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Original article

# Tumor contact with prostate capsule on magnetic resonance imaging: A potential biomarker for staging and prognosis

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## Abstract

**Background:** The high-spatial resolution of multiparametric magnetic resonance imaging (mpMRI) has improved the detection of clinically significant prostate cancer. mpMRI characteristics (extraprostatic extension [EPE], number of lesions, etc.) may predict final pathological findings (positive lymph node [pLN] and pathological ECE [pECE]) and biochemical recurrence (BCR). Tumor contact length (TCL) on MRI, defined as the length of a lesion in contact with the prostatic capsule, is a novel marker with promising early results. We aimed to evaluate TCL as a predictor of +pathological EPE (+pEPE), +pathological LN (+pLN), and BCR in patients undergoing robotic-assisted laparoscopic radical prostatectomy.

**Materials and methods:** A review was performed of a prospectively maintained single-institution database of men with prostate cancer who underwent prostate mpMRI followed by robotic-assisted laparoscopic radical prostatectomy without prior therapy from 2007 to 2015. TCL was measured using T2-weighted magnetic resonance images. Logistic and Cox regression analysis were used to assess associations of clinical, imaging, and histopathological variables with pEPE, pLN, and BCR. Receiver operating characteristic curves were used to characterize and compare TCL performance with Partin tables.

**Results:** There were 87/379 (23.0%) +pEPE, 18/384 (4.7%) +pLN, and 33/371 (8.9%) BCR patients. Patients with adverse pathology/oncologic outcomes had longer TCL compared to those without adverse outcomes (+pEPE: 19.8 vs. 10.1 mm, $P < 0.0001$, +pLN: 38.0 vs. 11.7 mm, $P < 0.0001$, and BCR: 19.2 vs. 11.2 mm, $P = 0.001$). On multivariate analysis, TCL remained a predictor of +pEPE (odds ratio: 1.04, $P = 0.001$), +pLN (odds ratio: 1.07, $P < 0.0001$), and BCR (hazard ratio: 1.03, $P = 0.02$). TCL thresholds for predicting +pEPE and +pLN were 12.5 and 19.7 mm, respectively. TCL alone was found to have good predictive ability for +pEPE and +PLN (pEPE: $TCL_{AUC}$: 0.71 vs. $Partin_{AUC}$: 0.66, $P = 0.21$; pLN:$TCL_{AUC}$: 0.77 vs. $Partin_{AUC}$: 0.88, $P = 0.04$).

**Conclusion:** We demonstrate that TCL is an independent predictor of +pEPE, +pLN, and BCR. If validated, this imaging biomarker may facilitate and inform patient counseling and decision-making. Published by Elsevier Inc.

*Keywords:* Biomarker; Capsule; Magnetic resonance imaging; Lymph node; Prostatic neoplasms

## 1. Introduction

Prostate cancer (PCa) remains the second leading cause of cancer-related deaths in men in the United States [1]. Accurate staging of PCa dictates treatment decisions and is one indication for multiparametric magnetic resonance imaging (mpMRI) [2–4]. Local staging of PCa includes

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assessment of extraprostatic extension (EPE), seminal vesicle involvement, and lymph node (LN) involvement, all of which guide planning of curative therapies. Current mpMRI parameters used to detect and predict final pathological EPE (pEPE), pathological LN (pLN) status, and local and biochemical recurrence (BCR) are mostly qualitative with high interreader variability owing to strong interpreter dependency and experience [5–7].

Objective mpMRI parameters with low interreader variation may predict disease outcomes. MRI-determined tumor contact length (TCL) with the prostatic capsule is an objective mpMRI-derived variable and is emerging as a stronger predictor of +pEPE [8,9]. Currently, MRI criteria to identify EPE are dependent on subjective reader visualization of the mechanical effects of macroscopic EPE, which is a relatively late development. By the time capsular bulging, periprostatic fatty tissue invasion, rectoprostatic angle obliteration, and neurovascular bundle asymmetry or involvement observed, cancer spread is likely beyond occult microscopic EPE [9]. Similarly, pretreatment evaluation of patients for LN involvement and BCR risk is limited. Lymph node evaluation is routinely dependent on size criteria on conventional computed tomography/magnetic resonance imaging (CT/MRI) [10]. Size criteria, though objective, have limited predictive value for small-to-normal-sized LNs [11]. Clinical variable–based nomograms [12–14] to predict LN staging and BCR were developed during the pre-mpMRI era, and therefore do not include novel imaging information. In this study, we aim to evaluate the association of TCL with pEPE, pLN, and BCR.

## 2. Methods

### 2.1. Patient selection

Patients were enrolled under an institutional review board–approved prospective trial (NCT00102544) at the National Cancer Institute from May 2007 to December 2015. A total of 428 patients, diagnosed with PCa, underwent robotic-assisted laparoscopic radical prostatectomy (RALRP). Of these, 44 patients (8, no mpMRI; 10, pre-RALRP treatment; 24, limited mpMRI [due to hip prosthesis or motion-related artifacts]; and 2, no mpMRI lesions) were excluded from the study. For the pEPE analysis, 5 additional patients were excluded owing to inconclusive evidence of +pEPE. Patients, who received any adjuvant therapy after RALRP ($n = 13$), were removed from the BCR analysis. Standard pelvic LN dissection involved the obturator and external iliac nodes only while extended dissection involved the obturator and iliac nodes to the aortic bifurcation.

### 2.2. Imaging protocol

Imaging was performed using a combination of an endorectal coil (BPX-30, Medrad) and a 16-channel cardiac surface coil (SENSE, Philips Healthcare) using a 3.0 T (Achieva, Philips Healthcare) scanner as previously described [15]. Sequences used for image interpretation comprised T1-weighted image, T2-weighted image, and diffusion-weighted image with apparent diffusion coefficient mapping, multivoxel 3D localized magnetic resonance spectroscopy, and axial 3D fast-field echodynamic contrast-enhanced MRI. Images were prospectively read by 2 experienced radiologists (B.T. and P.L.C. with prostate MRI experience of 8 and 16 years, respectively) to localize dominant prostate lesions. Suspicion for EPE on mpMRI was defined using conventional criteria of capsular obliteration, irregularity, bulging, neurovascular bundle asymmetry, or periprostatic fat extension. All included mpMRIs were reviewed to identify tumors in contact with the prostate capsule. TCL (mm) was measured (using axial T2-weighted image) by a research fellow under direct supervision of a radiologist dedicated to prostate MRI (B.T.) using the picture archiving and communication system freehand curved distance measurement tool (Fig. 1). In cases (6.2%, 24/384) where there was more than 1 lesion with capsular contact, the average of the TCLs was obtained. Lesions with no capsular contact were assigned a TCL of zero.

### 2.3. Data collection

Patient demographic, preoperative clinical, imaging, pathologic variables, and prostate-specific antigen (PSA) follow-up data were obtained from a prospectively maintained database built from institutional electronic records, referring physician, and outside medical records.

A single surgeon (>15-y experience) performed all RALRP procedures, and a single genitourinary pathologist (>25-y experience) reviewed all whole-mount pathology for variables such as EPE and LN status. Predicted probabilities of +pEPE and +pLN were obtained using online Partin tables [16]. Post-RALRP monitoring involved PSA testing at 1, 3, and 6 months, and yearly thereafter. BCR was defined as PSA > 0.2 ng/ml with a confirmatory value of > 0.2 ng/ml, a single PSA > 0.4 ng/ml, or receipt of salvage therapy per the guidelines of the American Urological Association of Localized Prostate Cancer Update Panel report [17].

### 2.4. Statistical analysis

Statistical analysis was performed using IBM SPSS (v21 Chicago, IL) and Stata version 13 (Statacorp, TX). Wilcoxon rank-sum test was used to compare differences in distribution of continuous variables, whereas the Fisher exact and Pearson Chi-square tests were used for categorical variables. Logistic regression was used to determine predictors of +pLN and +pEPE, and Cox regression for prediction of BCR. Receiver operating characteristics (ROC) curves were used to compare the predictive ability of TCL and Partin tables for +pEPE and +pLN.