Late Toxicity Following EBRT with LDR-BT Boost: A Single Institution Experience

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Introduction

- EBRT combined with LDR-brachytherapy boost (BT-boost) is considered a **recommended treatment** for unfavourable intermediate and high risk prostate cancer.
- The combination has shown **superior outcomes compared to dose-escalation EBRT alone**, with better overall survival demonstrated with LDR-BT-boost. [1]
- However, International studies – grade 3 or higher genitourinary (GU) toxicities **1.4% to 18.1** and gastrointestinal (GI) toxicities from **0 to 15%** (modified LENT-SOMA scale)
- We aim to assess the late grade 3 or higher GI and GU toxicity of our institution's over the past 10-year data and how it compares with other studies.

[1] G., Peyraga., et al. "Brachytherapy boost (BT-boost) or stereotactic body radiation therapy boost (SBRT-boost) for high-risk prostate cancer (HR-PCa).." Cancer Radiotherapie, 25 (2021).:400-409. doi: 10.1016/J.CANRAD.2020.11.004

Methods

- Retrospective chart review
- 2013-2023
- Patients with IR/HR Prostate cancer
- Pre-treatment analysis (baseline QOL symptoms recorded)
- EBRT 46 Gy in 23 fractions + Brachytherapy boost I125 1-4 weeks post EBRT
- Clinical follow ups at 1 months, 6 months and then yearly post-brachytherapy.
- Evaluate late grade 3 or higher GI and GU toxicities (Modified LENT-SOMA scale)

	1	2	3	4
GU	• Nocturia twice baseline. • Microscopic hematuria. • Light atrophy and minor telangiectasia. • Occasional (< weekly) use of incontinence pads.	• Moderate frequency. • Nocturia more than twice baseline. • Generalized telangiectasia. Intermittent macroscopic hematura. • Two or fewer coagulations. Intermittent (< daily use of incontinence pads.) • Regular nonnarcotic or occasional narcotic for pain.	• Severe frequency and dysuria. • **Nocturia more frequent than once every hour.** Minor surgical procedure (e.g. TURP, dilation). Reduction in bladder capacity (150 cc). • Frequent hematuria requiring **at least one transfusion**. More than two **coagulations** for hematuria. • **Hyperbaric oxygen** for bleeding/ulceration. • Persistent use of incontinence pads/. Regular narcotic for pain.	• **Severe hemorrhagic cystitis or ulcerations** with requirement for urinary diversion and/or cystectomy.
GI	• Excess bowel movements at least twice baseline. • Slight rectal discharge or blood.	• More than 2 antidiarrheals/week • Two or fewer coagulations for bleeding. • Occasional steroids for ulcerations. • Occasional dilations. • Intermittent use of incontinence pads. • Regular nonnarcotic or occasion narcotic for pain.	• **More than 2 antidiarrheals/day**. • **At least one blood transfusion or more than two coagulations** for bleeding. • Prolonged steroids per enema. • **Minor surgical procedure.** • Hyperbaric oxygen for bleeding/ulceration. • Regular dilation. • Persistent use of incontinence pads. • Regular narcotic for pain	• Dysfunction requiring **surgery.** • **Perforation.** • **Life -threatening bleeding**.

Modified LENT-SOMA *(Late Effects of Normal Tissuee Somatic, Objective, Management, Analytic)* ***Scale*** [1]

[1] Rodda, Sree, et al. "ASCENDE-RT: An Analysis of Treatment-Related Morbidity for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost with a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer." *International Journal of Radiation Oncology*Biology*Physics*, vol. 98, no. 2, 2017, pp. 286–95, https://doi.org/10.1016/j.ijrobp.2017.01.008.

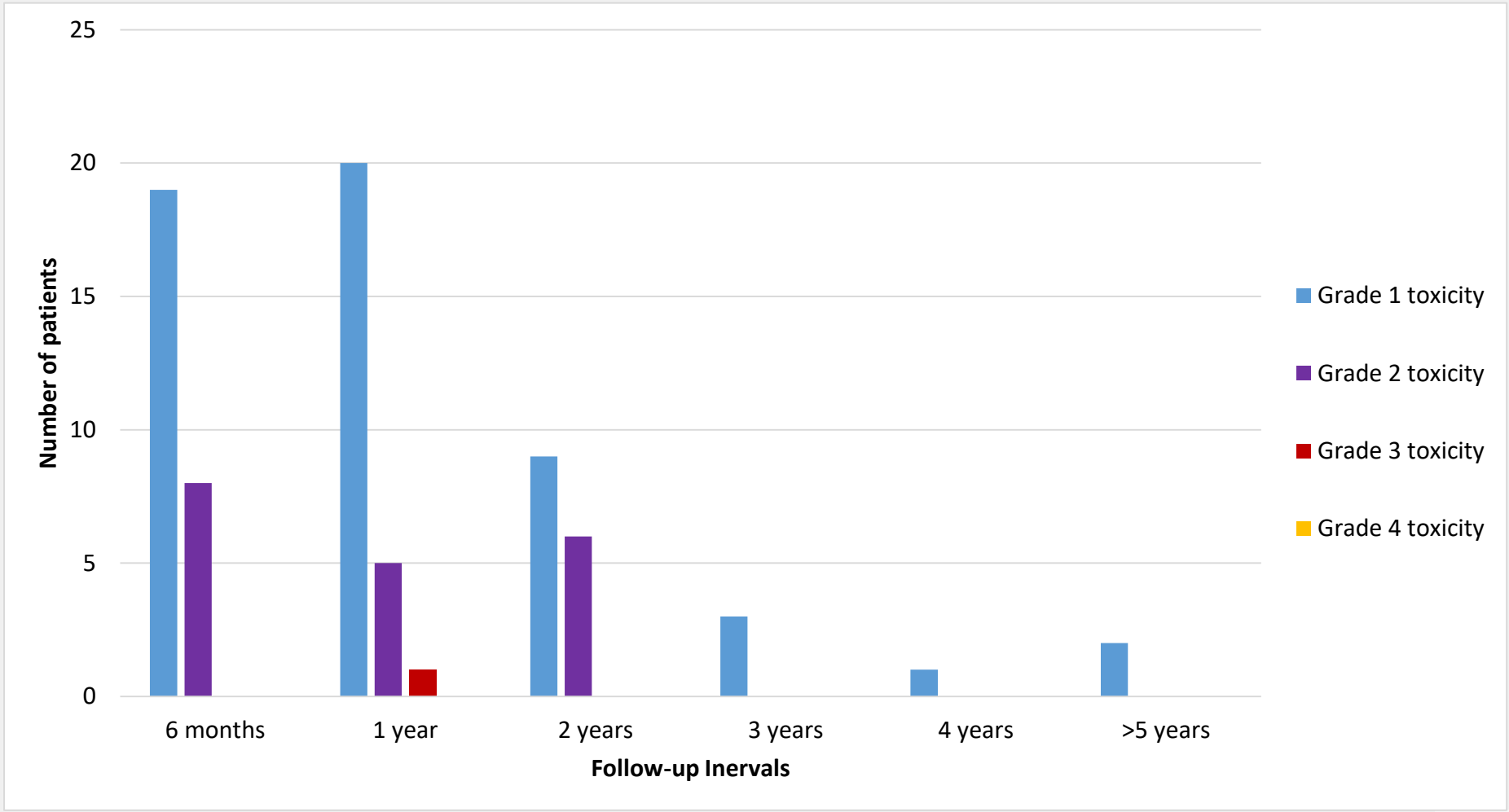
Radiation Treatment

- External beam radiotherapy (EBRT)
  - 46 Gy in 23#
  - 3D conformal and later VMAT
- Low-dose rate brachytherapy boost (LDR-BT)
  - I125 (110 Gy)
  - Loose and stranded seeds
  - Intraoperative dosimetry
  - Intraoperative planning

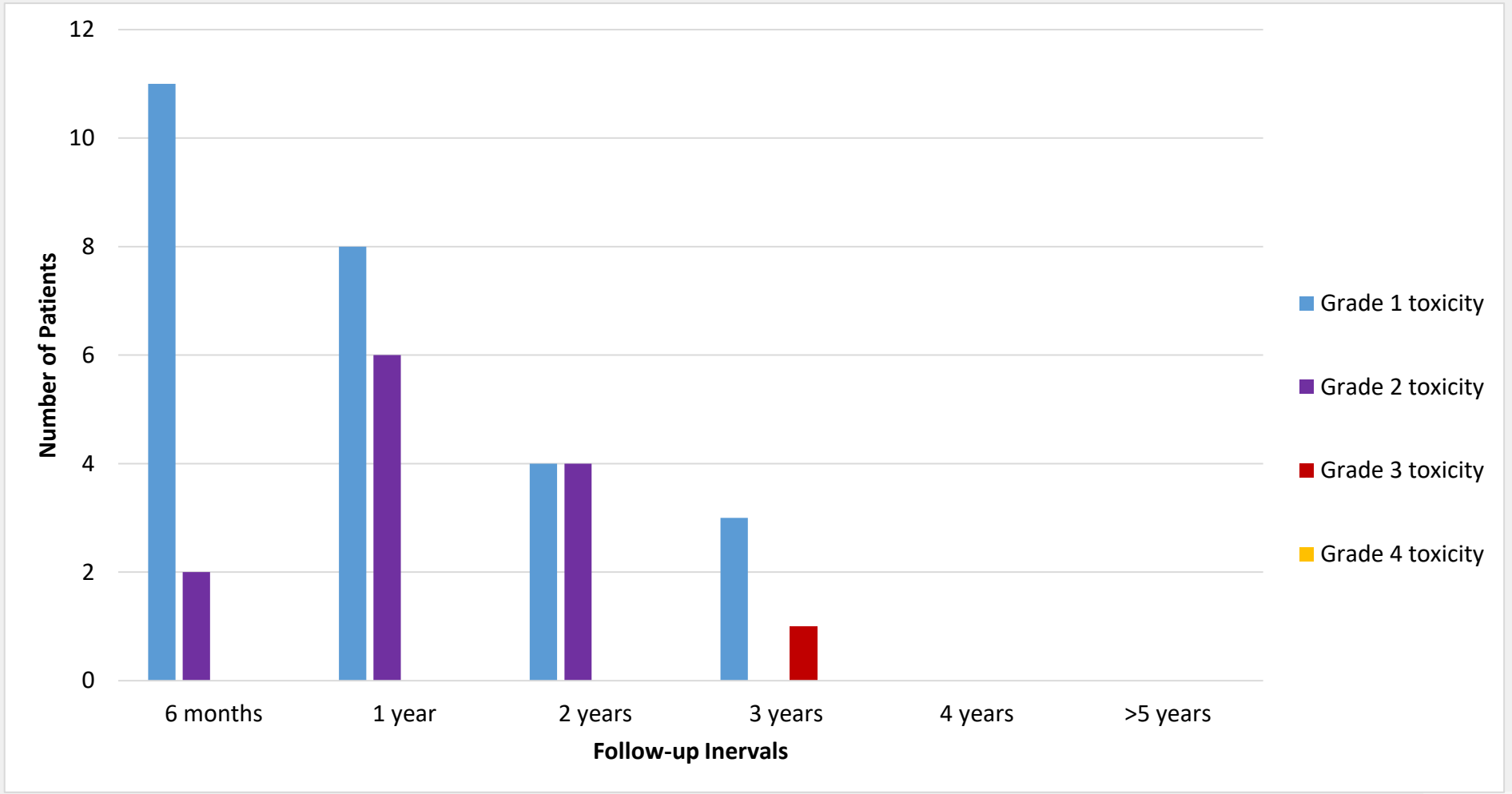
Results

- 57 patients
- Median age 66 years old (55-77)
- 49% (n=28) high risk and 51% (n=29) intermediate risk prostate cancer
- Of 28 HRPC patients, 22 (39% of all) received ENI
- Median iPSA 8.5 (range 5 – 37.7)
- 50 (88%) had at least 1 year of ADT (Casodex + Decapeptyl)
- Median follow up 3.1 years (1 – 10 years)
- Cumulative incidence of grade 3 or higher toxicity
  - GU = 1.75% (n=1)
  - GI = 1.75% (n=1)
- No biochemical relapse as of our last follow-up data

Genitourinary Toxicity Incidence



Gastrointestinal Toxicity Incidence



Outcomes in EBRT + LDR-BT Boost

Study	Median follow-up (Years)	Late Grade 3 GU Toxicity (%)	Late Grade 3 GI Toxicity (%)
Albert et al., 2003 [1]	2.8	N/A	**30**
Wong et al., 2009 [2]	4.8	**18**	**5**
Spratt et al., 2014 [3]	5.3	**1.4**	**1.4**
Hurwitz et al., 2011 [4]	6.0	**3**	**0**
Lawton et al., 2012 [5]	8.2	**15**	**15**
Rodda et al., 2017 (ASCENDE EBRT+ LDR arm) [6]	6.5	**18.4**	**8.1**
Qayoumi et al., 2024	3.1	**1.75**	**1.75**

[1] Albert, Michele, et al. "Late Genitourinary and Gastrointestinal Toxicity after Magnetic Resonance Image-Guided Prostate Brachytherapy with or without Neoadjuvant External Beam Radiation Therapy." *Cancer*, vol. 98, no. 5, 2003,
[2] Wong, William W., et al. "Radiation Dose Escalation for Localized Prostate Cancer." *Cancer*, vol. 115, no. 23, 2009, pp. 5596–606
[3] Spratt, Daniel E., et al. "Comparison of High-Dose (86.4 Gy) IMRT vs Combined Brachytherapy plus IMRT for Intermediate-Risk Prostate Cancer." *BJU International*, vol. 114, no. 3, 2014, pp. 360–67,
[4] Hurwitz, Mark D., et al. "Combination External Beam Radiation and Brachytherapy Boost with Androgen Deprivation for Treatment of Intermediate-Risk Prostate Cancer." *Cancer*, vol. 117, no. 24, 2011, pp. 5579–88
[5] Lawton, Colleen A., et al. "Long-Term Results of an RTOG Phase II Trial (00-19) of External-Beam Radiation Therapy Combined With Permanent Source Brachytherapy for Intermediate-Risk Clinically Localized Adenocarcinoma of the Prostate." *International Journal of Radiation Oncology*Biology*Physics*, vol. 82, no. 5, Apr. 2012, pp. e795–801
[6] Rodda, Sree, et al. "1 ASCENDE-RT: An Analysis of Treatment-Related Morbidity for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost with a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer." *International Journal of Radiation Oncology*Biology*Physics*, vol. 98, no. 2, 2017, pp. 286–95

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Discussion

- Our study demonstrates lower incidence of grade 3 or higher GU and GI toxicities in comparison to randomized international trials.
- Plausible explanations
  - Less conformal EBRT techniques (e.g. four-field box) may increase toxicity
  - Brachytherapy technique
    - Intraoperative planning – as opposed to pre-planning
    - Intraoperative dosimetry – enable modification of parameters
- Limitations: retrospective nature, limited number, single institution data

Discussion

- EBRT + LDR-BT boost were twice as likely to be free of biochemical failure at a median follow-up of 6.5 years.[1]
- ASCENDE-trial report:
  - Cumulative incidence of late grade 3 GU toxicity 18.4% for LDR-PB, versus 5.2% for DE-EBRT
  - Cumulative incidence of late grade 3 GI toxicity 8.1% for LDR-PB, versus 3.2% for DE-EBRT
  - 5-year prevalence: grade 3 GU morbidity for LDR-BT 8.6% vs 2.2% for DE-EBRT
  - 5-year prevalence: grade 3 GI toxicity for LDR-BT 1.0% vs 2.2% for DE-EBRT. [1]

[1] Morris, W. James, et al. "Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the ASCENDE-RT Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer." *International Journal of Radiation Oncology*Biology*Physics*, vol. 98, no. 2, 2017, pp. 275–85

Conclusion

- Our study demonstrates lower incidence of Grade ≥3 GU/GI toxicities in comparison to randomized international trials.
- This may be attributed to the utilisation of VMAT, intraoperative dosimetry, and intraoperative planning.
- EBRT + LDR Brachytherapy is a **safe** modality of treatment
- Further **prospective data** needed.

Contribution:

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