The Predictive Value of Tissue Change during Ultrasound Guided High Intensity Focused Ultrasound (USgHIFU) Focal Therapy of the Prostate on Treatment Success

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Tissue change measured as a function of ultrasound backscatter can be used to predict treatment success of focal HIFU therapy for localized prostate cancer.

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Intro

- High Intensity Focused Ultrasound (HIFU) focal therapy for localized prostate cancer has promising medium-term oncological outcomes
- Tissue change monitoring (TCM) is a novel feature by Sonablate Corp. that provides real-time feedback of ablation success potentially improving ablation efficacy
- TCM measures backscatter of ultrasound waves after passage through prostate tissue. Spectral analysis then estimates the tissue change.
- We sought to validate the association between tissue change and post-ablation oncologic outcomes

Methods

- 73 consecutive patients undergoing HIFU were enrolled
- All received mpMRI with fusion TRUS biopsy before and 12 months after focal therapy
- HIFU was performed with the Sonablate 500 device. TCM values from each ablation were measured
- Wilcoxon Rank Sum test and Prediction models were developed to evaluate the associations of:
  - 1. TCM and ablated tissue
  - 2. TCM and suspicious MRI lesions
  - 3. TCM and residual GG2 or higher cancer

Results

- 56 men were included in the study (19/56 or 33.9% had residual GG2 or higher disease after HIFU therapy)
- Higher TCM scores were associated with more tissue destruction (Figure 1)
- Mean TCM scores were higher in men with negative post-ablation mpMRI **(0.85 vs. 0.56; p=0.016)**
- Mean TCM of successful ablations were higher (0.97 vs. 0.70; p=0.017) than cases with residual ≥ GG2 cancer
- TCM was a strong predictor of treatment success (OR: 10.43, CI: 1.33-81.97)

Conclusions

- After focal HIFU therapy for prostate cancer, 34% of men have residual GG2 or higher cancer
- Measuring tissue change may allow for intra-ablation adjustments that improve outcomes
- Higher TCM scores correlate with more tissue ablation and less residual cancer at 12 months
- TCM is a strong predictor for treatment success and should be further optimized to improve HIFU outcomes

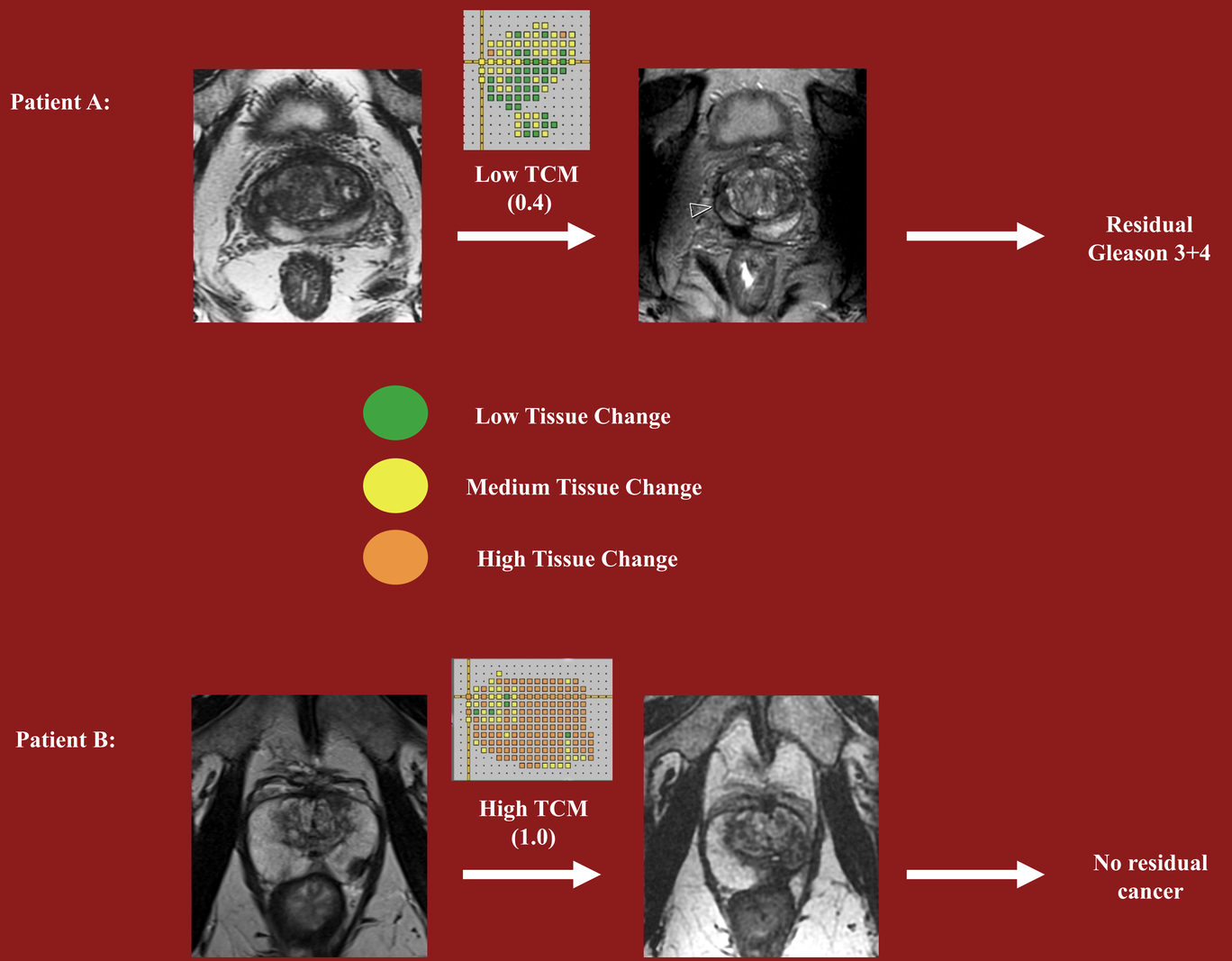

Table 1a. Comparison of the average TCM values by oncological outcomes of the 12-month targeted + systematic biopsy
A: Any cancer vs. No Cancer
B: Clinically significant cancer (≥GG2) vs. Non-clinically significant cancer (<GG2)

		Mean TCM within Tumor Contour
A	Any Cancer	0.79 (.35)
	No Cancer	1.10 (.43)
	p-value	0.015
B	<GG2	0.97 (.39)
	≥GG2	0.70 (.33)
	p-value	0.017

Table 1b. Comparison of patient characteristics in high vs. low TCM cases. High/low threshold was based off a cut-off of 0.557 (the median of all TCM scores).

	Low TCM	High TCM	*p*-value
PSA (ng/dL), Mean (SD)	4.5 (3.7)	2.5 (1.7)	0.02
Residual Positive Cores, Median [IQR]	2 [1,3]	1 [0,2]	0.002
PI-RADS Score, Median [IQR]	3 [0,2]	0 [0,4]	0.028

Table 2. Crude odds ratio and 95% confidence interval (CI), likelihood ratio test and AUC of clinically relevant predictors for negative biopsy 1-year post-HIFU.
A: Predictors for no clinically significant cancer (≤GG1) on biopsy.
B: Predictors for no cancer on biopsy

		Odds ratio (95% CI)[a]	Likelihood Ratio χ^2 [b]	AUC[c]
	Mean TCM (Tumor)	10.43 (1.33 – 81.97)	6.50 (p= 0.01)	0.72
	PSA (ng/mL)	0.87 (0.76 – 1.01)	5.80 (p = 0.02)	0.65
A	Gleason Grade Group	0.59 (0.31 – 1.12)	2.79 (p= 0.09)	0.63
	Volume (cc)	1.01 (0.98 – 1.05)	0.59 (p = 0.44)	0.54
	Positive cores	0.96 (0.79 – 1.16)	0.20 (p = 0.66)	0.53
	Age (years)	1.03 (0.95 – 1.11)	0.45 (p = 0.50)	0.46
	Mean TCM (Tumor)	7.57 (1.27 – 45.12)	5.55 (p = 0.02)	0.73
	PSA (ng/mL)	0.86 (0.70 – 1.06)	3.29 (p = 0.07)	0.66
B	Gleason Grade Group	0.96 (0.48 – 1.92)	0.02 (p = 0.90)	0.55
	Volume (cc)	0.99 (0.95 – 1.04)	0.06 (p = 0.81)	0.52
	Positive cores	0.82 (0.61 – 1.09)	2.28 (p = 0.13)	0.61
	Age (years)	1.04 (0.95 – 1.13)	0.60 (p=0.40)	0.60

[a]All estimates reported are from univariate analysis obtained from logistic regression models
[b]Values are likelihood ratio χ^2 statistics and associated *p*-values from the logistic regression model (a higher value indicates a better fit).
[c]Values are C index (a higher value indicates a better discrimination) calculated from the logistic regression model

Table 3. Prediction models for negative biopsy 1-year after HIFU treatment.
A: Prediction model for no clinically significant cancer (csc): 30 with no csc, 19 with csc.
B: Prediction model for no cancer: 12 with no cancer, 37 with cancer.

	Predictor	*β*-Coefficient (±SE)	Odds ratio (95% CI)[a]	*p*-value [b]
	Mean tumor TCM	2.07 (1.07)	7.96 (0.98 – 64.77)	0.05
A	PSA (ng/mL)	-0.15 (0.09)	0.86 (0.71 – 1.03)	0.10
	Gleason Grade Group	-0.42 (0.38)	0.66 (0.31 – 1.38)	0.27
B	Mean tumor TCM	2.11 (1.05)	8.25 (1.06 – 63.98)	0.04
	PSA (ng/mL)	-0.17 (0.13)	0.85 (0.66 – 1.08)	0.18
	Positive cores	-0.12 (0.17)	0.89 (0.64 – 1.23)	0.48
	Age (years)	0.05 (0.05)	1.05 (0.95 – 1.17)	0.34

[a] Estimates based from logistic regression model with 3 variable (model A) and 4 variable (model B); Intercept for prediction model A =1.10 (±1.57) and prediction model B = -4.85 (±4.17);
AUC for model A = 0.77 and for model B = 0.80, Hosmer and Lemeshow Goodness-of-Fit Test for model A: χ^2 = 7.49, p=0.48 and model B: χ^2 = 8.53, p=0.38
[b] *p*-value for Wald χ^2

Figure 1. ROC curves for final prediction models.
A: Prediction model for no clinically significant cancer on biopsy
B: Prediction model for no cancer on biopsy