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TITLE: Analysis of Novel Prostate Cancer Biomarkers and Their Predictive Utility in an Active Surveillance Protocol

PRINCIPAL INVESTIGATOR: Adam S. Feldman, M.D., M.P.H.

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The Research Project supported by this DOD PCRP Physician Research Training Award investigates novel biomarkers for prostate cancer and investigation of Active Surveillance of low risk prostate cancer. In this fifth year of my DOD PCRP PR TA, I have continued my productivity from both a translational laboratory and clinical research standpoint. We have continued to investigate our list of biologically relevant candidate prostate cancer biomarkers and have demonstrated promising results. We have also continued to investigate the expression of these markers in prostate cancer tissue and normal prostate using immunohistochemistry. We have had promising results with Tissue Inhibitor of Matrix Metalloproteinase Type 1 (TIMP-1), Semenogelin-2, and Leukocyte Elastase Inhibitor (SERPINB1). With these three biomarkers we have made significant strides in identifying differential expression patterns. In addition to success in our laboratory work, we have also continued to make significant accomplishments in analyzing our database of 469 men on active surveillance for prostate cancer over the past 15 years. Our analysis of this database has demonstrated freedom from intervention of 77% at 5 years and 62% at 10 years. Cancer specific survival was 100% at 10 years and overall survival was 95% at 5 years and 88% at 10 years. We are currently in the process of writing a manuscript to formally publish our results.

15. SUBJECT TERMS

Prostate Cancer; Biomarker; Proteomics; Active Surveillance

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Introduction:

The Research Project supported by this DOD PCRP Physician Research Training Award investigates novel biomarkers for prostate cancer detection and prediction of disease outcome. The goals and objectives of this study are summarized by the Specific Aims: 1. Evaluate the relative levels of expression of our panel of candidate biomarkers in urine, tissue and serum from patients with prostate cancer compared with normal controls to identify prostate cancer specific biomarkers. 2. Evaluate the relative urine, tissue and serum levels of these prostate cancer specific biomarkers within our active surveillance (AS) cohort to identify accurate biomarkers predictive of indolent vs. progressive prostate cancer. The funding from this Physician Research Training Award provides salary support for me to secure protected time as a translational and clinical investigator in prostate cancer research. It also provides salary support for a Research Assistant for my research.

Body:

The first four years of my DOD PCRP PRTA involved the identification of differentially expressed proteins in the urine from men with prostate cancer compared to samples from men without disease through mass spectrometry analysis. In summation, I used mass spectrometry (MS) to quantitatively compare the entire urinary proteome and identify differentially expressed proteins in the urine from men with prostate cancer as compared with those found in controls. The MS analysis identified >1400 unique proteins, and comparative analysis revealed 55 potential prostate cancer specific proteins. Over the ensuing period of this grant, we extensively investigated these potential candidate biomarkers via Western Blot, ELISA (enzyme-linked immunosorbent assay) and Immunohistochemistry (IHC). Our investigation of potential biomarkers includes serpinB1, tissue inhibitor of matrix metalloprotease type 1 (TIMP1), and semenogelin 2 (SEMG2); these three proteins represent only a select group amongst many other proteins of interest, which we have investigated and outlined in previous reports.

In this fifth year of funding, our focus on the validation of these three potential biomarkers, serpinB1, SEMG2, and TIMP1 as relevant prostate cancer biomarkers was continued. In addition to continuing our investigation of the expression of these proteins in patients with localized disease, we expanded our experiments to include patients with metastatic prostate cancer. Our patients are now divided into four groups; patients with no prostate cancer (control group), patients with Gleason score 6 prostate cancer, those with score 8 or above, and patients with metastatic prostate cancer. Using these four groups has allowed us to better observe differential expression patterns for our proteins of interest, specifically serpinB1, SEMG2, and TIMP1.

In addition to expanding our patient populations, this year has been marked by a heightened response to technical difficulties and shortcomings. Of utmost importance for the analysis and accurate representation of protein expression is the quantification of total protein in urine samples. While there are a number of methods to measure total protein concentration, some procedures are incompatible with protein sourced from urine samples and seemed to give inaccurate results. For this reason, it is imperative that an appropriate method of quantification is identified and consistently used. Some (but not all) previous data were generated using the widely applicable BCA assay for protein quantification, although recently we established this was a less acceptable way to measure the concentration in urine samples. While we do not have an exact mechanism for why the BCA assay fails to give accurate protein concentrations, our inconsistencies observed using this method were reflected in other partnering labs' experiences with quantifying urine samples. A more robust method of protein quantification, based on the Bradford assay, is now being used and our results reflect more reliable data.

Our previous data suggested the protein TIMP1 was upregulated in prostate cancer. The ongoing exploration of this protein's expression pattern uses Western blot and ELISA to observe levels in urine samples. We have repeatedly run into technical difficulties in Western blotting due to the nature of the samples, which have extremely variable concentrations and protein content. For this reason, we have coupled Westerns with ELISA, which serves as an accurate and fully quantitative method of protein identification. It is easily compatible with urine samples and has yielded especially interesting results for TIMP1 with the addition of the fourth patient population (men with metastatic disease).

The Western blot data for this protein, TIMP1, shows the protein may be generally expressed at higher levels in Gleason 6 samples than controls (fig. 1). Although we need to expand our enrollment numbers, preliminary ELISA results show these two groups may indeed differ in TIMP1 expression levels (fig. 2). Between localized disease groups, both Western blot and ELISA suggest there might actually be a significant decrease in TIMP1 expression in patients with Gleason score ≥ 8 as compared to those with Gleason 6 (fig. 1, 2). This downward trend in TIMP1 expression seems to continue to metastatic from Gleason ≥ 8 disease on ELISA, although Western blotting shows metastatic samples as having consistently moderate TIMP1 levels (fig. 1, 2). Because we only recently added this patient population, we need to replicate these experiments to confirm the correlation between TIMP1 and disease stage. In order to validate these observations and trends in Westerns, it will be necessary to compare quantifications of the band sizes between populations across all the membranes we generate. This is an ongoing next step of analysis. In ELISAs, we want to generate meaningful correlation coefficients for differences in median expression values, and for this more samples need to be analyzed. This reduced TIMP1 expression in high risk and metastatic disease may in effect allow a reduced

inhibition of matrix metalloproteinases (MMP), such as MMP-9, and has been demonstrated by others in tissue using IHC.^{1,2}

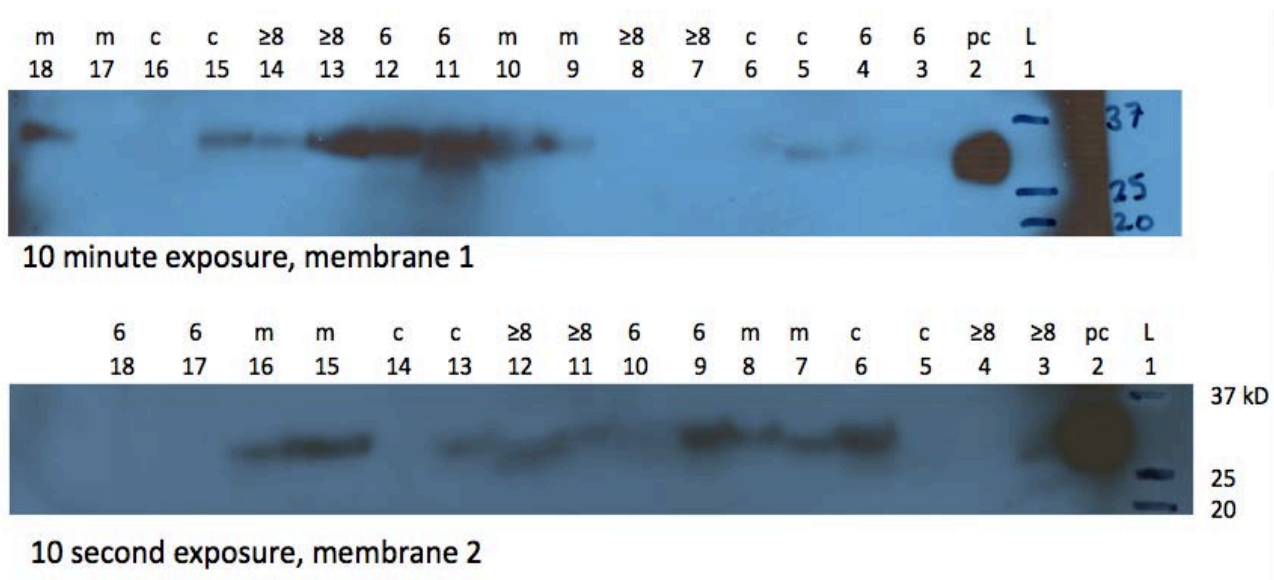


Figure 1 **TIMP1** expression in four prostate cancer patient populations on two different membranes. Four patients per population are represented in each blot. Populations are indicated by the following abbreviations; c- control (no prostate cancer), 6- Gleason score 6, ≥8- Gleason score of 8 or above, m- metastatic disease. The positive control, human recombinant TIMP1 protein, is indicated by “pc.” 40ug of total protein was loaded into each lane. All Western blots in this study are performed using PVDF membranes. Please note the two different membranes with different exposure times. The expected band size for this protein is 29kD.

¹ Reis ST, Viana NI, Iscaife A, et al. Loss of TIMP-1 immune expression and tumor recurrence in localized prostate cancer. *Int Braz J Urol.* (2015) 41(6):1088-95.

² Brehmer B, Biesterfeld S, Jakse G. Expression of matrix metalloproteinases (MMP-2 and -9) and their inhibitors (TIMP-1 and -2) in prostate cancer tissue. *Prostate Cancer and Prostatic Diseases* (2003) 6: 217–222.

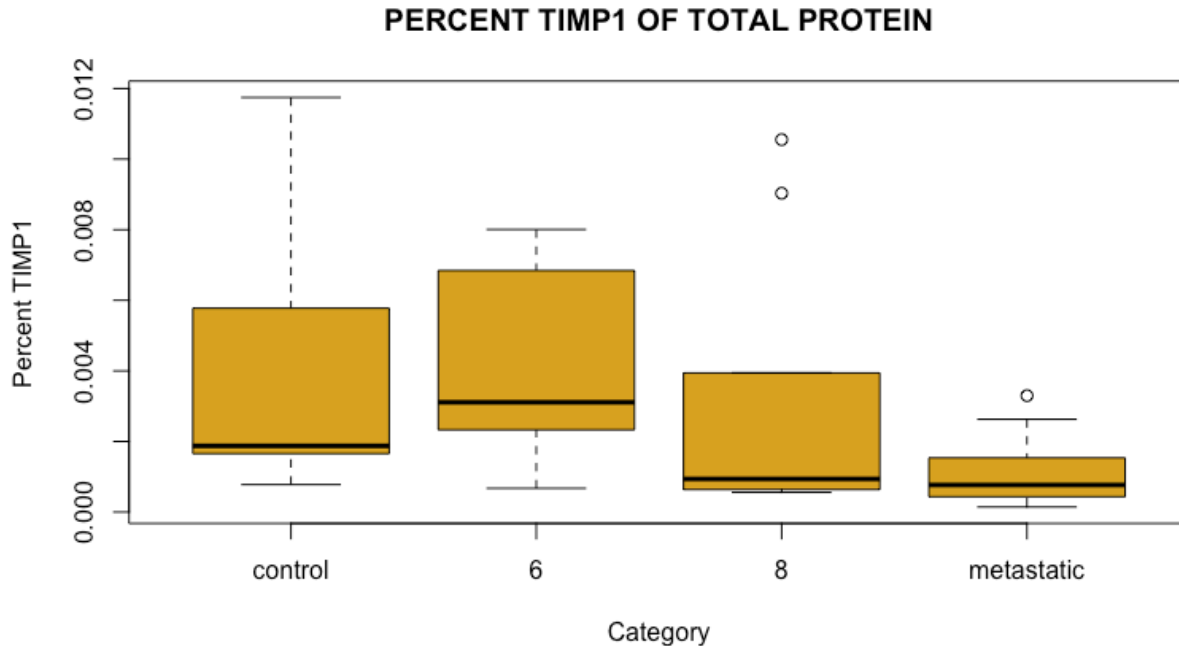


Figure 2 **Percent TIMP1 of total protein measured by ELISA. Box plots give representation of median value, interquartile range, range, and outliers. Patient populations are indicated by the following abbreviations; c- control (no prostate cancer), 6- Gleason score 6, 8- Gleason score of 8 or above, m- metastatic disease. Each category contained either nine or ten patients. In this figure, the concentration of TIMP1 is expressed as a percent of total protein.**

The next protein of interest, SerpinB1, also showed an interesting trend in expression pattern. On ELISA, the median value of SerpinB1 expression (represented as a percent of total protein) was highest in control samples, with a drop in value for all patients with any stage of prostate cancer (fig. 3). Because the ranges of SerpinB1 percent overlap for the groups, as well as the 95% confidence intervals for the median values, we will need to continue replications of this experiment to elucidate the consistency and significance of the trend (fig. 3). Of note, because the sample size is small (between six and eight patients per population), it is difficult to calculate a reliable confidence interval for the significance of the median values. For this reason, more repetitions of ELISA for SerpinB1 are warranted.

When visualized on Western blots, the pattern of SerpinB1 expression may not be as easily assessed. Similar to the TIMP1 immunoassays, these Westerns for SerpinB1 show nearly the opposite of what the ELISA analysis indicated. While the ELISA showed lower levels of SerpinB1 in prostate cancer as compared with disease-free urine samples, Western blotting had large bands indicative of high SerpinB1 expression in especially Gleason 6 samples while Gleason 8 or above and metastatic samples

may have lower than control levels (fig. 4). To make sure these qualitative observations are accurate, we will need to quantify Western bands using the computer program ImageJ and see if there is a consistent trend.

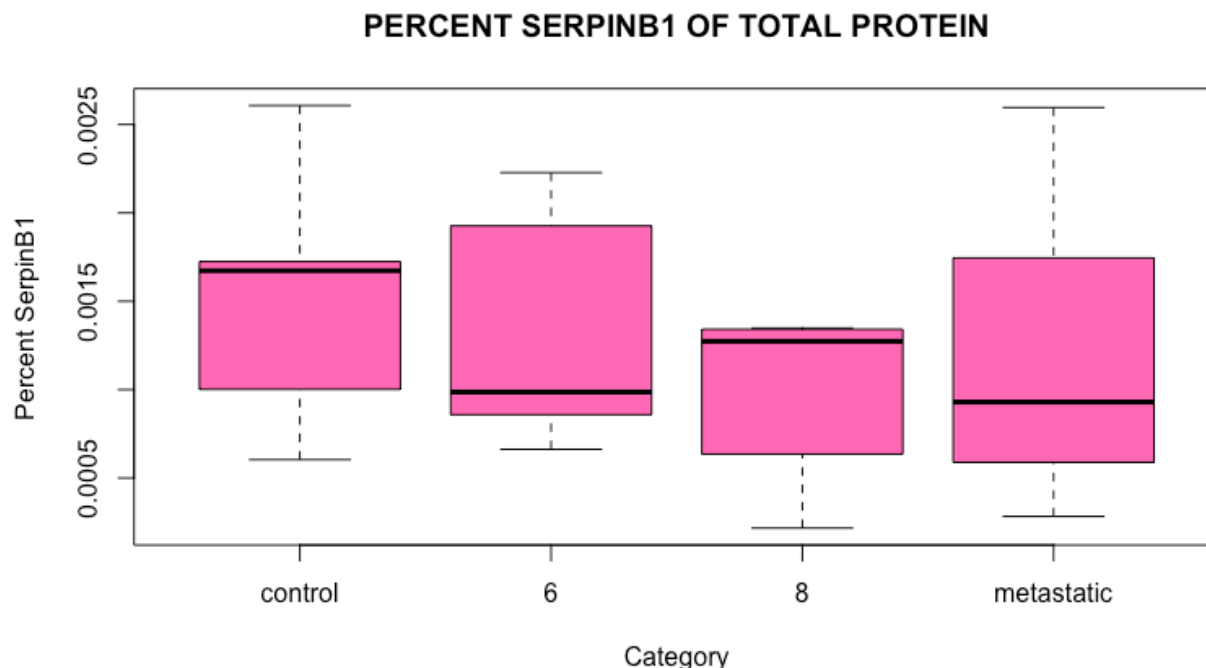
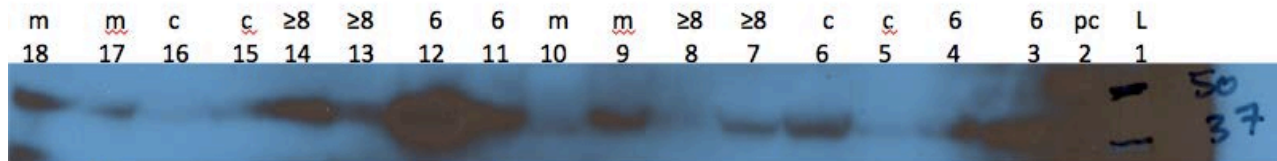


Figure 3 Box plot showing expression levels of SerpinB1 in four prostate cancer patient populations. Each group consists of six to eight patients. The concentration of SerpinB1 is expressed in this figure as a percent of total protein.

Our inconsistencies with Western blots and ELISA data are not new challenges, but our progress with accurately measuring protein concentration and understanding discrepancies that may affect results has allowed for continued experimentation. One reason we may observe dissimilarities between these immunoassays is the different antibodies used; unfortunately, this is a factor over which we have very little control. Another difference in the two methods involves the preparation of samples. While both use concentrated proteins isolated from urine, under-concentrated samples are extremely difficult to use for Western blots, so it is important sufficient concentration is reached before using these samples. High loading volumes (corresponding to low concentrations) may affect how much protein actually runs down the lane, which may result in a smaller band for the target protein. This volume issue is not a concern for ELISA, which can detect target protein in the least concentrated of samples.



12 minute exposure, membrane 1



5 minute exposure, membrane 2

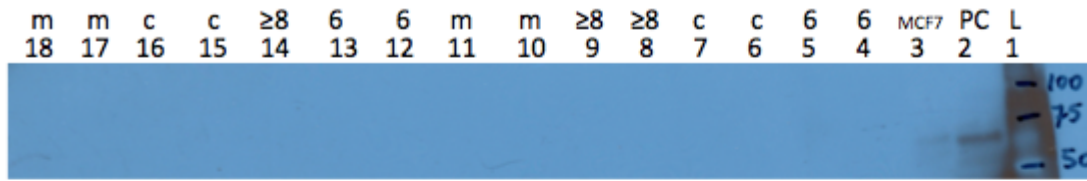


5 second exposure, membrane 3

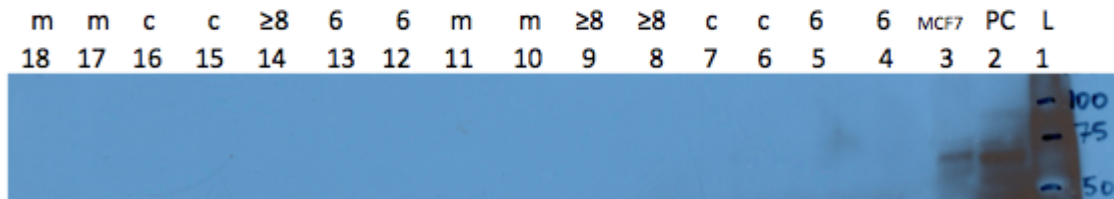
Figure 4 Three membranes showing SerpinB1 expression. Four patient populations are represented on each blot. In these three membranes, a total of 12 patients per population are assessed for SerpinB1 expression. The positive control, MCF7 cell lysate, is indicated by “pc.” 40ug of total protein was loaded into each lane. The expected size for this protein is 43kD.

The third protein of interest, SEMG2, has rarely been observed on Western blot by our group. This may be because there is very little SEMG2 in urine and Western blotting is not sensitive enough to detect it. We have tried a number of different antibodies and membrane conditions, but consistently only the positive control of COLO205 cell lysate shows a band (fig. 5). However, the levels of SEMG2 are sufficient enough to be detected by ELISA. When this immunoassay was performed for SEMG2, a similar trend to that of TIMP1 was observed (fig. 6). According to our ELISA, SEMG2 is expressed in higher concentrations in patients with Gleason 6 disease and then drops off to the lowest median value in metastatic patients (fig. 6). Interestingly, the control samples seem to have SEMG2 levels that fall within the ranges of Gleason 6 to metastatic expression levels, but the metastatic patients have almost no overlap with Gleason 6 expression levels (fig. 6). In fact, basic statistical analysis on these two groups, Gleason 6 and metastatic, indicates that the median values differ with 95% confidence. Aside from one outlier, the metastatic samples are all lower in expression than Gleason 6 samples. This interesting

finding encourages repetition of this particular ELISA with new patients, as well as continued attempts at showing the trend in a Western blot.



2 minute exposure



10 minute exposure

Figure 5 Western blots probing for SEMG2. Even after 10 minutes of exposure, the target protein is only observable in the positive control, COLO205 cell lysate, and MCF7 cell lysate lanes. This is suggestive of insufficient protein levels in urine samples. 40ug of total urinary protein was loaded into each lane. The expected band size for this protein is 65kD.

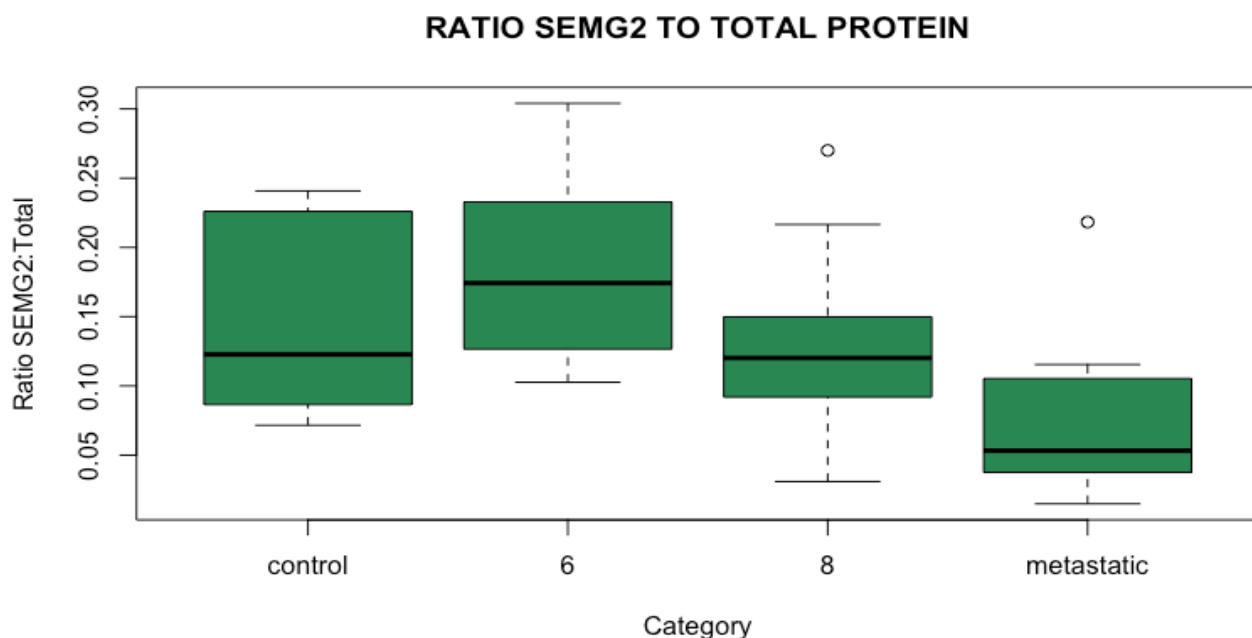


Figure 6 Box plots of ELISA data for SEMG2 in four patient categories. Basic statistical analysis indicates the median values for 6 and metastatic categories are different with 95% confidence. The concentration of SEMG2 is expressed in this figure as a ratio against the concentration of total protein.

Aside from focusing on these three protein biomarkers for prostate cancer, our group also has continued to expand our work in metabolomic evaluation of urine and tissue in prostate cancer patients. This work is in collaboration with Leo L. Cheng, Ph.D., here at the Massachusetts General Hospital. Our group has a long history of have investigating metabolomic signatures in prostatectomy specimens using *ex vivo* MR spectroscopy.^{3,4,5} Results from these studies of radical prostatectomy samples suggested the existence of metabolic or metabolomic fields, i.e. PCa metabolic information are observed to delocalize from PCa glands and into the surrounding structures that are benign tissue according to histology. These field effects likely create PCa “metabolomic lesions” that are larger than the histologic lesions. We have also continued to utilize multiparametric prostate MRI and MRI-Ultrasound fusion biopsy of the prostate to investigate biopsy cores taken from MRI targetable lesions and uninvolved prostate regions that appear normal by imaging criteria. Our current cohort of subjects in this study includes 25 patients, with suspicious lesions (PIRADS ≥ 3) undergoing MRI-Ultrasound fusion biopsy. From each patient, one targeted core biopsy and one standard template biopsy from a region appearing normal on MRI, immediately undergoes *ex vivo* MR spectroscopy to assess metabolite levels. Each specimen then is submitted for standard histopathologic analysis. Patient voided urine specimens, obtained just prior to the prostate biopsy, also undergo MR spectroscopy to assess metabolite levels. We are currently evaluating our data to assess for metabolic biomarkers, to distinguish malignant from benign, and clinically significant disease (Gleason ≥ 7) from clinically insignificant disease (Gleason 6). We will investigate the presence of potential metabolomic biomarkers in tissue, but also in urine from the same patients. We also will compare *ex vivo* biopsy metabolomic data with the *in vivo* pre-biopsy multiparametric prostate MRI data to assess for metabolomic characteristics of various PIRADS lesions. We look forward to analyzing and reporting these data in the near future.

³ Cheng LL, Burns MA, Taylor JL, He WL, Halpern EF, McDougal WS, Wu, CL. Metabolic characterization of human prostate cancer with tissue magnetic resonance spectroscopy. *Cancer Res.* 2005;65:3030-3034.

⁴ Maxeiner A, Adkins CB, Zhang Y, Taupitz M, Halpern EF, McDougal WS, Wu CL, Cheng LL. Retrospective Analysis of Prostate Cancer Recurrence Potential with Tissue Metabolomic Profiles. *The Prostate.* 2010; 70(7):710-717.

⁵ Wu CL, Jordan KW, Ratai EM, Sheng J, Adkins CB, DeFeo EM, Jenkins BG, Ying L, McDougal WS, Cheng LL. Metabolomic Imaging for Human Prostate Cancer Detection. *Sci. Transl. Med.* 2010;2(16):16ra8

My clinical research in active surveillance for low risk prostate cancer has also continued and we have made further progress in our investigation of our database of nearly 1000 men on active surveillance. In our work on assessing outcomes of men who initiate active surveillance when they are under 60 years of age, we have begun a collaborative analysis combining our cohort with that of Dr. Lawrence Klotz at Sunnybrook Health Sciences Centre in Toronto. We are currently performing the data analysis and expect manuscript submission within the next few months.

We also have investigated our cohort of men on active surveillance for those whom we would consider to be “borderline” candidates. Our guidelines for AS eligibility, formalized in 2008, include Gleason ≤ 6 , stage $\leq cT2a$, PSA < 10 ng/mL, ≤ 3 of 12 cores positive at diagnosis, and $\leq 20\%$ of any core involved at diagnosis. For this analysis, we defined borderline cases for AS as those patients with one or more of either Gleason score 7, PSA > 10 , stage $cT2a$, $> 33\%$ of cores positive at diagnosis, or $> 20\%$ of any core involved at diagnosis.

In the entire cohort ($n=990$), mean age at diagnosis was 66.9 years (± 7.9) and median PSA 5.1 (IQR 4-6.87). While the majority met all AS criteria, 312 patients (31.5%) met at least one of the borderline AS criteria; 2.4% of patients had Gleason 7, 7.6% had PSA > 10 , 8.0% were $cT2a$, 4.1% had $> 33\%$ of cores positive at diagnosis, and 18.4% had $> 20\%$ of any core involved. With mean follow-up 5.2 years, univariate survival analysis demonstrated no difference in freedom from treatment (FFT) between patients with Gleason 7 vs. ≤ 6 , $> 33\%$ vs. $\leq 33\%$ cores involved, or PSA > 10 vs. ≤ 10 . Lower FFT was noted among patients with $cT2a$ vs. $\leq cT1c$ disease (59.4% vs. 70.6%, $P=0.04$) and $> 20\%$ vs. $\leq 20\%$ of any core involved (56.5% vs. 69.5%, $P=0.01$). In multivariate analysis, $> 20\%$ core involvement remained a significant predictor for treatment, adjusting for PSA > 10 , Gleason > 6 , $> 33\%$ cores involved, and stage. Among the 312 borderline AS cases, there were only 5 (1.6%) cases of metastasis and 1 (0.3%) prostate cancer-specific death. These adverse outcomes were equivalent to the remainder of the cohort meeting strict AS criteria, which included 10 (1.5%) cases of metastasis and 2 (0.3%) prostate cancer-specific deaths.

We concluded that active surveillance remains a viable option for select patients who are borderline cases per current AS criteria. However, patients with higher volume disease may be more likely to progress to treatment. It is clear that long-term clinical outcomes in these patients should continue to be investigated, and we will continue to observe their outcomes over time. These analyses and results are being prepared as a manuscript for publication, which we anticipate in the next several months.

In addition to significant research accomplishments, I continue to meet my goals within the training program of this grant. I meet regularly with my two mentors, Drs. Matthew Smith and Bruce Zetter. In our regular meetings, we not only discuss research progress, but also focus on career planning and guidance. I attend regular urologic oncology clinical and research conferences at our institution and both attend and present at regional and national scientific meetings. I attend regular laboratory research meetings both for our own research progress, as well as reviewing other associated research in the current literature.

Key research accomplishments:

- Expanded analysis of three potential biomarkers to high score prostate cancer (Gleason score 8 or above) and metastatic disease
- Produced continued data indicative of differential expression between control and cancer groups for SerpinB1, and between disease progression for TIMP1 and SEMG2
- Optimized protocols to overcome previous setbacks and challenges in order to accumulate reliable and reproducible data
- Began metabolomic evaluation of tissue and urine in pilot cohort of men undergoing MRI-Ultrasound fusion targeted prostate biopsy
- Investigated outcomes of active surveillance in young men and men with borderline clinical features

Reportable Outcomes:

- *Preston MA, ***Feldman AS**, Coen JJ, McDougal WS, Smith MR, Paly JJ, Carrasquillo R, Wu CL, Dahl DM, Barrisford GW, Blute MB, Zietman AI. Active surveillance for prostate cancer: need for intervention and survival. *Urol Oncol*. 2015 Jun 6. pii: S1078-1439.
*Co-first Authorship
- Preston MA, Batista JL, Wilson KM, Carlsson SV, Gerke T, Sjoberg DD, Dahl DM, Sesso HD, **Feldman AS**, Gann PH, Kibel AS, Vickers AJ, Mucci LA. Baseline Prostate-Specific Antigen Levels in Midlife Predict Lethal Prostate Cancer. *J Clin Oncol*. 2016 Aug 10;34(23):2705-11
- Kuppermann D, Preston M, Paly J, Dahl D, Efstathiou JA, Blute ML, Zietman AL, **Feldman AS**. Active Surveillance for Low Risk Localized Prostate Cancer in Men Under 60 Years of Age. Abstract presented at the Mid-Atlantic and New England Sections of the American Urological Association national meeting, October 2015 and at Society of Urologic Oncology, December 2015

Conclusion

In summary, this fourth year of my DOD PCRP PRTA has been very productive. After identifying a number of potential biomarkers pertaining to prostate cancer, I have worked to explore the expression patterns' correlations with disease progression. In particular this year, I expanded my patient populations to include metastatic disease and conducted ELISAs on a number of proteins to get quantitative results. The quantifications allowed unambiguous comparisons across patient populations and revealed previously unobserved expression trends.

In addition to our work in proteomic biomarker evaluation, we have begun to explore metabolomic biomarkers and their relationship with MRI-based imaging. This collaborative project is very exciting and will complement our current work in proteomic biomarkers and active surveillance very well.

All of our projects are extraordinarily clinically relevant and have no trouble applying to “so what” criteria. While the prostate specific antigen (PSA) serves as the predictive biomarker for prostate cancer, new diagnostics with more consistent predictability and enhanced performance characteristics are sorely needed. The work funded by this grant directly addresses the challenge of discovering more predictive, dependable, and informative biomarkers; we are in the process of producing results to meet this goal.

Appendices:

Curriculum Vitae for Dr. Adam S. Feldman is included in this annual reporting.

Curriculum Vitae

Date Prepared: October 26, 2016

Name: Adam S. Feldman, M.D., M.P.H.

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Work E-Mail: afeldman@partners.org

Work FAX: 617-726-9150

Place of Birth: New York, NY

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)	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
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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

Other Professional 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

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

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

- 2012-13 Prostate Cancer Foundation Young Investigator Awards Review Committee
- 2013-15 Bladder Cancer Advocacy Network Young Investigator Awards Review Committee
- 2013-14 Prostate Cancer Foundation Challenge Awards Review Committee
- 2013-16 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

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

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 • 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 • 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 • 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 • 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

		• 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
2009-2010	Investigator	\$75,000 per year for 3 years. Harvard Catalyst Pilot Grant Program NIH UL1 RR 025758-02 Clinical and Translational Science Center Grant Sonoelastography for Tumor-Targeted Prostate Biopsy
2015	P.I.	• This study is a pilot study of the utility of sonoelastography for targeting biopsy to foci of cancer in the prostate. 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
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
2011-present	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-present	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
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.

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-present	HMS Surgical Clerkship Lecture on Urologic Surgery		<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-present	<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	

Laboratory and Other Research Supervisory and Training Responsibilities

2007-present	Supervision and mentoring of Research Fellow	5 hours/week
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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 [Invited Lecture]
2013	Ft. Lauderdale, FL	Faculty (CME Course): Winter Oncology Symposium – Holy Cross Hospital
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 –

2014	Cambridge, MA	Refresher course: Small renal mass (T1a) – the case for resection Faculty (CME Course): Primary Care Internal Medicine: Principles & Practice – Male Urology [Invited Lecture]
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 MGH Experience in MRI Fusion Prostate Biopsy
2014	Cambridge, MA	Faculty (CME Course): Primary Care Internal Medicine: Prostate in the Aging Male [Invited Lecture]
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

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 <i>[Invited Lecture]</i>
2015	Boston, MA	Management of the Small Renal Mass – Massachusetts General Hospital Department of Urology Grand Rounds <i>[Invited Lecture]</i>

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]

Regional Invited Presentations and Courses

2009	Dedham, MA	Urologic Oncology: An Overview. Massachusetts Health Information Management Association [Invited Lecture]
2010	Mt. Kisco, NY	Controversies in the Management of Small Renal Masses [Invited Lecture]
2011	Dedham, MA	Penile Cancer. Urology Nursing Society [Invited Lecture]
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
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 [Invited Lecture]
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

National Invited Presentations and Courses

2007	Hollywood, FL	Radical prostatectomy after inguinal hernia repair. The American Hernia Society [Invited Lecture]
2009	Boston, MA	Renal Cell Carcinoma: Surgical Management at Massachusetts General Hospital. Exchange Experience Program on Renal Cancer [Invited Lecture]
2009	Las Vegas, NV	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" [Invited Lecture]
2009	Scottsdale, AZ	Faculty (CME Course): Maximizing Bone Health for Patients With Prostate Cancer: Establishing the "Who, What, Why & How?" [Invited Lecture]
2010	San Francisco, CA	Faculty (CME Course): Master Class on Integrating Novel Antiresorptive Agents into the treatment of Prostate Cancer. [Invited Lecture]
2010	Boston, MA	Faculty (CME Course): Trauma and Critical Care Symposium – Penile and Genitalia Trauma. [Invited Lecture]
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 [Invited Lecture]
2013	New Orleans,	Faculty – 3D Laparoscopic Urology: Surgical Techniques and Hands-On

	LA	
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	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: First Global Summit on Precision Diagnosis for Prostate Cancer – Clinical Discussant

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

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.

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.
2. Banyard J, Bao L, Hofer MD, Zurakowski D, Spivey KA, **Feldman AS**, Hutchinson LM, Kuefer R, Rubin MA, Zetter BR. Collagen XXIII expression is associated with prostate cancer recurrence and distant metastases. *Clin Cancer Res*. 2007;13(9):2634-42.
3. **Feldman AS**, Banyard J, Wu C-L, McDougal WS, Zetter BR . Cystatin B as a tissue and urinary biomarker of bladder cancer recurrence and disease progression. *Clin Cancer Res*. 2009;15(3):1024-31.
4. Tanrikut C, **Feldman AS**, Altemus M, Paduch DA, Schlegel PN. Adverse effect of paroxetine on sperm. *Fertility and Sterility*. 2009. June 10, Epub ahead of print.
5. Kubota K, Anjum R, Yu Y, Kunz RC, Andersen JN, Kraus M, Keilhack H, Nagashima K, Krauss S, Pawletz C, Hendrickson RC, **Feldman AS**, Wu CL, Rush J, Villen J, Gygi SP. Sensitive multiplexed analysis of kinase activities and activity-based kinase identification. *Nature Biotechnology*. 2009; 27(10): 933-40.
6. Pandharipande PV, Gervais DA, Hartman RI, Harisinghani MG, **Feldman AS**, Mueller PR, Gazelle GS. Renal mass biopsy to guide treatment decisions for small incidental renal tumors: a cost-effectiveness analysis. *Radiology*. 2010; 256(3):836-46.
7. Coen JJ, **Feldman AS**, Smith MR, Zietman AL. Watchful waiting for localized prostate cancer in

the PSA era: what have been the triggers for intervention? BJU Int. 2010 Sep 22. Epub ahead of print.

8. Psutka SP, **Feldman AS**, Rodin D, Olumi AF, Wu CL, McDougal WS. Men With Organ-confined Prostate Cancer and Positive Surgical Margins Develop Biochemical Failure at a Similar Rate to Men With Extracapsular Extension. Urology. 2011 Mar 14. [Epub ahead of print]
9. **Feldman AS**, McDougal WS. Long Term Outcome of Excisional Organ Sparing Surgery for Carcinoma of the Penis. J Urol. 2011 Oct;186(4):1303-7.
10. Fernandez CA, Milholland JM, Zwarthoff EC, **Feldman AS**, Karnes JR, Shuber AP. A noninvasive multi-analyte diagnostic assay: combining protein and DNA markers to stratify bladder cancer patients. Research and Reports in Urology. 2012 Feb 22. [Epub]
11. Gershman B, Zietman AL, **Feldman AS**, McDougal WS. Transperineal Template-Guided Prostate Biopsy for Patients with Persistently Elevated PSA and Multiple Prior Negative Biopsies. Urol Oncol. 2013 Oct;31(7):1093-7.
12. *Psutka SP, ***Feldman AS**, McDougal WS, McGovern FJ, Mueller P, Gervais DA. Long-Term Oncologic Outcomes After Radiofrequency Ablation for T1 Renal Cell Carcinoma. Eur Urol. 2013 Mar;63(3):486-92.
*Co-first Authorship
13. Leung CP1, Klausner AP, Habibi JR, King AB, **Feldman A**. Audience response system: a new learning tool for urologic conferences. Can J Urol. 2013 Dec;20(6):7042-5.
14. Xu R, Horick N, McGovern FJ, Dahl DM, **Feldman AS**, Blute ML, Olumi AF, Michaelson MD. Prognostic significance of indeterminate lung nodules in renal cell carcinoma. Urol Oncol. 2014 Apr;32(3):355-61.
15. Sheth RA, **Feldman AS**, Walker TG. Renoduodenal Fistula After Transcatheter Embolization of Renal Angiomyolipoma. Cardiovasc Intervent Radiol. 2014 Apr 11. [Epub ahead of print]
16. Pollock CB, McDonough S, Wang VS, Lee H, Ringer L, Li X, Prandi C, Lee RJ, **Feldman AS**, Koltai H, Kapulnik Y, Rodriguez OC, Schlegel R, Albanese C, Yarden RI. Strigolactone analogues induce apoptosis through activation of p38 and the stress response pathway in cancer cell lines and in conditionally reprogramed primary prostate cancer cells. Oncotarget. 2014 Apr 2. [Epub ahead of print]
17. Yang P, Cornejo KM, Sadow PM, Cheng L, Wang M, Xiao Y, Jiang Z, Oliva E, Jozwiak S, Nussbaum RL, **Feldman AS**, Paul E, Thiele EA, Yu JJ, Henske EP, Kwiatkowski DJ, Young RH, Wu CL. Renal Cell Carcinoma in Tuberous Sclerosis Complex. Am J Surg Pathol. 2014 May 14. [Epub ahead of print]
18. Hedgire SS, Tabatabaei S, McDermott S, **Feldman A**, Dahl DM, Harisinghani MG. Diversion ahead: imaging appearance of urinary diversions and reservoirs. Clin Imaging. 2014 Jul-Aug;38(4):418-27.
19. Rodríguez D, Preston MA, Barrisford GW, Olumi AF, **Feldman AS**. Clinical features of leiomyosarcoma of the urinary bladder: Analysis of 183 cases. Urol Oncol. 2014 Oct;32(7):958-65.
20. Siddiqui MM, Heney NM, McDougal WS, Feldman AS (2015) Disparities in overall and urothelial carcinoma specific mortality associated with healthcare insurance status. Bladder 2(1):e10. doi: 10.14440/bladder.2015.39. *Accepted for publication.*
21. Ringer L, Sirajuddin P, Tricoli L, Waye S, Choudhry MU, Parasido E, Sivakumar A, Heckler M, Naeem A, Abdelgawad I, Liu X, **Feldman AS**, Lee RJ, Wu CL, Yenugonda V, Kallakury B,

- Dritschilo A, Lynch J, Schlegel R, Rodriguez O, Pestell RG, Avantaggiati ML, Albanese C. The induction of the p53 tumor suppressor protein bridges the apoptotic and autophagic signaling pathways to regulate cell death in prostate cancer cells. *Oncotarget*. 2014 Nov 15;5(21):10678-91
22. Hanske J, Sanchez A, Schmid M, Meyer CP, Abdollah F, **Feldman AS**, Kibel AS, Sammon JD, Menon M, Eswara JR, Noldus J, Trinh QD. A Comparison of 30-Day Perioperative Outcomes in Open Versus Minimally Invasive Nephroureterectomy for Upper Tract Urothelial Carcinoma: Analysis of 896 Patients from the American College of Surgeons-National Surgical Quality Improvement Program Database. *J Endourol*. 2015 Jun 11. [Epub ahead of print]
 23. Hanske J, Sanchez A, Schmid M, Meyer CP, Abdollah F, Roghmann F, **Feldman AS**, Kibel AS, Sammon JD, Noldus J, Trinh QD, Eswara JR. Comparison of 30-day perioperative outcomes in adults undergoing open versus minimally invasive pyeloplasty for ureteropelvic junction obstruction: analysis of 593 patients in a prospective national database. *World J Urol*. 2015 May 13. [Epub ahead of print]
 24. Huang J, **Feldman AS**, Dong L, Cornejo K, Liu Q, Dahl DM, Wu S, Blute ML, Huang Y, Wu CL. Preoperative Anemia as an Independent Prognostic Indicator of Papillary Renal Cell Carcinoma. *Clin Genitourin Cancer*. 2015 May 4. pii: S1558-7673
 25. Rodríguez D, Cornejo KM, Sadow PM, Santiago-Lastra Y, **Feldman AS**. Myopericytoma tumor of the glans penis. *Can J Urol*. 2015 Jun;22(3):7830-3.
 26. *Preston MA, ***Feldman AS**, Coen JJ, McDougal WS, Smith MR, Paly JJ, Carrasquillo R, Wu CL, Dahl DM, Barrisford GW, Blute MB, Zietman AI. Active surveillance for prostate cancer: need for intervention and survival. *Urol Oncol*. 2015 Jun 6. pii: S1078-1439
*Co-first Authorship
 27. Sanchez A, Rodríguez D, Allard CB, Bechis SK, Sullivan RJ, Boeke CE, Kuppermann D, Cheng JS, Barrisford GW, Preston MA, **Feldman AS**. Primary genitourinary melanoma: Epidemiology and disease-specific survival in a large population-based cohort. *Urol Oncol*. 2015 Dec 28. [Epub ahead of print]
 28. Sheth RA, **Feldman AS**, Paul E, Thiele EA, Walker TG. Angiographic and volumetric effects of mammalian target of rapamycin inhibitors on angiomyolipomas in tuberous sclerosis. *World J Radiol*. 2016 Mar 28;8(3):308-15.
 29. Preston MA, Batista JL, Wilson KM, Carlsson SV, Gerke T, Sjoberg DD, Dahl DM, Sesso HD, **Feldman AS**, Gann PH, Kibel AS, Vickers AJ, Mucci LA. Baseline Prostate-Specific Antigen Levels in Midlife Predict Lethal Prostate Cancer. *J Clin Oncol*. 2016 Aug 10;34(23):2705-11.
 30. Sheth RA, **Feldman AS**, Paul E, Thiele EA, Walker TG. Sporadic versus Tuberous Sclerosis Complex-Associated Angiomyolipomas: Predictors for Long-Term Outcomes following Transcatheter Embolization. *J Vasc Interv Radiol*. 2016 Aug 10.
 31. Baumann BC, Bosch WR, Bahl A, Birtle AJ, Breau RH, Challapalli A, Chang AJ, Choudhury A, Daneshmand S, El-Gayed A, **Feldman A**, Finkelstein SE, Guzzo TJ, Hilman S, Jani A, Malkowicz SB, Mantz CA, Master V, Mitra AV, Murthy V, Porten SP, Richaud PM, Sargos P, Efstathiou JA, Eapen LJ, Christodouleas JP. Development and Validation of Consensus Contouring Guidelines for Adjuvant Radiation Therapy for Bladder Cancer After Radical Cystectomy. *Int J Radiat Oncol Biol Phys*. 2016 Sep 1;96(1):78-86.

Other peer-reviewed publications:

1. **Feldman AS**, Bauer SB. Diagnosis and management of dysfunctional voiding. *Curr Opin Pediatr*. 2006;18(2):139-47.
2. **Feldman AS** and McDougal WS. Inguinal Node Dissection for Penile Carcinoma. AUA Update. 2008.
3. **Feldman AS**, McDougal WS, Harisinghani MG. The potential of nanoparticle-enhanced imaging. *The Journal of Urologic Oncology, Seminar Section*. 2008;26(1):65-73.
4. Kaufman DS, Shipley WU, **Feldman AS**. Bladder Cancer. *The Lancet*. 2009; 374(9685):239-49.
5. Eisner BH and **Feldman AS**. Nanoparticle imaging for genitourinary cancers. *Cancer Biomark*. 2009;5(2):75-9.
6. Siddiqui MM, **Feldman AS**. Advances in the evaluation and management of lymph node involvement in urothelial carcinoma of the bladder. *Expert Rev Anticancer Ther*. 2010;10(12):1855-9.
7. Kreydin EI, Barrisford GW, **Feldman AS**, Preston MA. Testicular cancer: what the radiologist needs to know. *AJR Am J Roentgenol*. 2013 Jun;200(6):1215-25.
8. Barrisford GW, Kreydin EI, Preston MA, Rodriguez D, Harisighani MG, **Feldman AS**. Role of imaging in testicular cancer: current and future practice. *Future Oncol*. 2015 Sep;11(18):2575-86.

Non-peer reviewed scientific or medical publications/materials in print or other media:

1. **Feldman AS**, Gargollo PC, Grocela JA. Genitourinary Trauma. In: Sheridan RL, Ed. *The Trauma Handbook of the Massachusetts General Hospital*. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. p. 584-508.
3. **Feldman AS** and Dahl DM. , 2006. June, 2-6, 2006. Laparoscopic Radical Prostatectomy. *US Oncological Disease 2006*. 2006: pp. 56-58.
4. **Feldman AS**, Mueller PR, McDougal WS. Radiofrequency Ablation. In: Ahmed HU, et al. Eds. *Interventional Techniques in Uro-Oncology*. Oxford, UK: Wiley; 2011. p. 68-85.
5. **Feldman AS**, Hsu C, Kurtz M, Cho KC. Etiology and evaluation of hematuria in adults. In: UpToDate 19.2. June 17, 2011.
6. Psutka SP, Daha A, McGovern FM, McDougal WS, Mueller PR, Gervais D, **Feldman AS**. Complication rates increase with radiofrequency ablation of large, central renal tumors. *AUA News*. November 2011. p. 9-10.
7. **Feldman AS** and McDougal WS. Evolving Imaging Modalities in the Diagnosis and Staging of Penile Cancer. In: Spiess P. Ed., *Penile Cancer: Diagnosis and Treatment*. Springer. New York. 2013.
8. **Feldman AS**, Lee RJ, Efsthathiou JE, Dahl DM, Michaelson MD, Zietman A. Cancer of the bladder, ureter, and renal pelvis. In: DeVita VT, Lawrence TS, Rosenberg SA, Eds. *Cancer: Principles & Practice of Oncology*, 10th edition. Lippincott, Williams and Wilkins. Baltimore, MD. 2014
9. **Feldman AS**. POINT: Is Immediate Radical Cystectomy Justified When Non-Muscle-Invasive Bladder Cancer First Presents as High-Grade T1 Urothelial Carcinoma on Re-Resection? *Oncology (Williston Park)*. 2016 Jun;30(6):541-2, 545.

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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 30% of my time. Teaching residents 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 and residents 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 a member of the MGH faculty. I also have formed a close collaborative relationship with Dr. Steven Gygi at the Taplin Mass Spectrometry Facility at HMS, working on biomarker discovery and investigating kinase activity in prostate and kidney cancers. My research projects have led to the presentation of several research abstracts at national meetings and publications, a patent on a novel biomarker, a peer-reviewed institutional grant, and corporate sponsored research funding. In 2008, I was awarded a three year Young Investigator Award from the Prostate Cancer Foundation for the discovery and development of novel biomarkers in prostate cancer and in 2011 I was awarded a five year Department of Defense Physician Research Training Award to continue my biomarker research in prostate cancer.

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 helping me achieve my academic goals by refining my ability to design and implement translational and clinical research and produce high quality independent investigations.

My clinical focus has been in Urologic Oncologic surgery. 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, including investigations of active surveillance for prostate cancer, nephron sparing techniques in renal cell carcinoma, the utility of renal mass biopsy and outcomes in penile sparing surgery for penile cancer. Clinical teaching has 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 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.