Prostate MRSI Predicts Treatment Failure after Radical Prostatectomy

Kristen Zakian[1], William Hatfield[2], Omer Aras[2], Kun Cao[3], Derya Yakar[4], Debra Goldman[2], Chaya Moskowitz[2], Amita Shukla-Dave[2], Yousef Mazaheri Tehrani[2], Samson Fine[2], James Eastham[2], and Hedvig Hricak[2]

[1]Memorial Sloan-Kettering Cancer Center, New York, NY, United States, [2]MSKCC, NY, United States, [3]Peking University Cancer Hospital, Beijing, China, [4]Radboud University of Nijmegen Medical Centre, Nijmegen, Netherlands

TARGET AUDIENCE: Radiologists, urologists, MR spectroscopic physicists, researchers in cancer metabolism and prognosis.

PURPOSE: We examined the long-term prognostic potential of ^{1}H-MRSI in prostate cancer in a large surgical population.

METHODS: Our sample included 262 untreated patients who underwent MRI/MRSI followed by radical prostatectomy (RP) from 2003-2007. A waiver of authorization was granted for this HIPPA-compliant study. MRI/MRSI was performed on a 1.5T scanner using a pelvic phased-array coil combined with an endorectal coil (Medrad, Pittsburgh, PA). Following T1 and T2-weighted MRI, PROSE acquisition (General Electric, Waukeshau, WI) was used incorporating PRESS (1) excitation and spectral-spatial pulses (2). MRSI data were acquired as 16x8x8 arrays (0.33 cm^3 voxel, TR/TE =1000/130 ms, 17 min. scan). Using information from a clinical database, each patient was assigned a low, intermediate, or high NCCN-based risk score based on clinical stage, PSA, and biopsy Gleason score (3). The date of last followup was August 2014, and treatment failure (TF) was defined as 1) biochemical recurrence (BCR), 2) persistently detectable PSA after RP, or 3) treatment initiated in the absence of BCR due to poor pathologic features. T2-weighted MRI stage was scored on a 7-point scale (4). MRSI voxels were designated as cancerous based on polyamine levels and [tCho+Cr]/Cit (5). Low, intermediate and high grade (HG) MRSI cancer voxels were designated (6). The largest cluster of cancer voxels was defined as the MRSI index lesion. MRI stage, index lesion number of voxels, and number of HG voxels were assessed for correlation with extracapsular extension (ECE), lesion Gleason score and TF. Univariate and multivariate Cox proportional hazards regression were used to determine the value of MR parameters in predicting TF.

RESULTS: Clinical: Thirty five of 262 patients experienced TF (median time to failure = 16.3 mos). **Pathology:** The number of MRSI lesion voxels was positively correlated with lesion Gleason score ($p = 0.0002$), and the number of MRSI cancer voxels in the gland was positively correlated with ECE ($p < 0.0001$). **Treatment Failure:** In the univariate analysis, NCCN risk score, number of positive biopsy cores (NPBC), MRI stage, number of MRSI index lesion voxels, number of HG voxels and number of zero-polyamine (ZP) voxels were associated with TF (all $p < 0.0001$). In the multivariate analysis, NCCN risk score and NPBC were significant in all models. When individually added to the clinical model, the number of MRSI lesion voxels, number of HG voxels and number of ZP voxels each remained significant. MRI stage was significant when combined with clinical variables but not when MRSI data were included (**Table 1**). **Figure 1** shows the result of Kaplan Meier analysis of TF in patients with a cutoff of ≤ 3 vs ≥ 4 voxels demonstrating the higher failure rate in patients with larger MRSI lesions.

DISCUSSION: In a large population with long-term followup, the current data confirm previous reports that the volume of MRSI abnormality is predictive of lesion Gleason score, ECE, and TF after radical prostatectomy (7-9). Further, the MRSI predictors remained significant when NPBC was included, suggesting that the volume of metabolic abnormality is independent of the number of positive biopsy cores. One weakness was the lack of diffusion-weighted data which occurred because DWI was not standard at our institution in 2003. DW-MRI has become a mainstay of prostate cancer detection although its effectiveness in predicting long term outcome is still under investigation. Others have shown that 3T field strength and use of efficient k-space sampling permits MRSI data collection in 10 minutes or less (10). Thus the combination of MRSI and DWI data acquisition could optimize the noninvasive prediction of long-term outcome in prostate cancer patients.

CONCLUSIONS: The MRSI tumor volume predicts TF after radical prostatectomy. MRSI has previously been shown to be insensitive to small, low grade tumors. The best application of this technique could be to help determine whether intermediate or high clinical risk patients should undergo RP with its substantial comorbidities.

Table1*. Models predicting treatment failure after radical prostatectomy.*

Model	***Variable***	**p-value**
1: Clinical	# Positive Biopsy Cores	***0.0004***
	NCCN Clinical Risk Score	***<.0001***
2: Clinical + MRI stage	# Positive Biopsy Cores	***0.0024***
	NCCN Clinical Risk Score	***<.0001***
	MRI Stage	***0.0378***
3: Clinical + MRI stage + MRSI voxels	# Positive Biopsy Cores	***0.0230***
	NCCN Clinical Risk Score	***<.0001***
	MRI Stage	0.16
	# MRSI Index Lesion Voxels	***0.0159***
4: Clinical + MRI stage + MRSI high grade voxels	# Positive Biopsy Cores	***0.0151***
	NCCN Clinical Risk Score	***<.0001***
	MRI Stage	***0.0458***
	# HG Voxels (MRSI)	***0.0016***
5: Clinical + MRI stage + MRSI number of zero-polyamine voxels	# Positive Biopsy Cores	***0.0097***
	NCCN Clinical Risk Score	***<.0001***
	MRI Stage	0.21
	# 0 Polyamine Voxels (MRSI)	***0.0056***

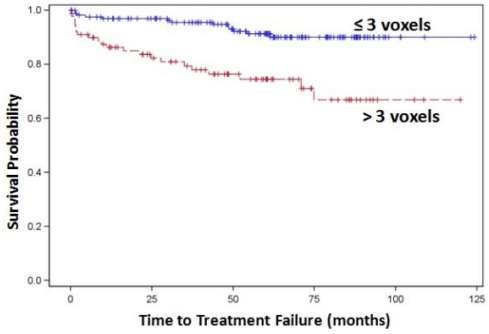

Figure 1. Kaplan-Meier analysis of time to treatment failure in patients with 3 or fewer MRSI index lesion voxels vs. patients with 4 or more voxels.

REFERENCES. 1. Bottomley P; USA patent 4,480,228. 1984. **2**. Schricker AA, et. al. Magn Reson Med 2001;46(6):1079-1087. **3**. Scherr D, et. al, Urology 2003;61(2 Suppl 1):14-24. **4**. Fuchsjager MH, et. al. BJU Int 2009;104(3):315-320. **5.** Shukla-Dave A, et. al. Radiology 2007;245(2):499-506. **6**. Pucar D, et. al. Clin Prostate Cancer 2004;3(3):174-181. **7**. Yu KK, et. al. Radiology 1999;213(2):481-488. **8**. Zakian KL, et. al. Radiology 2005;234(3):804-814. **9**. Zakian KL, et. al. J Urol. 2010;184(6):2320-2327. **10**. Futterer JJ, et. al. Invest Radiol 2004;39(11):671-680.