Image-Guided Catheter Placement for Prostate HDR Brachytherapy with Focal Tumor Boost using Deep Learning

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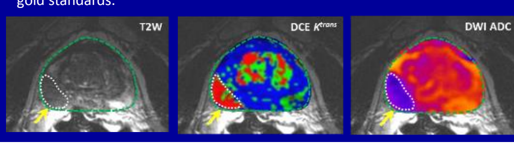
Background

- Dose-escalation strategies have improved local control, and higher doses of radiation have consistently demonstrated improved outcomes. However, increased radiation doses are frequently accompanied by severe side effects to the surrounding normal tissues.
- Histopathologic studies of recurrence after radiotherapy suggest that many men may have a **dominant focus** of disease in the prostate, which is frequently the source of local failure.
- Therefore, a better strategy is to irradiate the whole prostate but simultaneously boost doses to the dominant lesions using HDR brachytherapy.
- Compared to other imaging modalities, **multiparametric MRI (mp-MRI)** has the best performance to define **dominant lesions** as validated with pathology gold standards.



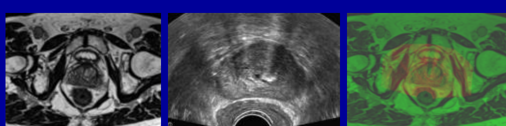
Purpose

- In the current MR-guided, CT- or US-based HDR brachytherapy with dominant intraprostatic lesion (DIL) boost, mp-MRI is firstly used to contour DILs, and these contours are then integrated into planning CT or US images for dose-boosting treatment plan though MRI-CT or MRI-US image registrations.
- In these boost studies, transrectal ultrasound (US) is routinely used to visualize and guide catheter placement, however, without considering the anatomic location and size of a DIL such catheter placement is still done "**blindly**", and thus over 50% patients cannot achieve the expected DIL boosting dose coverage with a generalized catheter distribution pattern, especially for the patients with smaller prostates.
- **To improve the probability of achievable optimal dose boost coverage, it is necessary to develop a method by which mp-MRI-defined DILs can be integrated to real-time US to guide catheter placement.**

Outline

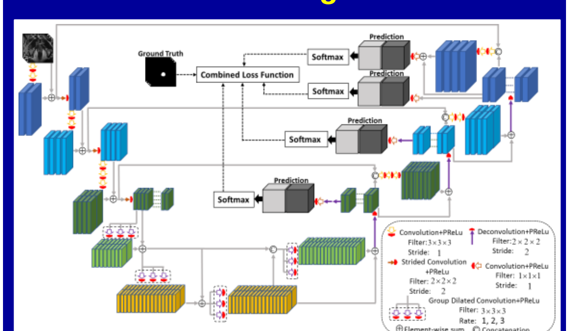
- Map mp-MRI to real-time Ultrasound (US) for tumor-targeted HDR catheter placement
  - Deformable MRI-US registration
- Online dose calculation
  - Automatic catheter reconstruct
- Investigate the feasibility and potential clinical impact
  - Retrospective dosimetric study

MRI-US Registration



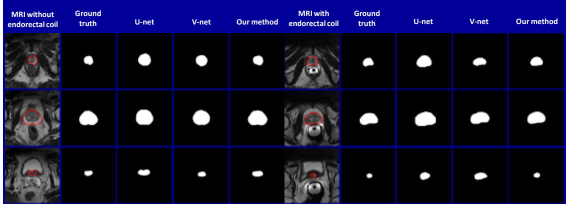
- We propose a new surface-driven MRI-US registration method using weekly supervised deep-leaning method to incorporate mp-MRI-defined DILs into real-time US imaging to guide HDR catheter placement.
- For surface-driven MRI-US registration, we need to segment prostate volume from MRI and US accurately.

MRI Prostate Segmentation



Wang B ... Yang X, *Medical Physics*, 46(4):1707-1718, 2019.

Segmentation Result



Method	DSC	MSD (mm)
3D U-net (Cicek *et al*, MCCAI 2016)	0.831±0.059	1.838±0.518
3D V-net (Milletari *et al*, 3DV 2016)	0.848±0.062	1.566±0.836
CUMED (Yu *et al*, AAAI 2017)	0.869	NA
3D DSD-FCN (Our)	0.883±0.049	1.015±0.346

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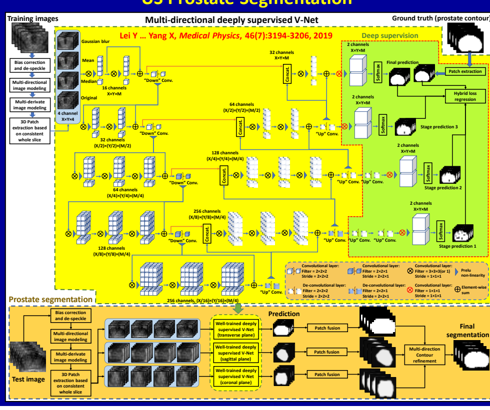
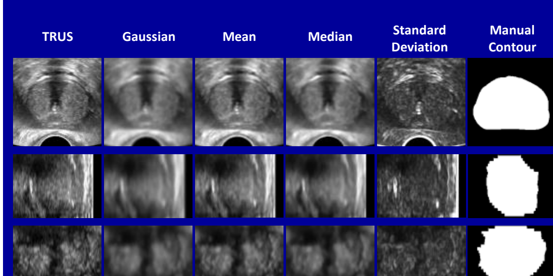
US Prostate Segmentation



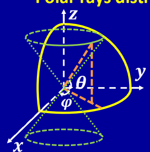
Multi-derivative Image



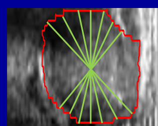
Lei Y … Yang X, *Medical Physics*, 46(7):3194-3206, 2019

Multi-directional-based Refinement

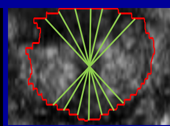
- **Polar rays distribution:**



Polar coordinate



Sagittal plane



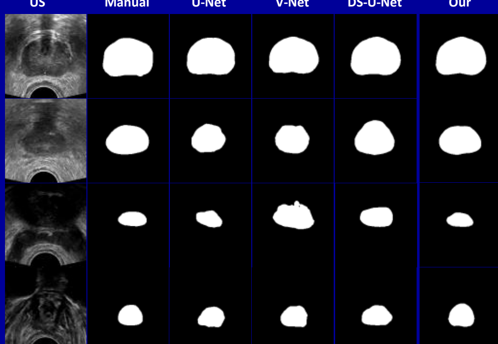
Coronal plane

- **Contour refinement:**

$$\hat{I}_{\text{final}}(n)=\begin{cases}\dfrac{\hat{I}_{\text{transverse}}(n)+\hat{I}_{\text{sagittal}}(n)+\hat{I}_{\text{coronal}}(n)}{3}, & if \quad d(n)<d_0\\[2ex] \dfrac{\hat{I}_{\text{sagittal}}(n)+\hat{I}_{\text{coronal}}(n)}{2}, & otherwise\end{cases}$$

$$d(n)=\left\|\hat{I}_{\text{transverse}}(n),\hat{I}_{\text{sagittal}}(n)\right\|+\left\|\hat{I}_{\text{transverse}}(n),\hat{I}_{\text{coronal}}(n)\right\|+\left\|\hat{I}_{\text{sagittal}}(n),\hat{I}_{\text{coronal}}(n)\right\|$$

Comparison with Start-of-art Methods



Lei Y ... Yang X, *Medical Physics*, 46(7):3194-3206, 2019

Comparison with Start-of-art Methods

Metric	DSC	Precision	Recall	HD(mm)	MSD(mm)	RMSD(mm)
U-Net	0.906±0.028	0.905±0.062	0.912±0.049	4.437±2.010	0.619±0.220	0.915±0.346
V-Net	0.905±0.030	0.881±0.060	0.935±0.035	4.643±1.926	0.657±0.270	0.977±0.410
DS-U-Net	0.911±0.03	0.901±0.05	0.926±0.05	3.963±1.51	0.599±0.21	0.892±0.33
Our	**0.919±0.028**	**0.906±0.055**	**0.938±0.043**	**3.938±1.550**	**0.599±0.225**	**0.900±0.377**

P-value	DSC	Precision	Recall	HD	MSD	RMSD
U-Net vs. Proposed	**<0.001**	0.854	<0.001	0.063	0.423	0.689
V-Net vs. Proposed	**<0.001**	<0.001	0.561	0.002	0.007	0.021
DS-U-Net vs. Proposed	**<0.001**	**0.009**	**0.005**	**0.013**	**<0.001**	**0.001**

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Outline

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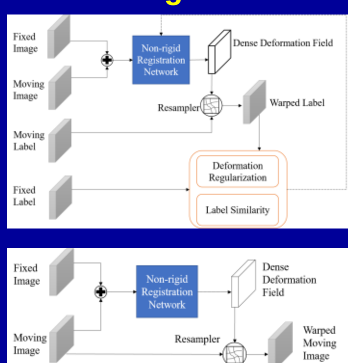
  - Retrospective dosimetric study

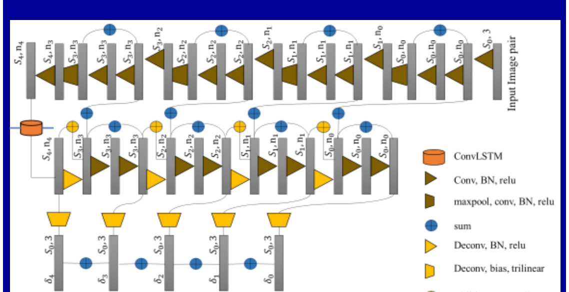
MRI-US Registration

Training Stage

Testing Stage

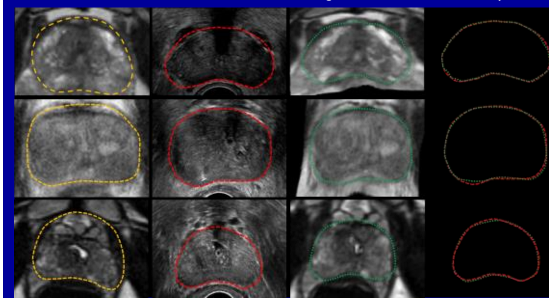


CNN-ConvLSTM Network



Qiu L, … Yang X. "Surface-driven MRI-US Registration Using Weakly-supervised Learning in Prostate Brachytherapy." AAPM 2019

Registration Result



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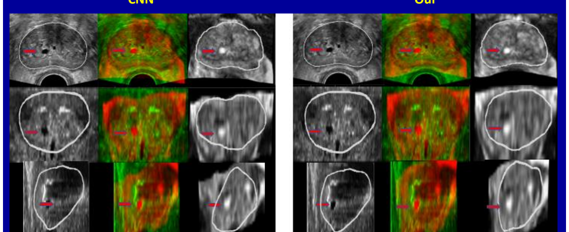

TRE (mm)		DSC	
Mean$\pm$Std	Percentiles [25^{th}, 50^{th}, 75^{th},]	Mean$\pm$Std	Percentiles [25^{th}, 50^{th}, 75^{th},]
1.30$\pm$0.90	[0.59, 1.00, 1.74]	0.87$\pm$0.04	[0.86, 0.88, 0.90]

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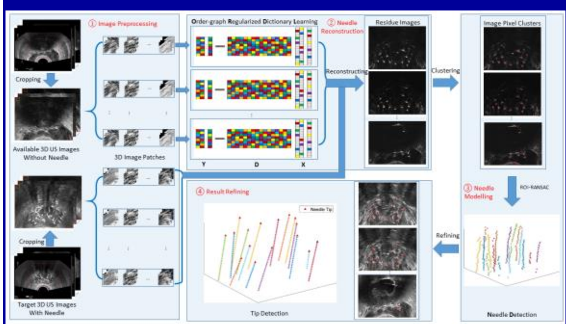
- Online dose calculation
  - **Automatic catheter reconstruction**
- Investigate the feasibility and potential clinical impact
  - Retrospective dosimetric study

Catheter Reconstruction

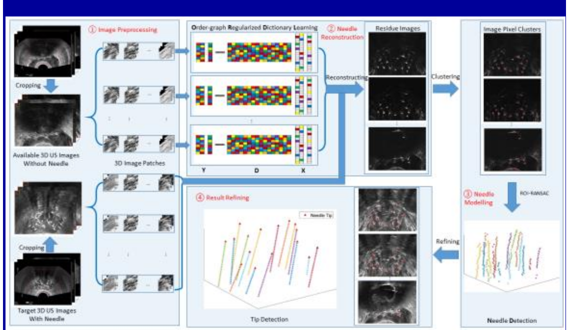
- Due to the low signal-to-noise ratio and image artifacts of US imaging, automatic multiple catheter reconstruction in US images remains a challenging problem.
- We propose an unsupervised dictionary learning method to quickly and accurately reconstruct multiple catheters in 3D US images.

Multi-catheter Reconstruction



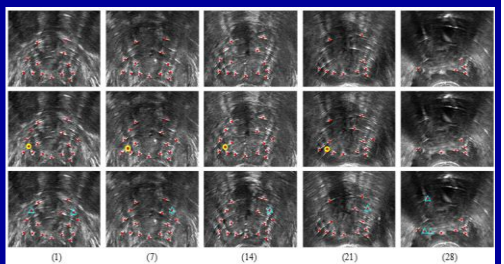
Zhang Y, … Yang X. " Order-graph Regularized Sparse Dictionary Learning for Unsupervised Multi-Needle Detection in 3D Ultrasound Images." AAPM 2019

Multi-catheter Reconstruction



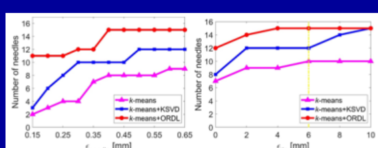
Zhang Y, … Yang X. " Order-graph Regularized Sparse Dictionary Learning for Unsupervised Multi-Needle Detection in 3D Ultrasound Images." AAPM 2019

Catheter Reconstruction Result



Zhang Y, … Yang X. " Order-graph Regularized Sparse Dictionary Learning for Unsupervised Multi-Needle Detection in 3D Ultrasound Images." AAPM 2019

Quantitative Result



(a) Needle localization error (b) Tip localization error

The cumulative distributions on the first prostate patient.

Quantitative results on the prostate data with total 318 needles.

Metrics	*k*-means	*k*-means + KSVD	*k*-means + ORDL
N_{incorr} (N_{all})	74 (286)	50 (304)	**16 (312)**
AVG. ε_{needle} [mm]	0.30±0.24	0.26±0.16	**0.19±0.13**
AVG. ε_{tip} [mm]	1.76±2.87	1.52±2.13	**1.01±1.74**

Outline

- Map mp-MRI to real-time Ultrasound (US) for tumor-targeted HDR catheter placement
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  - Automatic catheter reconstruct
- Investigate the feasibility and potential clinical impact
  - **Retrospective study**

Retrospective Study – Focal boost

- Investigate the feasibility and potential clinical impact of DIL dose boost in HDR brachytherapy based on CT simulation treatment planning.
- Determine the extent to which the DILs could be boosted while maintaining OAR sparing and prostate coverage, and to estimate its potential clinical benefit.

Patient Characteristics

- **Patients**
  - 17 patients treated with prostate HDR brachytherapy
  - Median age was 67 (range 45–79)
  - Clinical stage ≤T2a
  - Median PSA was 7 (range 0.9–20)
  - Median prostate volume was 53.3 cc measured on CT (range 25.1cc-124.9cc)
  - Gleason score was 6 or 7
  - 8 of 17 received HDR boost (15Gy x1) after 1.8Gy x25 EBRT
  - 9 of 17 received HDR mono (13.5Gy x2)
  - Mp-MRI: T1/T2/ADC/DCE (3 months before HDR treatment)
  - Average DIL volume 1.12cc (0.22-4.35cc among 21 DILs from 17 patients)

Boost Planning

- **Dose escalation to DILs**
  - **Clinical treatment plan "Original"**
    - standard catheter placement
    - Optimized to prescribed coverage on whole prostate and spare dose on OAR
    - DILs were not considered in optimization
  - **"Original Boost" plan**
    - Same standard catheter placement
    - Re-optimized for additional DIL dose coverage on clinical treatment plan
  - **"Additional Boost" plan**
    - Same standard catheter placement + one tumor-guided virtual catheter near DIL
    - Re-optimized for additional DIL dose coverage on clinical treatment plan
- **DIL localization**
  - Mp-MRI T1/T2/ADC/DCE
  - Deformable MRI-CT registration
- **Optimizing goals**
  - Prostate: D90>100%, V100>90%
  - Bladder and rectum: V75<1cc
  - Urethra: V125<1cc, D10<118%
  - DILs: Maximum attainable dose by starting at 130% Rx dose and increasing in 5% increments until OARs or conformity constraints were reached

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Evaluation

- **"Original" vs "Original Boost" vs "Additional Boost"**
  - Converted to equivalent dose in 2Gy/fx
  - Added EBRT dose for boost patients
  - DVH metrics on prostate-DIL, DIL, and OARs
  - Tumor control probability (TCP) and
  - Normal tissue complication probability (NTCP)

$$TCP = \frac{1}{\sigma_{\alpha}\sqrt{2\pi}} \int_0^{\infty} \prod_j \exp\left[-\rho_{clon} v_j \exp\left(\alpha D_j \left(1 + \frac{\beta}{\alpha} d_j\right)\right)\right] \cdot \exp\left[-\frac{\left(\alpha - \bar{\alpha}\right)^2}{2\sigma_{\alpha}^2}\right] d\alpha$$

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} \exp\left(-x^2/2\right) dx \quad t = \frac{EUD - TD_{50}}{mTD_{50}}$$

α/β(Gy)		$\bar{\alpha}$(Gy^{-1})	σ_{α}(Gy^{-1})	ρ_{clon}(cc^{-1})
1.5	Prostate-DIL[a]	0.155	0.058	6.2×10^4
	DIL	0.155	0.058	1×10^7
3	Prostate-DIL	0.217	0.082	6.2×10^4
	DIL	0.217	0.082	1×10^7
10	Prostate-DIL	0.301	0.114	6.2×10^4
	DIL	0.301	0.114	1×10^7

[a]Prostate - DIL = Prostate with DIL cropped.

		α/β(Gy)	TD_{50}(Gy)	m	n	Source
Bladder	Contracture/volume loss	3	76.9	0.13	0.09	Burman, et al.[41]
Rectum	Grade 2 + late toxicity or rectal bleeding	3	80.0	0.11	0.5	Michalski, et al.[42]
Urethra	Stricture requiring urethrotomy within 4 years after RT completion	5	70.7	0.37	0.3	Panettieri et al.[43]

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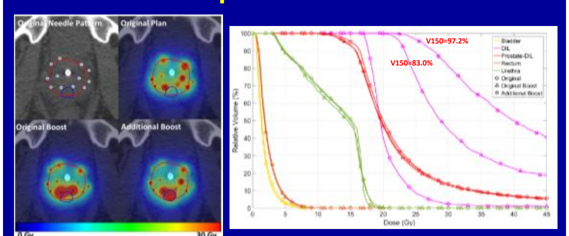
Example Case Result



- The "Original Boost" plan successfully deposited boost dose to the part of DIL close to one of the original catheter (V150 = 83.0% DIL coverage) but further dose escalation was limited in catheter location due to OAR constraints.
- The "Additional Boost" with an additional catheter around DIL achieved V150 = 97.2% among the three plans.

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DVH Statistical Result

- **Prostate and DIL**
  - "Original Boost": less coverage and higher hotspot on prostate-DIL
  - "Additional boost": significant DIL coverage improvement over "Original Boost"

	Prostate-DIL[a]				DIL				
	D90(%)	V100(%)	V150(%)	V200(%)	D90(%)	V100(%)	V150(%)	V175(%)	V200(%)
I[b]	106.6 ± 1.7	94.7 ± 1.2	35.9 ± 3.7	14.0 ± 1.7	114.6 ± 21.9	94.4 ± 9.7	46.4 ± 28.6	26.3 ± 21.4	19.1 ± 16.6
II	105.3 ± 2.6	93.7 ± 1.7	37.1 ± 4.0	15.1 ± 1.9	151.6 ± 22.8	98.7 ± 4.8	87.0 ± 15.5	69.3 ± 20.9	52.9 ± 21.9
III	106.3 ± 3.1	93.9 ± 1.9	37.1 ± 4.0	14.6 ± 2.1	164.5 ± 21.1	99.4 ± 2.5	93.0 ± 14.1	79.5 ± 18.6	65.2 ± 16.8
P-values									
I vs II	0.149	0.049	0.163	0.015	<0.001	<0.001	<0.001	<0.001	<0.001
I vs III	0.979	0.326	0.215	0.070	<0.001	<0.001	<0.001	<0.001	<0.001
II vs III	0.393	0.836	0.717	0.179	0.001	0.250	<0.001	0.002	0.020

[a]Prostate - DIL = Prostate with DIL cropped.
[b]I, II and III are "Original", "Original Boost" and "Additional Boost" plans, respectively.

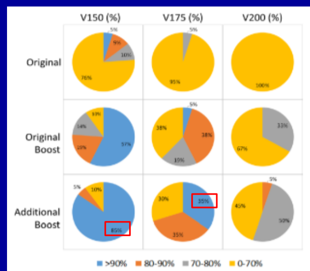
- **OAR**
  - A little more dose on rectum and urethra
  - Statistically significant, may not clinically significant

	Bladder		Rectum		Uretha
	D2cc(%)	V75(cc)	D2cc(%)	V75(cc)	V125(cc)
I[a]	8.68 ± 1.06	0.48 ± 0.46	8.00 ± 1.01	0.19 ± 0.28	0.00 ± 0.01
II	8.67 ± 0.96	0.51 ± 0.34	8.24 ± 1.05	0.28 ± 0.34	0.03 ± 0.03
III	8.56 ± 0.97	0.46 ± 0.41	8.31 ± 1.09	0.31 ± 0.35	0.02 ± 0.02
P-values					
I vs II	0.758	0.796	0.039	0.168	0.001
I vs III	0.423	0.679	0.016	0.094	0.003
II vs III	0.756	0.421	0.918	0.998	0.856

[a]I, II and III are "Original", "Original Boost" and "Additional Boost" plans, respectively.

Percentage of DILs Receiving Different Dose Coverage

- **Prostate and DIL**
  - "Additional Boost"
    - 85% of DILs got 150% Rx dose coverage
    - 35% of DILs got 175% Rx dose coverage
  - Benefit
    - compared with "Original Boost", ~30% DILs can receive high dose coverage (V175(%)>90%)



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TCP and NTCP Result

		TCP, α/β=1.5 Gy		TCP, α/β=3 Gy		TCP, α/β=10 Gy	
		Prostate-DIL[a]	DIL	Prostate-DIL	DIL	Prostate-DIL	DIL
Patients with EBRT (8)	I[b]	89.3 ± 4.8	61.7 ± 28.5	83.2 ± 6.2	58.4 ± 33.2	63.3 ± 11.7	25.3 ± 33.0
	II	87.8 ± 4.9	83.6 ± 13.9	83.4 ± 6.1	73.9 ± 19.8	60.5 ± 11.5	45.8 ± 33.9
	III	87.4 ± 6.0	90.1 ± 7.5	83.1 ± 6.9	85.2 ± 11.3	60.7 ± 12.1	59.1 ± 27.1
		P-values					
	I vs II	0.250	0.008	0.195	0.016	0.250	0.008
	I vs III	0.469	0.016	0.469	0.016	0.297	0.016
	II vs III	0.297	0.031	0.219	0.031	0.219	0.031
Patients without EBRT (9)	I	94.8 ± 0.7	89.5 ± 16.9	91.1 ± 1.1	84.5 ± 21.0	70.8 ± 2.9	63.0 ± 25.3
	II	94.5 ± 1.1	96.1 ± 5.2	90.6 ± 1.6	93.5 ± 8.4	69.9 ± 4.1	80.3 ± 19.6
	III	94.3 ± 1.4	97.3 ± 3.0	90.3 ± 2.2	95.3 ± 5.2	69.0 ± 5.5	84.8 ± 14.9
		P-values					
	I vs II	0.258	0.004	0.250	0.004	0.426	0.004
	I vs III	0.219	0.004	0.301	0.004	0.359	0.004
	II vs III	0.805	0.008	0.734	0.008	0.652	0.008

		NTCP		
		Bladder	Rectum	Urethra
Patients with EBRT (8)	I	10.5 ± 9.8	0	71.0 ± 2.1
	II	11.1 ± 7.3	0	72.1 ± 1.8
	III	8.5 ± 6.2	0	71.8 ± 1.8
		P-values		
	I vs II	0.945	N/A	0.008
	I vs III	0.938	N/A	0.016
	II vs III	0.297	N/A	0.688
Patients without EBRT (9)	I	0.1 ± 0.2	0	46.1 ± 5.9
	II	0.5 ± 1.2	0	48.4 ± 6.3
	III	0.2 ± 0.4	0	48.9 ± 6.9
		P-values		
	I vs II	0.652	N/A	0.004
	I vs III	0.570	N/A	0.008
	II vs III	0.426	N/A	0.250

[a]Prostate - DIL = Prostate with DIL cropped.
[b]I, II and III are "Original", "Original Boost" and "Additional Boost" plans, respectively.

- **TCP**
  - "Additional Boost" is more effective for
    - HDR boost
    - HDR mono when large α/β
- **NCTP**
  - Urethra
    - <3% increase

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Summary

- We have developed a surface-driven weekly supervised MRI-US registration using weakly supervised deep-learning model. Through this MRI-US registration, we could incorporate MRI-defined DILs into real-time US imaging to guide HDR catheter placement.
- We have developed a unsupervised learning-based needle detection method which can correctly reconstruct multiple needles from noisy US images, which lays the foundation for real-time dose calculation during HDR catheter placement.
- Through the retrospective study, we investigated the feasibility and potential clinical impact of DIL dose boost in tumor-guided HDR brachytherapy, and found that accurate catheter location could provide more freedom in boost plan optimization and improve boost dose coverage and level for the DILs.
- Successful integration of mp-MR into real-time US imaging to guide HDR catheter placement could enable accurate dose planning and personalize treatment delivery, and potentially enhance prostate HDR treatment outcome.

Acknowledgements

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- **DoD W81XWH-17-1-0439 (AJ)**
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