A study of endorectal MRI and MRSI of the prostate as predictive biomarkers of biochemical relapse after radical prostatectomy

K. Zakian[1], H. Hricak[2], N. Ishill[3], V. Reuter[4], S. Eberhardt[5], C. Moskowitz[3], A. Shukla-Dave[6], L. Wang[7], P. Scardino[8], J. Eastham[9], and J. Koutcher[6]
[1]Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY, United States, [2]Radiology, Memorial Sloan-Kettering Cancer Center, New York, NY, United States, [3]Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, [4]Pathology, Memorial Sloan-Kettering Cancer Center, [5]Radiology, University of New Mexico, [6]Medical Physics, Memorial Sloan-Kettering Cancer Center, [7]Radiology, Memorial Sloan-Kettering Cancer Center, [8]Surgery, Memorial Sloan-Kettering Cancer Center, [9]Memorial Sloan-Kettering Cancer Center

Introduction Radical prostatectomy (RP) has substantial long-term side effects. Pre-operative information which could predict the long-term success or failure of RP would be highly valuable to both patient and physician. The purpose of this exploratory study was to determine whether pre-treatment, combined endorectal MRI/MRSI has the potential to predict biochemical relapse (BCR) after RP.
Experimental Design 202 patients who had endorectal MRI/MRSI from Jan. 2000 to Dec. 2002 followed by RP were studied. All patients gave informed consent. Prostatectomy specimens were whole-mounted and step-sectioned. Of the 202 patients, 72 were excluded for the following reasons: biopsy < 6 weeks prior to MRI/MRSI (N = 9), MRSI data unusable due to technical failure/artifact (N = 27), tumor only in transition zone (TZ) (N = 9), pathology unavailable (N =3), prior treatment (N=24). The data acquisition procedure is described in (1). In brief, MRI/MRSI was performed on a 1.5 Tesla G.E. Signa Horizon scanner (GE, Milwaukee, WI) using a combined pelvic phased array and endorectal coil (Medrad, Indianola, PA). T1 and T2-weighted images were acquired. MRSI data were obtained using software which employed PRESS (2) with BASING water and lipid suppression (3-7). Specimens were fixed in formalin, whole-mounted and sectioned at 3-4 mm intervals. Cancer foci were outlined in ink. MRSI data processing was performed as described in (7). Peak areas were calculated by numerical integration. Voxels were classified as suspicious for cancer if (Cho+Cr)/Cit (CC/C) was at least 2 standard deviations above the mean healthy CC/C for the peripheral zone (PZ) (8). Only PZ voxels were considered in this analysis; patients with tumor only in the TZ were censored because the MRSI software used at the time did not always encompass the TZ. Spatial correlation between MRI/MRSI data and pathological sections was performed as previously described (1). **MRI Scoring.** A 7 point scoring system was used to rank the risk of recurrence based on clinical MRI findings: 1 no tumor seen; 2 tumor seen, no extracapsular extension (ECE); 3 tumor seen, can't exclude ECE; 4 unilateral ECE; 5 bilateral ECE; 6 seminal vesicle invasion; 7 lymph node invasion. **MRSI Scoring.** The largest lesion identified by MRSI was designated as the "index lesion". If 2 lesions had the same volume (number of voxels), the lesion with the greater mean CC/C was chosen. If pathological comparison indicated that the MRSI index lesion was a false positive, the lesion was still included in the analysis. An MRSI grade representing the extent of metabolic abnormality (9) was assigned to each voxel in the index lesion: low grade (LG) ($0.5 \le CC/C \le 0.6$), intermediate (IG) ($0.7 \le CC/C < 3.0$) or high grade (HG)($CC/C \ge 3.0$). Time to BCR was measured from the date of radical prostatectomy until the first documented BCR, and was estimated using the methods of Kaplan and Meier (10). Associations between MRI and MRSI variables, TNM stage, pre-treatment PSA, biopsy Gleason score and time to recurrence were evaluated using Cox Proportional Hazards regression.
Results Within a mean followup period of 68 months, there were 26 biochemical failures in 130 patients. MRI risk score, MRSI index lesion mean and maximum CC/C, MRSI index lesion volume and the number of high MRSI grade voxels each correlated with time-to-BCR. Categorical MRSI variables were generated which represented lesion volume and metabolic abnormality. **MRSI index lesion volume**: MRSI index lesions were divided into those with ≤ 3 voxels vs. those with > 3 voxels; patients with index lesions in the latter category had significantly shorter time to BCR (p = <0.0001, Fig. 1A). **MRSI index lesion grade**: When index lesions were divided into those with zero HG voxel vs. those with at least one HG voxel, patients in the latter category also had a significantly shorter time to BCR (p <0.0001, Fig. 1B). Patients whose index lesions had > 3 voxels *and* at least one HG voxel, fared significantly worse than patients with only one of these characteristics (p < 0.0001) (Fig. 1C). In a multivariate analysis including clinical stage, biopsy Gleason score, and pre-operative PSA, the number of voxels in the index lesion and the presence of at least one HG voxel were significant predictors of BCR (number of voxels in lesion, p = 0.002; at least one HG voxel, p = 0.02). The MRI risk score remained significant unless either of the MRSI variables was included.
Conclusions MRI risk score, MRSI index lesion volume and the presence of high grade MRSI voxels correlate with time-to-biochemical failure after RP even when adjusted for clinical stage, biopsy Gleason score and PSA. Patients with large lesions and a higher degree of metabolic abnormality had shorter times to BCR. These results suggest predictive utility for endorectal MRI/MRSI in patients considering RP.

This work was supported by NIH R01-CA076423

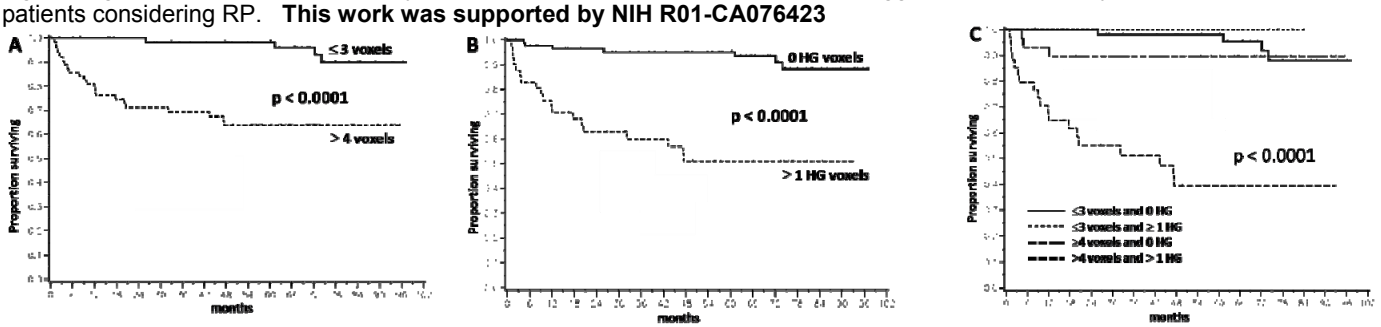

Figure 1. Kaplan-Meier time-to- BCR plots for 130 patients segregated by MRSI index lesion characteristics: A) ≤ 3 voxels vs ≥ 4 voxels, B) no high grade voxels vs. ≥ 1high grade voxels, C) 4 groups: (i) ≤ 3 voxels and no high grade voxels (ii) ≤ 3 voxels and ≥ 1 high grade voxel (iii) ≥ 4 voxels and no high grade voxels (iv) ≥ 4 voxels and at least one high grade voxel.

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