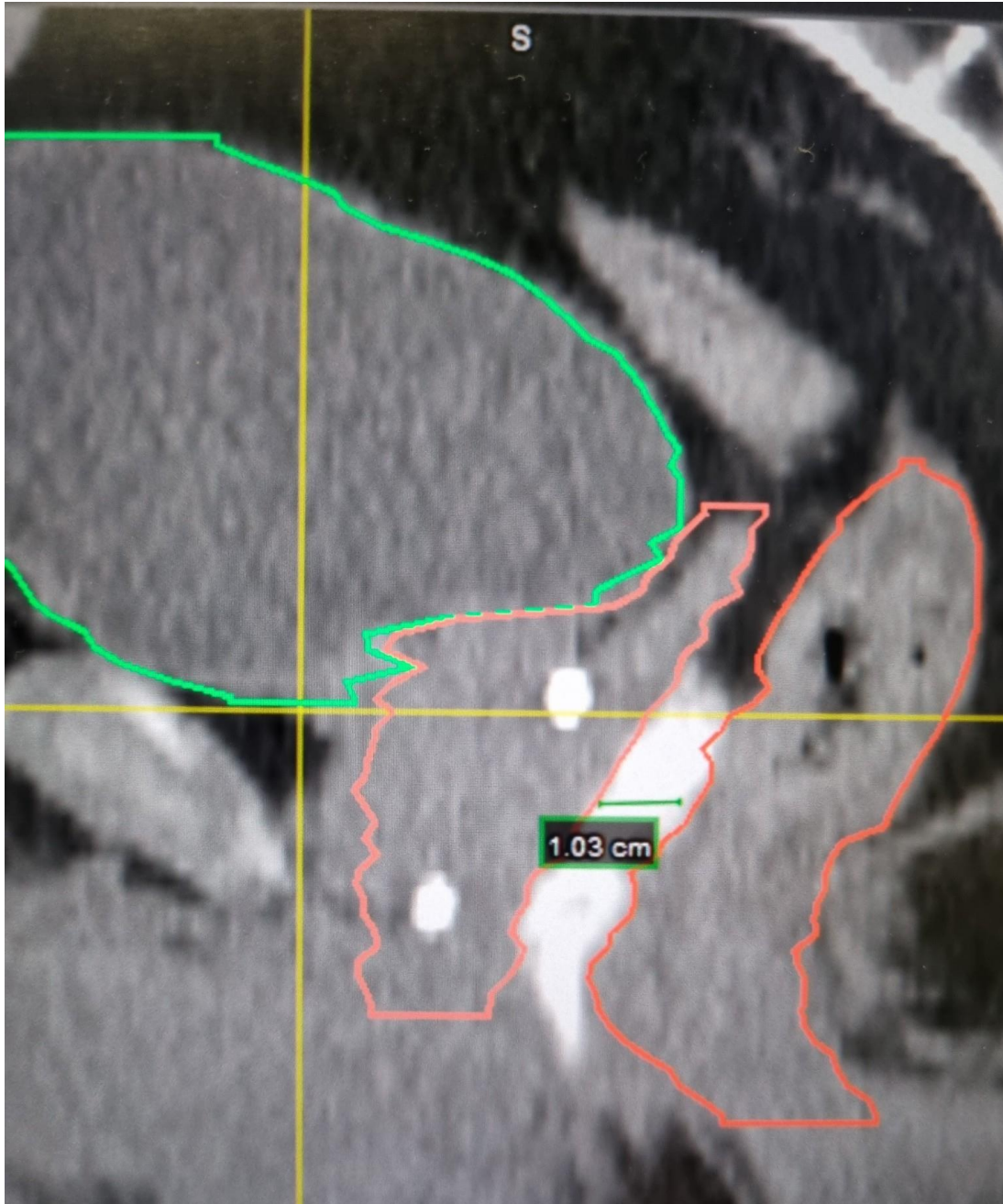
## Radiation Therapy Oncology Group (RTOG) criteria for long-term normal tissue toxicity

<b>Symptoms</b>
<b>Diarrhea</b>
Frequent loose bowel movements without associated rectal irritation
<b>Proctitis</b>
Rectal irritation or urgency, and the presence of mucous or blood in the stool, with or without frequent or sometimes loose bowel movements
<b>Cystitis</b>
Irritative bladder symptoms such as frequent dysuria; hematuria may or may not be a part of the clinical picture
<b>Grades</b>
<b>Grade 0</b>
No symptoms
<b>Grade 1</b>
Minor symptoms requiring no treatment
<b>Grade 2</b>
Symptoms that respond to simple outpatient management and do not affect lifestyle
<b>Grade 3</b>
Distressing symptoms affecting lifestyle; may necessitate hospital admission or minor surgical intervention (eg, urethral dilation)
<b>Grade 4</b>
Major surgical intervention or long stay in the hospital necessary (eg, laparotomy, colostomy, or cystectomy)
<b>Grade 5</b>
Fatal complications

Data from: Rubin P, Constine LS, Fajardo LF, Phillips TL, Wasserman TH. RTOG Late Effects Working Group. Overview. Late Effects of Normal Tissues (LENT) scoring system. *Int J Radiat Oncol Biol Phys* 1995; 31:1041.

# Gastro-intestinal toxicities

- Acute proctitis or enteritis (5-30%)-abdominal cramping, tenesmus, urgency, and frequency of defecation.
  - After RT is completed, acute symptoms usually resolve within three to eight weeks.
- Late gastrointestinal side effects ( $\geq$  Gd III: 1-5%)
  - can manifest as persistent diarrhea, tenesmus, rectal urgency, or hematochezia.
  - Rectal or anal strictures, fecal incontinence, ulcers, and perforation are rare.



# Rectal spacer

- Improve rectum dosimetry, Reduce rectal toxicities
- Operator dependent
- Aim for 1cm separation at mid gland level
- Cost- covered by private health fund
- Not suitable for patients with large prostate gland (>80 c.c.) and/or extra-prostate extension (T3)

JAMA Oncology | [Original Investigation](#)

## Hyaluronic Acid Spacer for Hypofractionated Prostate Radiation Therapy A Randomized Clinical Trial

Mariados N et al. Hydrogel Spacer Prospective Multicenter Randomized Controlled Pivotal Trial: Dosimetric and Clinical Effects of Perirectal Spacer Application in Men Undergoing Prostate Image Guided Intensity Modulated Radiation Therapy. *Int J Radiat Oncol Biol Phys.* 2015 Aug 1;92(5):971-977. doi: 10.1016/j.ijrobp.2015.04.030. Epub 2015 Apr 23. PMID: 26054865.

# Urinary toxicities

- Acute:
  - 50% will have some degrees of frequency, dysuria, and/or urgency due to cystitis, urethritis, or both. Symptoms typically resolve within four weeks after the completion of therapy.
- Late:
  - $\geq$ Gd 3  $\approx$  8%
  - urethral strictures, cystitis, hematuria, and bladder contracture.
  - 50% these were attributed to urethral stricture that could be managed with dilation.

# Bleeding in anticoagulated patients

- Patients on Warfarin, clopidogrel
- One single institution reported a retrospective incidence of ~15% compared to 3%
- GI bleeding more common than GU bleeding
- Generally self-limiting and rarely requires transfusion



# Erectile dysfunction

- 30-45% in those previously potent.
- Incidence increases over time

# Fatigue

- Incidence and severity increase during radiotherapy
- Two randomized trials found that aerobic and resistance exercise ameliorated fatigue in the short term,
- Resistance exercise may offer additional conditioning benefits

# Pelvic Insufficiency fracture

- No prospective long term follow up data
- Incidence ~6% at 5 years (one single institution retrospective series)
- Important to rule out bony metastasis

*Insufficiency fractures after pelvic radiotherapy in patients with prostate cancer. Iğdem S, Alço G, Ercan T, Barlan M, Ganiyusufoğlu K, Unalan B, Turkan S, Okkan S. Int J Radiat Oncol Biol Phys. 2010;77(3):818.*

# Secondary malignancies

Not increased compared to population-based registries

*Second primary cancers after radiation for prostate cancer: a systematic review of the clinical data and impact of treatment technique. Murray L, Henry A, Hoskin P, Siebert FA, Venselaar J, PROBATE group of GEC ESTRO Radiother Oncol. 2014;110(2):213. Epub 2014 Jan 30.*

# RT toxicities- prostate and pelvis

- Gd II blood/marrow late toxicities: Moderately hypocellular or  $>25$  –  $\leq 50\%$  reduction from normal cellularity for age **4.4%**
- Gd III blood/marrow late toxicities: Severely hypocellular or  $>50$  –  $\leq 75\%$  reduction cellularity from normal for age **2.1%**
- Note FBC was only collected for another 6 months after RT was completed

*Pollack A, Karrison TG, Balogh AG et al. The addition of androgen deprivation therapy and pelvic lymph node treatment to prostate bed salvage radiotherapy (NRG Oncology/RTOG 0534 SPPORT): an international, multicentre, randomised phase 3 trial. Lancet. 2022 May 14;399(10338):1886-1901. doi: 10.1016/S0140-6736(21)01790-6. PMID: 35569466; PMCID: PMC9819649.*