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PRINCIPAL INVESTIGATOR:	Michael A. Liss, M.D., M.A.S.
CONTRACTING ORGANIZATION:	University of Texas Health Science Center San Antonio
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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 am 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. 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 has mentored my entry into the NCI-Early Detection Research Network. 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. I also was awarded the NCI Cancer Clinical Investigator Team Leadership Award (CCILTA) and the VA NAVIGATE award to increase NCTN clinical trials at the South Texas Veterans Affairs Healthcare System.

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 the 12 credit hours to complete the program. I decided to continue my education by transferring the credits to Ph.D. program. I was accepted to the **Translational Science Ph.D.** at through a joint program between UT Austin, UT Health San Antonio, and UT San Antonio beginning in the Fall 2018 semester and have requested a no cost extension to finish this work. My home institution for the PhD program is UT Austin and my mentor is John DiGiovanni in the College of Pharmacy. I have completed 17 credit hours of courses towards this PhD. I have completed all 8 domains of translational science to include translational science, responsible conduct, research methods, research analysis, leadership, cultural proficiency, communication and business of translational science. I passed my written qualifying exam and on September 3rd, 2019 I completed and passed

my verbal exam and proposal defense. I was officially accepted as a Ph.D. Candidate on Monday September 9th, 2019. I plan to complete all remaining coursework by the end of Fall Semester 2020. Additionally, I have completed the **Translational Researcher Awareness Program** (TRAP) with Dr. Thompson.

I became a member of the Mays Cancer Center at UT Health San Antonio in 2015 and have remained heavily involved with the GU Working group. In addition, I joined SWOG in 2016 and have attended all semi-annual meetings for the past 3 years. 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 led 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 4 years and we have already been selected as an **NCI Cancer Trials Support Unit - High Performance Site Initiative** for our four year in a row**.**

I was awarded the NCI Cancer Clinical Investigator Team Leadership Award in Sept 2018. This award is a two year supplement to our cancer center's P30 award and will remain active until the end of July 2020. As Cancer Clinical Investigator Team Leader, my role is to promote team science by working with clinical investigators and translational scientists to enhance the cancer center's capability to develop and engage in scientifically well designed and critical biomarker studies in clinical trials.

In addition, I have been involved in the Prostate Active Surveillance Study (PASS) and am currently the site principal investigator for this study. I developed the MRI data collection forms with statisticians at Fred Hutchison Cancer Research Center and have expanded enrollment to our South Texas Veterans Hospital. We submitted a proposal to NCI and were awarded a U01 in which I am the site principal investigator for UT Health San Antonio.

I attended the annual meeting at Stanford University on September 26, 2019 and discussed PASS MRI project along with implications of this DOD grant on what we can validate in the PASS cohort. I also provided an update on a project. This study allows me to learn the collaborative nature of multi-disciplinary research in a multi-institutional, prospective prostate cancer cohort.

I have also become involved 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. I have personally been involved in over 300 exams and enrollments. 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. This has allowed me to learn about prostate cancer biomarkers, management of a longitudinal cohort, long-term regulatory issues, and has allowed me to be part of EDRN. I recently became an Associate Member of the EDRN and expanding my networking and collaborators. In order to further investigate the influence of Restricted Spectrum Imaging and Inflammation of prostate cancer, I applied and received additional funding from EDRN in September 2018 for 2 years to explore these questions.

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 incorporated medical students, residents, and fellows into research and are actively publishing manuscripts with them.

Mentoring:

SWOG: Dr. Thompson has provided opportunities within our cancer center and SWOG for involvement and leadership roles including the site principal investigator for SWOG. I am one of the very few surgeons to hold this title. I have a 6/8ths appointment at our South Texas Veterans Healthcare System and have been encouraging clinical trial enrollment. I have successfully competed for support from the Hope Foundation-SWOG VA Integration program to start SWOG clinical trials program at our VA. This led to a large effort to obtain NCI IRB and organize our site to successfully compete for the new NAVIGATE program grant which integrates the NCTN trials from the NCI to the VA. I also have been chosen to be the SWOG champion of EA8171 entitled "Multiparametric MRI (mpMRI) for Preoperative Staging and Treatment Planning for Newly-Diagnosed Prostate Cancer." These have been initiated at the VA and we are currently enrolling in trials.

NCI-EDRN: I have successfully been incorporated in each of these cohorts and am able to utilize the for future research questions. I also have successfully competed for a position as an Associate Member of the National Cancer Network Early Detection Research Network (EDRN). My project is to extend my current project into detection of false positive lesions using the network to help with grading inflammation on pathology and access to developing biomarkers. Additionally, I assisted with protocol development of a new EDRN Prostate MRI study that will enroll men prior to initial prostate biopsy with an MRI and include various collection techniques for biomarker assessment led by John Wei M.D. at the University of Michigan. We have completed the design and now are embarking on the trial to start in the next few months.

PASS/SABOR: I am now the site-PI for the Canary Prostate Active Surveillance Study (PASS) and is a longitudinal, observational study of men on active surveillance. PASS participants also qualify for the research project supported by the DOD Physician Training Grant. Moreover, I helped design the MRI imaging case report forms nearly 2 years ago and we will be writing the results soon regarding the implications of prostate MRI in the active surveillance population. We are in the final process of approval from PASS and I plan to submit to Journal of Urology in the next month. I am also the Co-Investigator with Dr. Thompson on the San Antonio Biomarkers of Risk (SABOR) cohort which has allowed me to gather men as healthy controls. The cohort needs funding to continue so we will start investigating various avenues to investigate utilization of the SABOR screening cohort.

Research Imaging Institute: 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). We are now working with Anders Dale and Nate White at UCSD to upgrade the acquisition protocols after wen enrolled our 120th patient. Dr. Fox continues to be instrumental in facilitating the resolution of this issues and allowing me to utilize his staff regarding the maintenance of the MRI images in the XNAT platform for banking. We are also expanding our imaging cohort to side effects on the brain from androgen deprivation therapy and seek to put in an R01 with a multidisciplinary team in February 2020.

Associated Mentors: 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, Dr. Ronald Rodriguez is a mentor and Chair of the Department of Urology has continued to be very supportive of my research and training goals.

Academic Promotion: I was promoted Associate Professor of Urology in September 2018. I have no doubt that this research grant has assisted me in this process. I also won the UT Health San Antonio **Presidential Distinguished Junior Research Scholar Award 2019**.

Research:

Despite initial delays in implementation due to the different MRI hardware systems at UCSD and UTHSCSA in the first year, we have successfully implemented the acquisition portion of the RSI MRI. We have utilized the initial RSI processing but has since undergone some upgrading. We did enroll 123 patients thus far. We have made progress and have finalized the RSI grading as well as Apparent Diffusion Coefficients (ADC's) to compare RSI to traditional DWI methods. I have been able to share this data with UCSD and Moffit who will conduct additional "Habitat" scoring of the images.

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.

Blood-based biomarkers: We will run PSA and likely discuss the newer blood based biomarkers with EDRN for biomarker discovery in that prostate health index (PHI; PSA, free PSA and [-2] proPSA) has been shown to have some relevance. Dr. Dan Chan at John's Hopkins ran the Phi testing along with help from Beckman-Kolter grant that supplied the reagents for the test.

Urine-based biomarkers: We collaborated with Arul Chinnaiyan M.D. Ph.D. at the University of Michigan to utilize there novel MiPS biomarker and include T2:Erg fusion status and PCA3 testing.

Tissue 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. After discussion with them via phone conversation, it was felt this process would be dropped do to very small amounts of tissues and would be best to target tissue processing with a specific hypothesis rather than hypothesis generating approach.

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

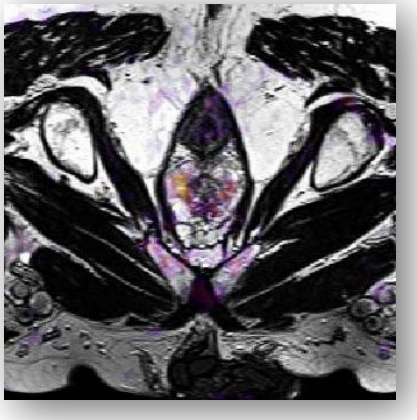


Figure 1: RSI-MRI imaging performed at UTHSCA Research Imaging Institute. Yellow/Red indicates high suspicion of tumor.

Figure 2

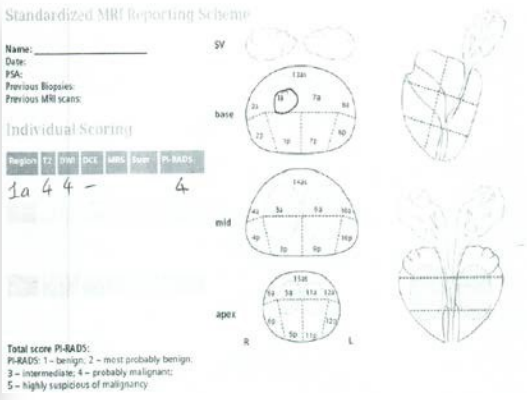


Figure 2: Radiology reading report in the same patient indicated a lesion in the same location given a PI-RADS 4 score.

Figure 3

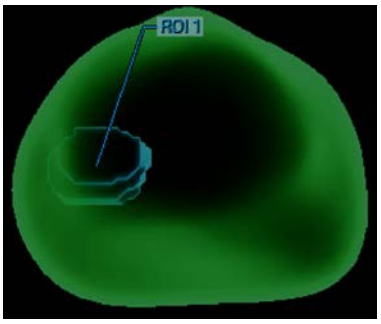
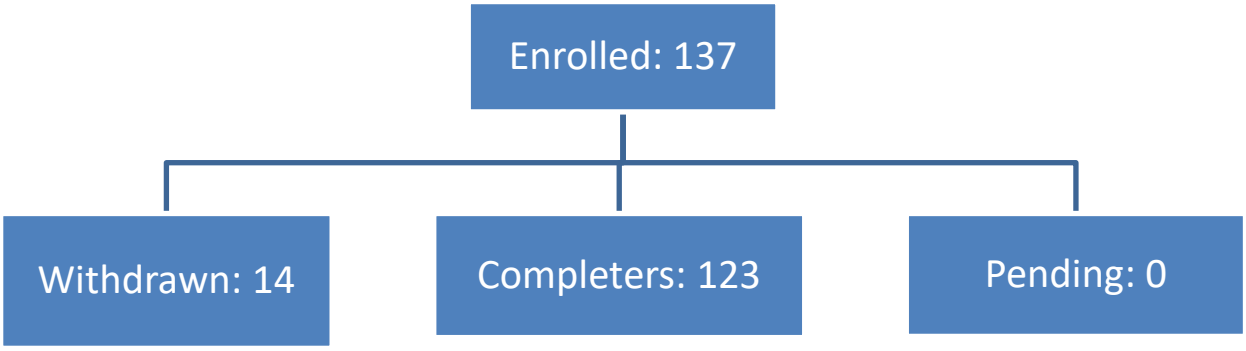


Figure 3: Three-dimensional rendering of the prostate utilizing the RSI-MRI then DynaCAD software for targeted prostate biopsy with Gleason 3+4 cancer.

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 137 subjects to obtain an MRI and prostate biopsy.

Figure 1: Flow Diagram



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 have 111 evaluable patients and will import the MRI data soon. As for the biomarker evaluation, T2:ERG fusion status seemed to be the strongest predictor of prostate cancer upgrading among Phi, PCA3 and genetic risk score. T2:ERG also outperformed the conglomerate MiPS test for high risk cancer that combines many tests with PCA3.

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. Moreover, we may be able to improve MRI to reduce false positives on MRI that lead to unnecessary biopsies. RSI and biomarkers could allow for the distinction of high grade, lethal tumors from low grade, non-lethal tumors to better inform clinical care.

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. I also have been nominated as an **Associate Member of NCI-EDRN** and promoted to **Associate Professor** in just 4 years.

How were the results disseminated to communities of interest?
American Urologic Association Annual Meeting on 5/19/2018 – Best poster award
EDRN meeting in Boston, A on 9/5/2018

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 – **Accomplished**
    - John Semmes Lab has samples and is performing Proteomics on urine samples looking for PSA variants
    - Moffit Cancer Center has access to images to perform habitat scoring.
d. Continue TRAP article review with mentors – **Accomplished**
    - Completed

e. Attend national MRI conference / workshop – **Accomplished**
    - Won Best Poster at American Urological Association (MP20-06 - FALSE POSITIVE LESIONS ON MRI FUSION PROSTATE NEEDLE BIOPSY AND INFLAMMATION) May 18, 2018.
f. Continue Certificate in Translational Science coursework – **Accomplished**
g. Transitioned into Translational Science Ph.D. - Ongoing

My plans for the next period include:

a. Aggressive pursuit of funding for MRI and biomarker studies
    a. PAR 18-009 - Academic-Industrial Partnerships to Translate and Validate in vivo Cancer Imaging Systems (R01 Clinical Trial Optional) – Submitted and Not Discussed
    b. PAR 16-089 0- Imaging and Biomarkers for Early Detection of Aggressive Cancer (U01) – Plan for December 2019 Submission

b. Present findings at national meetings
    - American Urological Association (AUA)
    - Genitourinary American Society of Clinical Oncologists (GU ASCO)

c. 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 but rapidly approaching conclusion. I will be able to utilize this study to slecet the best biomarker for the R01, but has also opened many collaborations across the nation. These collaborations have led to increase speed in biomarker development and implementation of biomarkers along with imaging into active surveillance strategies. Based on our current subjects, the MRI seems to have value in men with low-grade prostate cancer on active surveillance. 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. More recently, we have formed a transdisciplinary team to add bioinformatics, genetics, proteomics and other team members that will accelerate biomarker discovery.

What was the impact on technology transfer?

Part of the team at UCSD has formed a company looking to transfer there intellectually protected property to market. We did not have any role in the technology but only the utilization of the technology in human prostate cancer to test its applicability. We have formed a close relationship with them and look forward in being a future testing site of the commercial version of the software, which is the topic of an upcoming R01 we will apply for jointly.

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?
More investment into education for the Translational Science Ph.D. courses.

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.
1. Rourke E, Sunnapwar A, Mais D, Kukkar V, DiGiovanni J, Kaushik D, Liss MA. Inflammation appears as high Prostate Imaging-Reporting and Data System scores on prostate magnetic resonance imaging (MRI) leading to false positive MRI fusion biopsy. Investig Clin Urol. 2019 Sep;60(5):388-395. doi: 10.4111/icu.2019.60.5.388. Epub 2019 Jul 30. PMID: 31501802

2. Liss MA, Al-Bayati O, Gelfond J, Goros M, Ullevig S, DiGiovanni J, Hamilton-Reeves J, O'Keefe D, Bacich D, Weaver B, Leach R, Thompson IM. Higher baseline dietary fat and fatty acid intake is associated with increased risk of incident prostate cancer in the SABOR study. Prostate Cancer Prostatic Dis. 2019 May;22(2):244-251. doi: 10.1038/s41391-018-0105-2. Epub 2018 Nov 1. PMID: 30385837

Pending:

1. Canary PASS MRI study

2. Ankerst – Family History and prostate cancer calculator

Presentations

American Urological Association Annual Meeting
MP 19-3790
Assessment of MRI Performance in the Canary Prostate Active Surveillance Study (PASS)
Michael Liss*, San Antonio, TX, Michael Garcia, Yingye Zheng, Lisa Newcomb, Seattle, WA, Christopher Filson, Atlanta, GA, Hilary Boyer, Seattle, WA, James Brooks, Stanford, CA, Peter Carroll, San Francisco, CA, Martin Gleave, Vancouver, Canada, Francis Martin, Virginia Beach, VA, Todd Morgan, Ann Arbor, MI,

Peter Nelson, Seattle, WA, Andrew Wagner, Boston, MD, Ian Thompson, San Antonio, TX, Daniel Lin, Seattle, WAChicago, Illinois 5/2019
Acknowledgement of federal support (yes)

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

Other publications, conference papers, and presentations
none

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:	Allison Sherrill
Project Role:	Research Area Specialist
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	4.8
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?

Yes, 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

Other Support *(Italic font notes updates from the last year)*
MICHAEL A. LISS, M.D., MAS

PREVIOUS (award period of performance ending within the past 5 years)

Title	Relationship of the Intestinal Microbiota and Benign Prostatic Hypertrophy
Time Commitments	1%
Supporting Agency	UTHSCSA Department of Urology
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris Green; grants@uthscsa.edu
Performance Period	03/01/2016-02/28/2017
Level of Funding	$25,000
Brief description of the project's goals	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.
List of Specific Aims	Aim 1: To determine intestinal microbiome diversity associated with benign prostatic hypertrophy. Aim 2: To investigate biomarkers leading to symptomatic benign prostate hypertrophy.
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*
Time Commitments	*1%*
Supporting Agency	*UT Health San Antonio Cancer Center*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	*Chris Green; grants@uthscsa.edu*
Performance Period	*11/01/2014-06/14/2017*
Level of Funding	*$25,000*
Brief description of the project's goals	*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.*
List of Specific Aims	*Aim 1: A negative or low risk MRI can safely replace initial prostate biopsy to investigate elevated PSA. Aim 2: Comparison Prostate MRI risk prediction of prostate cancer risk compared to the Prostate Cancer Prevention Trial Risk Calculator.*
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
Time Commitments	1%
Supporting Agency	Duke University
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Jennifer McCallister; Jennifer.mccallister@duke.edu
Performance Period	06/01/2016-11/30/2018
Level of Funding	$48,199
Brief description of the project's goals	Primary object is to identify the relative abundance for 27 genera, which represent a mean bacterial abundance in patients with and without fluoroquinolone resistance.
List of Specific Aims	Aim 1: Comparing the fecal microbiome in men with and without FQR organisms prior to prostate biopsy. Aim 2: Identify additional fluoroquinolone resistant *E. coli* clonal groups.
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
Time Commitments	2%
Supporting Agency	Agency for Healthcare Research & Quality
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Brian Campbell; brian.campbell@ahrq.hhs.gov
Performance Period	07/01/2016-12/31/2018
Level of Funding	$79,365
Brief description of the project's goals	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.
List of Specific Aims	Aim 1: Assess the impact of a rapid qPCR guided point-of-care test on antibiotic choices for prostate biopsy prophylaxis. Aim 2: Impact of implementation of a point of care test on healthcare system and clinic flow.
If overlap with other existing and pending research projects; if none state "None"	None

Title	An Interventional Study to Reduce Folate Levels in Men on Active Surveillance for Prostate Cancer
Time Commitments	1%
Supporting Agency	UT Health San Antonio Mays Cancer Center
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris Green; grants@uthscsa.edu
Performance Period	08/15/2016-01/31/2019
Level of Funding	$52,081

Brief description of the project's goals	Results in the laboratory strongly implicate dietary folate/folic acid intake in the promotion of prostate cancer. The goal of this study is to determine if dietary education can reduce red blood cell and serum folate levels in men under active surveillance for prostate cancer to provide preliminary data for a future clinical intervention.
List of Specific Aims	
If overlap with other existing and pending research projects; if none state "None"	None

Title	Transitional Care of Service Members with Genitourinary Injury
Time Commitments	0%
Supporting Agency	Military Health Institute
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris Green; grants@uthscsa.edu
Performance Period	09/01/2016-09/30/2018
Level of Funding	$50,000
Brief description of the project's goals	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.
List of Specific Aims	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	*The Virome Effect on Immune Function in the Tumor Microenvironment*
Time Commitments	*1%*
Supporting Agency	*San Antonio Area Foundation*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	*Lydia Saldaña, Program Officer, lsaldana@saafdn.org*
Performance Period	*03/01/2018-02/28/2019*
Level of Funding	*$30,680*
Brief description of the project's goals	*Our research explores how the microbiome (viruses in particular) impact cancer outcomes.*
List of Specific Aims	*Aim 1: To compare the virome diversity between tumor and normal adjacent tissue in various ethnicities.* *Aim 2: To determine the correlation between virome profile and potential impact on the immune system.*
If overlap with other existing and pending research projects; if none state "None"	*None*

Title	*2017 SWOG/Hope VA Integration Support Program*
Time Commitments	*0%*
Supporting Agency	*The Hope Foundation*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	*Johanna Horn, jo@thehopefoundation.org*
Performance Period	*01/01/2018-12/31/2018*
Level of Funding	*$24,270*
Brief description of the project's goals	*The grant is to provide funding to initiate SWOG clinical trials at VA centers and increase enrollment of United States Veterans into NIH clinical trials. The support has been approved by VA pharmacy, nursing, chief of staff, and ACOS for research. Funds will provide a research coordinator time for enrollment and regulatory with close communication with our cancer center.*
List of Specific Aims	
If overlap with other existing and pending research projects; if none state "None"	*None*

CURRENT

Title	Incorporation of Novel MRI and Biomarkers Into Prostate Cancer Active Surveillance Risk Assessment, W81XWH-15-1-0441
Time Commitments	40%
Supporting Agency	Department of Defense (DOD)
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Kathy Robinson; Kathy.e.robinson.civ@mail.mil
Performance Period	09/01/2015-8/31/2020 (NCE)
Level of Funding	$520,000
Brief description of the project's goals	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 master's in applied science in Clinical Research.
List of Specific Aims	
If overlap with other existing and pending research projects; if none state "None"	None

Title	Clinical Trial of Angiotensin Receptor Blockers in the Treatment of Stage 1 Renal Cancer: A Pilot Study
Time Commitments	1%
Supporting Agency	San Antonio Cancer Council /CTRC
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Chris Green; grants@uthscsa.edu

Performance Period	12/01/2016-02/24/2020
Level of Funding	$21,473
Brief description of the project's goals	In this pilot study, we seek to use an angiotensin receptor blocker (ARB) commonly used for hypertension and to prevent chronic kidney disease in diabetic patients to potentially slow the growth of small renal masses and avoid aggressive interventions. We have selected a small pilot study in order to guide medication dose (50mg vs. 100mg), imaging, and biomarker selection for implementation in a larger randomized clinical trial.
List of Specific Aims	
If overlap with other existing and pending research projects; if none state "None"	None

Title	LOngitudinal Study for Prostate cAncer Determinants of RESistance
Time Commitments	1%
Supporting Agency	Los Padres Prostate Cancer Foundation
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	Johnny and Joni Reyna, 8637 Fredericksburg Road, Suite 100, San Antonio, TX 78240
Performance Period	12/01/2017-12/01/2018
Level of Funding	$25,000
Brief description of the project's goals	Los Padres is a San Antonio based prostate cancer charitable foundation interested in prolonging quality life for prostate cancer patients.
List of Specific Aims	Aim 1: To determine genetic biomarkers of resistance to prostate cancer therapy and identify therapeutic targets. Aim 2: Initiate an investigation into microbial interactions and the immune system in prostate cancer.
If overlap with other existing and pending research projects; if none state "None"	None

Title	***CTRC Clinical Investigator Team Leadership Award***
Time Commitments	*15%*
Supporting Agency	*National Institutes of Health/NCI*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	*Dr. Jennifer Hayes, Program Director, hayesjf@mail.nih.gov*
Performance Period	***08/01/2018-07/31/2020***
Level of Funding	*$76,686*
Brief description of the project's goals	*The Cancer Clinical Investigator Team Leadership Award (CCITLA) is an administrative supplement award which recognizes and supports outstanding clinical investigators with records of developing and promoting a culture of successful clinical research.*
List of Specific Aims	

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

Title	*Early Detection of Castration-Resistant Prostate Cancer by Assessing Interactions Between Circulating Tumor Cells and Accompanying Immune Cells*
Time Commitments	*1.5%*
Supporting Agency	*DOD/CDMRP*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	
Performance Period	*09/01/2018 – 08/31/2021*
Level of Funding	*$915,000*
Brief description of the project's goals	*To develop a procedure to early identify CR patients with a risk score based on mechanical/ immunocytochemical profiling of blood-isolated cells. For its future clinical use, collection and analysis of cells' mechanical parameters, vetted for essentiality in this study, will be condensed into a bed side device. Specific Aims: 1 – We will determine the role of EMT in mechanical fitness of CTCs by measuring their mechanical properties with atomic force microscopy (AFM). We will recapitulate the EMT in cell culture to follow mechanical fitness related biophysical and gene expression changes in model CTCs. Aim 2 – We will define the role of CTC-macrophage interactions in mechanical fitness of CTCs. We will classify the macrophage populations and determine mechanical and gene expression phenotypes of interacting CTCs. We will recapitulate the interactions in cell culture and follow phenotypic changes in model CTCs contacting macrophages. Aim 3 - We will construct a model for patients' stratification predicting the risk of castration resistance based on the mechanical fitness of CTCs collected before the start of ADT.*
List of Specific Aims	
If overlap with other existing and pending research projects; if none state "None"	*None*

Title	*Biomarkers with MRI Targeted Biopsy for Prostate Cancer in Men on Surveillance*
Time Commitments	*1%*
Supporting Agency	*National Institutes of Health/EDRN*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	*Dr. Christos Patriotis, Program Director, patriotisc@mail.nih.gov*
Performance Period	*04/01/2018-03/31/2020*
Level of Funding	*$100,000*
Brief description of the project's goals	*We plan to investigate imaging as a biomarker in an active surveillance cohort with multi-parametric MRI imaging along with a novel Restricted Spectrum Imaging (RSI).*

List of Specific Aims	*Aim 1: To determine the predictive ability of any biomarker to compared to MRI imaging level of suspicion. Aim 2: Determine the best biomarker or biomarkers that predict cancer progression on active surveillance.*
If overlap with other existing and pending research projects; if none state "None"	*None*

Title	*SPOP Mutant Prostate Cancer as a Therapeutic Target in Castration Resistant Prostate Cancer*
Time Commitments	*1%*
Supporting Agency	*UTHSCSA Mays Cancer Center*
Name & Address of the Funding Agency's procuring Contracting/Grants Officer	
Performance Period	*06/15/2018-06/14/2020*
Level of Funding	*$10,000*
Brief description of the project's goals	*We therefore propose that hyperactivated GLI3-dependent SHH signaling drives castration-resistant growth of SPOP mutant tumors, suggesting that SHH pathway inhibitors might prove effective to block CRPC in this prostate cancer subtype.*
List of Specific Aims	
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	Completed
Subtask 2: Seminars in Translational Research symposium	Completed
Subtask 3: Translational Researcher Awareness Program	60/60 (100%) articles Completed
Subtask 4: Mentorship of Residents	Completed
Subtask 5: Case Presentations at GU Oncology Conference	Continuous
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 3. Leading NAVIGATE to increase NCI trials at VA.
Subtask 2: **SABOR** biomarker study	SABOR food frequency Questionnaire Submitted to PCAN
Subtask 3: Prostate Active Surveillance Study (PASS)	PASS MRI manuscript Needed to wait for maturing data, pulling data this week.
Major Task 3: MRI Biomarker and Risk Assessment	
Subtask 1: Prostate MR Imaging National Meetings	American Urological Association Annual Meeting May, 2018 San Francisco, USA 1. Presentation 2. Prostate MRI Courses
Subtask 2: Formal course work in MRI	Not Completed
Subtask 3: Attend the SWOG Imaging Committee	Chicago 9/2017 San Francisco 3/2018 Chicago 10/2018

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 90% for PASS Contribute to SABOR Weekly
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 106 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