A multi-observer study investigating the effectiveness of prostatic mpMRI to dose escalate corresponding histologic lesions using high dose rate brachytherapy.

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Introduction

- Post-radiotherapy prostate cancer recurrence often occurs at dominant intraprostatic lesions (DILs), motivating focal dose escalation.
- HDR brachytherapy (HDR-BT) is performed by:
  1) Inserting approximately 15 hollow needles into the prostate using 3D transrectal ultrasound (TRUS).
  2) Designing a dose profile to uniformly cover the entire prostate.
  3) Moving a single radioactive source through each needle to deliver the dose.
- The current whole-gland approach to dosimetry aims to deliver the prescription dose to the entire prostate without focally targeting DILs.
- Multiparametric magnetic resonance imaging (mpMRI) has demonstrated potential for lesion localization.
- However, observer variability and error in MRI contouring has been shown, in comparison to gold-standard whole-mount histopathology.
- The aim of this study is to measure the effect of mpMRI-based DIL targeting based on the dose received to the DIL as defined on co-registered whole-mount histopathology.

Objectives

- **Objective 1:** To build an accurate registration procedure mapping MRI DIL contours to intraprocedural 3D TRUS.
- **Objective 2:** To focally increase the dose to the MRI DILs by modifying the dwell times the of the original whole-gland treatment plan.
- **Objective 3:** To register the ground-truth histopathology into the treatment plans to determine what dose the actual cancer would have received.

JULY 12–16 2020 VIRTUAL JOINT AAPM | COMP MEETING EASTERN TIME (GMT-4)

Materials & Methods

- 12 patients had pre-procedural multiparametric MRI scans (ADC, T2W and DCE) followed by radical prostatectomy.
- Four radiologists contoured DILs on ADC and DCE using PIRADS scoring and two pathologists contoured all cancer of the mid gland, yielding digital whole-mount histopathology with ground truth DILs.
- Both mpMRI and corresponding histology DILs were mapped and deformed to two previously performed standard intraprocedural 3D TRUS treatment plans. The prescribed dose for the entire prostate was 15 Gy.
- Using BrachyVision 13.6, plans were then adjusted to focally escalate the dose to the MRI defined lesions to 20.25 Gy.
- The dose delivered to the high- and low- grade histology DILs both prior to plan adjustment and following plan adjustment were recorded for analysis.

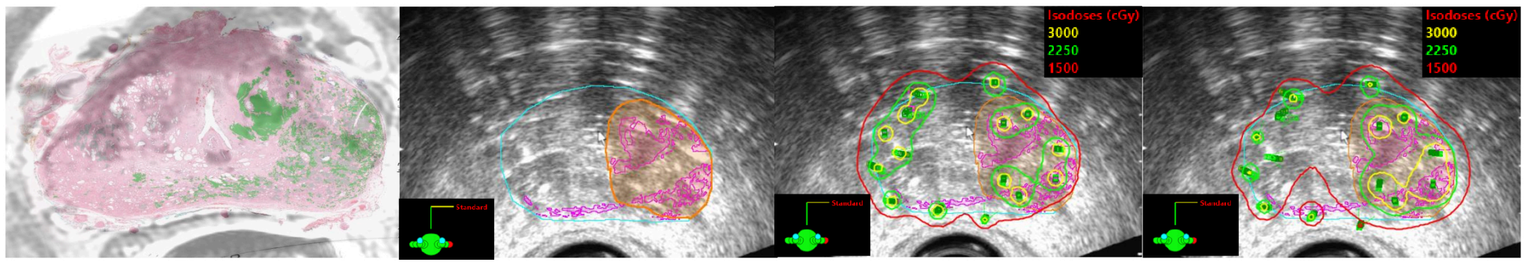

Figure 1. Starting from left to right. (1) Co-registered digital histology with T2W MRI. The histology-defined cancer delineated in green. (2) Intraprocedural TRUS with the prostate contoured in cyan. digital histology cancer contoured in magenta, and T2W MRI interpretation delineated in orange. (3) Whole-gland HDR-BT treatment with overlaid isodose lines. (4) mpMRI focal-boost treatment with overlaid isodose lines.

Results

- 212 mpMRI DIL-targeted HDR-BT plans were analyzed.
- The median D98 dose delivered to high-grade histology by mpMRI-boosting was significantly greater than the standard treatment plans. (Table 1, Figure 2)
- There was no significant difference in median D98 dose to the low-grade histology due to mpMRI boosting.
- By mpMRI boosting, the percentage of patients that could receive a given D98 dose to high-grade histology increased in comparison to standard treatment planning. (Figure 3)

Table 1. Median [interquartile range] dose metrics delivered to the high- and low-grade histology defined disease. High-grade histology is defined as any histology with any Gleason grade 4 or greater, and low-grade is any histology with only Gleason grade 3.

		High-grade (Gy)	Low-grade (Gy)
D98	Standard	16.9 [15.8–17.7]	15.3 [14.6–15.8]
	Boosted	18.2 [16.7–19.4]	15.4 [14.9–16.2]
	p-value	p=0.01	p=0.2

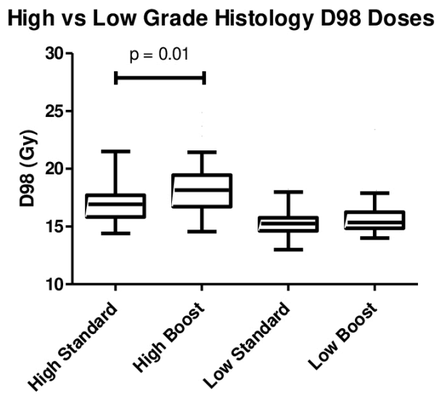

Figure 2. A box-and-whisker plot of the D98 delivered to the high-grade and low-grade digital histopathology within standard planned HDR-BT treatment plans and corresponding mpMRI focally-boosted treatment plans. Whiskers are the 5th and 95th percentiles.

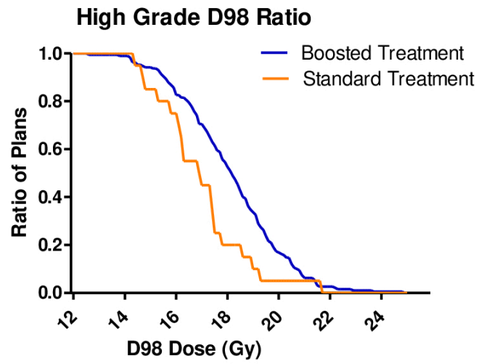

Figure 3. Line graph of the percentages of focally boosted plans and whole gland plans which deliver a given D98 to the high-grade histology.

Discussion

- mpMRI boosting successfully escalated dose to high-grade histologically defined disease. However, this was only a modest median D98 increase of 1.3 Gy in comparison to the standard plans.
- Low-grade disease would not have received a significantly different dose due to mpMRI boosting.
- This led us to the conclusion that improved DIL contouring accuracy is required, and that mpMRI-boosting should only be used for patients who present with high-grade disease.
- Training observers and machine learning systems for mpMRI DIL contouring using an accurately registered histologic reference standard may be valuable steps towards maximizing efficacy of dose escalation to intraprostatic lesions.
- Future work will be to investigate if an expansion margin to the mpMRI DIL can help improve the boost- dose that would be delivered to the underlying ground truth disease.

Acknowledgements

London Health Sciences Centre
Ontario
Prostate Cancer Canada
LAWSON HEALTH RESEARCH INSTITUTE

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