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Urologic Oncology: Seminars and Original Investigations 30 (2012) 150–154

UROLOGIC ONCOLOGY

Original article

# 111-In-capromab pendetide imaging using hybrid-γ camera-computer tomography technology is not reliable in detecting seminal vesicle invasion in patients with prostate cancer

Matvey Tsivian, M.D.[a,*], Tiera Wright, DrPH[a], Marva Price, DrPH[b], Vladimir Mouraviev, M.D., Ph.D.[a], John F. Madden, M.D., Ph.D.[c], Masaki Kimura, M.D.[a], Terrence Wong, M.D., Ph.D.[d], Thomas J. Polascik, M.D.[a]

[a] *Duke Prostate Center and Division of Urologic Surgery, Department of Surgery, Duke University Medical Center, Durham, NC 27710, USA*
[b] *School of Nursing, Duke University Medical Center, Durham, NC 27710, USA*
[c] *Department of Pathology, Duke University Medical Center, Durham, NC 27710, USA*
[d] *Department of Radiology/Nuclear Medicine, Duke University Medical Center, Durham, NC 27710, USA*

Received 13 November 2009; received in revised form 3 December 2009; accepted 4 December 2009

**Abstract**

**Objectives:** In this study, we evaluate the diagnostic utility of a hybrid **γ**-camera-computer tomography (SPECT-CT) indium-111 (111-In)-capromab pendetide scan in detecting seminal vesicle invasion (SVI) in select patients evaluated for primary surgical treatment of prostate cancer (CaP).

**Methods and materials:** We retrospectively analyzed a prospective database of patients who underwent preoperative SPECT-CT imaging with 111-In-capromab-pendetide as part of a staging evaluation who were subsequently treated with radical surgery in our center. Only patients with clinically localized disease were included. We calculated diagnostic properties of the hybrid scan in detecting SVI compared with final pathology. Regression analyses were performed, including scan and preoperative variables to predict SVI.

**Results:** We retrieved 50 medical records matching our criteria. Median patient age was 61 years (range 45–74). Most patients had a clinical T1c CaP and biopsy Gleason score of 7 or higher. On final pathology, SVI was found in 12 (24%) specimens and radiotracer signal in the seminal vesicle region was reported in 15 (30%) imaging studies. Hybrid SPECT-CT imaging had a sensitivity of 25%, specificity of 61.9%, positive and negative predictive values of 20% and 74.3%, respectively, for detecting SVI. SPECT-CT results did not contribute significantly to SVI prediction on univariate ($P = 0.627$) or multivariate ($P = 0.754$) analyses.

**Conclusions:** SPECT-CT imaging with 111-In-capromab-pendetide is not reliable in detecting or excluding SVI in this select cohort. High rates of positive radiotracer signals from healthy seminal vesicles raise concerns regarding pharmacologic properties of this radiotracer molecule. 

*Keywords:* Prostate cancer; 111-In-capromab pendetide scan; Seminal vesicle

## 1. Introduction

Currently, preoperative evaluation of patients with prostate cancer (CaP) is unable to deliver precise information on disease localization and its characterization. To date, nomograms [1–3] are the best tools available to the urologist to predict local extent of CaP, namely extracapsular extension (ECE) and seminal vesicle invasion (SVI). If SVI is known before therapy, the treatment strategy may be changed to address the increased risk of recurrence associated with SVI [4]. Although considered excellent tools, these nomograms have significant departures from ideal predictions [5], limiting their implementation in clinical practice. In order to offer the appropriate treatment to an individual patient, new imaging techniques that better define the extent of disease are required. Presently, this need remains unmet.

Molecular imaging is the new frontier in noninvasive diagnostics since it offers the possibility to precisely localize a specific molecular target. Capromab pendetide is a

* Corresponding author. Tel.: +1-919-684-0787; fax: +1-919-684-5220.
*E-mail address:* matvey.tsivian@duke.edu (M. Tsivian).

1078-1439/$ – see front matter 
doi:10.1016/j.urolonc.2009.12.005

Food and Drug Administration (FDA)-approved imaging agent for the detection of metastatic disease in patients with CaP. A scintigraphic indium-111 (In-111) radiolabeled murine immunoglobulin G1 monoclonal antibody reactive with prostate specific membrane antigen (PSMA) forms the basis of the capromab pendetide imaging study (ProstaScint; Cytogen Corp., Princeton, NJ). Although capromab pendetide immunoscintigraphy has been shown to potentially yield clinically useful information in the evaluation of metastatic disease, there is no general consensus on its utility in evaluating patients for primary treatment of CaP.

In this study, we evaluate the diagnostic properties of hybrid-$\gamma$ camera computer tomography (CT) In-111-capromab pendetide scans in detecting SVI in select patients evaluated for primary surgical treatment of CaP. To the best of our knowledge, this is the first study directly comparing hybrid In-111-capromab pendetide scans with surgical pathology specimens for the detection of SVI.

## 2. Materials and methods

We retrospectively analyzed our center's prospective database to retrieve records of a select cohort of patients who underwent a preoperative imaging study with hybrid-$\gamma$ camera-CT (SPECT-CT) In-111-capromab pendetide at the Duke University Medical Center. We included in the present study patients with clinical T1-T2 CaP, according to the American Joint Commission on Cancer (AJCC) 2002 staging system [6], who had a diagnostic In-111-capromab pendetide scan as part of a staging evaluation and subsequently underwent radical prostatectomy. Final pathology results were compared with hybrid SPECT-CT imaging results, focusing on SVI.

The following variables regarding our cohort were recorded: patient age, race, serum prostate-specific antigen (PSA) level at diagnosis, biopsy Gleason score, clinical stage of disease using the TNM classification, Gleason score on final pathology, prostate weight, percent of tumor involvement (PTI), ECE, surgical margins (positive versus negative), SVI, and pathologic stage.

Regarding hybrid SPECT-CT imaging, the presence of radiotracer uptake in the seminal vesicles region, as determined by the radiologist, was considered positive. Our technique of co-registered imaging was previously described [7]; briefly, 180–220 MBq (5–6 mCi) of In-111 capromab pendetide was administered by slow intravenous injection. The patient was asked to void before imaging, and no Foley catheter was used. Imaging was performed on a dual-head scanner (Discovery VH; GE Healthcare, Chicago, IL) with an integrated CT scanner built onto the same rotating gantry as the camera heads. Single-photon emission CT (SPECT) images were reconstructed by using 2 iterations of ordered subsets expectation maximization with CT-based attenuation correction and a final Butterworth filter (10th order, cutoff at 0.26 Nyquist frequency). The interactive display software allows reconstruction and review of the images in axial, coronal, and sagittal planes, and display of the fused CT and SPECT images.

Descriptive statistics along with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were computed. Preoperative parameters and fusion CT-capromab scan results were incorporated in multivariate regression models to assess their independent predictive value; $P < 0.05$ was considered statistically significant. Statistical analysis was carried out using the SPSS ver. 15 software package (SPSS Inc., Chicago IL). This study was approved by the Institutional Review Board.

## 3. Results

A total of 50 patients matching our selection criteria were identified. Patient median age was 61 years (range 45–74) with Caucasians accounting for 68%, African American 24%, and other backgrounds for 8%. Median serum PSA at diagnosis was 8.7 ng/ml (1.2–161). Tumor clinical features are detailed in Table 1. Most patients had clinical T1c disease. According to the D'Amico classification [8], 20 (40%) patients had high risk CaP, 19 (38%) patients met the criteria for intermediate risk, and 11 (22%) had low risk disease.

Hybrid In-111-capromab SPECT-CT was positive in the seminal vesicle region in 15 (30%) patients and negative in the remaining 35 (70%). Local signals in the prostatic region were observed in all 50 cases. Median interval from scan to surgery was 28.4 days (1–116). Final pathology reported ECE in 50% of the specimens and positive margins in 52%. Pathologic stage was T2 in 24 (48%) patients and T3 in 26 (14 T3a and 12 T3b).

Diagnostic properties of hybrid In-111-capromab pendetide SPECT-CT studies are reported in Table 2. Sensitivity and specificity of hybrid In-111-capromab pendetide SPECT-CT were 25% and 61.9%, respectively. The NPV was 74.3% and the PPV was 20%.

Logistic regression results are detailed in Table 3. On univariate analysis, several preoperative factors were significantly associated with SVI, including serum PSA ($P = 0.015$) and biopsy Gleason sums ($P = 0.003$). SPECT-CT results regarding the seminal vesicles region were not significant ($P = 0.627$). On multivariate analysis, only biopsy Gleason sums were independently associated with SVI ($P = 0.033$, OR=2.74). CT/SPECT results were not associated with SVI ($P = 0.754$).

## 4. Discussion

For the most part, CaP imaging has not yet met the needs of reliability and accurate detection of disease, defining its extension beyond prostatic capsule or into the seminal vesicles. Despite promising background and initial reports, immunoscintigraphy with In-111-capromab pendetide has