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TITLE: Evaluation of Lipid Poor Renal Masses with Magnetic Resonance Spectroscopy in Tuberous Sclerosis Complex

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14. ABSTRACT The Research Project supported by this DOD Award investigates the potential of <i>in vivo</i> and <i>ex vivo</i> MRS in characterizing the metabolomic spectra of TSC-associated renal masses. In an effort to optimize our <i>in vivo</i> image acquisition protocol, we began by scanning healthy volunteers and have formalized our novel <i>in vivo</i> MRS protocol, which will be submitted for publication. Subsequently, our overall enrollment of TSC patients with lipid poor renal masses has been lower than expected. For this reason and in order to meet our goals of gaining more metabolomic data on renal masses, we have expanded our subjects to include TSC patients with lipid rich masses, non-TSC patients with lipid poor and lipid rich renal masses. We continue to enroll patients and analyze our current and ongoing data. Our analysis cohort also will be expanded with the utilization of our genitourinary oncology tumor bank, including AML and other renal tumor tissue. The findings from this study will help the TSC community gain an understanding of the metabolomics of AML and other renal tumors.					
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Introduction:

The Research Project supported by this DOD Award investigates the potential of *in vivo* and *ex vivo* Magnetic Resonance Spectroscopy (MRS) in characterizing the metabolomic spectra of Tuberous Sclerosis Complex (TSC)-associated lipid poor renal masses. We have hypothesized that MRS metabolomic profiling of lipid poor renal masses will provide clinical biomarkers to noninvasively differentiate benign from malignant tumors and can help predict the tumor grades and pathological stages defined by histopathology, thus improving decision making for patient care. This information is urgently needed in today's TSC clinic to help clinicians to assess the malignant potentials of specific tumors, improve prognostic accuracy, and select the most appropriate therapy for individual patients.

Keywords:

Tuberous Sclerosis Complex; Metabolomics; Kidney Cancer; Biomarker

Accomplishments:

- **What were the major goals of the project?**

There are three defined major goals of the project to be accomplished over the course of a 24 month period, with a 12 month no-cost extension:

Major Task 1: Administrative startup tasks; Subject recruitment (total n=80); *In vivo* MRI/MRS acquisition and interpretation, with correlation of MRS data with multiparametric MRI data; Histopathologic analysis of biopsy and surgical specimens; Correlation of *in vivo* MRS data with histopathology and clinical data.

Major Task 2: *Ex vivo* MRS performance on biopsy and surgical specimens; Correlation of *ex vivo* MRS data with histopathology and clinical data; Assess consistency of *in vivo* and *ex vivo* MRS metabolomic signatures and correlate signatures with tumor tissue assessment for mutations of the cellular metabolic pathway and direct measurement of

tumor metabolite levels.

Major Task 3: Correlation of *ex vivo* and *in vivo* MRS data; GC-MS and qRT-PCR of surgical tissue specimens; Correlation of all MRS, histopathologic and clinical data with GC-MS and qRT-PCR data.

What was accomplished under these goals?

General update:

We were given local IRB approval for the research project in January 2018. Subject enrollment began in February 2018 with patients recruited from the Urology Clinic at Massachusetts General Hospital. Given that there has been limited data in performing *in vivo* MRS of the kidney, healthy volunteers were first consented to the project to undergo *in vivo* MRS and help develop the imaging protocol for ultimate subject scans.

Since the project start, 17 research subjects have been consented and scheduled for multiparametric MRI and MRS of the kidneys. Ten of the subjects have confirmed diagnoses of Tuberous Sclerosis Complex, while 7 of the subjects have sporadic renal masses. Fifteen subjects have undergone clinically-indicated MRIs of the kidneys with the additional *in vivo* MRS sequence. Three have undergone clinically-indicated renal mass biopsy (RMB) with core biopsy specimens evaluated with *ex vivo* MRS immediately after RMB. Three subjects have had partial nephrectomies and had tissue evaluated with *ex vivo* MRS immediately after. Two subjects are scheduled to undergo MRI and MRS in the near future along their imaging follow-up protocol for their TSC care.

Given the slow rate of recruitment, we have and will continue to focus our efforts on consenting a greater volume of TSC and sporadic renal mass patients. One difficulty with recruitment has been that as a referral institution, many patients who we see have already had their appropriate renal mass imaging performed and therefore, an additional study cannot be justified in their clinical care. We also believe that it will be important to gain data on the MRS profile of lipid rich AML in addition to lipid poor masses so that we can better understand the normal metabolic spectra of AML and renal masses in general. For this reason, we will include imaging of lipid

rich lesions as well. These TSC patients will get periodic renal MRI as part of their routine screening, and therefore they are ideal candidates to include in this study. In addition, in order to improve our numbers and meet our goals of *ex vivo* analysis, we have initiated IRB approval process in order to take advantage of our previously collected and annotated MGH GU Oncology Frozen Tumor Bank. This tumor bank includes fresh frozen tissue from renal masses, including benign renal neoplasms, angiomyolipoma and RCC. We have previously tested and demonstrated (data not shown) that the metabolomic spectra are consistent between fresh and fresh frozen RCC and renal tissue. Therefore, we are confident that this can be used as a resource to investigate the metabolomic profiles of renal masses which are appropriate for this study. In addition, we are analyzing metabolomic spectra across patients to assess for any consistency in expression between tumor types.

Detailed info on *in vivo* work:

Seven subjects underwent clinically-indicated MRI of the kidneys with the additional *in vivo* MRS sequence during this reporting period. The routine multi-parametric renal MRI includes multiecho gradient-echo, diffusion weighted images with 3 b values (0, 500 and 1000) and dynamic enhanced images with temporal resolution of 6 seconds. Two single voxels (Volume of interest (VOI) = 2 x 2 x 2 cm³) are targeted over the area of interest for the *in vivo* MRS spectra. We ran prior axial and coronal imaging sequences with non-breath hold technique to use as references for the MRS sequences. Metabolic spectra of both the tumor(s) of interest and regions of benign parenchymal tissue were recorded and analyzed. We used a respiratory-gated Point Resolved Spectroscopy (PRESS) sequence with and without water suppression using TE/TR=135ms/1500ms and number of averages (NA) = 32 for the water-suppressed spectrum and NA = 4 for the water-unsuppressed sequence. .

In the first quarter of the year, there were three patients, one had a sporadic large 8cm AML requiring embolization, the second patient had a sporadic renal mass confirmed to be ccRCC on histopathologic analysis, and the final had a confirmed diagnosis of TSC with a history of bilateral AMLs and RCCs. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figs. 1-3).

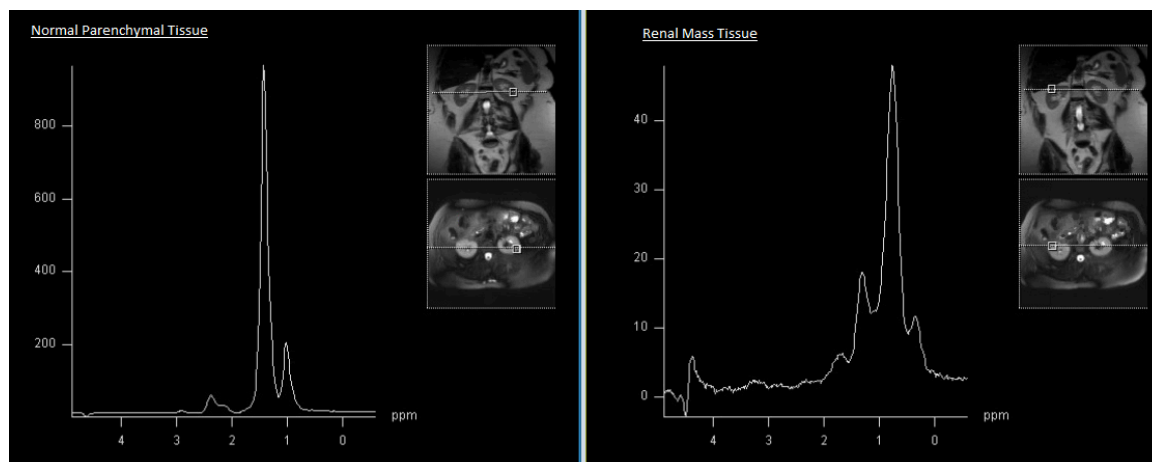


Figure 1: Example of in vivo MRS spectra from a patient without a history of TSC. The image on the left obtained with targeting of large angiomyolipoma requiring embolization. Image on the right obtained with targeting contralateral normal kidney tissue.

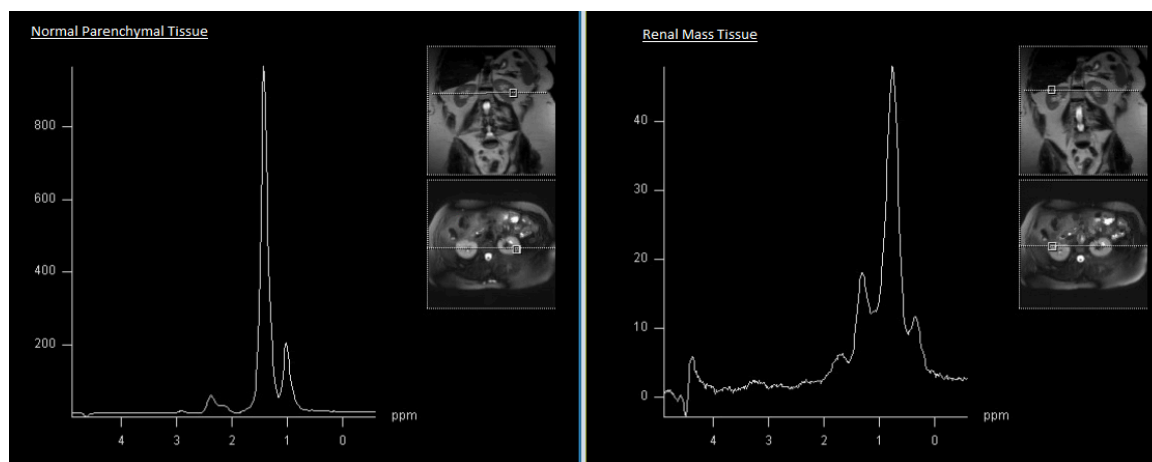


Figure 2: Example of in vivo MRS spectra from a single patient with sporadic renal mass, no history of TSC. The image on the right obtained with targeting of sporadic renal mass, RCC-likely due to radiographic evidence. Image on the left obtained with targeting contralateral normal kidney tissue.

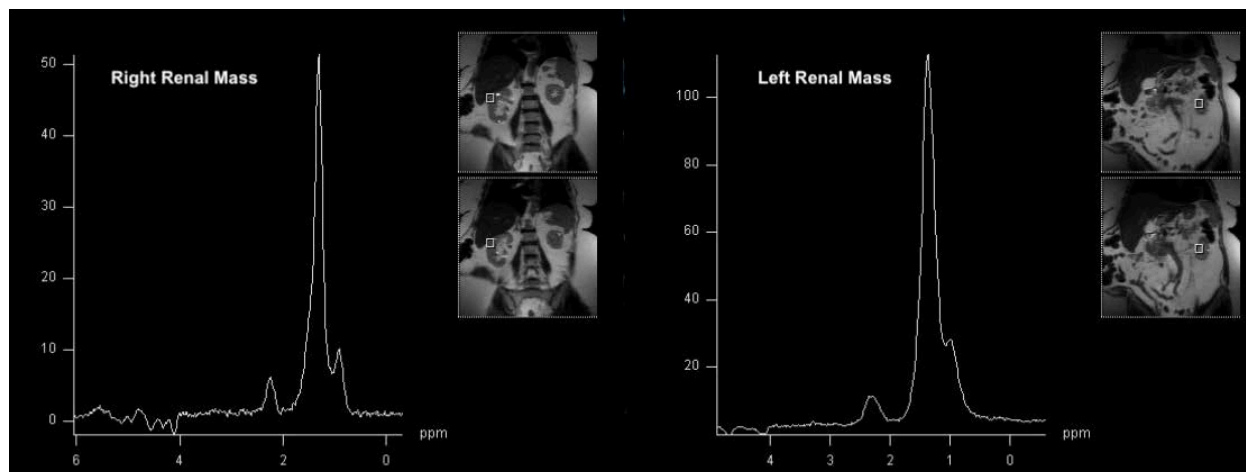


Figure 3: Example of *in vivo* MRS spectra from a single patient with history of TSC and bilateral renal AMLs and RCCs. The image on the left obtained with targeting the right renal mass. The image on the right obtained with targeting the left renal mass.

In the second quarter of the year, there were two patients, one had no history of TSC with a 2.8 cm left renal neoplasm scheduled for partial nephrectomy, and the second patient had a confirmed diagnosis of TSC with a history of numerous bilateral AMLs. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figs. 4-6).

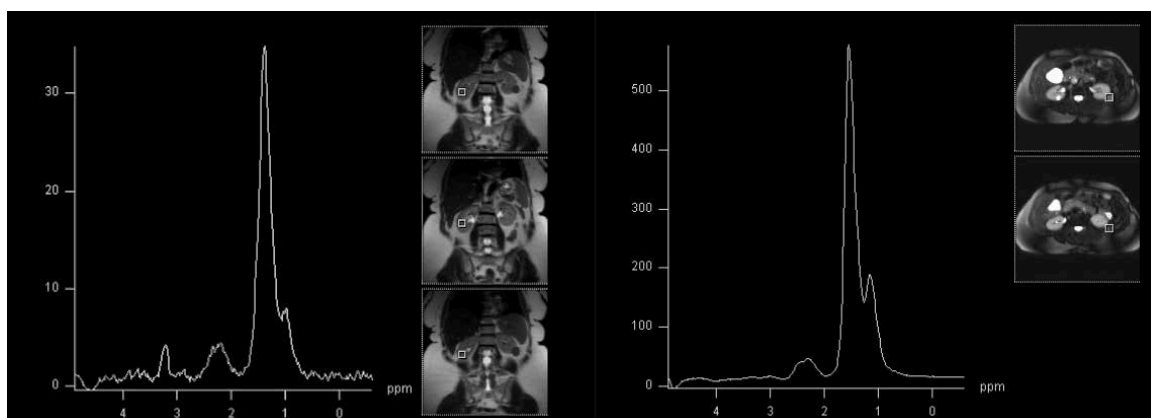


Figure 4: Example of *in vivo* MRS spectra from a patient without a history of TSC. The image on the left obtained with targeting of normal renal parenchymal tissue. Image on

the right obtained with targeting contralateral, left renal lesion, RCC favored by radiographic review.

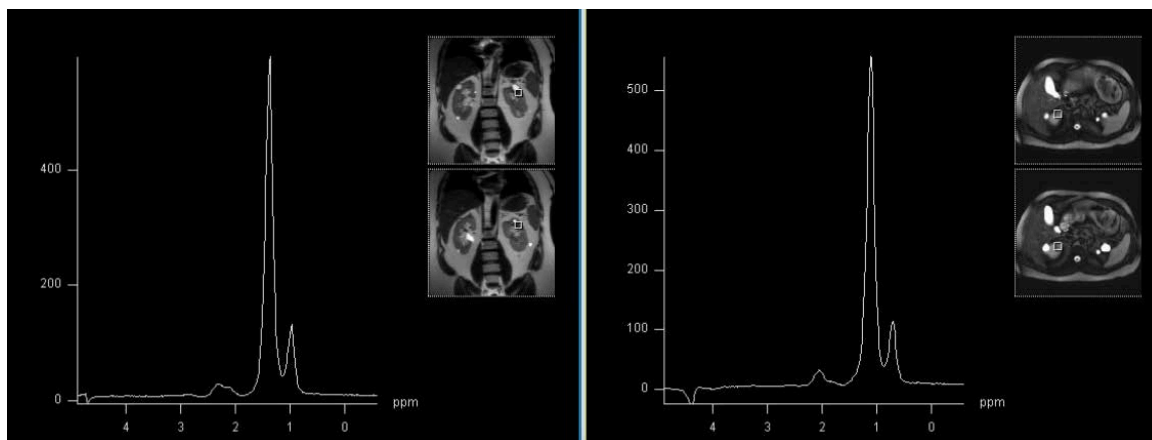


Figure 5: Example of *in vivo* MRS spectra from a single patient with history of TSC and numerous bilateral renal AMLs. The image on the left obtained with targeting the largest, suspicious left renal mass (3.3 cm). The image on the right obtained with targeting the largest, suspicious right renal mass (3.1 cm). Both are favored to be AMLs on radiographic review

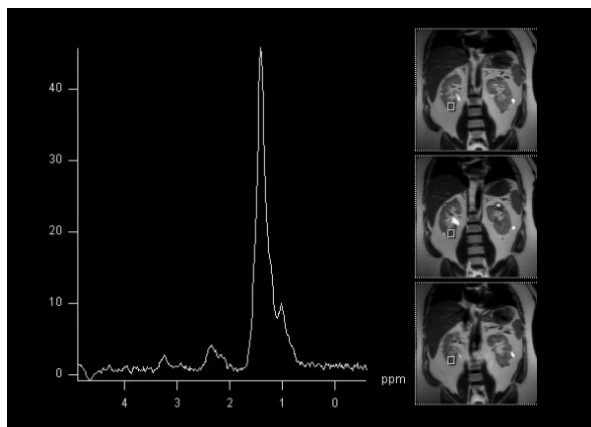


Figure 6: Example of *in vivo* MRS spectra images from single patient with history of TSC and numerous bilateral renal AMLs. The image depicts metabolomic spectrum from right lower pole normal appearing renal parenchymal tissue. Compared to figure 2 of the same patient.

In the third quarter of the year, there were four patients, one had no history of TSC with a 1.8 cm left renal neoplasm scheduled for partial nephrectomy, second had no history of TSC with a 4.3

cm left renal neoplasm scheduled for partial nephrectomy. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figure 7). Two patients, one with history of TSC one without history of TSC, consented during this reporting period and are scheduled for MRI with MRS in the future near the time of their clinically-indicated follow-up visit.

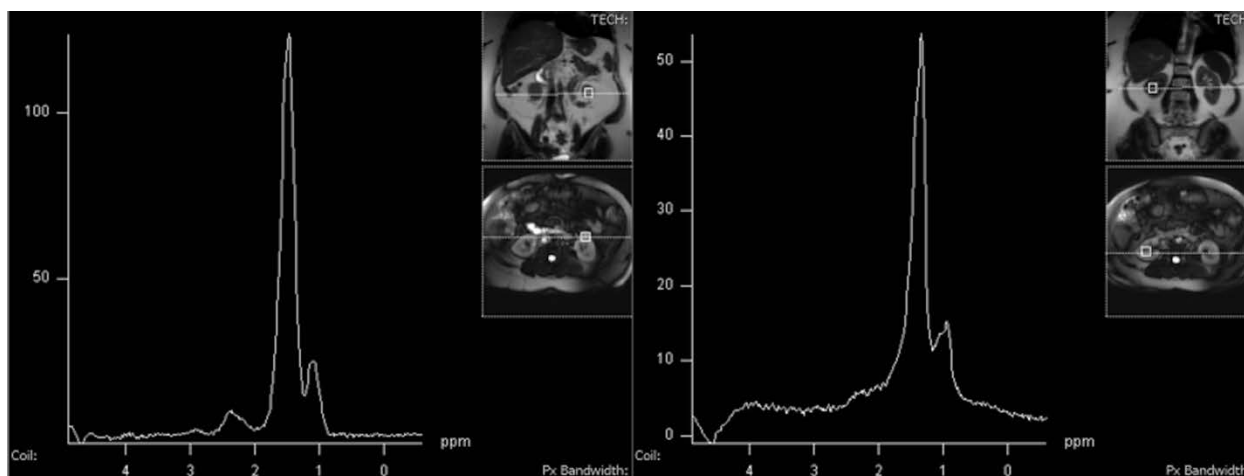


Figure 7: Example of *in vivo* MRS spectra from patient without a history of TSC. The image on the right obtained with targeting of normal renal parenchymal tissue. Image on the left obtained with targeting contralateral, left renal lesion, RCC favored by radiographic review.

Detailed info on *ex vivo* analysis of percutaneous renal mass biopsy tissue:

In the past year from the current cohort of subjects, one patient with a confirmed diagnosis of TSC was consented and underwent renal mass biopsy (RMB) as clinically indicated from imaging results demonstrating a suspicious lipid poor renal mass. Immediately after RMB, core biopsy specimens were transported on ice to the A.A. Martinos Center for Biomedical Imaging at MGH for *ex vivo* MRS. Following MRS, the specimens were transported to the MGH Pathology department for routine histopathologic processing. The metabolic spectra of the core biopsy

specimens were recorded and analyzed. These were compared to the *in vivo* MRS results to assess for consistency between the metabolic signatures.

Histopathologic analysis of the core biopsy specimens showed lipid-poor Angiomyolipoma. On immunohistochemical stain, the tumor cells are positive for MiTF and SMA and focally positive for Melan A and HMB45, supporting the diagnosis. The example of this spectra is present in Figure 8.

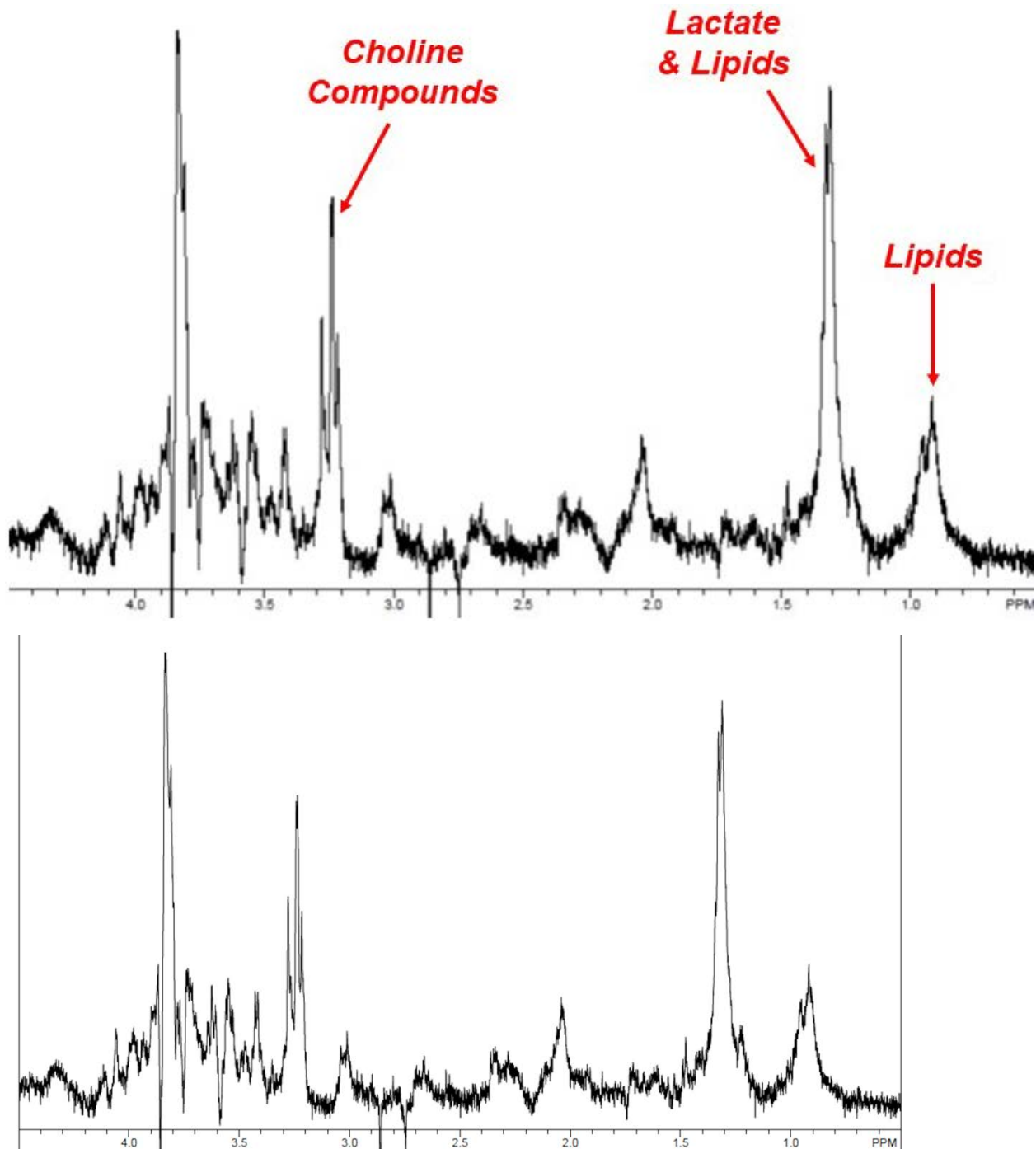


Figure 8: Example of high-resolution magic angle spinning (^1H HRMAS) *ex vivo* MRS spectra image obtained with intact biopsy-core specimen from fat-poor angiomyolipoma kidney tissue from single patient

Detailed info on *ex vivo* analysis of renal mass surgical specimens:

There have been three non-TSC patients, with sporadic renal masses, who underwent clinically-indicated MRIs of the kidneys with the additional *in vivo* MRS sequence and then proceeded to partial nephrectomy. Following resection, the specimens were taken to the Surgical Pathology lab as soon as possible to minimize changes in the metabolomic profile from devascularization. One portion of the tissue was provided for *ex vivo* MRS and another portion from the same location for an immediate snap freeze in liquid nitrogen.

An example of the spectral image obtained from the renal mass is present in Figure 4. The remaining portion of tissue was stored at minus 80 degrees Celsius for future GC-MS analysis and qRT-PCR to examine the metabolomic profile and enzymes implicated in central carbon metabolism.

For one patient, the histopathologic analysis of the surgical specimen was consistent with clear cell Renal Cell Carcinoma (ccRCC), stage T1a, grade 2, with no evidence of tumor necrosis or lymphovascular invasion. The example of this spectra is present in Figure 9. For the second patient, the histopathologic analysis of the surgical specimen was consistent with clear cell Renal Cell Carcinoma (ccRCC), stage T1b, grade 2, with no evidence of tumor necrosis or lymphovascular invasion. For the third patient the histopathologic analysis of the surgical specimen was consistent with Type 1 papillary Renal Cell Carcinoma, stage T1a, grade a, with no evidence of tumor necrosis or lymphovascular invasion. The example of this spectra is present in Figure 10.

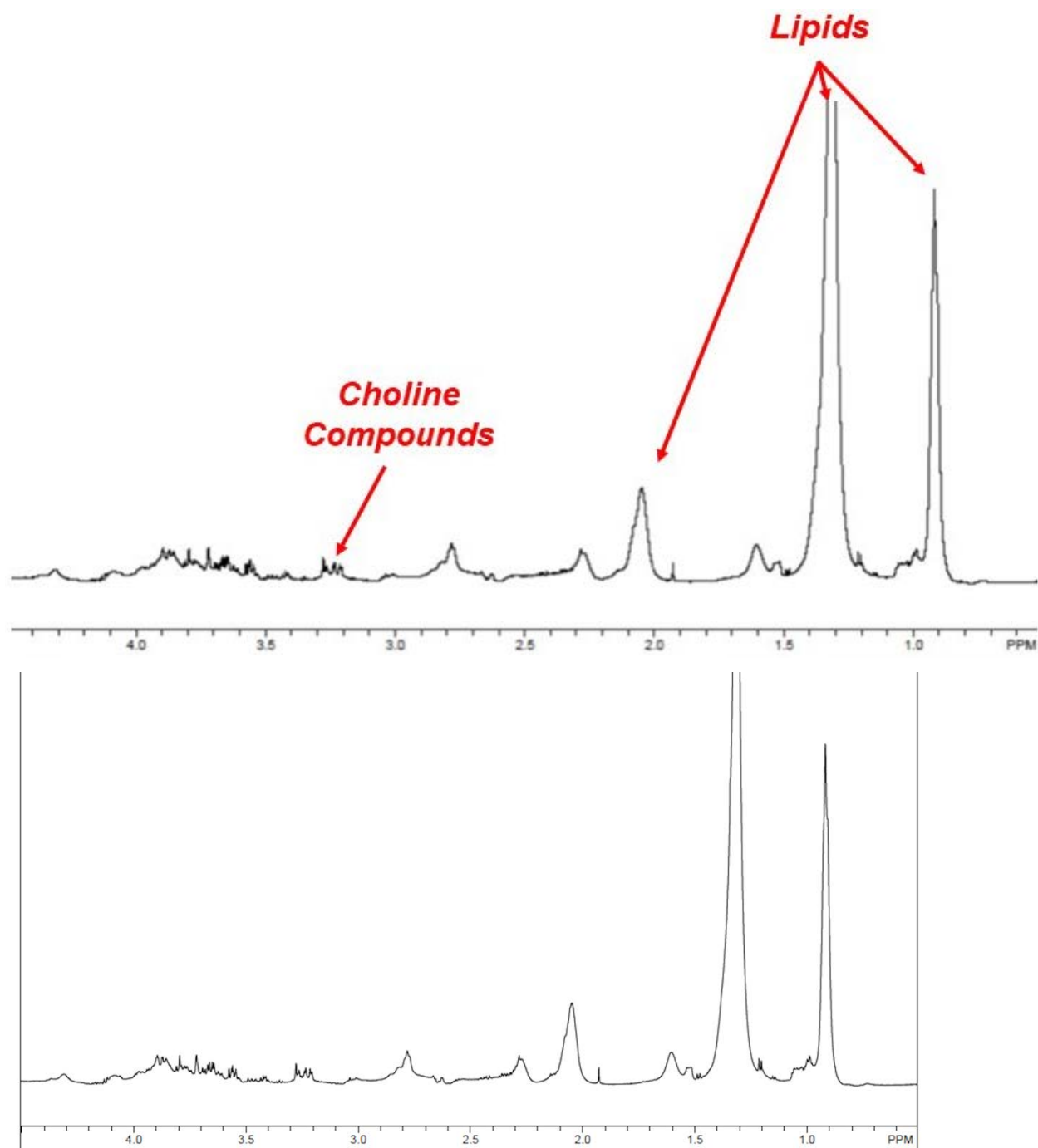


Figure 9: Example of high-resolution magic angle spinning (^1H HRMAS) *ex vivo* MRS spectra image obtained with intact partial nephrectomy specimen from renal cell carcinoma, clear cell type kidney tissue from single patient.

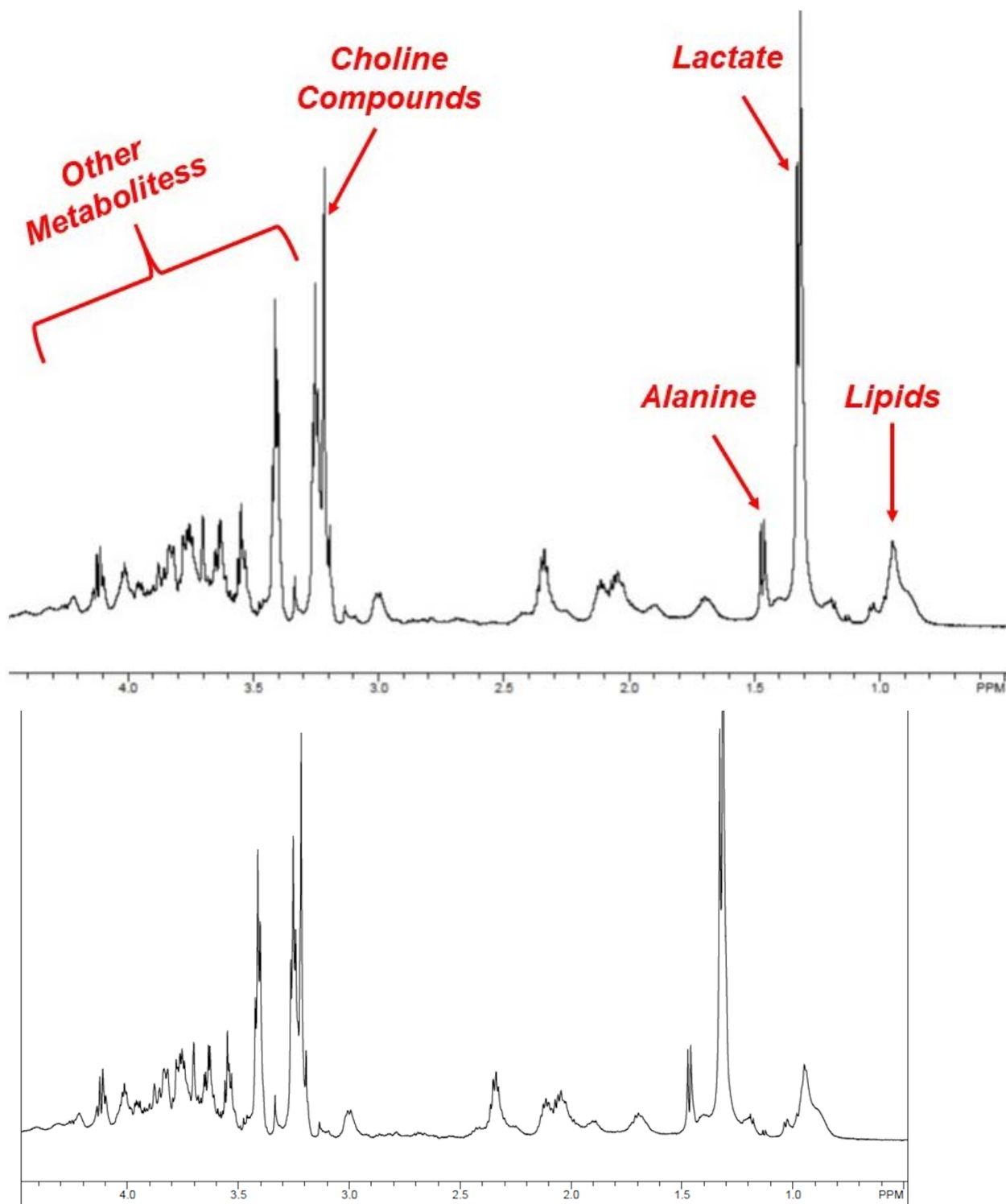


Figure 10: Example of high-resolution magic angle spinning (^1H HRMAS) *ex vivo* MRS spectra image obtained with intact partial nephrectomy specimen from renal cell carcinoma, Type 1 papillary type kidney tissue from single patient.

- **What opportunities for training and professional development has the project provided?**

This project has provided multiple opportunities for training and professional development by increasing our understanding of how to successfully perform *in vivo* metabolomic imaging of the kidney and renal masses.

- **How were the results disseminated to communities of interest?**

We have communicated the results to the multidisciplinary members of our research group, however, have not yet disseminated results to the larger TSC community as we are awaiting additional data and analysis.

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

Our primary task to accomplish the listed goals of the research project is to recruit a greater number of TSC patients with lipid rich and poor renal masses and patients with sporadic renal masses and lipid rich AMLs to record more data on the metabolomic signatures of renal masses from *in vivo* and *ex vivo* MRS. This will also help update and improve the current *in vivo* MRS protocol to better reflect the metabolic profile of the tumor(s) being targeted. Additionally, we will utilize previously collected and annotated tissue from our MGH GU Oncology Frozen Tumor Bank to expand our ability to

investigate the metabolomic profiles of renal masses. To investigate Task 3, we will perform GC-MS and qRT-PCR of surgical tissue specimens and banked specimens to correlate metabolomic profiling.

Impact:

- **What was the impact on the development of the principal discipline(s) of the project?**

Our optimization of protocols for *in vivo* MRS has allowed us to better utilize this method and measure the metabolomic profiles of renal tumor tissue non-invasively. This is novel work and will be published in a peer-reviewed journal. Our ability to do *ex vivo* MRS of the associated AML tumor tissue is also novel work and will allow us to gain a better understanding the metabolomic profiling of AML in TSC and sporadic patients.

- **What was the impact on other disciplines?**

The findings from this work will help gain insight into the active metabolic pathways in AML in TSC and sporadic patients. This may lead to improvements in *in vivo* imaging, but also potentially therapeutics targeting the metabolic pathway.

- **What was impact on technology transfer?**

Nothing to report.

- **What was the impact on society beyond science and technology?**

We are hopeful that the findings from this study will ultimately improve the clinical care of patients with TSC, who suffer from renal involvement, including AML and other tumors.

Changes/Problems:

- **Changes in approach and reasons for change**

During the past reporting period, we decided to consent a greater number of healthy

volunteers and patients with sporadic renal masses. The volunteers helped us improve the technique used for the *in vivo* MRS sequence given our initial difficulties with B₀ shimming to obtain good SNR MRS data. We also began consenting patients with sporadic renal masses to accumulate more MRS data on lipid-poor renal masses due to the slow enrollment of patients diagnosed with TSC. Recruitment has now increased and we have improved our *in vivo* MRS data acquisition with better shimming for our respiratory-gated MRS sequence. Furthermore, we will be including a short echo-time (TE = 30 ms) for our next patients to include additional metabolites which can be captured by *ex-vivo* MRS.

Given the slow rate of recruitment, we also continue to focus our efforts on consenting a greater volume of TSC and sporadic renal mass patients. In addition, we have initiated IRB approval process in order to utilize renal mass tissue from the MGH GU Oncology Frozen Tumor Bank for *ex vivo* MRS. Once IRB approval is received, we will begin this process and report our findings.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

We anticipated initial slow enrollment into the research study, which was resolved by consenting patients with sporadic lipid-poor renal masses. Part of the delay was related to our prolonged process for IRB approval, but part of it also can be attributed to improving the *in vivo* MRS sequence technique to limit signal interference. This was accomplished by consenting healthy volunteers prior to TSC-associated renal mass patients intended for the study. Given the length in time of the MRS sequence, we had to begin using non-breath hold gating when targeting the tumor of interest. These actual problems have been resolved and we anticipate to consent a greater number of participants according to the schedule for year 2 of the research study.

We also had a delay with our local IRB in approval of our use of the GU Oncology Tissue Bank. We have reached out to the appropriate institutional representatives and

have made sure that this part of the project will be approved soon. Once that has occurred we will begin metabolomic evaluation of these specimens to supplement our current data.

- **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.

Products:

- **Publications, conference papers, and presentations**

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Imaging data and associated clinical databases; biospecimen collections

Participants & Other Collaborating Organizations:

- **What individuals have worked on the project?**

Name:	<i>Adam S. Feldman, MD, MPH</i>
Project Role:	<i>PI</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3
Contribution to Project:	<i>Dr. Feldman is responsible for the overall performance of this study. He consents patients in his clinic and then oversees the progress. He coordinates meetings with the various members of the project research team to discuss progress, data and troubleshoot difficulties.</i>
Funding Support:	

Name:	<i>Edouard Nicaise</i>
Project Role:	<i>Research Assistant</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6
Contribution to Project:	<i>Mr. Nicaise coordinates subject scheduling for MRI with in vivo MRS, records and maintains all data, coordinates the acquisition of all specimens and assists with laboratory preparation of specimens for ex vivo MRS and other analyses.</i>
Funding Support:	

Name:	<i>Eva Ratai, PhD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	

Nearest person month worked:	1
Contribution to Project:	<i>Dr. Ratai has expertise in in vivo MRS and has worked on the development of our in vivo MRS protocol in the kidney and interpretation of MRS data</i>
Funding Support:	

Name:	<i>Mukesh Harisinghani, MD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Harisinghani has expertise in diagnostic multiparametric MRI of the kidney. He has worked to interpret the clinical MRI images and will help to correlate our metabolomic data with standard multiparametric MRI imaging data.</i>
Funding Support:	

Name:	<i>Leo Cheng, PhD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Cheng has expertise in ex vivo MRS and has worked on the development of our ex vivo MRS protocol for renal tissues and interpretation of MRS data</i>

Funding Support:	
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Name:	<i>Chin-Lee Wu, MD, PhD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Wu has expertise in genitourinary pathology, kidney cancer in TSC and angiomyolipoma. He reviews all pathology associated with this study.</i>
Funding Support:	

Name:	<i>Elizabeth Thiele, MD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Thiele is the Director of the Herscot TSC Center here at MGH and is very involved in the referral of patients to Dr. Feldman for clinical care and also for consideration of this study. As we collect and analyze more data, she will help with continued interpretation and clinical correlation.</i>
Funding Support:	

Name:	<i>Elizabeth Henske, MD</i>
Project Role:	<i>Co-Investigator</i>

Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Henske is a leader in the care of TSC patients and an active part of our local TSC community. She is very involved in the referral of patients to Dr. Feldman for clinical care and also for consideration of this study. As we collect and analyze more data, she will help with continued interpretation and clinical correlation</i>
Funding Support:	

Name:	<i>Othon Iliopoulos, MD</i>
Project Role:	<i>Co-Investigator</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Dr. Iliopoulos has expertise in the clinical and basic biology of RCC, and specifically has expertise in the metabolic pathways in RCC pathogenesis. As we collect and analyze more data, she will help with continued interpretation and clinical correlation.</i>
Funding Support:	

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

Nothing to report.

- **What other organizations were involved as partners?**

Nothing to report.

Special Reporting Requirements:

Nothing to report.

Appendix:**Curriculum Vitae****Date Prepared:** September 16, 2019**Name:** Adam S. Feldman, M.D., M.P.H.**Office Address:**

Department of Urology
 Massachusetts General Hospital
 55 Fruit Street, GRB 1102
 Boston, MA 02114 United States

Education

1994	B.A. - Biological Basis of Behavior	University of Pennsylvania
1996	M.A. (Alpha Epsilon Lambda) - Medical Sciences	Boston University School of Medicine
2000	M.D. (Alpha Omega Alpha) School	University of Massachusetts Medical School
2009	M.P.H. – Clinical Effectiveness	Harvard School of Public Health

Postdoctoral Training

07/00-06/01 Intern in Surgery, Massachusetts General Hospital
 07/01-06/02 Resident in Surgery, Massachusetts General Hospital
 07/02-06/05 Resident in Urology, Massachusetts General Hospital
 07/05-06/06 Chief Resident in Urology, Massachusetts General Hospital
 07/06-06/08 Fellow in Urologic Oncology, Massachusetts General Hospital

Faculty Academic Appointments

2000-2006 Clinical Fellow in Surgery, Harvard Medical School, Boston, MA
 2006-2010 Instructor in Surgery, Harvard Medical School, Boston, MA
 2010-present Assistant Professor of Surgery, Harvard Medical School, Boston, MA

Appointments at Hospitals/Affiliated Institutions

2006-present Assistant in Urology, Massachusetts General Hospital, Boston, MA

Major Administrative Leadership Positions

2011 Scientific Program Chair, American Urological Association, New England and Mid-Atlantic Sections, Annual Meeting
 2015-present Director, Combined Harvard Urologic Oncology Fellowship
 2018-present Director of Research, Department of Urology, Massachusetts General Hospital

Other Professional Leadership Positions

2012 American Urological Association Representative, Lower Anogenital Squamous Terminology Standardization (LAST) Consensus Conference, 2012
 2012 Member: Scientific Program Committee, American Urological Association, New England Section Annual Meeting
 2012-present Board Member: Sean Kimerling Testicular Cancer Foundation
 2013-present Co-Leader of the Career Development Program: DFCI/HCC Prostate Cancer SPORE
 2016 Scientific Co-Chair: DF/HCC Kidney Cancer Program Retreat
 2016 Course Director: State of the Art Imaging in the Diagnosis and Management of Prostate Cancer
 2017 Course Director: State of the Art Imaging in the Diagnosis and Management of Prostate Cancer
 2019 Course Director: State of the Art Imaging in the Diagnosis and Management of Prostate Cancer

Committee Service - Local

2012-present Member: Surgical Coordination Committee, Department of Urology, MGH
 2013-2015 Member: MGH eCare Big Data and Data Repository Workgroup
 2013-present Urology Representative: Clinical Research Workgroup of the Continuous of the Continuous Research Operations Improvement (CROI) Task Force
 2016-present Urology Representative: MGH Research Council
 2018 Urology Representative: MGH Frigoletto Committee on Physician Well-Being
 2018-present Member: Department of Urology Executive Committee
 2015-present Member: Department of Urology Education Committee

Committee Service - Regional

2012-present Member: Massachusetts Medical Society Committee on Men's Health

Committee Service - National

2013-present Member: Eastern Cooperative Oncology Group (ECOG) Genitourinary Committee

Professional Societies

1998-present Massachusetts Medical Society, Member
 2002-present American Urological Association, Member
 2004-present American Association of Clinical Urologists, Member
 2009-present Society of Urologic Oncology, Member

Grant Review Activities

- 2012-19 Prostate Cancer Foundation Young Investigator Awards Review Committee
- 2013-15 Bladder Cancer Advocacy Network Young Investigator Awards Review Committee
- 2013-19 Prostate Cancer Foundation Challenge Awards Review Committee
- 2013-19 DFCI/HCC Prostate Cancer SPORE Review Committee

Editorial Activities

- 2006 Ad-Hoc Reviewer, International Braz J Urol
- 2007-present Ad-Hoc Reviewer, Journal of Urology
- 2010-present Ad-Hoc Reviewer, Urology
- 2010-present Ad-Hoc Reviewer, Prostate Cancer and Prostatic Diseases
- 2010-present Ad-Hoc Reviewer, Urologic Oncology
- 2011-present Ad-Hoc Reviewer, BJU International
- 2012-present Ad-Hoc Reviewer, Molecular Cancer Research
- 2013-present Ad-Hoc Reviewer, European Urology
- 2014-present Ad-Hoc Reviewer, Journal of Endourology
- 2015 Ad-Hoc Reviewer, JAMA

Editorial Board

- 2015-present Editorial Board Member, BMC Urology
- 2017-present Editorial Board Member, Urologic Oncology: Seminars and Original Investigations

Honors and Prizes

- 1996 Alpha Epsilon Lambda - Graduate Honors Society, Boston U. School Of Medicine
- 2000 Senior Scholar - Department of Surgery, U. Of Massachusetts Medical School
- 2000 Alpha Omega Alpha Honor Medical Society, U. Of Massachusetts Medical School
- 2003 Resident Abstract Travel Award, American Urological Association - New England Section
- 2005 Merit Award for Outstanding Abstract, The ASCO Foundation Grants Program – Multidisciplinary Prostate Cancer Symposium
- 2006 Gerald P. Murphy Scholar, American Urological Association
- 2008 Merit Award for Outstanding Abstract, The ASCO Foundation Grants Program – Multidisciplinary Genitourinary Cancers Symposium
- 2009 AUA Foundation Research Forum – AUA New England Section Nominee
- 2008 Prostate Cancer Foundation Young Investigator Award
- 2011 CINE Golden Eagle Award – CBS Public Service Announcement on Prostate Cancer
- 2011 Best Poster - Annual Meeting of the American Urological Association, Washington, D.C.
- 2012 AUA Foundation Research Forum – AUA New England Section Nominee
- 2018 Best Poster - Annual Meeting of the American Urological Association, San Francisco

2018 Summa Cum Laude Award at the 2018 Annual Meeting of the International Society for Magnetic Resonance in Medicine

Report of Funded and Unfunded Projects

Funding Information

Past:

1997	Student	Institutional Grant, Joseph P. Healy Grant, Pre-clinical Intercultural Program, University of Massachusetts Medical School <ul style="list-style-type: none"> • Summer intercultural immersion program in clinical medicine in Latino community in Miami, FL
1997-1998	Project Director	Institutional Grant, Community Service Grant funding Creating Our Future Program, University of Massachusetts Medical School <ul style="list-style-type: none"> • Program in which medical students tutored and mentored children of homeless families in Worcester, MA
2007-2008	P.I.	Claire and John Bertucci Prostate Cancer Research Fund, A Proteomic Approach to Prostate Cancer Biomarker Discovery <ul style="list-style-type: none"> • Use proteomic techniques for urine biomarker discovery in men with prostate cancer • \$25,000 award
2007-2009	P.I.	Company – Predictive Biosciences; Evaluation of Urine Based Protein Biomarkers in Bladder Cancer <ul style="list-style-type: none"> • Analyze urinary proteins as novel diagnostic and surveillance markers in bladder cancer • Sponsored Research Agreement
2009-2010	P.I.	Claire and John Bertucci Prostate Cancer Research Fund - Active Surveillance for Prostate Cancer: Management Patterns, Outcomes, and Quality of Life <ul style="list-style-type: none"> • Funding supports research personnel for data mining and management • \$25,000 award
2008-2012	P.I.	Prostate Cancer Foundation – Young Investigator Award; Proteomic Discovery and Analysis of Novel Biomarkers in Prostate Cancer

- Use proteomic mass spectrometry techniques for identification of novel prostate cancer biomarkers in urine and serum

		\$75,000 per year for 3 years.
2009-2010	Investigator	Harvard Catalyst Pilot Grant Program NIH UL1 RR 025758-02 Clinical and Translational Science Center Grant Sonoelastography for Tumor-Targeted Prostate Biopsy
		<ul style="list-style-type: none"> • This study is a pilot study of the utility of sonoelastography for targeting biopsy to foci of cancer in the prostate.
2015	P.I.	Project Title: A Collaborative Study Using Primary Prostate Cells and their Reprogramming for the Study of Progression to Castrate Resistant Prostate Cancer Role on the Project: Site PI Supporting Agency: Georgetown University/GHUCCTS/Clinical and Translational Science Awards Level of Funding: \$10,000
2014-2015	Site-P.I.	An Open registry to Measure the Impact of Adding Genomic Testing (Prolaris) on the Treatment Decision Following Biopsy in Newly Diagnosed Prostate Cancer Patients by Specialists (CTA:PROCEDE-2000) Myriad Genetic Labs, Inc. The objective of this registry is an estimation study intended to evaluate the impact of genomic test results towards selecting a first-line therapy option for newly diagnosed localized prostate cancer patients
2011-2016	P.I.	Department of Defense Prostate Cancer Research Program - Physician Research Training Award; Analysis of Novel Prostate Cancer Biomarkers and Their Utility in an Active Surveillance Protocol The research project will investigate novel biomarkers in prostate cancer detection and prediction of disease outcome. \$130,000 per year for 5 years
2013-2016	P.I.	Project Title: Validating Conditionally Reprogrammed Cells to Advance Personalized Medicine for Prostate Cancer Role on the Project: Site PI Supporting Agency: Georgetown University/DoD (W81XWH-12-PCRP) Level of Funding: \$50,000
2014-2017	Site P.I.	Project Title: An Open registry to Measure the Impact of Adding Genomic Testing (Prolaris) on the Treatment Decision Following Biopsy in Newly Diagnosed Prostate Cancer Patients by Specialists (PROCEDE-2000) Role on the Project: Site PI Supporting Agency: Myriad Genetic Labs., Inc.

Current:

- 2009-present Investigator RTOG 0712: A Phase II Randomized Study for Patients With Muscle-Invasive Bladder Cancer Evaluating Transurethral Surgery and Concomitant Chemoradiation by Either BID Irradiation Plus 5-Fluorouracil and Cisplatin or QD Irradiation Plus Gemcitabine Followed by Selective Bladder Preservation and Gemcitabine/Cisplatin Adjuvant Chemotherapy
- 2013-present Investigator RTOG0938: A Randomized Phase II Trial of Hypofractionated Radiotherapy for Favorable Risk Prostate Cancer
- 2013-present Investigator Phase III randomized clinical trial of proton therapy vs IMRT for low or low-intermediate risk prostate cancer
- 2013-present Investigator Characterizing Prostate Cancer by ex vivo MRS Signature (Cheng)
NIH/NCI, R01CA115746
The proposed project is aimed at permitting translation of our pre-clinical human study results into new diagnostic and evaluation paradigms for the PCa clinic
- 2014-present P.I. Prognostic Utility of CCP Score in Patients with Renal Cell Carcinoma
Myriad Genetics, Inc.
The specific aims are: 1) to evaluate the prognostic utility of the CCP score generated from nephrectomy to predict recurrence and cancer-specific mortality in patients who have undergone radical nephrectomy; 2) to evaluate the correlation between CCP scores generated from biopsies and nephrectomy tissue in patients with paired samples; and 3) to evaluate the association between CCP score from biopsy and observed tumor growth rate in patients with RCC managed by active surveillance.
- 2015-present Site-P.I. Tissue-based Genomics for Risk Stratification in Localized Renal Cell Carcinoma
University of Michigan/NCCN
The goal of this subcontract work is to collaborate with University of Michigan to provide clinical specimens and clinical data to Myriad Genetics on the clinical management of patients with RCC.
- 2013-2019 Site-P.I. DF/HCC SPORE in Prostate Cancer
Dana Farber Cancer Institute/NIH-NCI
The specific aims for Administrative Core are: 1) monitor research progress and plan for the future; 2) foster collaborative research within and between SPOREs and integrate the DF/HCC Prostate Cancer SPORE into the structure of DF/HCC; 3) provide necessary resources and fiscal oversight; 4) promote rapid dissemination of significant research findings and free and open; and 5) communication and resource exchange between the DF/HCC SPORE and other institutions.
- 2017-2019 P.I. Evaluation of Lipid Poor Renal Masses with Magnetic Resonance Spectroscopy in Tuberous Sclerosis Complex
Department of Defense - W81XWH-17-1-0468

The major goals of this project are to assess in vivo and ex vivo metabolomic profiles of renal masses in patients with Tuberous Sclerosis Complex in order to differentiate malignant from benign lesions.

Project Role: Principal Investigator

Unfunded Projects

Past:

1991	Research Assistant	Isolation and sequencing of a conserved domain of the DnaJ family of chaperonins. Department of Surgical Research, Children's Hospital, Boston, MA.
1994-1995	Research Assistant	Evaluation of Critical Pathways for CHF, DVT, and Normal Vaginal Delivery with 24 hour LOS. Brigham and Women's Hospital, Boston, MA.
1994-1995	Research Assistant	Adverse Drug Events Prevention Study Group. Brigham and Women's Hospital, Harvard School of Public Health.
1999-2000	Research Fellow	Characterization of Angiogenic Markers in the Rat Genitourinary System. Laboratory for Cellular Therapeutics and Tissue Engineering, Department of Urology, Children's Hospital, Boston, MA.
2002-2004	Investigator	Development of bladder cancer in a murine model for Cables knock-out mice exposed to N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). Laboratory of Urology/Pathology, Massachusetts General Hospital, Boston, MA.
2002-2004	Investigator	The Role of Cables, a novel cell-cycle regulatory protein in human transitional cell carcinoma and prostate cancer. Laboratory of Urology/Pathology, Massachusetts General Hospital, Boston, MA.
2004-2005	Investigator	Proteomic analysis of voided urine specimens for biomarker discovery and validation in prostate and bladder cancer. Laboratory of Urology/Pathology, Massachusetts General Hospital. Department of Vascular Biology, Children's Hospital, Boston, MA.
2007-2008	Investigator	Laparoscopic and Open Radical prostatectomy after laparoscopic inguinal hernia repair. Massachusetts General Hospital, Boston, MA.
2010	Investigator	Outcomes of Organ Sparing Surgery in Penile Cancer. Massachusetts General Hospital, Boston, MA.
2010- 2012	Investigator	Multi-Institutional Bladder Cancer Quality Care Initiative for non-metastatic muscle invasive transitional cell carcinoma of the bladder.

Current:

2008-present P.I.		A comparison of nephron sparing techniques: percutaneous radiofrequency ablation (RFA) vs. open and laparoscopic partial nephrectomy. Massachusetts General Hospital, Boston, MA.
2009-present P.I.		Active Surveillance in Prostate Cancer: Retrospective analysis of quality of life and outcomes and development of a prospective cohort. Massachusetts General Hospital, Boston, MA.
2010-present P.I.		Renal Biopsy for Small Renal Masses. Massachusetts General Hospital, Boston, MA.
2013-present Investigator		PARTIQoL (Prostate Advanced Radiation Technologies Investigating Quality of Life) Registry

Report of Local Teaching and Training

Teaching of Students in Courses

2006-present	<u>Urologic Surgery</u>		<i>contact time</i>	<i>prep time</i>
	Attending	30 Medical Students 8 Residents	10 hours/week for 50 week(s)	none reported
2008-2010	<u>Patient Doctor II</u>		<i>contact time</i>	<i>prep time</i>
	Attending	5 Medical Students	8 hours/year for 1 year(s)	none reported
2010, 2015	<u>HMS2 Pathophysiology</u>		<i>contact time</i>	<i>prep time</i>
	Attending	25 Medical Students	3 hours/year for 1 year(s)	3 hours
2013-2017	<u>HMS Surgical Clerkship Lecture on Urologic Surgery</u>		<i>contact time</i>	<i>prep time</i>
	Attending	10 Medical Students	4 hours/year for 1 year(s)	3 hours

Formal Teaching of Residents, Clinical Fellows and Research Fellows (post-docs)

2007	<u>Surgical Chief's Rounds - Department of Surgery - Injuries to the Urogenital Tract</u>		<i>contact time</i>	<i>prep time</i>
	Lecturer	25 Residents	1 hour	5 hours
2008-2013	<u>Ambulatory Teaching Rounds - Department of Medicine – Uro-oncology for the primary care physician; Management of Small Renal Masses</u>		<i>contact time</i>	<i>prep time</i>
	Lecturer	30 Residents	4 hours/year	10 hours/year
2010	<u>General Surgery Teaching Rounds – Department of Surgery – Bladder Cancer Review</u>		<i>contact time</i>	<i>prep time</i>
	Lecturer	25 Residents	0.5 hour	3 hours

Clinical Supervisory and Training Responsibilities

2006-present	Urological Surgery – Training of Residents/Fellows	15 hours/week
2008-2012	Sub-specialty Faculty Advisor for the Acute Care Surgery fellow	10 hours/year
2015-present	Director, Combined Harvard Urologic Oncology Fellowship	
2018-present	Director of Research, Department of Urology, Massachusetts General Hospital	

Laboratory and Other Research Supervisory and Training Responsibilities

2007-present Supervision and mentoring of Research Fellow

5 hours/week

Formally Mentored Harvard Medical, Dental and Graduate Students:

Sarah Psutka (HMS): 2010 – Research Rotation

David Kuppermann (HMS): 2014-2015 – Research Year

Yefri Baez (HMS): 2019 – Research Rotation

Other Mentored Trainees and Faculty:

- M. Minhaj Siddiqui, MD
 - Current position – Urologic Oncologist, Director of Urologic Robotic Surgery, University of Maryland School of Medicine
 - Mentored Dr. Siddiqui as a Urology resident on clinical disparities research in bladder cancer
- Sarah Psutka, MD, MSc
 - Current position – Urologic Oncologist, University of Washington
 - Mentored Dr. Psutka as a Urology resident on clinical outcomes research in prostate cancer, bladder cancer, and renal cell carcinoma
- Sameer Deshmukh, MD
 - Current Position – Urologist, Kaiser Permanente, Mid-Atlantic Permanente.
 - Mentored Dr. Deshmukh as a Urology resident on clinical outcomes research in renal cell carcinoma and the management of small renal masses
- Mark Preston, MD, MPH
 - Current position – Urologic Oncologist, Brigham and Women’s Hospital, Boston, MA.
 - Mentored Dr. Preston as a Urologic Oncology Fellow in clinical outcomes research in active surveillance in prostate cancer
- Glen Barrisford, MD, MPH
 - Current position – Urologic Oncologist, Kaiser Permanente, Santa Rosa, CA.
 - Mentored Dr. Barrisford as a Urologic Oncology Fellow in clinical outcomes research in renal cell carcinoma and the management of small renal masses
- Jed-Sian Cheng, MD, MPH
 - Current position – Urologic Oncologist, MD Anderson Cancer Center at Cooper, Camden, NJ.
 - Mentored Dr. Cheng as a Urologic Oncology Fellow in clinical outcomes research in renal cell carcinoma and prostate cancer
- Alejandro Sanchez, MD
 - Current Position - Urologic Oncologist, University of Utah
 - Mentored Dr. Sanchez as a Urology resident in clinical outcomes research in urologic oncology

- Dayron Rodriguez, MD
 - Current Position – Fellow in Female Pelvic Medicine & Reconstructive Surgery, Neuro-Urology and Voiding Dysfunction, UT Southwestern
 - Mentored Dr. Rodriguez as a Urology resident in clinical outcomes research in urologic oncology
- Sarah Prophet, BA
 - Current Position – Graduate Student, Cell Biology, Yale University
 - Mentored Ms. Prophet as a Research Assistant for two years between undergraduate and graduate school
- Nawar Hanna, MD
 - Current Position – Urologic Oncologist, University of Montreal
 - Mentored Dr. Hanna as a Urologic Oncology Fellow in clinical outcomes research in prostate cancer
- Ross Krasnow, MD, MPH
 - Current Position – Urologic Oncologist, Georgetown University/MedStar
 - Mentored Dr. Krasnow as a Urologic Oncology Fellow in clinical outcomes research in bladder cancer
- Keyan Salari, MD, PhD
 - Current Position – Urologic Oncology Fellow, Memorial Sloan Kettering Cancer Center
 - Mentored Dr. Salari as a Urology resident in clinical outcomes research in prostate cancer
- Matthew Mossanen, MD
 - Current Position – Urologic Oncologist, Brigham and Women’s Hospital
 - Mentored Dr. Mossanen as a Urologic Oncology Fellow in clinical outcomes research in bladder cancer
- Naren Nimmagadda, MD
 - Current Position – Fellow in Endourology, Vanderbilt University
 - Mentored Dr. Nimmagadda as a Urology resident in clinical outcomes research in renal cell carcinoma
- Eduoard Nicaise, BA
 - Current Position – Medical Student, Chicago Medical School
 - Mentored Mr. Nicaise as a Research Assistant for two years between undergraduate and medical school

Formal Teaching of Peers (e.g., CME and other continuing education courses)

1996-1997	Worcester, MA	Teaching Assistant/Tutor in Biochemistry, University of Massachusetts Medical School Responsibility: Tutor fellow medical students in Biochemistry.
2009	Las Vegas, NV	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?"
2009	Scottsdale, AZ	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?"
2010	San Francisco, CA	Faculty (CME Course): Master Class on Integrating Novel Antiresorptive Agents into the treatment of Prostate Cancer

2010	Boston, MA	Faculty (CME Course): Trauma and Critical Care Symposium – Penile and Genitalia Trauma
2011	Boston, MA	Faculty (CME Course): Society of Translational Oncology Prostate Cancer Symposium – Prostate Cancer: Progress and Promise
2011	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Case Studies in Urology [<i>Invited Lecture</i>]
2013	Ft. Lauderdale, FL	Faculty (CME Course): Winter Oncology Symposium – Holy Cross Hospital – Management of the Small Renal Mass
2013	Waltham, MA	Faculty (CME Course): Men’s Health Symposium – Prostate Cancer: Screening, Management and Controversy
2013	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2014	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Male Urology [<i>Invited Lecture</i>]
2014	Boston, MA	Faculty (CME Course): 17th Biennial Urologic Cancer Course – Bladder Cancer Biomarkers
2014	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2015	Video Series	Faculty (CME Course): Comprehensive Review of Urology – Penile and Urethral Cancer
2015	Boston, MA	Faculty (CME Course): UroTrack – Renal Mass Biopsy
2015	Boston, MA	Faculty (CME Course): UroTrack – MGH Experience in MRI Fusion Prostate Biopsy
2014	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Prostate in the Aging Male [<i>Invited Lecture</i>]
2015	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2016	Baltimore, MD	Faculty (CME Course): UroTrack – Renal Mass Biopsy Debate - Pro
2016	Boston, MA	Faculty (CME Course): 18th Biennial Urologic Cancer Course – Role of Biomarkers in Diagnosis and Followup of Bladder Cancer
2016	Boston, MA	Faculty (CME Course): State of the Art Imaging in the Diagnosis and Management of Prostate Cancer - Rising PSA, Prior Negative Biopsy
2017	Boston, MA	Faculty (CME Course): Trauma & Critical Care Symposium – Approaches to the Ureters and Bladder: High and Low
2017	Boston, MA	Faculty (CME Course): State of the Art Imaging in the Diagnosis and Management of Prostate Cancer – Utilization of Other
2017	Boston, MA	Faculty (CME Course): State of the Art Imaging in the Diagnosis and Management of Prostate Cancer – Tips and Tricks: Fusion vs. Cognitive Biopsy
2017	Boston, MA	Faculty (CME Course): UroTrack – To Biopsy or Not to Biopsy: Role of Renal Mass Biopsy
2018	Ft. Lauderdale, FL	Faculty (CME Course): Winter Oncology Symposium – Holy Cross Hospital – To Biopsy or not to Biopsy: Role of the Renal Mass Biopsy
2018	Boston, MA	Faculty (CME Course): National Comprehensive Cancer Network Prostate Cancer Tumor Board Webinar

2018	Santo Domingo, Dominican Republic	Faculty (CME Course): Latin America Prostate Cancer Summit – Management of Patients post-radical prostatectomy [<i>Invited Lecture</i>] Management of Hormone Sensitive Prostate Cancer [<i>Invited Lecture</i>]
2018	San Francisco, CA	Course Director and Faculty: AUA Course – Trimodality Therapy for Management of Muscle Invasive Bladder Cancer
2018	New York, NY	Faculty (CME Course): UroTrack – Active Surveillance for Prostate Cancer in Young Men
2018	New York, NY	Faculty (CME Course): UroTrack – Long-term Results of Ablation vs. Partial Nephrectomy for Stage T1 Renal Masses
2018	Boston, MA	Faculty (CME Course): 18th Biennial Urologic Cancer Course – Role of Biomarkers in Diagnosis and Followup of Bladder Cancer
2019	Chicago, IL	Course Director and Faculty: AUA Course – Trimodality Therapy for Management of Muscle Invasive Bladder Cancer
2019	Boston, MA	Faculty (CME Course): BOTSOGO Tumor Board
2019	Baltimore, MD	Faculty (CME Course): UroTrack – Penile Cancer Guidelines

Report of Regional, National and International Invited Teaching and Presentations

Local Invited Presentations and Courses

2008	Boston, MA	Comparative Analysis of Nephron Sparing Techniques. Update on Urologic Oncology – Massachusetts General Hospital, Harvard Medical School [<i>Invited Lecture</i>]
2008	Boston, MA	Prostate Cancer: Diagnosis and Management. Prostate Cancer Support Group, Massachusetts General Hospital [<i>Invited Lecture</i>]
2011	Boston, MA	Controversies Around the Management of Small Renal Masses – DF/HCC Kidney Cancer Program [<i>Invited Lecture</i>]
2011	Boston, MA	Proteomic Discovery of Novel Biomarkers in Prostate Cancer – Massachusetts General Hospital Department of Urology Centennial Academic Program [<i>Invited Lecture</i>]
2011	Cambridge, MA	Management of Small Renal Masses – Harvard University Health Services Grand Rounds [<i>Invited Lecture</i>]
2011	Boston, MA	Incidental Radiologic Findings: "Incidental Renal Masses" – Massachusetts General Hospital Medical Grand Rounds [<i>Invited Lecture</i>]
2012	Concord, MA	Controversies in the Management of the Small Renal Mass – Emerson Hospital Medical Grand Rounds [<i>Invited Lecture</i>]

2014	Boston, MA	Management of Renal Lesions in Tuberous Sclerosis Complex – Massachusetts General Hospital Department of Pathology Grand Rounds [Invited Lecture]
2015	Boston, MA	Management of the Small Renal Mass – Massachusetts General Hospital Department of Urology Grand Rounds [Invited Lecture]
2015	Boston, MA	Prostate Cancer: Facts and Misconceptions – Massachusetts State House, Prostate Cancer Awareness Day [Invited Lecture]
2016	Cambridge	Evaluation and Management of the Small Renal Mass – Cambridge Health Alliance, Department of Surgery Grand Rounds [Invited Lecture]
2016	Boston, MA	Evaluation and Management of the Small Renal Mass – Massachusetts General Hospital Department of Urology Grand Rounds [Invited Lecture]
2017	Boston, MA	Penile and Urethral Cancer– Massachusetts General Hospital Department of Urology Grand Rounds [Invited Lecture]
2018	Boston, MA	MGH/MIT Center for Ultrasound Research & Translation (CURT) Lecture Series - I'm still trying to figure it out: A busy surgeon's evolving journey in translational and clinical research [Invited Lecture]
2018	Boston, MA	MGH Chief's Council – Urologic Oncology at MGH: Research and Scholarly Activity
2018	Cambridge, MA	Harvard University Health Services: Grand Rounds – Bladder Cancer Review [Invited Lecture]

Regional Invited Presentations and Courses

2009	Dedham, MA	Urologic Oncology: An Overview. Massachusetts Health Information Management Association [<i>Invited Lecture</i>]
2010	Mt. Kisco, NY	Controversies in the Management of Small Renal Masses [<i>Invited Lecture</i>]
2011	Dedham, MA	Penile Cancer. Urology Nursing Society [<i>Invited Lecture</i>]
2012	Boston, MA	AUA Update in Bladder and Prostate Cancer. AUA New England Section, Annual Meeting
2013	Ft. Lauderdale, FL	Faculty (CME Course): Winter Oncology Symposium – Holy Cross Hospital – Management of the Small Renal Mass
2013	Waltham, MA	Faculty (CME Course): Men's Health Symposium – Prostate Cancer: Screening, Management and Controversy
2015	Bahamas	Renal Mass Biopsy Should Be Used Selectively Prior To a Treatment Decision [<i>Invited Lecture</i>]
2016	Boston, MA	DF/HCC Kidney Cancer Program Retreat - Metabolomic imaging of RCC using MR Spectroscopy: Proposal for a comparative <i>in vivo</i> and <i>ex vivo</i> study
2016	Portland, ME	Multiparametric MRI for the Detection of Prostate Cancer. AUA New England Section, Annual Meeting

2017	Boston, MA	First Annual Herscot Center for Tuberos Sclerosis Complex Symposium – Management of Renal Masses in Tuberos Sclerosis Complex
2018	Ft. Lauderdale, FL	Faculty (CME Course): Winter Ongology Symposium – Holy Cross Hospital – To Biopsy or not to Biopsy: Role of the Renal Mass Biopsy

National Invited Presentations and Courses

2007	Hollywood, FL	Radical prostatectomy after inguinal hernia repair. The American Hernia Society <i>[Invited Lecture]</i>
2009	Boston, MA	Renal Cell Carcinoma: Surgical Management at Massachusetts General Hospital. Exchange Experience Program on Renal Cancer <i>[Invited Lecture]</i>
2009	Las Vegas, NV	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" <i>[Invited Lecture]</i>
2009	Scottsdale, AZ	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" <i>[Invited Lecture]</i>
2010	San Francisco, CA	Faculty (CME Course): Master Class on Integrating Novel Antiresorptive Agents into the treatment of Prostate Cancer. <i>[Invited Lecture]</i>
2010	Boston, MA	Faculty (CME Course): Trauma and Critical Care Symposium – Penile and Genitalia Trauma. <i>[Invited Lecture]</i>
2011	Boston, MA	Faculty (CME Course): Society of Translational Oncology Prostate Cancer Symposium – Prostate Cancer: Progress and Promise
2011	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Case Studies in Urology <i>[Invited Lecture]</i>
2012	Washington, DC	Society of Urologic Oncology – December, 2012: To biopsy or not to biopsy: Results of 1000 renal mass biopsies at a single institution
2013	New Orleans, LA	Faculty – World Congress of Endourology (Industry Sponsored Symposium) - 3D Laparoscopic Urology: Surgical Techniques and Hands-On
2013	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2014	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Male Urology <i>[Invited Lecture]</i>
2014	Boston, MA	Faculty (CME Course): 17th Biennial Urologic Cancer Course – Bladder Cancer Biomarkers
2014	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2015	New Orleans, LA	Society of Urologic Oncology, May 2015 – Primary Penile Sparing: Treatment Approaches
2015	Chicago, IL	Faculty (CME Course): Radiologic Society of North America – Refresher course: Small renal mass (T1a) – the case for resection
2016	San Francisco, CA	Myriad Genetics, Inc. Advisory Board on Renal Cell Carcinoma – Evaluation of CCP Score Genomic Signature in Renal Cell Carcinoma
2016	Boston, MA	Faculty: World Conference on Interventional Oncology – Partial Nephrectomy Remains the Gold Standard

2016	Baltimore, MD	Faculty (CME Course): UroTrack – Renal Mass Biopsy Debate - Pro
2016	Boston, MA	Faculty (CME Course): 18th Biennial Urologic Cancer Course – Role of Biomarkers in Diagnosis and Followup of Bladder Cancer
2016	Boston, MA	Faculty: First Global Summit on Precision Diagnosis for Prostate Cancer – Imaging Tools in a Population of Men With Proven Prostate Cancer: Clinical Case Presentations.
2017	Boston, MA	Faculty: AdMeTech Second Global Summit on Precision Diagnosis for Prostate Cancer - Precision Oncology and Advanced Prostate Cancer: Genomic Testing.
2018	Dallas, TX	Advanced Urology Fellows Course: Identification, Resection & Treatment of Non-Muscle Invasive Bladder Cancer –Complications and Management of TURBT
2018	San Francisco, CA	Course Director and Faculty: AUA Course – Trimodality Therapy for Management of Muscle Invasive Bladder Cancer
2018	Boston, MA	Faculty (CME Course): 18th Biennial Urologic Cancer Course – Role of Biomarkers in Diagnosis and Followup of Bladder Cancer

International Invited Presentations and Courses

2011	Mallorca, Spain	5 th International Urology Forum – The Potential of Nanoparticle Enhanced Imaging in the Accurate Detection of Lymph Node Metastases [<i>Invited Lecture</i>]
2012	Mallorca, Spain	6 th International Urology Forum – Renal Mass Biopsy [<i>Invited Lecture</i>]
2016	Tel Aviv, Israel	Faculty: Friends of Israel Urology Symposium – Nephron sparing surgery for multiple renal tumors [<i>Invited Lecture</i>] Partial Nephrectomy: How I do it with less than 20 minutes warm Ischemia time [<i>Invited Lecture</i>] Session Chair: Oligometastases in Prostate Cancer
2017	Hachioji, Japan	Olympus Corporation - Future of Urologic Surgery [<i>Invited Lecture</i>]
2018	Santo Domingo, Dominican Republic	Latin America Prostate Cancer Summit – Management of Patients post-radical prostatectomy [<i>Invited Lecture</i>] Management of Hormone Sensitive Prostate Cancer [<i>Invited Lecture</i>]
2018	Tel Aviv, Israel	Faculty: Friends of Israel Urology Symposium – Active Surveillance for Prostate Cancer in Young Men [<i>Invited Lecture</i>] Trimodality Therapy for Muscle Invasive Bladder Cancer [<i>Invited Lecture</i>]

Report of Clinical Activities and Innovations

Current Licensure and Certification

2002 Diplomate, National Board of Medical Examiners
2004 Massachusetts Registered Physician

Practice Activities

Urology/Urologic Oncology, Laparoscopy and Endourology Massachusetts General Hospital
Attending Urologic Surgeon, Polycystic Kidney Disease Clinic Massachusetts General Hospital

Report of Technological and Other Scientific Innovations

Patents

1. Zetter BR, Feldman AS, McDougal WS. Methods for diagnosis and prognosis of epithelial cancers. U.S. provisional Patent Application. 2006 Mar 8.
 - Potential use of biomarkers as diagnostic or prognostic markers in bladder cancer. These are currently under investigation and are not yet being used in clinical care
 - My contribution was and is the discovery and analysis of the patented biomarkers

Report of Education of Patients and Service to the Community

Activities

1996-1998 Director (1997-1998) Volunteer (1996-1997), Creating Our Future Program - Worcester Family Health and Social Services Center

Educational Material for Patients and the Lay Community:

2010 **Feldman AS.** Essay on Prostate Cancer. CBS Cares: Prostate Cancer Campaign. cbscares.com.
2011 **Feldman AS.** Essay on Testicular Cancer. CBS Cares Valentine's Day Campaign on Testicular Cancer. cbscares.com.
2011 **Feldman AS.** Patient information: Blood in the urine (hematuria) in adults. UpToDate 19.3. October 14, 2011.
2014 **Feldman AS.** Prostate Cancer: Screening, Management and Controversy. Lecture given at Temple Beth Avodah, Newton, MA.
2015 **Feldman AS.** Prostate Cancer: Screening and Awareness. Lecture given at Leon De Juda Church, Boston, MA.
2015 **Feldman AS.** Prostate Cancer: Screening, Diagnosis and Treatment. Lecture given at The 7th Annual Prostate Cancer Awareness Day. Massachusetts State House, Boston, MA.

Report of Scholarship

Peer Reviewed Publications in print or other media:

Research Investigations:

1. Eisner BH, **Feldman AS**, Chapin BF, Dretler SP. "Blind coning"--using the Stone Cone for removal of intramural ureteral calculi. *Urology*. 2007;69(4):773-5.
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36. **Feldman AS**, Banyard J, Fergus M, Jedrychowski M, Huttlin E, Gygi S, Smith M, Zetter B. Discovery and analysis of prostate cancer biomarkers in a standard non-post-DRE voided urine specimen. Abstract presented at the American Urological Association national meeting, May 2012.
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39. Psutka SP, McDougal WS, McGovern FJ, Mueller P, Gervais DA, **Feldman AS**. Radiofrequency Ablation Achieves Comparable Oncologic Control to Partial Nephrectomy for T1 Renal Cell Carcinoma in Poor Surgical Candidates. Abstract presented at the American Urological Association, New England Section, 2012, Podium Presentation
40. **Feldman AS**, Deshmukh SM, Dhyani M, McGovern FJ, McDougal WS, Olumi A, Dahl DM, Arellano RA, Samir A, Blute ML. To biopsy or not to biopsy: results of 1000 renal mass biopsies at a single institution. Society of Urologic Oncology 2012, Podium Presentation
41. Kurtz M, Thiele E, Paul E, Blute ML, Walker TG, **Feldman AS**. Lipid-Poor Lesions of Tuberos Sclerosis; A Role for Percutaneous Biopsy. Abstract presented at the American Urological Association national meeting, May 2013.
42. Psutka S, McDougal WS, Dahl DM, McGovern FJ, Mueller P, Gervais D, **Feldman AS**. Radiofrequency ablation achieves comparable local oncological control to partial nephrectomy for T1 renal cell carcinoma. Abstract presented at the American Urological Association national meeting, May 2013.
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- American Urological Association national meeting, October 2015 and at Society of Urologic Oncology, December 2015.
61. Hanna N, **Feldman A**, Meyer C, Sanchez A, Reznor G, Hanske J, Nguyen PL, Choueiri TK, Lipsitz S, Sun M, Trinh QD. Morbidity, mortality and cost in locally advanced prostate cancer: a population based-analysis comparing radical prostatectomy and external beam radiation. Presented at the Society of Urologic Oncology, December 2015.
 62. Krasnow R, Roberts H, Drumm M, Niemierko A, Wu CL, **Feldman A**, Wszolek M, Lee R, Blute M, Zietman A, Shipley W, Efstathiou J. Clinical outcomes of patients with histologic variants of bladder cancer treated with trimodal bladder-sparing therapy. Abstract presented at the American Urological Association national meeting, May 2016.
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 64. Salari K, Kuppermann D, Preston MA, Dahl DM, Wu CL, Blute ML, Zietman AL, **Feldman AS**. Active Surveillance Is A Viable Option For Men With Borderline Low-Risk Prostate Cancer. Abstract presented at the American Urological Association New England Section, September 2016 and the American Urological Association national meeting, May 2017
 65. Hanna N, Wszolek MF, Gelpi-Hammerschmidt FJ, Salari K, Harisinghani M, Dahl DM, Blute ML, **Feldman AS**. Multiparametric MRI/Ultrasound Fusion Biopsy Improves But Does Not Replace Standard Templatebiopsy For The Detection Of Prostate Cancer. Abstract presented at the American Urological Association New England Section, September 2016 and the Society of Urologic Oncology, December 2016.
 66. Prophet S, **Feldman A**, Fergus M, Zetter B. Urine Expression of TIMP1, Serpin B1, and Semenogelin 2 may differentiate men with low-risk or no evidence of prostate cancer from men with high-risk or metastatic disease. Abstract presented at the American Urological Association national meeting, May 2017 and the American Urological Association New England Section, September 2017
 67. Salari K, Kuppermann D, Preston MA, Dahl DM, Efstathiou J, Blute ML, Vesprini D, Loblaw A, Zietman AL, Klotz L, **Feldman AS**. Active Surveillance for low-risk prostate cancer in men under 60 years of age. Abstract presented at the American Urological Association national meeting, May 2017 and the American Urological Association New England Section, September 2017
 68. Mossanen M, Krasnow RE, Pieretti AC, **Feldman AS**, Efstathiou JA, Blute ML, Heney NM, Wszolek MF. Comparing complications and survival of primary cystectomy vs. salvage cystectomy after triomodal therapy. Abstract presented at the American Urological Association national meeting, May 2017
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- Y, Wu CL, Checng LL. Metabolomic evaluation of MRI/US fusion biopsies differentiates malignant from Benign. Abstract presented at the American Urological Association national meeting, May 2018
- 71 Salari K, Zlatev D, Kuppermann D, Preston M, Dahl D, Efstathiou J, Blute M, Zietman A, **Feldman AS**. The prognostic impact of a negative confirmatory biopsy in men on active surveillance for prostate cancer. Abstract presented at the American Urological Association national meeting, May 2018
- 72 Nimmagadda N, Hsieh G, Kuppermann D, Grant M, Psutka S, Allard CB, McGovern F, Dahl D, Blute M, Arellano R, Gervais D, **Feldman A**. Long-term Oncologic Comparison of Radiofrequency Ablation to Partial Nephrectomy for T1 Renal Cell Carcinoma using Propensity Score Analysis. Abstract presented at the American Urological Association New England Section meeting, September 2018
- 73 Pieretti A, Krasnow R, Nimmagadda N, **Feldman A**, Wszolek M. Complications and Survival of Primary Cystectomy, Primary Cystectomy with History of Pelvic or Abdominal Radiation and Salvage Cystectomy after Trimodality Therapy. Abstract presented at the American Urological Association New England Section meeting, September 2018
- 74 Zlatev D, Salari K, Kuppermann D, Pucheril D, Blute M, Feldman A. Prognostic Impact of Increased Prostate-Specific Antigen Density in Men on Active Surveillance for Prostate Cancer. Abstract presented at the American Urological Association New England Section meeting, September 2018
- 75 Yu A, Baloda T, Nicaise E, Gusev A, Harisingani M, Mojhed A, Dahl D, Wszolek M, Zietman A, Feldman AS. Widespread use of multiparametric MRI in an active surveillance cohort results in earlier identification and treatment of clinically significant prostate cancer. Abstract presented at the American Urological Association national meeting, May 2019.
- 76 Nicaise E, Yu A, Gusev A, Baloda T, Kuppermann D, Zietman A, Preston M, Dahl D, Blute M, Feldman A. Need for intervention and survival in a cohort of patients on active surveillance for prostate cancer. Abstract presented at the American Urological Association national meeting, May 2019.

Narrative Report

My activities at the Massachusetts General Hospital and at Harvard Medical School are in the field of Urologic Oncology. My clinical service activity in both operative and office urology requires approximately 70% of my time. My research activities in clinical and translational research comprises about 20% of my time. My administrative responsibilities require approximately 10% of my time. Teaching residents, fellows and medical students clinical and operative urology is integrated into my clinical time and a significant proportion of my research time is devoted to mentoring and working with my research fellows, residents and students on our clinical and translational research projects.

My exposure to basic science and clinical research have fostered my interests in combining these

skills in translational and clinical research endeavors. As an undergraduate, I worked in the Department of Surgical Research at Children's Hospital learning molecular biology and basic science methodology. After my undergraduate years I conducted clinical outcomes research at Brigham and Women's Hospital and learned fundamentals of answering a research question in my Master's thesis at Boston University School of Medicine. As a Senior Scholar medical student, I worked as a Research Fellow in the Laboratory for Cellular Therapeutics and Tissue Engineering at Children's Hospital, Boston. This research experience gave me a solid foundation in molecular biology, immunohistochemistry and tissue culture methods.

As a Urology resident at MGH, I continued to develop basic science techniques with the development of a murine model of bladder cancer in Cables (novel cell regulatory protein) knock-out mice and investigated the expression of Cables in bladder and prostate cancers using immunohistochemistry. Later in residency I moved into translational biomarker research, mentored by Dr. Bruce Zetter at Children's Hospital and Dr. Matthew Smith at MGH. This research focused on the development of novel biomarkers for bladder and prostate cancers. I continued to develop these investigative projects throughout my Fellowship in Urologic Oncology and as an early member of the MGH faculty. In an effort to further my education in sound clinical and translational research, I pursued a Masters degree in Public Health in Clinical Effectiveness at the Harvard School of Public Health. Awarded in November 2009, this degree is still helping me achieve my academic goals by refining my ability to design and implement translational and clinical research and produce high quality independent investigations.

In 2008, I received a three year Prostate Cancer Foundation Young Investigator Award for my work in novel biomarkers in prostate cancer and in 2011 was awarded a five year Congressionally Directed Medical Research Program Physician Research Training Award by the Department of Defense for my research in prostate cancer biomarkers and active surveillance. In 2013 I was a co-PI on a Department of Defense Synergistic Idea Development Award on the development of conditionally reprogrammed cells in prostate cancer and a co-investigator on a National Institutes of Health RO1 on metabolomic imaging in prostate cancer. I am currently the PI on a DOD Exploratory Hypothesis Development Award investigating metabolomic imaging in renal masses. In addition to federal funding, I have had several industry sponsored research grants in prostate, bladder and kidney cancers. In addition to my translational research work in bladder and genitourinary cancer biomarkers, I have also developed institutional clinical databases in active surveillance in prostate cancer, use of imaging and fusion biopsy in prostate cancer, surgical and ablative treatments for renal cell carcinoma, renal mass biopsy, and penile carcinoma.

My clinical focus has been in Urologic Oncology. During my residency and fellowship I learned and developed my skills in both open and laparoscopic techniques and in the clinical management of patients with genitourinary cancer. As a clinician interested in research, I have also directed some of my research efforts toward clinical projects in genitourinary cancers. I have worked to develop institutional clinical databases in active surveillance in prostate cancer, use of imaging and fusion biopsy in prostate cancer, surgical and ablative treatments for renal cell carcinoma, renal mass biopsy, and penile carcinoma. Clinical teaching has also always been an integral part of my roles as resident, chief resident, fellow and now attending urologic surgeon. In clinical research, I have mentored residents, fellows, medical students and our

research associates, overseeing and teaching investigational method and presentation of data. On a national and international level, I have served on the faculty for several CME courses and served as the Scientific Program Chair for the 2011 American Urological Association New England and Mid-Atlantic Sectional Meeting. I founded and am co-Director of the biennial HMS CME course, State of the Art Imaging in the Diagnosis and Management of Prostate Cancer.