The Role of 3-Dimensional Mapping Biopsy in Decision Making for Treatment of Apparent Early Stage Prostate Cancer

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Abbreviations and Acronyms

3D = 3-dimensional

3DMB = 3D mapping biopsy

5ARI = 5α-reductase inhibitor

AS = active surveillance

PCa = prostate cancer

PSA = prostate specific antigen

TRUS = transrectal ultrasound

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Purpose: We determined the impact of a grid based, transperineal 3-dimensional mapping biopsy on decision making for primary management of early stage prostate cancer.

Materials and Methods: We prospectively performed 3-dimensional mapping biopsy on 180 consecutive men who presented to our clinic between 2006 and 2009 with early stage, organ confined prostate cancer based on transrectal ultrasound guided 10 to 12-core biopsy, and on 35 with prior negative transrectal ultrasound biopsies.

Results: At presentation median patient age was 60.5 years (range 43 to 77), median prostate specific antigen was 4.8 ng/ml (range 0.5 to 72.4) and median prostate volume was 35 cc (range 9 to 95). The median number of cores acquired by transrectal ultrasound and 3-dimensional mapping biopsy was 12 and 56, and the median number of positive cores was 1 and 2, respectively. We documented Gleason score upgrade in 49 of 180 cases (27.2%) and up-stage in 82 (45.6%). The incidence of urinary retention catheter requirement of greater than 48 hours was 3.2% and the incidence of transient orthostatic hypotension was 5%. No urinary tract infections were documented. A total of 38 men received radical extirpative therapy, 11 radiation and 45 cryotherapy while 60 enrolled in a targeted focal therapy study, 44 entered active surveillance and 5 underwent other focal investigational treatments. Post-mapping data on 12 men were not available for analysis.

Conclusions: Three-dimensional mapping biopsy revealed that a significant portion of men initially diagnosed with apparently low risk disease harbored clinically significant cancers requiring more aggressive therapy. The technique also enabled a number of men with low risk disease to elect surveillance or another less morbid option.

Key Words: prostate, prostatic neoplasms, biopsy, ultrasonography, decision making

Since the advent of the PSA era, the proportion of PCa diagnoses that is low stage and low risk has increased significantly. This stage migration is well documented and new controversies surrounding management for low volume, well differentiated, indolent disease has come to the forefront. Concordantly although modern biopsy techniques have evolved considerably since the first sextant biopsy technique was described in 1989 by Hodge et al,[1] these methods routinely miss aggressive cancers in up to a third of cases.[2,3]

Urologists and patients are now faced with the dilemma of possible overtreatment based on the results of

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a standard, extended 12-core TRUS guided prostate biopsy, particularly when single cores with minimal volumes of adenocarcinoma are present or patients present with persistently increased or increasing PSA in the face of 1 or more negative biopsies. These clinical entities remain difficult in regard to discussion of risk, monitoring and decision making.[4]

Recent innovations in magnetic resonance imaging, such as combination spectroscopy, dynamic contrast enhanced and diffusion sequences, have attempted to address this problem and define disease extent without the need for invasive procedures and associated morbidity. However, the sensitivity and specificity of these imaging techniques vary considerably (66% to 86% sensitivity and 77% to 94% specificity) and until further studies prove that they are beneficial and cost-effective, traditional diagnostic methods, ie biopsy, will continue to be used.[5,6]

Taking into account uncertainties associated with initial diagnosis using modern TRUS guided biopsy, we assessed 3DMB as a treatment decision tool for a select group of patients. This approach takes advantage of a 5 mm perineal grid to systematically sample the aggregate zones of the prostate to better clarify disease extent, grade and stage in men with low volume, lower risk disease on TRUS biopsy. This in turn is used clinically to inform patient and physician in decision making around a plan of care.

The primary goal of this study was to use 3DMB to determine the size and location of cancer foci better than standard biopsy schemes and enable patients to more appropriately elect therapy, including AS and less invasive targeted therapies, as part of other ongoing studies at our institution.

METHODS

Patient Selection

This prospective, institutional review board approved study recruited 180 men through physician-patient relationships at our institution from 2006 to 2009. Eligible patients presented with a histological diagnosis of PCa (Gleason 7 or less) on prior TRUS guided biopsy read predominantly by community pathologists. They were considering AS or targeted focal therapy, which requires 3DMB for enrollment according to our institutional protocol. A total of 35 patients with prior negative TRUS guided biopsies were also offered 3DMB and analyzed separately. All patients underwent TRUS evaluation in clinic to determine eligibility. If prostate volume was greater than 65 cc or the anterior prostate was inaccessible due to pubic arch obstruction, patients were given the option to begin a trial of 5ARI in an attempt to shrink prostate volume. These patients were reevaluated every 3 months for followup TRUS to determine eligibility for 3DMB.

3DMB and 3D-Reconstruction

The procedure was performed in the operating room under monitored anesthesia care. A TRUS probe mounted on a stepper was attached to a standard 5 mm grid (fig. 1). As part of ongoing investigational treatments for focal therapy, 2, 1.2 × 3 mm gold fiducial markers were inserted to aid as internal landmarks. We captured prostate gland cross-section dimensions at 5 mm increments from apex to base to render a 3D reconstruction. Transperineal biopsies were obtained at 5 mm intervals using a standard 18 gauge biopsy gun. Deeper (base) vs shallow (apex) passes at the same grid position were performed to ensure complete gland coverage. Each biopsy was labeled with x-y-z coordinates and placed in separate jars.

Pathological review was performed elsewhere for the first 150 patients and subsequently by 4 dedicated uropathologists at our institution. Coordinates of positive samples were imported into the specialized computer program ProVIEW (Applied Coherent Technology, Herndon, Virginia), which was used to reconstruct the prostate and cancer foci in 3 dimensions (fig. 2). This enabled the patient and physician to visualize the extent and grade of cancer foci, and design an appropriate treatment plan.

Statistical Analysis

Using covariates obtained from pathological findings we defined 4 possible transitions that could occur between the results of the original TRUS guided biopsy and 3DMB, including Gleason score upgrade or downgrade (eg 7 to 6) and up-stage or down-stage. Upgrade could occur if the 3DMB Gleason score was greater than the TRUS biopsy Gleason score or a transition from Gleason 3 + 4 = 7 to 4 + 3 = 7. Up-stage was defined as an increase in the number of positive cores on mapping biopsy by 2 or more than that on TRUS biopsy. Alternatively up-stage could also occur if 3DMB detected bilateral disease compared to unilateral foci on TRUS guided biopsy. Downgrade and down-stage were defined similarly but in the opposite directions. Data were entered and stored in a FileMaker® Pro 7.0 database and transferred to SAS® 9.2 for analysis.

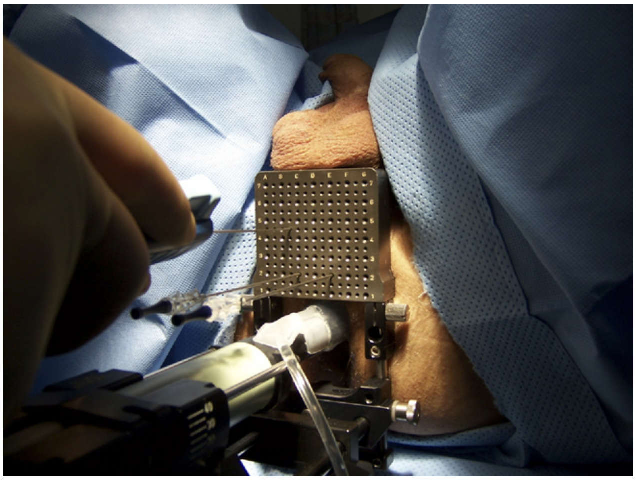

Figure 1. TRUS transducer placement in relation to perineal 5 mm biopsy grid.