AWARD NUMBER: W81XWH-15-1-0441

TITLE: Incorporation of Novel MRI and Biomarkers into Prostate Cancer Active Surveillance Risk Assessment

PRINCIPAL INVESTIGATOR: Michael A. Liss, M.D., M.A.S.

CONTRACTING ORGANIZATION: University of Texas Health Science Center San Antonio
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this research is to improve the baseline and longitudinal risk assessment of prostate cancer patients electing active surveillance (AS) as their management strategy. Our broad objective is two-fold: [1] to improve the ability to select candidates who safely choose active surveillance as a prostate cancer management strategy and [2] to improve current monitoring for progression of prostate cancer. We subsequently aim to improve non-invasive means to monitor prostate cancer and improve the ability to decide when to intervene with therapeutic intent. Additionally we seek to reduce the number of biopsies, in turn reducing the morbidity of the AS strategy.

15. SUBJECT TERMS
Prostate Cancer, Imaging, Magnetic Resonance Imaging, Active Surveillance, Prostate Biopsy, Diffusion weighted imaging, PSA, Biomarkers, Risk calculator

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1 INTRODUCTION:

Prostate cancer is a prevalent disease among men with over 230,000 new cases reported each year. More than two-thirds of these men are diagnosed with low-risk prostate cancer (Gleason 6 or less). An increasing number of men in this low-risk group are choosing Active Surveillance (AS) over aggressive treatment thereby subjecting themselves to serial prostate biopsies. Prostate biopsies can be inaccurate and cause significant pain, bleeding, infection, and anxiety over the years men with low-risk prostate cancer are followed.

Improving non-invasive techniques to monitor prostate cancer status will enhance clinical decision-making regarding timing of therapeutic interventions. This should result in a decrease in serial biopsies; thereby, reducing the overall morbidity of men who choose the active surveillance strategy.

This grant is a training award. I have engaged my mentors, enrolled in courses and conferences to augment my knowledge of translational science and MRI imaging, and I have developed and am managing my first clinical trial. My long-term goal is to become a leader in the field of urology as a clinical researcher. My focus is to improve the lives of patients with prostate cancer by implementation of imaging and biomarkers at the point of care.

2 KEYWORDS:

Prostate Cancer Active
Surveillance Prostate Biopsy
Imaging
Magnetic Resonance Imaging Diffusion
weighted imaging PSA
Biomarkers
Risk calculator

3 ACCOMPLISHMENTS:

What were the major goals of the project?

This Prostate Cancer Physician Training Award is divided into three integrated components, **training, mentorship, and research,** each of which has its own set of specific major goals.

The **training component** is comprised of three goals that are integral in the preparation for a career in clinical research. These goals include 1) training in T1 translational research; 2) training in the development and management of clinical trials, and 3) training in MRI biomarker and risk assessment techniques. Translational research training includes formal coursework to obtain the Certificate in Translational Research as well as engaging in the Translational Research Awareness Program (TRAP). My training in clinical trials includes participating in the GU working group meetings at the cancer center, completion of a young investigators training course, and involvement in ongoing clinical trials with Dr. Thompson. I am heavily involved in SWOG and have been recently selected to become the study champion of EA8171 Multiparametric MRI (mpMRI) for Preoperative Staging and Treatment Planning for Newly-Diagnosed Prostate Cancer. The third goal includes additional training in MRI imaging through a series of prostate specific imaging courses as well as several MRI specific formal courses offered at UTHSCSA. In order to gain a working knowledge of how imaging is incorporated into the overall clinical diagnosis and treatment plans, I attend the semi-annual **SWOG Imaging committee** meetings along with the general SWOG meetings.

The **mentorship** component included Dr. Ian Thompson as my Mentor, Dr. Peter Fox as my Co-Mentor, and Dr. Robin Leach as a collaborating mentor. Each mentor is an expert in one of the integral focus areas of this award.

Dr. Thompson is a leader in prostate cancer clinical research and chairs the Genitourinary Committee at SWOG, a member of NCTN (national clinical trials network). In addition to basic mentoring tasks, we have identified four sources of mentorship in particular to my career, which include opportunities at the UT Health San Antonio Cancer Center, SWOG, PASS, and the SABOR clinical trials.

Dr. Fox is a leader in imaging research and is the Director of the Research Imaging Institute. He has a working relationship with my previous MRI Mentors at UCSD where I received my fellowship training and completed preliminary studies using the novel restriction spectrum imaging (RSI) MRI techniques. We have submitted a U01 in Imaging and Biomarkers for Early Detection of Aggressive Cancer based on our work at UT Health San Antonio.

Dr. Leach is an expert in Biomarker evaluation as well as the Director of the Biobanking and Genome Analysis Research Core at UTHSCSA. She has been an advocate for me on the national level and accompanied me to the NCI-Early Detection Research Network annual meeting (EDRN, Seattle, WA September 7-9, 2017) to present this project for expansion to other sites within EDRN. My mentorship plan includes regularly scheduled individual and group meetings with each mentor as well as an advisory committee that includes Drs. Thompson, Fox, and Leach to oversee my progress through the DOD Prostate Cancer Physician Research Training program.

The **research** component is a clinical research project that investigates a novel MRI technique called Restricted Spectrum Imaging (RSI) in men undergoing active surveillance for low risk prostate cancer. Our broad objective is two-fold: [1] to improve the ability to select candidates who safely choose active surveillance as a prostate cancer management strategy and [2] to improve current monitoring for progression of prostate cancer. We subsequently aim to improve non-invasive means to monitor prostate cancer and improve the ability to decide when to intervene with therapeutic intent. Additionally we seek to reduce the number of biopsies, in turn reducing the morbidity of the active surveillance strategy.

Our specific aims are:

Aim 1: Prostate MRI to predict Progression on Active Surveillance.

Aim 2: Biomarker testing to predict active surveillance outcomes.

Aim 3: Incorporation of Imaging and Biomarker data into the PROMISS calculator.

What was accomplished under these goals? Training:
I was accepted into the **Certificate in Translational Research** program on 12/14/2015 and completed MEDI 6101 Topics in Translational Science (part 2) and MEDI 5070 Responsible conduct of Patient-Oriented Clinical Research. I am currently enrolled in MEDI 5071 Patient Oriented Research Methods I and MEDI 5078 Introduction to Intellectual Property and Tech Communication. I have reviewed 18 articles (30%, 18/60) of the **Translational Researcher Awareness Program** (TRAP) with Dr. Thompson.

I became a member of the UT Health San Antonio Cancer Center in 2015. I have been heavily involved in the GU Working group and have attended all meetings at the cancer center. In addition, I joined SWOG and attended both semi-annual meetings in 2016. I attend both the GU Committee weekly working group meetings and the monthly general Genitourinary meeting where leaders in the field discuss new and continuing clinical trials. Fortunately, my involvement has lead to my selection as the **site principal investigator for SWOG**, which requires me to represent UTHSCSA at the bi-annual Board of Governors meetings. I have been in this role for 1 year and we have already been selected as a **NCI Cancer Trials Support Unit - High Performance Site Initiative.**

In addition, I have been involved in the Prostate Active Surveillance Study (PASS). I developed the MRI data collection forms with statisticians at Fred Hutchison Cancer Research Center. We will be reporting on our first 100 subjects within the next 6 months. I have been selected as the **site principal investigator for the PASS** study and have expanded enrollment to our South Texas Veterans Hospital. I attended the annual meeting at Stanford University on May 3-4, 2017 and presented PASS MRI project. I also provided an update on a project I am working on with Dr. Leach using the PASS cohort entitled the *Identification of Genetic Variants Associated with Poor Outcome*.

I have also become involved in a second ongoing clinical research study entitled San Antonio Biomarkers of Risk (SABOR) for prostate cancer. SABOR is a community based cohort initiated 15 years ago involving men undergoing prostate cancer screening. This important longitudinal cohort has been funded by the Early Detection Research Network (EDRN) as part of the National Cancer Institute and continues to provide important research in the study of prostate cancer development and biomarker research.

I was selected to be the **Director of the Genitourinary Tissue Bank** in January 2017 and oversee requests for tissue and the production of tissue microarrays that may be utilized for biomarker evaluation. In addition, my peers selected me as the **UT Health San Antonio Cancer Center Clinical Investigator of the Year** (academic year 2016-2017).

An important part of my training plan is developing my ability to train others. I am the leader of the Urologic Oncology morning conference every other Friday and hold regular journal clubs for our Urology residents. I have created an Active Surveillance clinic at the South Texas Veterans Hospital in San Antonio where I see a majority of men with prostate cancer and can now enroll patients directly from this clinic into my clinical trials.

I have received additional training in MRI imaging by attending the MRI Ultrasound Fusion Guided Prostate biopsy II session at the American Urological Association 2017 annual meeting along with several poster/podium presentations. Our UTHSCSA radiologists and I hold monthly Prostate MRI conferences where we read new MRI's together and review MRI targeted biopsies to improve quality of the scans and reads.

Mentoring:

Drs. Thompson and Leach have been integral and very involved in the mentoring process. We meet nearly every Monday morning for 1-2 hours with our research group. Drs. Thompson and Leach are preparing a prostate SPORE application to be submitted to the NCI in January of 2018. I will be a co-investigator on their Project 1, which attempts to identify high-grade prostate cancer in men with low PSA incorporating the RSI imaging, for which this project has provided the groundwork and experience. I have recruited and enrolled 30 patients in a pilot study regarding this project. We have diagnosed 5 men with prostate cancer, 4 of which were high grade and underwent prostatectomy. In addition to these activities, Dr. Thompson has provided opportunities within our cancer center and SWOG for involvement and leadership roles. I have been involved with the SABOR and PASS clinical trials under his guidance and mentorship as well. My co-mentor, Dr. Peter Fox, has been very helpful with navigating the Research Imaging Institute and providing a connection with a fantastic medical physicist, Dr. Geoffrey Clarke. We experienced some delays with implementation due to having a different MRI hardware system (Siemens) at UTHSCSA than at UCSD (GE). Dr. Fox was instrumental in facilitating the resolution of this issue in as timely a manner as possible. Dr. Robert Svatek is a non-formal advisor and has been very helpful in navigating the intricacies of clinical research and he has activated his first national cooperative group clinical trial, SWOG S1602 with BCG vaccination in bladder cancer. Additionally, the Dean of UTHSCSA, Dr. Ronald Rodriguez and my Chair of the Department of Urology, Dr. Stephen Kraus have been very supportive of my research and training goals and have accommodated my clinical schedule to ensure the protected time I need to meet the goals of my grant and career development.

Research:

We have successfully implemented the acquisition portion of the RSI MRI. There were some initial delays in implementation due to the different MRI hardware systems at UCSD and UTHSCSA in the first year. Additional time was needed to modify the sequences and then do practice scanning to ensure the images were consistent across the two systems. Under the guidance of Dr. Clarke, I was able to correct the scanner differences. We then underwent practice scanning for comparison and quality control from UCSD. The images were uploaded utilizing XNAT (Extensive Neuroimaging Archive Toolkit). UCSD then viewed and analyzed our images securely and remotely and we were able to ensure the consistency of the scans and readings across the two hardware systems.

We have also successfully implemented the software component of the RSI MRI at UTHSCSA. There were some software issues that we had at the initiation of the project mostly related to non-static IP address; however, that also has been resolved. After 60 scans, we have re-evaluated our protocol to improve the field of view and incorporation into the Uronav biopsy system (Invivo Inc.). I am now transferring de-identified images to UCSD for secondary review and RSI data analysis. We will perform whole gland RSI analysis on men who had a negative MRI and biopsy for control and compare to those men with a negative MRI and a positive biopsy and/or progression of prostate cancer. The largest limitation to the project seems to be the false positive rate of PIRADS 3 tumors. We will start investigating whether the RSI technology can predict this event.

The project received UTHSCSA IRB approval (HSC20150160H) and we began enrolling subjects on 2/5/2016. Biologics (blood and urine) were collected on all subjects for application of Aim 2 biomarkers. We also have secured the material transfer agreement with Dr. Dobi at the Center for Prostate Disease Research for application of the Nanostring technology to our biopsy samples. Utilizing the MRI, without implementation of the RSI component. I have summarized our current findings to date in the next sections.

Background and objectives

Active surveillance is a strategy used to monitor low risk prostate cancer in order to delay or avoid aggressive therapies with the option to intervene yearly in the disease process with curative intent if progression is detected. Unfortunately, the initial and secondary prostate biopsies suffer from a 30% sampling error. Progression is usually detected by repeating the prostate biopsy, in some cases yearly. Prostate biopsies can cause significant pain, bleeding, infection, and anxiety. The primary objective of this project is to investigate if a novel screening MRI can predict prostate biopsy outcomes and eventually replace the prostate biopsy as the primary means to follow these patients. The secondary purpose is to use biomarkers from blood, urine, or prostate tissue to identify those men who are likely to progress while on active surveillance.

Methods

Our primary population is men who are diagnosed with prostate cancer and choose active surveillance. We plan to enroll 160 subjects to undergo a prostate MRI prior to their TRUS prostate biopsy. Both conventional MRI with IV gadolinium contrast and Restriction Spectrum Imaging (RSI) techniques will be employed (Figure 1). Images will be evaluated using a five- point scale (PI-RADS) to determine suspicion of clinically significant prostate cancer (Figure 2). PI-RADS will also be used to grade the RSI images with secondary radiology review. After the MRI, the patient will undergo targeted and template prostate biopsy and pathology compared to PI-RADS (Figure 3). Other study endpoints will include Gleason 6 tumor (low-grade) or a negative biopsy. After pathologic review the paraffin embedded tissue will be sent the CPDR in Rockville, MD for the Aim 2b NanoString technology investigation.

Figure 1

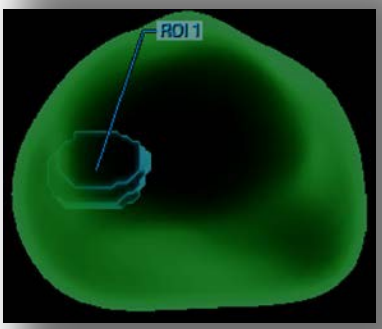

Figure 1: RSI-MRI imaging performed at UTHSCA Research Imaging Institute. Yellow/Red indicates high suspicion of tumor.

Figure 2

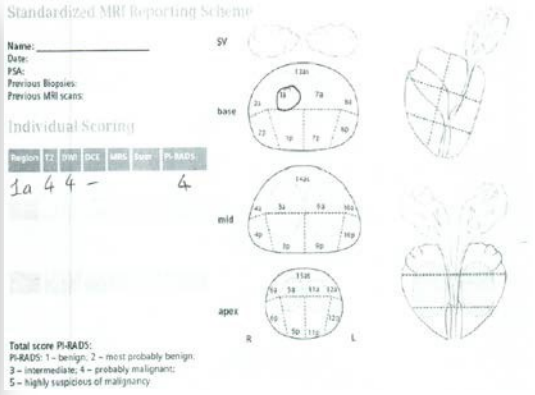

Figure 2: Radiology reading report in the same patient indicated a lesion in the same location given a PI-RADS 4 score.

Figure 3

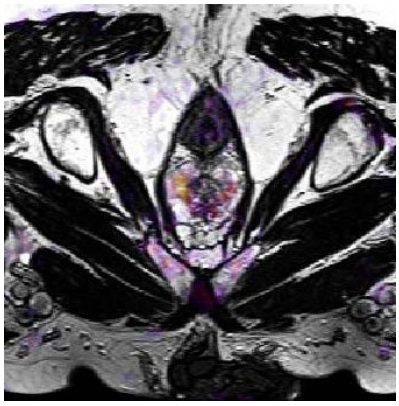

Figure 3: Three-dimensional rendering of the prostate utilizing the RSI-MRI then DynaCAD software for targeted prostate biopsy with Gleason 3+4 cancer.

Results To Date

To date we have completed the IRB protocol and attained approval for imaging in men undergoing active surveillance for prostate cancer who have an upcoming prostate biopsy. We have enrolled 67 subjects to obtain an MRI and undergo cognitive or MRI-Fusion targeted prostate biopsy from 2/5/2016 to present. We have enrolled 68 patients in the study and have complete data on 38 patients thus far. Figure 1 represents our current enrollment status and the Tables 1-4 represent contingency tables regarding the sensitivity and specificity of the MRI with particular parameters.

Figure 1. Study Enrollment

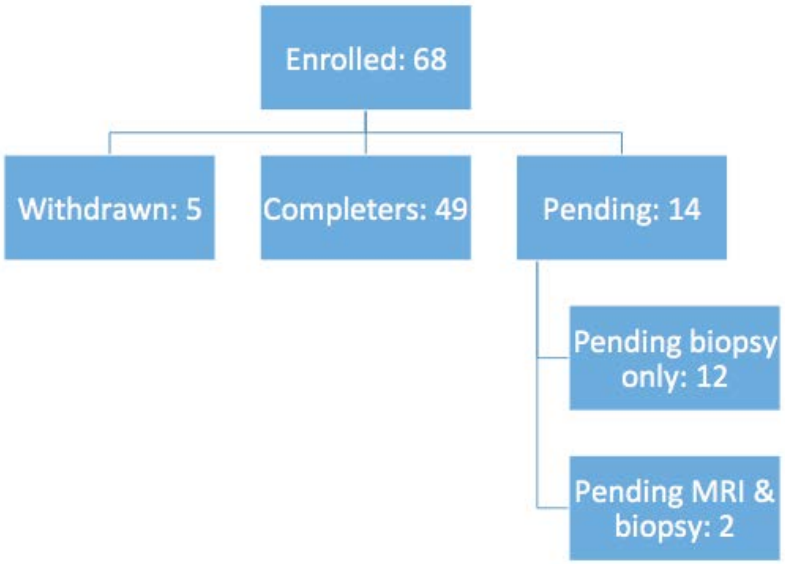

Table 1: Contingency table for MRI PIRADS >2 prior to prostate biopsy in men on active surveillance for prostate cancer.

	Positive (Target) Biopsy	**Negative (Target) Biopsy**
MRI Positive	9	10
MRI Negative	13	6

Sensitivity: 43%
Specificity: 40%
Positive Predictive Value: 32%
Negative Predictive Value: 53%
P=0.21

Table 2: Contingency table for MRI PIRADS >3 prior to prostate biopsy in men on active surveillance for prostate cancer.

	Positive (Target) Biopsy	**Negative (Target) Biopsy**
MRI Positive	9	4
MRI Negative	15	10

Sensitivity: 38%
Specificity: 69%
Positive Predictive Value: 37%
Negative Predictive Value: 40%
P=0.72

Table 3: Contingency table based on MRI result of PIRADS > 2 and patients deemed as progression on active surveillance

	Progression	**No Progression**
MRI Positive	10	9
MRI Negative	7	12

Progression = Any 3+4, >3 cores of any cancer, Greater than 50% any core
Sensitivity: 58%
Specificity: 57%
Positive Predictive Value: 53%
Negative Predictive Value: 63%
P=0.51

Table 4: Contingency table based on MRI result of PIRADS > 3 and patients deemed as progression on active surveillance

	Progression	**No Progression**
MRI Positive	10	3
MRI Negative	7	18

Progression = Any 3+4, >3 cores of any cancer, Greater than 50% any core
Sensitivity: 59%
Specificity: 86%%
Positive Predictive Value: 78%
Negative Predictive Value: 72%
P=0.006

Conclusions

We have successfully implemented our Prostate MRI study at the University of Texas HSC San Antonio. From our preliminary results, PI-RADS 4 and 5 lesions are more significant findings on prostate biopsy. Importantly a negative MRI indicates no cancer or very low risk cancer is present and may guide future biopsy decisions. Currently, we suggest that using the PIRADS score of 4 or higher would be more accurate in active surveillance prediction protocols. We look forward to continuing this research in order to obtain a better power to more accurately describe our results.

Impact statement

Our research is directed towards improving the quality of life of prostate cancer patients in the form of reduction of prostate biopsies and more accurate selection of active surveillance candidates.

What opportunities for training and professional development has the project provided?
The grant provided a validation of the research I am doing and my dedication to translational science. It has provided platform to be more involved in SWOG and the EDRN. Since receiving this training award, I have been elected to serve as the **SWOG site Principal Investigator** and have also been appointed as the **Medical Director for Clinical Research** at University Hospital in San Antonio, Texas.

How were the results disseminated to communities of interest?
I have presented this work at the EDRN meeting in Seattle, Washington on 9/13/2017.

What do you plan to do during the next reporting period to accomplish the goals?

Previous Plan

a. Implement RSI MRI software component - **Accomplished**
   Specifically, we now have full capability of automated RSI processing of MRI imaging in the XNAT system with the ability to share data.
b. Continue subject enrollment – **Accomplished**
c. Aggressive pursuit of funding for MRI and biomarker studies – **On going**
d. Continue TRAP article review with mentors – **Accomplished**
e. Attend national MRI conference / workshop – **On going**
f. Continue Certificate in Translational Science coursework - **Accomplished**

My plans for the next period include:

a. Aggressive pursuit of funding for MRI and biomarker studies
b. Attend national MRI conference / workshop
c. Present our results at a meeting
d. Write a manuscript regarding results from this grant
e. Continue resident or student educational opportunities

4 IMPACT:

What was the impact on the development of the principal discipline(s) of the project?
The project is still ongoing. Based on our current subjects, the MRI seems to have value in men with low-grade prostate cancer on active surveillance. We are now researching how to standardize the imaging across multiple hardware systems, reduce the cost of the imaging, and provide faster results to providers and patients. We plan to change the clinical management of men with low-grade prostate cancer by incorporating imaging as a standard procedure in follow up visits thereby reducing unnecessary interventions such as prostate biopsies and the morbidities associated with those interventions.

What was the impact on other disciplines?
The core of our project is a joint venture between Urology and Radiology. Both fields will be impacted by the study as it may set a new standard for prostate cancer treatment. We also feel that a standardized, non-invasive scan would set a baseline quality study that could be compared across scanners and institutions. Additionally, we will investigate imaging as a biomarker and incorporate into a risk calculator, which will impact the field of prostate cancer biomarkers and prevention research. The knowledge gained from this project can be applied to research on cancers in other organ sites.

What was the impact on technology transfer?
Nothing to report

What was the impact on society beyond science and technology?
If successful, this project has the potential to change the standard of care of prostate cancer in daily clinical practice and long-term management. By focusing on non-invasive techniques, patient comfort and individualized risk assessment we hope to change patient behaviors in order to increase compliance with long term treatment / management plans. These non-invasive techniques can reduce morbidities and increase the quality of life for patients on active surveillance treatment plans.

5 CHANGES / PROBLEMS:

Changes in approach and reasons for change?
Nothing to Report.

Actual or anticipated problems or delays and actions or plans to resolve them?
Nothing to Report

Changes that had a significant impact on expenditures?
Nothing to Report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents?
Nothing to Report.

Significant changes in use or care of human subjects: No Changes
Significant changes in use or care of vertebrate animals: Not Applicable
Significant changes in use of biohazards and/or select agents: No Changes

6 PRODUCTS:
Publications, conference papers, and presentations

Journal publications.
Liss MA, Ehdaie B, Loeb S, Meng MV, Raman JD, Spears V, Stroup SP.
An Update of the American Urological Association White Paper on the Prevention and Treatment of the More Common Complications Related to Prostate Biopsy.
J Urol. 2017 Mar 29. pii: S0022-5347(17)42253-1. doi: 10.1016/j.juro.2017.01.103.
Acknowledgement of federal support (no).

Galván GC[1], Johnson CB[1], Price RS[2], Liss MA[3], Jolly CA[1], deGraffenried LA[1].
Effects of Obesity on the Regulation of Macrophage Population in the Prostate Tumor Microenvironment. Nutr Cancer. 2017 Sep 25:1-7. doi: 10.1080/01635581.2017.1359320.
Acknowledgement of federal support (no).

Presentations

Early Detection Research Network, National Cancer Institute

Title: Novel Prostate MRI Technique as a Prostate Cancer Screening Biomarker
Seattle, Washington, USA 9/13/2017
Acknowledgement of federal support (yes).

Books or other non-periodical, one-time publications.
None

Other publications, conference papers, and presentations
Poster presentation entitled ” Incorporation of Novel MRI and Biomarkers into Prostate Cancer Active Surveillance Risk Assessment” at DOD IMPACT meeting in Baltimore, MD on August 5, 2016.

7 PARTICIPANTS & OTHER COLLABORATING

ORGANIZATIONS What individuals have worked on the project?

Name:	*Michael A. Liss, M.D., M.A.S.*
Project Role:	*Principal Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*4.8*
Contribution to Project:	*Oversight: study design / development / implementation*
Funding Support:	

Name:	Kerri Kendrick, P.A.
Project Role:	Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3.4
Contribution to Project:	IRB approval, patient enrollment, organization of patient MRI and follow up.
Funding Support:	*Department of Urology departmental funds*

Name:	Allison Sherrill
Project Role:	Research Area Specialist
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1.2
Contribution to Project:	patient enrollment and data management
Funding Support:	*Department of Urology departmental funds*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

No, complete, active other support is provided in the appendices.

What other organizations were involved as partners?

Organization Name: Audie L. Murphy Veterans Hospital San Antonio
Location of Organization: *San Antonio, Texas*
Partner's contribution to the project *Providing patients for enrollment, supporting protected research time*
In-kind support *Dedicated research time*
Facilities: clinic space for recruitment, use of VA computers

Organization Name: University of California San Diego
Location of Organization: *San Diego, California*
Partner's contribution to the project *Providing sequence data for the generation of the RSI MRI and providing a quality check of the scans.*
Facilities: Multi-model Imaging Laboratory, Off site
Collaboration: David Karow, Nathan White, and Anders Dale

8 SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:
Not Applicable

QUAD CHARTS:
Not Applicable

9 APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text.*

Other Support – Michael Liss
Annotated SOW
Certificate in Translational Research acceptance letter
Prostate MR Imaging Symposium schedule
ARRS CME Transcript PASS
publication SABOR publication
IMPACT 2016 Poster

Other Support
MICHAEL A. LISS, M.D., MAS
CURRENT

Title	**Transitional Care of Service Members with Genitourinary Injury**
Role	PI
Time Commitments	1%
Supporting Agency	UTHSCSA IIMS Pilot Award
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris G. Green, CPA, Office of Sponsored Programs, 7703 Floyd Curl Drive, San Antonio, TX 78229
Performance Period	09/01/2016-12/31/2018
Level of Funding	$31,560
Brief description of the project's goals List of Specific Aims	This study will be the first to address genitourinary trauma access to care issues and propose solutions regarding veterans transitioning to Veteran's Affairs Health System. Aim 1: To identify the characteristics and access to care patterns of veterans that sustained battlefield genitourinary injuries. Aim 2: To identify areas of improvement in the initial assessments and management of veterans with genitourinary injuries during transition to care in the Veteran's Affairs Health System.
If overlap with other existing and pending research projects; if none state "None"	None

Title	**Prostate MRI as a Screening Tool to Detect Prostate Cancer**
Role	PI
Time Commitments	1%
Supporting Agency	UTHSCSA CTRC CPPS Pilot Award
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris G. Green, CPA, Office of Sponsored Programs, 7703 Floyd Curl Drive, San Antonio, TX 78229
Performance Period	11/01/2014-06/14/2017
Level of Funding	$25,000
Brief description of the project's goals List of Specific Aims	The project is currently assessing novel MRI software to improve cancer detection in men undergoing either their first prostate biopsy or a repeat prostate biopsy in men with low-grade prostate cancer on active surveillance. The novel MRI is faster and does not require IV contrast material. The study compares the new software to traditional multi-parametric MRI to determine if the information obtained is similar or better so that future studies could be less invasive and costly.
If overlap with other existing and pending research projects; if none state "None"	None

Title	**Incorporation of Novel MRI and Biomarkers Into**

	Prostate Cancer Active Surveillance Risk Assessment, W81XWH-15-1-0441
Role	PI
Time Commitments	40%
Supporting Agency	Department of Defense/U.S. Army Medical Research and Materiel Command Congressionally Directed Medical Research Programs
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Kathy Robinson, Contracting Officer, 301-619-8803, Kathy.e.robinson.civ@mail.mil
Performance Period	09/01/2015 – 06/30/2019
Level of Funding	$561,600
Brief description of the project's goals List of Specific Aims	The award provides salary support to engage in additional training in incorporating translational research into clinical trials. No money is allocated to research endeavors as this is a career development award. A novel MRI is being utilized in men prior to active surveillance biopsy to test accuracy and utility of the novel technique. As the training component I will earn a certificate of translational research from UTHSCA to augment my Masters in Applied Science in Clinical Research. As a mentorship component, Dr. Thompson will guide me in clinical trials research and offer assistance to gain access to SWOG and the workings of current clinical trials. Dr. Fox is the director of the Research Imaging Institute at UTHSCSA and will mentor my imaging component.
If overlap with other existing and pending research projects; if none state "None"	None

Title	**Relationship of the Intestinal Microbiota and Benign prostatic hypertrophy**
Role	PI
Time Commitments	1%
Supporting Agency	UTHSCSA Department of Urology
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Gabe Hernandez, Vice Dean for Finance, 7703 Floyd Curl Drive, San Antonio, TX 78229
Performance Period	03/01/2016-02/28/2017
Level of Funding	$25,000
Brief description of the project's goals List of Specific Aims	In this proposal we seek to investigate various aspects of intestinal microbiota and its potential influence of BPH as a pilot study for future funding.
If overlap with other existing and pending research projects; if none state "None"	None

Title	**ARLG-ESI: Microbiota Colonization in the Presence of Intestinal Fluoroquinolone Resistant E. coli, UM1 AI104681-04**
Role	PI
Time Commitments	1%

Supporting Agency	Duke University
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Keri R Baum, Clinical Research Associate Clinical Operations, Antibiotic Resistance Leadership Group (ARLG). Duke Clinical Research Institute (DCRI), 2400 Pratt Street, Durham, NC 27703 Office (919) 668-8681, Keri.baum@duke.edu
Performance Period	06/01/2016-11/30/2017
Level of Funding	$63,000
Brief description of the project's goals List of Specific Aims	Primary object is to identify the relative abundance for 27 genera, which represent a mean bacterial abundance in patients with and without fluoroquinolone resistance.
If overlap with other existing and pending research projects; if none state "None"	None

Title	**Rapid PCR to Guide Antibiotic Therapy at the Time of Prostate Biopsy, R03HS024810**
Role	PI
Time Commitments	2%
Supporting Agency	Agency for Healthcare Research and Quality/DHHS
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Brian Campbell, brian.campbell@ahrq.hhs.gov, 301-427-1266, 5600 Fishers Lane, Rockville, MD 20857
Performance Period	07/01/2016-12/31/2017
Level of Funding	$100,000
Brief description of the project's goals List of Specific Aims	In this proposal, we evaluate the use of a rapid test to detect the presence of a strain of bacteria that is a major cause of infection after a prostate biopsy.
If overlap with other existing and pending research projects; if none state "None"	None

If overlap with other existing and pending research projects; if none state "None"	None

Training Goals

Major Task 1: *T1 Translational Research*	**Percent Complete Or Tasks Completed**
Subtask 1: Certificate in Translational Research	11/16 Hours Currently enrolled in 3 hrs
Subtask 2: Seminars in Translational Research symposium	Not Attended due to schedule conflicts
Subtask 3: Translational Researcher Awareness Program	10/60 (17%) articles reviewed
Subtask 4: Mentorship of Residents	Resident 1st author manuscripts 1 Accepted 2 Submitted 2 Writing
Subtask 5: Case Presentations at GU Oncology Conference	Every Other Friday
Major Task 2: Clinical Trial Education	
Subtask 1: SWOG Young Investigators Training Course	1. SWOG Study Champion for ECOG EA8171 Multiparametric MRI (mpMRI) for Preoperative Staging and Treatment Planning for Newly-Diagnosed Prostate Cancer 2. Elected Jr. Investigator with Guru Sonpavde on a PDL-1 trial within SWOG
Subtask 2: **SABOR** biomarker study	SABOR food frequency Questionnaire (pending)
Subtask 3: Prostate Active Surveillance Study (PASS)	PASS MRI manuscript (pending)
Major Task 3: MRI Biomarker and Risk Assessment	
Subtask 1: Prostate MR Imaging National Meetings	American Urological Association Annual Meeting March, 14, 2017 Boston, MA, USA Prostate MRI Courses
Subtask 2: Formal course work in MRI	Not Completed
Subtask 3: Attend the SWOG Imaging Committee	Chicago 9/2016 San Francisco 3/2017

Mentoring Specific Tasks

Major Task 1: ***Incorporation into leadership roles (Dr. Thompson)***	**Percent Complete Or Tasks Completed**
Subtask 1: Lead CTRC GU Working Group	Complete, Continued
Subtask 2: SABOR data collection and biomarker requests	Complete, Continued
Subtask 2: SWOG GU Committee	Complete, Continued
Subtask 3: PASS Meeting	Complete, Continued
Milestone(s) Achieved: Attendance at Meetings	100% for SWOG, Missed 1 PASS meeting due to sisters wedding.
Major Task 2: ***MRI Image Analysis (Dr. Fox)***	
Subtask 1: Present for acquisition of MRI and data collection	Complete, Continued
Subtask 2: Interaction with Imaging Scientists	Complete, Continued
Milestone(s) Achieved: Give a summary MRI lecture at Grand Rounds	Yearly Starting 1/20/2017

Research-Specific Tasks:

Specific Aim 1: Prostate MRI to predict cancer progression in men on active surveillance	**Percent Complete Or Tasks Completed**
Major Task 1: Clinical trail initiation	
Subtask 1: Complete IRB	Completed
Subtask 2: Incorporate imaging protocols of mpMRI and RSI MRI	Completed
Subtask 3: Patient enrollment	Enrolled 68 Patients
Specific Aim 2: Biomarker testing to predict active surveillance outcomes.	
Major Task 2: Serum PSA, Free PSA, and biopsy tissue collection and storage logistics	
Subtask 1: Serum Banking	With enrollment
Subtask 2: Complete material transfer sheets for NanoString and confirm logistics of transfer.	Completed
Subtask 3: Analysis of PSA biomarkers	Not started
Subtask 4: Identify a target gene for exploration in immunohistochemistry (IHC)	Not Started
Specific Aim 3*:* Incorporation of Imaging and Biomarker data into the PROMISS calculator.	
Major Task 3: Incorporation of Imaging and Biomarker data into the PROMISS calculator.	
Subtask 1: Incorporation of Imaging and Biomarker data into the PROMISS calculator.	Not Started
Subtask 2: Manuscript Preparation	Started

American Urological Association

Certificate of Credit

The American Urological Association certifies that **Michael A. Liss, MD** has participated in the live activity titled below at the location and on the date(s) indicated below and is awarded **3.00** *AMA PRA Category 1 Credits™*.

Code	Title	Location	Date	*AMA PRA Category 1 Credits™*
16SAN102HO	MR Fusion Guided Prostate Biopsy 2: Refining Techniques for the Advanced User	San Diego, CA	5/7/16	3.00

Accreditation
The American Urological Association is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Victor Nitti, M.D.
Chair, Office of Education

Shelby Englert
Director, Office of Education

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