MRI DERIVED QUANTITATIVE RISK MAPS FOR PROSTATE CANCER DIAGNOSIS USING TARGETED BIOPSY

Principle Investigators:

Aytekin Oto, M.D., Professor of Radiology

Co-Investigators:

Scott Eggener. MD

Tatjana Antic, MD

Greg Karczmar, Ph.D.

Yulei Jiang, Ph.D.

Ambereen Yousuf, M.D

Aritrick Chatterjee, Ph.D.

Ajit Devaraj, Ph.D.

Milica Medved Ph.D.

Xiaobing Fan Ph.D.

Luke Reynolds, M.D.

Location: University of Chicago Medical Center, Department of Radiology

A. BACKGROUND AND RATIONALE

Prostate cancer (PCa) is the most frequently diagnosed cancer and the second most common cause of cancer death in US men (3). Approximately 26,730 men in the US will die of PCa in 2017 (3). Current methods for detecting and diagnosing PCa are seriously flawed since they frequently produce inconsistent and unreliable results, often with high cost. PCa screening is driven by the serum prostate specific antigen (PSA) test, with definitive diagnosis from histologic analysis of 12–24 tissue cores sampled randomly from the prostate with trans-rectal ultrasound (TRUS)-guided biopsy. This approach is prone to under-sampling the prostate (only 1% of the prostate tissue is sampled) and under-diagnosing clinically significant PCa. Typically, only 30% of the first TRUS-guided biopsy is positive for PCa but unfortunately, a negative biopsy does not rule out PCa, and repeat biopsies are often required. Furthermore, Gleason score—one of the most important prognostic factors for PCa—is not reliably assessed from TRUS-guided biopsy, and is upgraded in 30% of cases in repeat biopsies or prostatectomies (4, 5). Every year, approximately 1.2 million prostate biopsies are performed in the US (6), which cost the US health care system an estimated $2 billion/year (7-10). As a result, there are currently no effective, widely accepted and reliable methods for risk assessment, detection and diagnosis of PCa. Consequently, the number of early cancers detected is also decreasing

significantly, and therefore increased incidence of metastatic PCa and disease specific mortality is expected, beginning in approximately 2017 (11). In addition, inefficient diagnosis algorithms and unreliable risk prediction leads to "overtreatment"—it is estimated that, for 30–40% PCa patients, prostatectomy does not impact survival but exposes them to significant complications (impotence and incontinence). There is a critical and immediate need for accurate and non-invasive diagnostic tools to improve PCa diagnosis and grading. At the time of initial diagnosis, we need a diagnostic tool for evaluation of the entire prostate, to identify PCa foci, and to differentiate clinically significant cancer (requires aggressive treatment) from indolent disease (does not require aggressive treatment), to reduce financial, logistical, and emotional costs from PCa and improve the outcome of PCa management.

Currently there is no consensus on the definition of clinically significant prostate cancer. In this proposal we define significant cancer based on pathologic criteria. For biopsy, based on the Canadian recommendations (12), clinically significant cancers include all tumors with Gleason score >6 (3+3) (ISUP grade group 1), and with Gleason score ≤6 (3+3) (ISUP grade group 1) if not localized.

Multi-parametric MRI (MP-MRI) is an MRI protocol optimized for PCa and embraced worldwide by the radiology community. MP-MRI is a combination of two or more of the following imaging sequences: T_2-weighted (T_2w), diffusion-weighted (DW), and dynamic contrast enhanced (DCE). One promising solution for improving PCa detection is targeted biopsy of the prostate using MP-MRI. When performed by experts, Mp-MRI targeted biopsies result in higher detection rates of clinically significant cancer with a reduced upgrading of cancers at surgery, improving confidence in the biopsy results (13-16). MR-targeted biopsies can be performed either by fusing MR images to real time US images or directly under MR guidance (in-bore MR guided biopsy).

A.1 Current status and shortcomings of prostate magnetic resonance imaging (MRI)

Performance of MRI-targeted biopsy depends on accurate and reproducible interpretation of MR images leading to accurate identification of targets for biopsy. Images from MP-MRI are complementary and synergistic in diagnostic information, but they are also complex and difficult to decipher by radiologists. T_2w and DW MR images are the mainstay of MP-MRI, and can depict PCa with high sensitivity. T_2w and DW-MRI are the main imaging techniques for PI-RADS, the standardized reporting approach to MP-MRI (17). Currently, all commercially available PCa MP-MRI protocols are based on subjective and qualitative interpretation by radiologists, and none is truly quantitative, well defined, and reproducible. Interpretation of prostate MP-MRI varies greatly among radiologists, because of a lack of reproducible and quantitative MRI acquisition protocols, and because of a lack of decision support system (DSS) tools to assist radiologists interpret the images. This problem is exacerbated by limited number of radiologists who have substantial experience and expertise in interpretation of prostate MP-MRI. Success of MP-MRI achieved in select centers of excellence cannot be reproduced easily worldwide. **We propose to evaluate a quantitative prostate MRI acquisition protocol, and a novel Risk Map DSS tool for image interpretation, to enable widespread clinical translation of PCa MRI.** If these emerging results are reproduced widely, MRI has the potential to revolutionize PCa management, reduce unproductive biopsies and

unnecessary radical therapies (e.g., prostatectomy and radiation), and achieve more accurate and efficient diagnosis, effective follow-up, and targeted eradication of aggressive disease.

We will use a new MRI technique to obtain quantitative tissue composition maps based on a new hybrid multi-dimensional MRI (HM-MRI) approach that combines T2 and ADC measurements and detects tissue heterogeneity at the microscopic level in an innovative way.

Our group has developed two novel approaches that have potential to substantially improve multi-parametric MRI in prostate: the kT-T2 sequence (18-21) and the hybrid multi-dimensional MRI (HM-MRI) (22-25). The kT-T2 sequence provides a direct assessment of the prostatic micro-environment and HM-MRI provides an assessment of the prostatic tissue micro anatomy which allows us to find water signals that are characteristic of cancers. This is important new information that **cannot be obtained** from conventional T2 and ADC measurements.

HM-MRI data can be analyzed to produce accurate tissue composition maps showing volume fractions of stroma, epithelia, and lumen. These maps have been shown in preliminary studies from this laboratory to enhance diagnostic accuracy (26) , as summarized in Preliminary Results (**Section A.3.1.**). Information from these tissue composition maps will be incorporated into the DSS tool.

A.2. Protocol overview:

We propose to test a Risk Map DSS image interpretation tool for automated interpretation of prostate MR using research sequences, which will include quantitative kT-T_2, and HM-MRI acquisition, in the clinical MRI protocol. This will also allow straightforward comparison of kT-T2 and HM-MRI vs. conventional T2 and ADC images. This, in turn, will be used for reliable determination of clinically significant cancer in prostate which will be targeted by MR-targeted biopsies at the time of diagnosis. The goal is to achieve clinical translation of advanced and innovative technology for accurate and reliable PCa diagnosis, to provide patients and treating physicians with quantitative and objective data, and to enable them to make informed treatment decisions.

A.3. Preliminary results:

Preliminary results and research accomplishments directly related to this proposal are listed below.

A.3.1. Tissue composition estimate from HM-MRI data, and correlation with histology:

A preliminary study demonstrates that HM-MRI has potential to significantly enhance the diagnostic accuracy of PCa detection and diagnosis (26). This analysis included 21 PCa patients who underwent preoperative 3T HM-MRI. Axial images using HM-MRI were acquired with TE = 47, 75, 100 ms and *b*-values of 0, 750, 1500 s/mm^2, resulting in a 3×3 array of data for each voxel. Volume fractions of three tissue components—epithelium, stroma, and lumen—were estimated by fitting the HM-MRI data to a three-component signal model (see section c.2.3.iv) with distinct ADC and T_2 values for each component. Figure 1 shows an example Gleason 4+5 cancer outlined on H&E slides and superimposed on estimated ADC and T2 maps (top row), stromal, luminal, and epithelial volume fraction maps (2nd row, and 3rd row, left), and finally a tissue composition map (3rd row, right). This aggressive cancer is clearly evident on conventional ADC and T2 images, but is shown here with greater contrast in the tissue composition map. We analyzed 28 PCa and 71 normal tissue ROIs outlined by an expert radiologist. The volume fractions of normal tissue are similar to histological studies (27-29). Stromal volume was highest in AFMS followed by transition zone, epithelium volume was highest in central zone, and lumen volume was highest in PZ (Fig. 1, 4th row). The volume fractions were significantly different in cancers than in normal tissue (Table 1 for cancer and normal PZ, and Fig. 1, 4th row, for cancer vs. normal tissue in all zones). PCa has significantly increased epithelium than normal tissue (48.8±9.2 vs. 23.2±7.1%), reduced lumen (14.0±5.2 vs. 26.4±14.1%), and reduced stroma (37.2±9.1 vs. 50.5±15.7%) fractional volumes. The volume fractions also correlate more strongly with Gleason Score (ρ = 0.65 for epithelium, -0.44 for stroma, and -0.39 for lumen) than T_2 (ρ = -0.29) and ADC (ρ = -0.32). The AUC value for differentiating

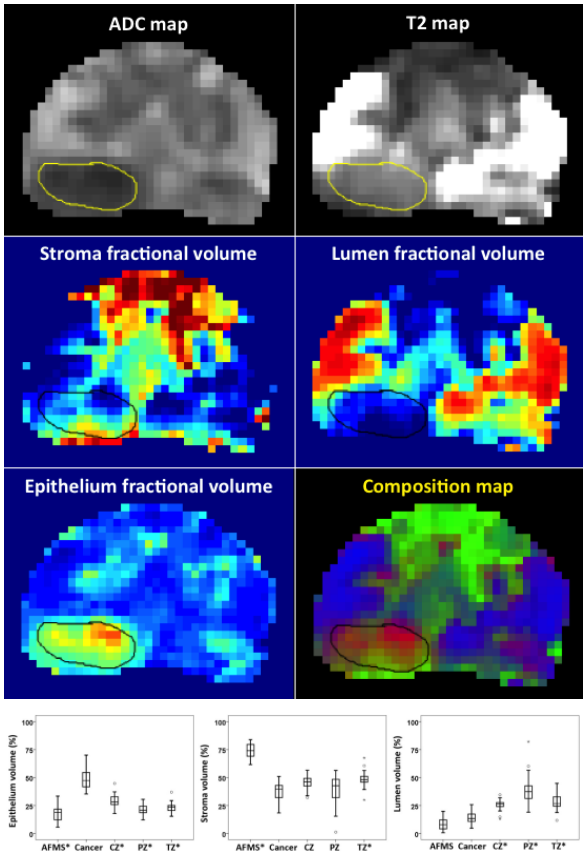


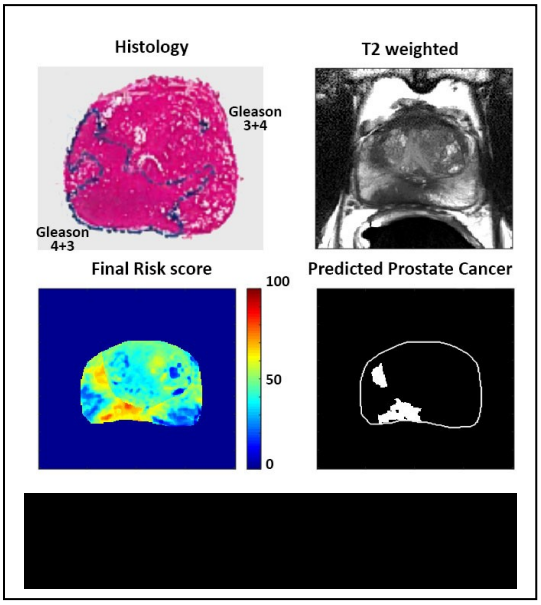
Figure 1. Representative tissue composition maps estimated from HM-MRI for an ROI of histologically confirmed Gleason Grade 4+5 cancer. The red color in the "composition map" which combines the stroma (1), lumen (blue), and epithelium (2) maps is consistent with increased epithelial and reduced lumen and stromal volume fraction in this cancer. The box plots show epithelial, stromal, and luminal volume fractions in the AFMS, CZ, PZ, TZ, and cancer.

Table 1. Comparison of Tissue Composition

	Study	Stroma (%)	Epithelium (%)	Lumen (%)
Normal Peripheral Zone Tissue	Langer et al 2010	38.2	31.2	29.6
	Chatterjee et al 2016	38.3±1.4	32.0±1.5	30.1±1.2
	HM-MRI	39.0±13.6	21.5±4.6	39.4±14.1
Prostate Cancer	Langer et al 2010	38.6	46.2	13.5
	Chatterjee et al 2016	27.9±1.0	60.9±1.9	11.2±1.1
	HM-MRI	37.2±9.1	48.8±9.2	14.0±5.2

PCa from normal tissue was 0.99 for epithelium, 0.80 for lumen, 0.79 for stroma, and 0.71 for T_2 (AUC for ADC was not evaluated because cancer ROIs were outlined in ADC maps). These results suggest that HM-MRI non-invasively provides 3-dimensional information that is similar to the information obtained from 2D *ex vivo* histology slices, and that prostate tissue composition measured non-invasively by using HM-MRI have potential to improve PCa diagnosis and assessment of PCa aggressiveness. The study also resulted in a filed patent application (30).

A.3.2. PCa risk maps derived from quantitative MRI data



We have developed a preliminary risk map based on mpMRI: ADC, T2, and DCE signal enhancement rate (α). These parameters were calculated on a voxel-by-voxel basis for the entire, co-registered prostate. Each parameter was normalized (to 0-100) with low T2, low ADC, and high α signify high risk. The final risk score is a weighted sum of the parameters (ADC 40%, T2 40%, DCE 20%) with higher risk for low T2, low ADC, and high α values. We analyzed preoperative 3T mpMRI of 22 PCa patients, and used five patients as the training set to find the optimal threshold for predicting PCa and 17 patients as the test set. A sector-based analysis (18 sectors per prostate) on the 17 test patients showed the following PCa detection performance: sensitivity 75% (105/140), specificity 89% (147/166), positive predictive value 85% (105/124), negative predictive value 81% (147/182), and AUC 0.82 (95% CI [0.77, 0.87]). Importantly, the risk map correctly identified all index lesions. This study suggests that the risk map can detect PCa and guide targeted biopsies for improved PCa diagnosis.

A.3.3. Pilot DSS study:

We developed a pilot DSS based on T_2w and DW-MRI (31). A radiologist and a pathologist identified 104 ROIs (61 cancer and 43 normal tissue) based on correlation of histological and MR findings. AUC values in the differentiation of PCa from normal tissue foci of 10th percentile ADC, average ADC and T_2w skewness were 0.92, 0.89, and 0.86 respectively. The combination of the 10th percentile ADC, average ADC, and T_2w skewness yielded an AUC value of 0.95 for the same task. Gleason score correlated moderately with the 10th percentile ADC (ρ=-0.34, p=0.008) and with the average ADC value (ρ=-0.30, p=0.02). The combination of 10th percentile ADC, average ADC, and T_2w skewness were promising in differentiation of PCa from normal tissue, and ADC image features correlated moderately with Gleason score (31).

A.3.4. Validation study of pilot DSS:

We validated the pilot Risk Map DSS on preoperative 1.5T MP-MR images (with endorectal coil) of 119 PCa patients (GE scanners, n=71; Philips scanners, n=48) and 265 PCa and normal peripheral zone ROIs identified through histology-MR consensus review (32). AUC values of the pilot DSS image features combined were 0.95 and 0.88

on the Philips and GE dataset (leave-one-patient-out evaluation), respectively, and 0.96 and 0.89 when training on the GE dataset and testing on the Philips dataset, and vice versa, respectively. Spearman correlation coefficients between ROI-specific Gleason scores and the ADC features were between -0.27 and -0.34. This previous work (32) demonstrates that a pilot DSS tool developed based on data from Philips scanners can be effective with data from other scanners, and supports the feasibility of the proposed Risk Map DSS tool.

B. PURPOSE

The purpose of the proposed research is to test and validate **an artificial intelligence-based Risk Map decision-support system (DSS) for PCa MRI interpretation and identification of clinically significant tumor site based on MRI acquisition of a protocol covering the entire prostate which will include the kT-T2 and the hybrid multi-dimensional MRI (HM-MRI) sequences.**

We will test an artificial intelligence-based Risk Map DSS tool we have developed, which is based on and expanded from previously identified key MR image features that are effective for identifying PCa from normal prostate tissue, and which also correlates moderately with Gleason scores (ADC, T2, and tissue composition maps). The DSS tool will assist radiologists interrogate suspicious areas in the prostate that are potentially clinically significant PCa foci, and will identify up to two potential clinically significant tumor sites. In addition to systematic biopsies and the targets identified by the radiologist, up to two targets determined by the DSS tool will be biopsied. Biopsy histology results of all cores will be used as the reference standard to evaluate the performance of the Risk Map DSS tool.

C. METHODOLOGY

C.1. Study Design:

This is a prospective, single-arm, unblinded study of patients with known or suspected prostate cancer. A total of 125 patients will be enrolled.

Recruitment: We will recruit patients with known or suspected prostate cancer who have been referred to the Department of Radiology at the University of Chicago Medical Center for a diagnostic MRI exam of the prostate, to be followed by an MRI-guided fusion biopsy of the prostate, per standard clinical protocol.

All patients will be scanned using a standard clinical prostate MRI protocol. Research sequences will be added to the routine clinical exam. The research sequences will not exceed 15 minutes. The patients will not receive intravenous contrast agent as part of the research protocol.

All patients will then undergo a 12-core TRUS-guided or transperineal US-guided sextant random biopsy by their urologist at the Urology Clinic as their standard of care treatment. Additional biopsy targets may be selected based on an expert radiologist's interpretation of the patient’s clinical MRI, as part of the clinical, standard of care MR targeted biopsy procedure. Up to two additional biopsy targets per patient will be selected by the Risk

Map DSS tool, if different from the already selected targets by the radiologist per standard of care. Ultimately, the clinical radiologist will make the final decision on the targets to be biopsied. MR-targeted biopsies will be done by using a Uronav MR-US fusion device. The following results will be recorded for each core: (1) the reason of biopsy (random biopsy; DSS tool alone; radiologist alone) (2) location (sextant and zone), and (2) histology result. Research cores will be evaluated by expert genitourinary pathologist, Dr. Antic, and results will be communicated to the urologist.

Studies will be carried out using FDA approved 3 Tesla Philips, GE and Siemens MRI units at the University of Chicago Medical Center. All of the research MR sequences will be in compliance with FDA safety requirements and MR contrast agents will not be injected for research purposes.

C.2. MRI Data acquisition methods:

The data acquisition will consist of obtaining the standard clinical protocol and research sequences, in compliance with FDA safety requirements. Research sequences may include, but will not be limited to (1) kT-T2 sequence (high spatial resolution axial ME-TSE for T_2 measurements and anatomy visualization), and (2) axial HM-MRI with 4 b-values and 4 TEs for diffusion and T2 measurements. MR images will be acquired using Philips, GE or Siemens 3T clinical MR systems with a phased array surface receiver coil.

C.3. Study Endpoints and Statistical Analysis

The major goal of this study is to compare the accuracy of the Risk Map DSS tool against the clinical accuracy of experienced radiologists in the context of the reference standard of biopsy histology. The primary endpoints will be ROC curve, AUC value, the secondary endpoint will be sensitivity, specificity, PPV, and NPV, and the tertiary endpoint will be correlation strength between the DSS tool output and tumor-specific Gleason scores. Both per-patient and per-tumor analyses will be conducted. For the per-patient analysis, patients who are diagnosed with PCa from the biopsy procedure will be considered as positive for PCa, and patients who are not diagnosed with PCa from the biopsy procedure will be considered as negative for PCa. For the per-tumor analysis, each individual PCa tumor diagnosed from the biopsy procedure will be analyzed separately, and biopsy sites that do not yield PCa diagnosis will be considered as negative for PCa. To ascertain a true positive biopsy, the finding and the biopsy must match in sextant and zone. If ambiguity in biopsy site arises with regard to indications from the DSS tool, or the radiologist's opinion, and the biopsy, expert radiologist (Dr. Oto) and pathologist (Dr. Antic) will review each case to make the determination. This will allow us to calculate the performance of: (1) the Risk Map DSS tool, (2) the radiologist, and (2) the standard sextant biopsy. We will evaluate these performance endpoints on clinically significant PCa (but we will have data for all tumors). Spearman correlation coefficient will be estimated in the usual manor.

C.4. Statistical power consideration

We expect the following level of performance: AUC 0.90±0.03, sensitivity 90±5%, specificity 90±4%, and statistically significant (Spearman's) correlation strength of 0.8 with tumor-specific Gleason scores. Variances are estimated based on the expectation of PCa diagnosis in 35% of 125 patients, and based on an empirical rule-of-thumb formula

for AUC and binomial probability for sensitivity and specificity. The estimated 95% confidence intervals (CIs) are: for AUC [0.87, 0.93], for sensitivity [0.85, 0.95], and for specificity [0.86, 0.94]. These uncertainty estimates do not include analysis of biopsy by sextant and zone of the 12-20 cores per patient; estimates of 12 by-location-analyses per patient reduce all uncertainties to about 1%. These estimates suggest that this protocol will produce meaningful performance estimates.

D. DURATION OF THE PROTOCOL

The probable duration of the study will be 3 years with review, at least annually, to recruit the target number of patients and complete all data analysis.

E. LOCATION WHERE RESEARCH WILL BE CONDUCTED

The study will be conducted on the FDA approved 3 Tesla Philips, GE or Siemens MRI scanners at the University of Chicago Medical Center, 5841 South Maryland Avenue, Chicago, IL 60637.

F. SAFETY MONITORING

We do not anticipate any adverse events. However, adverse events related directly to the study will be reported to the Cancer Center Clinical trials office following standard operating procedures outlined in the Cancer Center data safety and monitoring plan.

G. DESCRIPTION OF EXPERIMENTAL CONTROLS AND USE OF PLACEBOS

N.A.

H. TYPE AND NUMBER OF EXPERIMENTAL SUBJECTS

We will recruit 125 patients who will receive a diagnostic MRI exam of the prostate, to be followed by an MRI-guided fusion biopsy of the prostate.

Inclusion Criteria

We will recruit patients with known or suspected prostate cancer who have been referred to the Department of Radiology at the University of Chicago Medical Center for a diagnostic MRI exam of the prostate, to be followed by an MRI-guided fusion biopsy of the prostate. Written informed consent will be signed by the patients before the MRI examination.

Exclusion Criteria

Subjects will be screened and excluded per standard clinical protocol.

Also excluded are:

- Subjects incapable of giving informed written consent;

- Subjects who cannot adhere to the experimental protocols for any reason, or have an inability to communicate with the researcher;
- Subjects with psychiatric disorders that affect their ability to consent for themselves will be excluded and not the entire population of patients with psychiatric disorders.
- Prisoners;
- Minor children (under the age of 18 years old).
- Previous treatments (surgery, radiation, focal ablation, hormone or other chemotherapy) for prostate cancer.

Data to be collected

Demographic information will be collected from each recruited subject. The research team will also collect clinic visit, laboratory, imaging and pathology results relevant to the clinical question for each subject.

J. SHARING RESEARCH RESULTS:

At times, the advancement of research or the development of healthcare devices is aided by the sharing of de-identified image data, pathology data, genetic data and clinical information with other organizations. De-identified copies of image data, pathology data, genetic data and clinical information may be sent outside of The University of Chicago for such purposes, including as part of an image library. If this occurs, scientists outside of The University of Chicago will be unable to identify the subject from medical images, pathology data, genetic data or from clinical information, because all identifying information will have been removed from the images and records. Insurance agencies will not have access to this information.

K. POTENTIAL RISKS AND BENEFITS TO SUBJECTS

Risks Associated with Magnetic Resonance Imaging

The risks below are the risks of standard MR imaging which the patients will undergo for clinical indications. The research component will not cause any additional risk to the existing minimal risks of clinical MR imaging. The research sequences will be designed in compliance with FDA requirements, and intravenous contrast material will not be administered for research purposes.

The presence of devices, implants, or other objects containing metal: Metal objects pose a serious risk to all patients undergoing MRI exams. This includes internally implanted objects such as surgical clips, biosupport devices (e.g., pacemakers), and artificial joints which contain metal.

Claustrophobia: Some individuals may experience claustrophobia during the MRI exam due to the limited space available inside the bore of the magnet.

Breach of confidentiality: There is a minimal risk that patient confidentiality may be breached.

Protection against risks associated with MRI

Protection against risks related to presence of metals, devices and other metal containing material: Participants are questioned carefully before MRI imaging to insure that they do not have metal implants. Prospective study participants who have such implants will be excluded from the study. Patients who have worked in or near machine shops and electronics shops and may have had metal slivers become trapped in their eyes, posing a potential hazard if exposed to a strong magnetic field, will also be excluded from the study. In addition, metal objects such as heavy key chains that are carried into the scan room can cause serious accidents. Participants will be cautioned to remove all metal objects before entering the scan room. Access to the scan room is carefully controlled to insure that no ferrous metal is inadvertently brought in.

Protection against claustrophobia: Prospective participants will be counseled about this possibility before the exam. The magnet is equipped with an intercom system enabling study subjects to communicate with the operators at any time during the exam. If they report any discomfort during the MRI examination they will be removed from the magnet immediately.

Protection against the breach of confidentiality: Patient identifiers will be kept and used only for the purpose of correlating patient data between radiology, urology and pathology. Patient identifiers will be removed from data analysis unless it becomes necessary to correlate results of the analysis to other clinical data, which we do not expect. Patient identifiers will be removed from all presentations and publications; only data from a group of patients will be reported so that data from any individual patient cannot be identified.

Risks associated with Transrectal and Transperineal Ultrasound-Guided Prostate Biopsy:

The risks will be those associated with standard MRI-guided fusion biopsy of the prostate, which the patients will undergo for clinical indications. The research component (upto two additional biopsy targets) will cause a minimal increase in the risk of bleeding and infection.

Benefits

There may or may not be any direct medical benefit to patients who are enrolled in the study.

There will be a long-term benefit to society in general if this research leads to the development of a new technology that improves clinical practice.

Alternatives

If patients decide not to participate in this study, they will undergo routine clinical examination ordered by their referring physician.

L. PAYMENT TO SUBJECTS

Patients will not be paid or compensated for their participation in this study.

M. OBTAINING WRITTEN CONSENT

The Principal Investigator or Co-Investigators or the Clinical Research Coordinator will be responsible for obtaining written informed consent signatures from the patients based on the research plan and consent form approved by University of Chicago Institutional Review Board.

Confidentiality will be insured by use of an encrypted patient ID numbering system for all research data to maintain confidentiality and anonymity.

N. CONFIDENTIALITY OF RECORDS

In accordance with the regulations promulgated by the Federal Food and Drug Administration, all records will be treated with strict adherence to professional standards of confidentiality. Care will be taken during the review of medical records to maintain as much privacy as possible. Only the treating physician or study staff will review the medical records. Records will be kept locked, and the database will have restricted access (password protected).

Security and Privacy:

This protocol is designed to respect proper attention to patient privacy and prevention of breach of confidentiality. For each patient, the study protocol number and the patient`s medical record number will be entered into a restricted database by selected research personnel. Additional relevant general clinical information will be included. Access to the database will be password protected. All personnel are trained to maintain confidentiality of patient information according to HIPAA regulations. All of the images will be maintained in the password protected University of Chicago PACS.

Research charts, including signed consent forms, will be stored in a locked file cabinet in the clinical research coordinator’s office at University of Chicago Medical Center, Room Q200. Although each chart, radiographic study, and MRI examination will contain the patient’s name, and as such will not be anonymous, no individual identities will be used in any publications resulting from this study. Officials from examining bodies such as the U.S. Food and Drug Administration or NIH may inspect records pertaining to this study.

O. PATIENT RECRUITMENT:

We will recruit patients referred by the UCMC Urology Department, who are scheduled for diagnostic MRI exam of the prostate, to be followed by an MRI-guided fusion biopsy of the prostate. In addition, patients may also be referred to the study team from other

medical centers/hospitals. The study protocol will be discussed with the patient and the study coordinators will consent the patient.

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