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14. ABSTRACT

The Research Project supported by this DOD Award investigates the potential of *in vivo* and *ex vivo* MRS in characterizing the metabolomic spectra of TSC-associated renal masses. In an effort to optimize our *in vivo* image acquisition protocol, we began by scanning healthy volunteers and have formalized our novel *in vivo* MRS protocol, which will be submitted for publication. Subsequently, our overall enrollment of TSC patients with lipid poor renal masses had been lower than expected. For this reason and in order to meet our goals of gaining more metabolomic data on renal masses, we 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 was also expanded with the utilization of our MGH Genitourinary Oncology Tumor Bank, including AML and other renal tumor tissue. Our *ex vivo* work from the tumor bank was presented virtually at the 2020 American Urological Association national meeting and was awarded Best Poster. The manuscript is currently under preparation. The findings from this study will help the TSC community gain an understanding of the metabolomics of AML and other renal tumors.

15. SUBJECT TERMS

Kidney Cancer; Metabolomics; Tuberous Sclerosis Complex

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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, 22 research subjects have been consented and underwent multiparametric MRI and MRS of the kidneys. Fourteen of the subjects have confirmed diagnoses of Tuberous Sclerosis Complex, while eight of the subjects have sporadic renal masses. Four have undergone clinically-indicated renal mass biopsy (RMB) with core biopsy specimens evaluated with *ex vivo* MRS immediately after RMB. Five subjects have had partial nephrectomies and had tissue evaluated with *ex vivo* MRS immediately after.

As noted in previous reports, given the slow rate of recruitment of patients with TSC, we elected to augment our study with *ex vivo* MRS analysis on 89 specimens from 55 subjects from our MGH GU Oncology Frozen Tumor Bank. 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. The specimens for *ex vivo* MRS from our tissue bank were collected from 55 unique patients who underwent radical or partial nephrectomy. Seven specimens were of angiomyolipoma, 13 papillary RCC, 21 clear cell RCC, 13 chromophobe RCC, 10 oncocytoma, and 25 benign tissue specimens adjacent to one of the previously mentioned. High-resolution magic angle spinning (1H HRMAS) ex vivo MRS spectra images were obtained. This work has been presented

virtually at the 2020 American Urological Association national meeting and was awarded Best Poster. The manuscript is currently under preparation.

It is also important to note that this past year has been a challenge due to COVID and the related restrictions. In the Spring of 2020, the COVID shutdown halted our clinical and research activity through the early summer. In addition, our research assistant on the project moved on to medical school and our institutional hiring freeze led to further research delays. For these reasons, a second no-cost extension was requested and granted.

Detailed info on prospective patient *in vivo* and *ex vivo* work:

Since the prior reporting period, five additional patients underwent clinically-indicated MRI with in vivo MRS according to the previously described protocol. 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 who underwent *in vivo* MRS. Two patients who underwent MRI with in vivo MRS had no history of TSC, but had sporadic renal masses. The first patient had a 1.8 cm right anterior interpolar region lesion and the second patient had a 4.3 cm left inferior pole lesion. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figure 1).

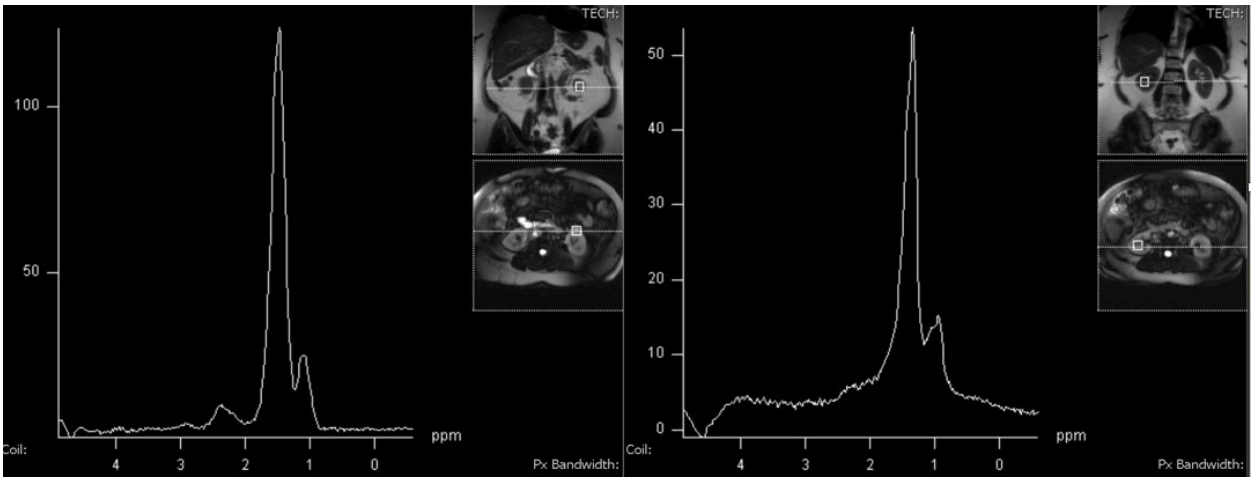

Figure 1: Example of in vivo MRS spectra from a patient without a history of TSC. The image on the right obtained with targeting of normal renal parenchymal tissue. Image on the left obtained with targeting contralateral, left renal lesion, RCC favored by radiographic review.

Subsequently, both of these patients went on to partial nephrectomy. On final pathology, the first patient was found to have a stage T1a, grade 2 clear cell renal cell carcinoma, while the second patient had a stage T1b, grade 2 clear cell renal cell carcinoma, respectively. Following resection, both specimens were immediately taken for ex vivo MRS according to the previous described protocol. The ex vivo MRS results from these will be used for comparison and correlation with their in vivo results. Metabolic spectra of the lesion of interest were obtained (Figure 2).

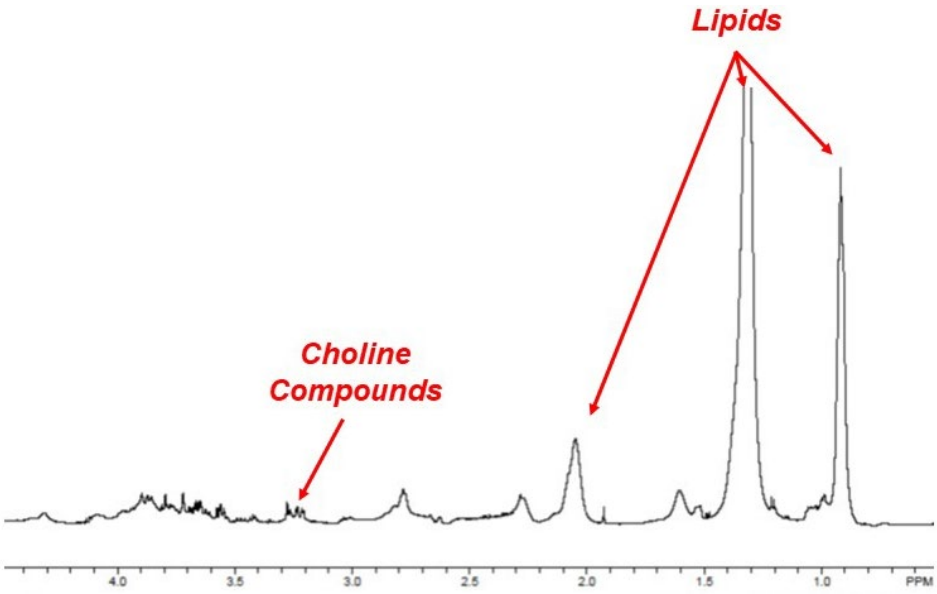

Figure 2: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained with intact partial nephrectomy specimen from renal cell carcinoma, clear cell type kidney tissue from single patient.

One patient with a history of TSC also underwent clinically-indicated MRI with in vivo MRS according. In the left kidney, this patient was found to have a unchanged 2.0 cm enhancing lesion in the upper pole, consistent with previous biopsy-proven oncocytoma. In the right kidney, the patient has several lesions: a 3.1cm enhancing mass consistent with a previous biopsy-proven AML, a 1.1 cm hypointense enhancing lateral mid/lower pole lesion which does not contain fat and could represent lipid-poor AML or papillary RCC, and two enhancing lesions containing fat in the mid pole, measuring 1.3 cm and 8mm. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figure 3).

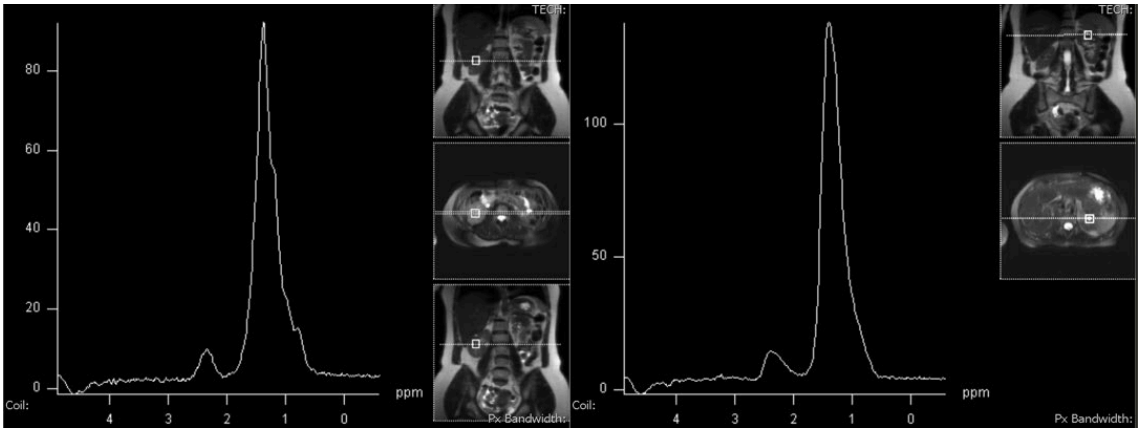

Figure 3: Example of in vivo MRS spectra from a single patient with history of TSC. The image on the left obtained with targeting normal parenchymal renal tissue. The image on the right obtained with targeting the previous biopsy-proven oncocytoma.

One patient with a history of TSC with numerous bilaterial AMLs underwent renal mass biopsy with ex *vivo* MRS. Two lesions were targeted in the lower pole of the right kidney: one was a 2.6 cm heterogeneously enhancing exophytic lesion, the second was a 1.9 cm complex cyst with thick enhancing septations and no internal fat. Biopsy pathology of the first lesion was found to be a fat-poor angiomyolipoma, while the second lesion was non-diagnostic but contained atypical spindled and oncocytic cells. Following biopsy, both specimens were immediately taken for ex vivo MRS according to the previous described protocol. Metabolic spectra of the lesion of interest were obtained (Figure 4).

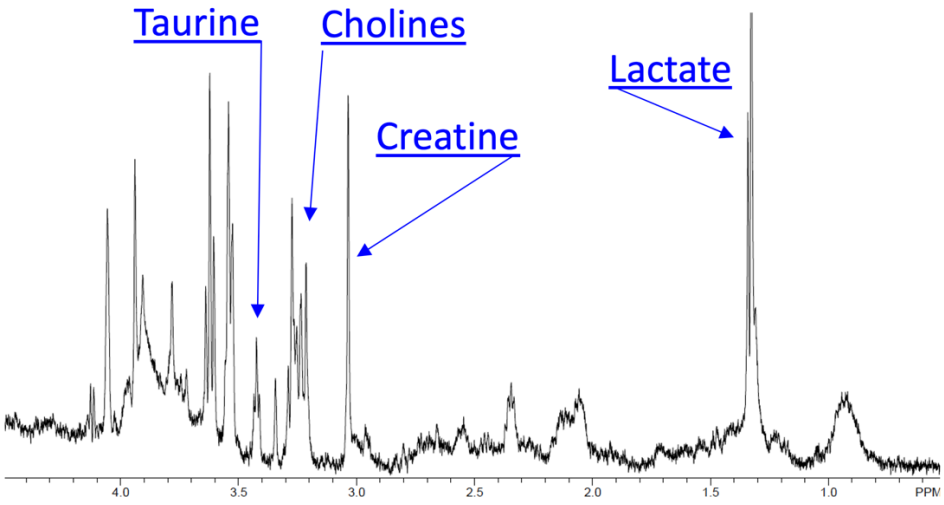

Figure 4: Example of high-resolution magic angle spinning (1H HRMAS) ex vivo MRS spectra image obtained with intact biopsy-core specimen from fat-poor angiomyolipoma kidney tissue from single patient

Additionally a sporadic renal mass patient, who underwent in vivo MRS with MRI from the prior reporting period, underwent partial nephrectomy of a left posterior midpole lesion. Histopathologic analysis confirmed Type 1 Papillary Renal Cell Carcinoma. On immunohistochemical stain, the tumor cells are positive for CK7, CD10 and focally positive for

CD57 and negative for WT1 and BRAF, supporting the diagnosis. Metabolic spectra of the lesion of interest were obtained (Figure 5).

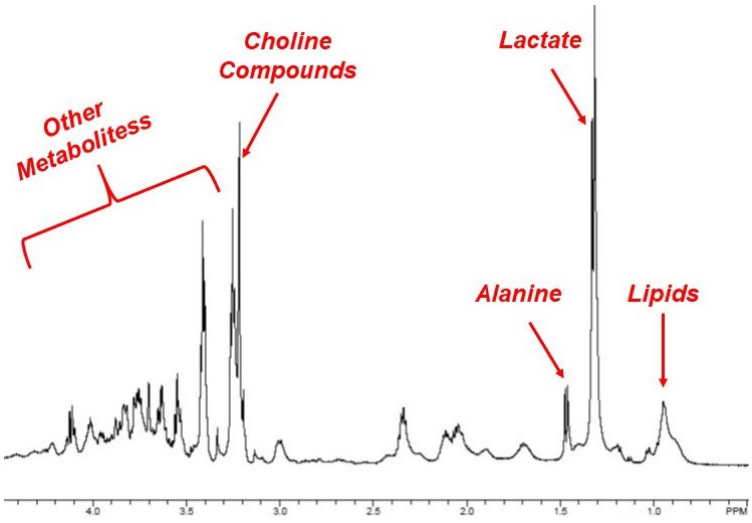

Figure 5: Example of high-resolution magic angle spinning (1H HRMAS) ex vivo MRS spectra image obtained from partial nephrectomy specimen of Papillary Type 1 RCC.

In the second quarter of the year, one patient with a history of TSC underwent clinically-indicated MRI with *in vivo* MRS. This patient was found to have an unchanged 2.3 cm lobular lesion arising from the anterolateral right renal lower pole. It is favored to represent a lipid-poor angiomyolipoma based on imaging characteristics. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figure 6). A second patient with a history of TSC was consented during a previous reporting period, but underwent clinically-indicated MRI with *in vivo* MRS during this reporting period. He was found to have multiple fat-containing lesions in the bilateral kidneys, consistent with lipid-rich angiomyolipomas, the largest measuring 3.3 cm on the right, and a smaller 5mm T2 hypointense lesion likely representing a lipid-poor angiomyolipoma.

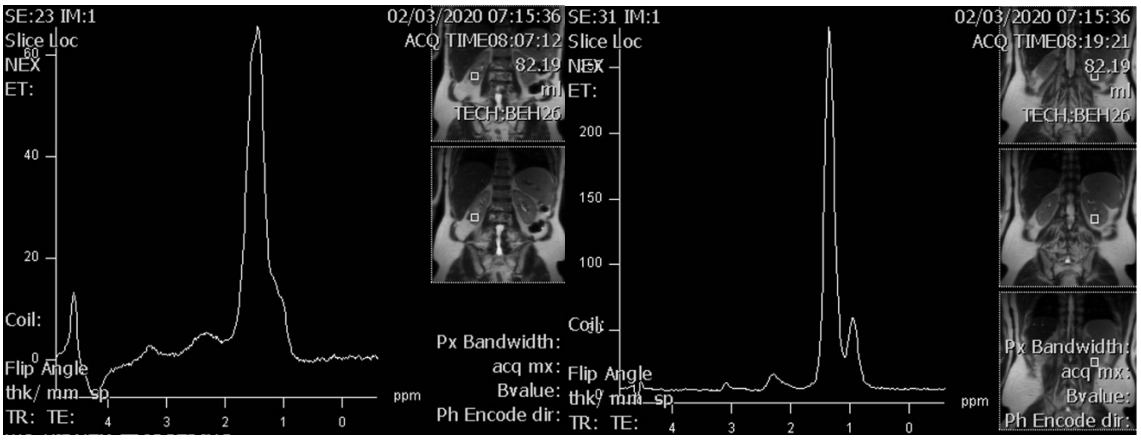

Figure 6: Example of in vivo MRS spectra from a single patient with history of TSC. The image on the right obtained with targeting normal parenchymal renal tissue. The image on the left obtained with targeting the lesion, favored to be a lipid-poor angiomyolipoma by radiographic review.

During the third quarter of the year, we as most of the US and world were shut down clinically and our research labs shut down as well. For this reason, no new patients were enrolled and the majority of the research that occurred was done remotely as members of our lab were not allowed to be physically in the research laboratory. That being said, we did make significant achievements in our analysis of the data from banked *ex vivo* specimens and this is reported in the section later in this report.

During the fourth quarter of the year once clinical research activity resumed, one additional patient underwent clinically-indicated MRI with *in vivo* MRS according to the previously described protocol. There were no renal mass biopsies or nephrectomies performed at this time. One patient with a history of TSC underwent clinically-indicated MRI with *in vivo* MRS. This patient was found to have a 2.4 cm exophytic right upper pole renal mass. It is favored to represent a lipid-poor angiomyolipoma based on imaging characteristics. Metabolic spectra of the lesion of interest and healthy parenchymal tissue, as comparison, were obtained (Figure 7).

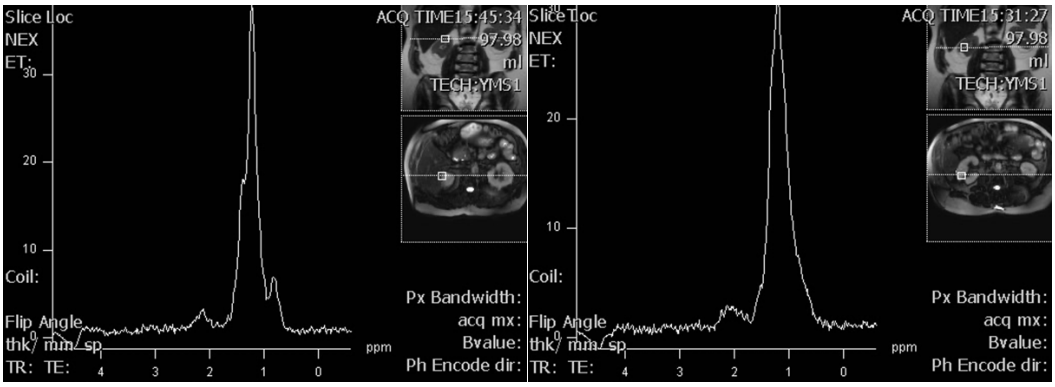

Figure 7: Example of in vivo MRS spectra from a single patient with history of TSC. The image on the left obtained with targeting the lesion, favored to be a lipid-poor angiomyolipoma. The image on the right obtained with targeting normal parenchymal renal tissue.

Detailed info on *ex vivo* analysis of MGH GU Tumor Bank fresh frozen tissue:

In order to improve our subject size and meet our goals of *ex vivo* analysis, we have taken advantage of our previously collected and annotated MGH GU Oncology Frozen Tumor Bank. Our internal IRB for utilization of tissue bank specimens was approved on 2/27/2020. After approval we began our analysis of these specimens. 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 were 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 analyzed metabolomic spectra across patients to assess for any consistency in expression between tumor types.

We completed ex vivo MRS on 89 specimens stored in the tumor bank. These were collected from 55 unique patients who underwent radical or partial nephrectomy. Seven specimens were of angiomyolipoma, 13 papillary RCC, 21 clear cell RCC, 13 chromophobe rcc, 10 oncocytoma,

and 25 benign tissue adjacent to one of the previously mentioned. High-resolution magic angle spinning (1H HRMAS) ex vivo MRS spectra images were obtained and example spectra are presented below (Figures 8-12).

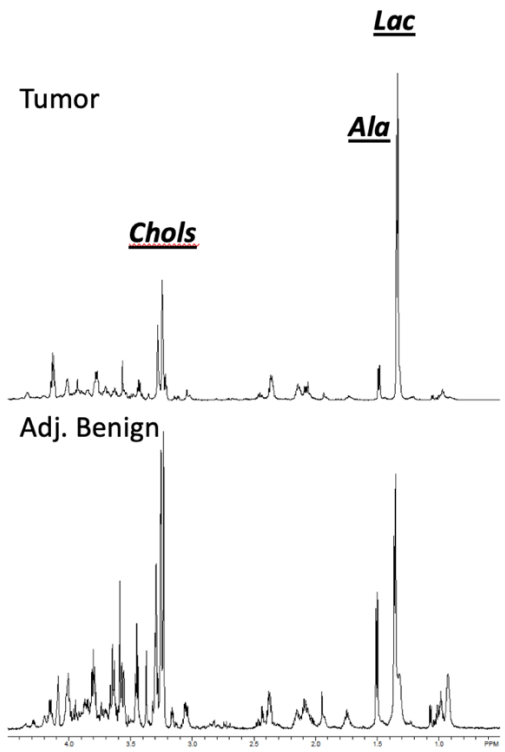

Figure 8: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained from fresh frozen tumor bank specimen of intact partial nephrectomy specimen from renal cell carcinoma, clear cell type kidney tissue and adjacent benign tissue from single patient.

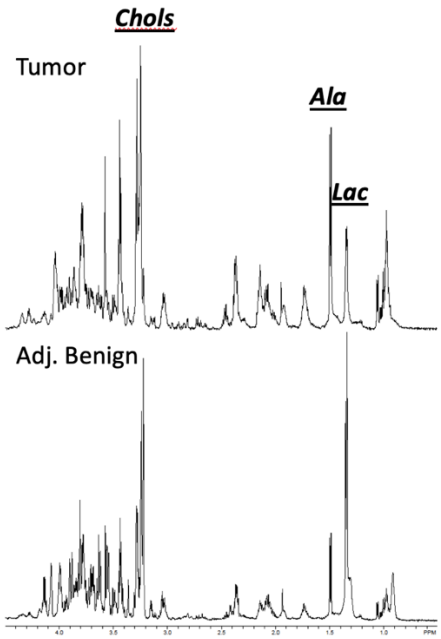

Figure 9: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained from fresh frozen tumor bank specimen of intact partial nephrectomy specimen from renal cell carcinoma, papillary type kidney tissue and adjacent benign tissue from single patient.

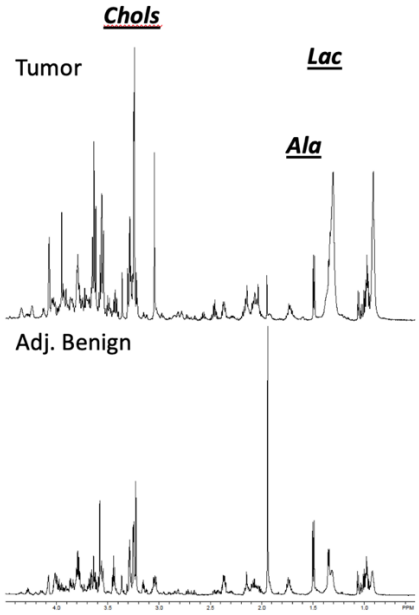

Figure 10: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained from fresh frozen tumor bank specimen of intact partial nephrectomy specimen from renal cell carcinoma, chromophobe type kidney tissue and adjacent benign tissue from single patient.

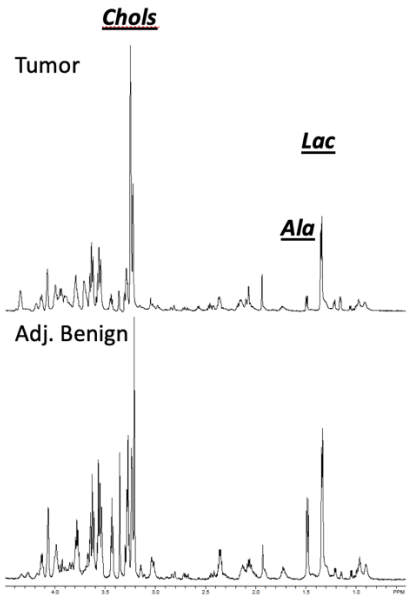

Figure 11: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained from fresh frozen tumor bank specimen of intact partial nephrectomy specimen from oncocytoma kidney tissue and adjacent tissue from single patient.

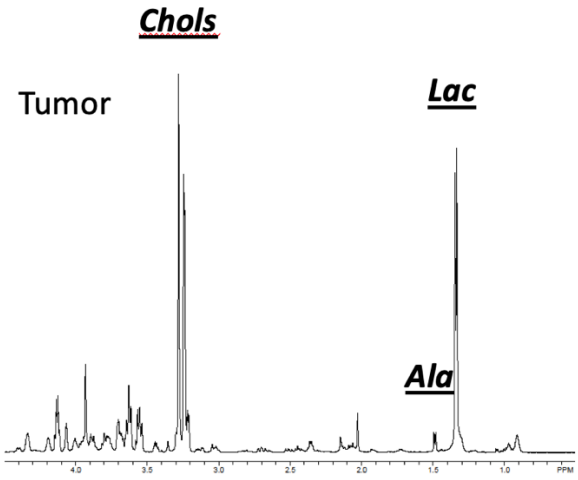

Figure 12: Example of high-resolution magic angle spinning (^{1}H HRMAS) *ex vivo* MRS spectra image obtained from fresh frozen tumor bank specimen of intact partial nephrectomy specimen from angiomyolipoma kidney tissue from single patient.

To further investigate the metabolomic profile of RCC, we compared 38 RCC (16 clear cell, 11 papillary, 11 chromophobe) and 13 adjacent normal tissue specimens (matched pairs). A

MatLab-based curve fitting program developed by our laboratory was used to process the spectra to produce relative intensities for each analyzed spectral region of interest. Our outcome of interest was to identify metabolites indicative of renal cell carcinoma rather than benign tissue. Metabolomic profiles of RCC & adjacent benign renal tissue were compared, and false discovery rates (FDR) were used to account for multiple testing. Regions of interest (ROI) with FDR <0.05 were selected as potential predictors of malignancy. The Wilcoxon rank sum test was used to compare median MRS relative intensities for the candidate predictors. Logistic regression was used to determine odds ratios for risk of malignancy based on abundance of each metabolite.

We found Metabolic predictors of malignancy based on FDR to include histidine, phenylalanine, phosphocholine, serine, phosphocreatine, creatine, glycerophosphocholine, valine, glycine, myo-inositol, scylla-inositol, taurine, glutamine, spermine, acetoacetate & lactate (Table 1 and Figure 13). Higher levels of spermine, histidine & phenylalanine at 3.15-3.13 ppm were associated with a decreased risk of RCC (OR 4x10-5, 95% CI 7.42x10-8, 0.02), while 2.84-2.82 ppm increased the risk of malignant pathology (OR 7158.67, 95% CI 6.3, 8.3x106), and the specific metabolites characterizing this region remain to be identified. Tumor stage did not appear to affect the metabolomics of malignant tumors, suggesting that metabolites are more dependent on histologic subtype.

	RCC (N=38)	Adjacent benign parenchyma (N=13)	P-value			
Age (years)	55.3 ± 11.4	50.8 ± 7.3	0.1818			
Males (n, %)	27 (71.1)	8 (61.5)	0.7302			
Race (n, %)	37 (97.4)	13 (100)	1.00			
Median MRS relative intensities (IQR)				**FDR P-value**	**Odds ratios (OR, 95% CI)**	**P-value for OR**
4.07-4.05 (Myo-Inositol)	0.80 (0.48, 1.32)	1.84 (1.27, 2.24)	0.0026	0.027	0.38 (0.18, 0.82)	0.013
4.02-4.00 (TBD)	1.21 (0.68, 2.07)	0.50 (0.06, 0.88)	0.0073	0.034	3.12 (1.10, 8.84)	0.032
3.99-3.96 (Histidine, Phenylalanine, Phosphocholine, Serine)	1.26 (0.84, 1.93)	2.56 (1.19, 3.50)	0.0092	0.013	0.34 (0.16, 0.71)	0.004
3.95-3.94 (Serine, Phosphocreatine)	0.77 (0.33, 1.24)	0.30 (0, 0.53)	0.0006	0.003	29.2 (2.47. 345.24)	0.007
3.93-3.91 (Creatine, Glycerophosphocholine)	1.28 (0.90, 1.61)	0.69 (0.24, 1.34)	0.0071	0.012	8.17 (1.77, 37.78)	0.007
3.61-3.59 (Myo-Inositol, Glycerophosphocholine, Phosphocholine, Valine)	0.96 (0.63, 1.24)	1.68 (1.39, 1.96)	0.0006	0.005	0.13 (0.03, 0.49)	0.003
3.55-3.52 (Glycine)	1.92 (0.77, 3.17)	4.02 (2.87, 4.42)	0.0019	0.024	0.59 (0.39, 0.90)	0.014
3.36-3.34 (Scylla-Inositol)	0.55 (0.35, 0.78)	1.34 (0.75, 1.54)	0.0019	0.005	0.08 (0.02, 0.42)	0.003
3.24-3.23 (Myo-Inositol, Taurine)	5.86 (3.95, 9.46)	4.32 (2.43, 5.40)	0.0267	0.030	1.35 (1.04, 1.76)	0.027
3.22-3.21 (Phosphocholine, Glycerophosphocholine, Histidine)	0.69 (0.22, 2.16)	4.23 (3.05, 5.53)	<0.001	<0.001	0.41 (0.35, 0.67)	<0.001
3.15-3.13 (Spermine, Histidine, Phenylalanine)	0.21 (0.11, 0.35)	0.83 (0.49, 1.02)	<0.001	<0.001	4×10^{-5} (7.42×10^{-8}, 0.02)	0.001
2.84-2.82 (TBD)	0.28 (0.18, 0.45)	0.18 (0.10, 0.23)	0.0021	0.009	7158.67 (6.3, 8.3×10^{6})	0.013
2.45-2.42 (Glutamine)	0.51 (0.30, 0.74)	0.32 (0.21, 0.38)	0.0098	0.017	121.5 (2.16, 6820)	0.02
2.15-2.11 (TBD)	1.45 (1.15, 1.97)	1.95 (1.46, 2.50)	0.0370	0.035	3.96 (1.18, 13.28)	0.026
1.93-1.92 (Acetoacetate)	0.31 (0.18, 0.67)	0.77 (0.54, 2.83)	0.0008	0.012	0.38 (0.13, 1.09)	0.072
1.35-1.33 (Lactate)	8.74 (5.26,13.23)	5.2 (3.06, 8.30)	0.0150	0.033	1.22 (1.03, 1.45)	0.023

*TBD denotes that the specific metabolites characterizing this region remain to be identified

Table 1: Metabolites with median MRS relative intensities that were statistically significantly different between the malignant and adjacent benign tissues. Certain metabolites still remain to be identified and are indicated by TBD. On the right side of the table, we have reported odds ratios for risk of malignancy,

and we found the metabolomic profile demonstrated that metabolites in the 3.15-3.13 ppm spectral region in particular were present in lower levels in malignant tissue, while higher levels of metabolites in the 2.84-2.82 ppm region substantially increased the risk of RCC.

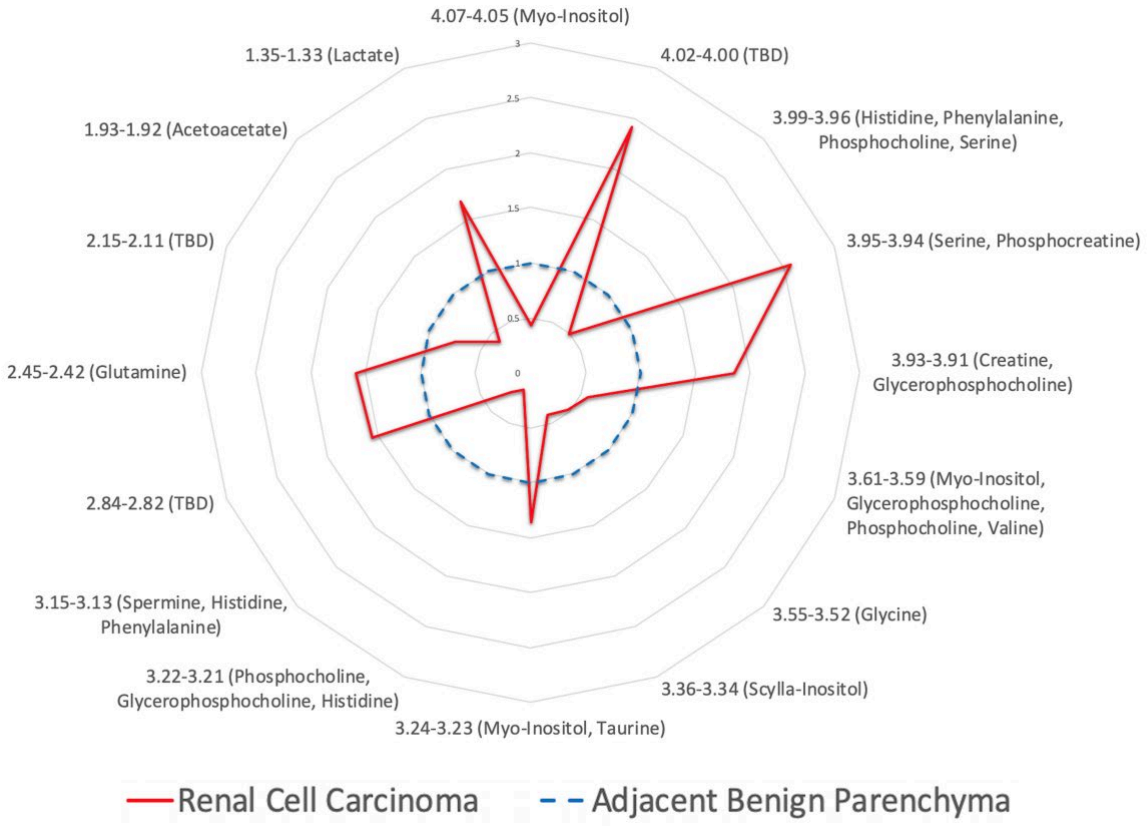

Figure 13: Radar plot of metabolomic predictors of malignancy compared to benign tissue

We performed a second analysis to evaluate the metabolomic profile of AML and compare it to that of clear cell RCC using 16 ccRCC samples & 7 AML specimens. The methodology of the analysis was similar to the aforementioned, with comparison of metabolomic profiles of AML and RCC with FDRs. Our outcome of interest was to identify metabolites indicative of renal cell carcinoma rather than fat-poor AML. A MatLab-based curve fitting program was used to process the spectra to produce relative intensities for each analyzed spectral region of interest. ROIs with FDR <0.05 were considered potential predictors of ccRCC rather than AML. The Wilcoxon rank sum test was used to compare median MRS relative intensities for candidate predictors. Logistic

regression was used to determine odds ratios for risk of malignancy based on abundance of each metabolite.

Candidate predictors of malignancy rather than AML based on FDR p-values include histidine, phenylalanine, phosphocholine, serine, alanine, glutamate, glutathione, glycerophosphocholine, & glutamine. While an abundance of these metabolites is associated with higher risk of malignancy, the odds ratio was particularly high in the 3.5-3.49 ppm spectral region (OR 2.99x106, 95% CI 3.27, 2.73x1012, p=0.033) in ccRCC samples (Table 2 and Figure 14).

	ccRCC (N=16)	AML (N=7)	P-value			
Median MRS relative intensities (IQR)				**FDR P-value**	**Odds ratios (OR, 95% CI)**	**P-value for OR**
4.67-4.66 (TBD)	1.22 (0.55, 4.62)	0.042 (0, 0.455)	0.007	0.00046275	4723.55 (1.54, 1.45x10^7)	0.039
4.02-4 (TBD)	0.80 (0.56, 1.32)	0.46 (0.01, 0.67)	0.0299	0.03685893	17.89 (1.00, 319.6)	0.05
3.99-3.96 (Histidine, Phenylalanine, Phosphocholine, Serine)	1.80 (0.97, 2.61)	0.32 (0.03, 0.49)	0.0009	0.00052614	109.72 (1.25, 9.63x10^3)	0.04
3.9-3.89 (TBD)	0.84 (0.56, 0.85)	0.10 (0.01, 0.42)	0.0019	0.00105305	674.29 (2.87, 1.58x10^5)	0.019
3.84-3.81 (TBD)	1.51 (1.22, 1.89)	0.15 (0.03, 0.76)	0.0009	0.00055658	59.25 (2.15, 1.63x10^3)	0.016
3.8-3.78 (Alanine, Glutamate, Glutamine, Glutathione)	2.34 (1.18, 3.23)	1.11 (0.02, 1.43)	0.0083	0.00293991	9.94 (1.08, 91.66)	0.043
3.77-3.74 Alanine, Glutamate, Glutamine)	2.75 (2.42, 3.31)	0.62 (0.03, 2.38)	0.0029	0.01004921	3.48 (1.26, 9.55)	0.016
3.57-3.56 (TBD)	1.83 (1.44, 2.45)	0.04 (0.02, 0.70)	0.0009	0.00046275	29.61 (2.23, 393.8)	0.01
3.5-3.49 (TBD)	0.53 (0.27, 0.63)	0.008 (0, 0.12)	0.0013	0.00052614	2.99x10^6 (3.27, 2.73x10^{12})	0.033
3.48-3.46 (TBD)	0.64 (0.36, 1.16)	0.01 (0.006, 0.35)	0.0045	0.0016087	1258.41 (3.2, 4.9x10^5)	0.019
3.45-3.43(TBD)	1.31 (0.42, 2.13)	0.42 (0.03, 0.87)	0.0083	0.00418794	25.24 (1.21, 527.58)	0.037
3.42-3.39 (TBD)	1.73 (0.98, 2.81)	0.54 (0.02, 0.78)	0.0045	0.00534601	8.37 (1.14, 61.31)	0.037
3.22-3.21(Phosphocholine, Glycerophosphocholine, Histidine)	1.81 (1.03, 2.95)	0.03 (0, 0.19)	0.0003	0.00020209	888.36 (1.31, 6.04x10^5)	0.041
2.38-2.37 (TBD)	0.22 (0.19, 0.28)	0.04 (0.008, 0.14)	0.0009	0.00052614	2.44x10^{16} (0.73, 8.13x10^{32})	0.052
2.36-2.31 (Glutamate)	2.37 (1.67, 3.15)	0.90 (0.04, 1.33)	0.0015	0.00105305	15.05 (1.37, 165)	0.026
2.15-2.11 (TBD)	1.89 (1.43, 2.56)	0.68 (0.002, 1.27)	0.0009	0.00052614	62.62 (1.24, 3.12 x10^3)	0.038

Table 2: Statistically significantly different metabolite intensities in ccRCC compared to fat-poor AML. Certain metabolites still remain to be identified and are indicated by TBD. On the right side of the table, we have reported odds ratios for risk of malignancy, and we found the metabolomic profile demonstrated that metabolites in the 3.5-3.49 ppm spectral region in particular increased the risk of harboring RCC rather than fat-poor AML. The 2.38-2.37 had very a high odds ratio but did not meet statistical significance.

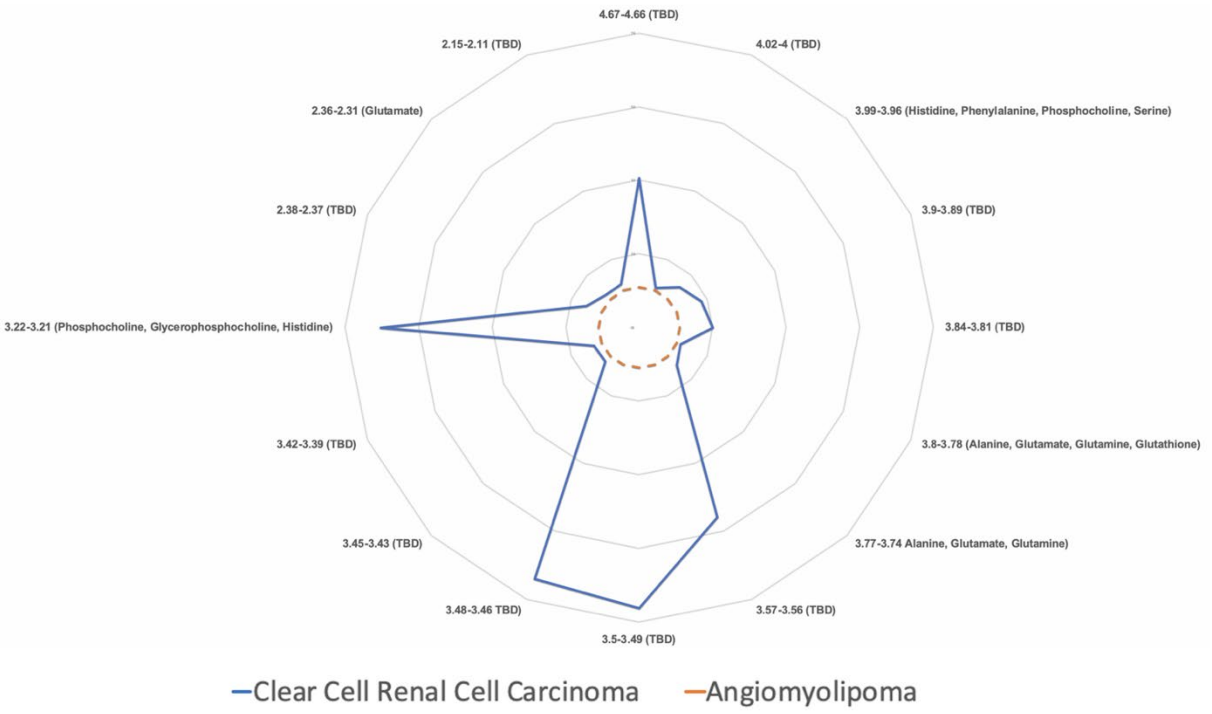

Figure 14: Radar plot of metabolomic predictors of malignancy compared to AML

In summary, these analyses showed that HRMAS MRS identified metabolites that may help differentiate fat-poor AML from ccRCC and RCC from adjacent benign parenchyma. We are thrilled to report that these results were presented virtually at the Annual Meeting of the American Urologic Association in May 2020, where we were awarded Best Poster for our work. Our manuscript for these results is currently in progress and will be submitted in the near future.

- **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 perform *in vivo* metabolomic imaging of the kidney and renal masses, as well as investigating and discovering the *in*

vivo and *ex vivo* metabolomic profiles of benign and malignant renal masses.

- **How were the results disseminated to communities of interest?**
  We have communicated the results to the multidisciplinary members of our research group and as discussed above, have presented our data at the Annual Meeting of the American Urologic Association in May 2020.

- **What do you plan to do during the next reporting period to accomplish the goals?**
  In the next reporting period, we will plan to finalize our manuscript of the discussed *ex vivo* analysis of tumor tissue from our GU Oncology Tumor Bank. In addition, we will plan to further analyze the *in vivo* data from our entire cohort of patients who underwent MRI/MRS of renal masses and compare the metabolomic findings with our *ex vivo* metabolomic data. 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 *ex vivo* MRS of benign and malignant renal tumor tissue, including AML and RCC is also novel work and will allow us to gain a better understanding the metabolomic profiling of these tumors in TSC and sporadic patients. This is also novel work and will be published in a peer-reviewed journal.

- **What was the impact on other disciplines?**
  The findings from this work will help gain insight into the active metabolic pathways in AML and RCC 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**

  Given the slow rate of recruitment to the study, we utilized fresh frozen renal mass tissue from the MGH GU Oncology Frozen Tumor Bank for *ex vivo* MRS. As discussed above, this approach was successful in allowing us to increase our numbers in metabolomic analysis.

- **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 and TSC patients with lipid-rich renal masses.

- **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**
  Our *ex vivo* MRS metabolomic analysis of fresh frozen MGH GU Tumor Bank tissue was presented at the Annual Meeting of the American Urologic Association in May 2020, where we were awarded Best Poster for our work. Our manuscript for these results is currently in progress and will be submitted in the near future.

- **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:	*Adam S. Feldman, MD, MPH*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*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.
Funding Support:	

Name:	*Edouard Nicaise*
Project Role:	*Research Assistant*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*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.*
Funding Support:	

Name:	*Andrew Gusev*
Project Role:	*Medical Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*6*
Contribution to Project:	*Mr. Gusev helped to coordinate subject scheduling for MRI with in vivo MRS, record and maintain data, coordinate the acquisition of specimens and assisted with laboratory preparation of specimens for ex vivo MRS and other analyses.*
Funding Support:	

Name:	*Eva Ratai, PhD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	*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*
Funding Support:	

Name:	*Mukesh Harisinghani, MD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	*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.*
Funding Support:	

Name:	*Leo Cheng, PhD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	

Nearest person month worked:	1
Contribution to Project:	*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*
Funding Support:	

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

Name:	*Elizabeth Thiele, MD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	*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.*
Funding Support:	

Name:	*Elizabeth Henske, MD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	*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*
Funding Support:	

Name:	*Othon Iliopoulos, MD*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	*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.*
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:

The Faculty of Medicine of Harvard University
Curriculum Vitae

Date Prepared: November 16, 2020

Name: Adam Scott Feldman

Office Address:

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

Work Phone: 857-238-3838

Work E-Mail:

afeldman@mgh.harvard.edu **Work FAX:**

617-726-9089

Education

1994	B.A. - Biological Basis of Behavior	University of Pennsylvania
1996	M.A. - Medical Sciences	Boston University School of Medicine
2000	M.D.	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

2006-2010 Instructor in Surgery, Harvard Medical School, Boston, MA
2010- Assistant Professor of Surgery, Harvard Medical School, Boston, MA

Appointments at Hospitals/Affiliated Institutions

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

2019- Urologic Oncolgist, Newton Wellesley Hospital, Newton, MA

Other Professional Leadership Positions

2012-2018	Board Member: Sean Kimerling Testicular Cancer Foundation	2 days per year
2014, 2016, 2018	Scientific Advisory Board – Myriad Genetics, Inc.	2 days per year
2015	Scientific Advisory Board – Sanofi Pasteur, Inc.	2 days per year
2015-	Consultant – Olympus America, Inc.	5 days per year
2016	Consultant – Cerulean Pharma, Inc.	1 day per year
2019	Scientific Advisory Board – Ferring Pharmaceuticals	2 days per year

Major Administrative Leadership Positions

Local

2013-2019	Course Director, Fundamentals in Laparoscopic Surgery for Urology Residents, Department of Urology, Massachusetts General Hospital
2013-	Co-Leader of the Career Development Program: DFCI/HCC Prostate Cancer SPORE
2015-	Director, Combined Harvard Urologic Oncology Fellowship
2018-	Director of Research, Department of Urology, Massachusetts General Hospital
2016	Scientific Co-Chair: DF/HCC Kidney Cancer Program Retreat
2016,17,19,21	Course Co-Director: State of the Art Imaging in the Diagnosis and Management of Prostate Cancer – HMS CME Course

Regional

2011 Scientific Program Chair, American Urological Association, New England and Mid-Atlantic Sections, Annual Meeting

National

2019 Scientific Co-Chair: Clinical Society of Genitourinary Surgeons Annual Meeting

Committee Service

Local

2012-	Member: Surgical Coordination Committee, Department of Urology, MGH
2013-2015	Member: MGH eCare Big Data and Data Repository Workgroup
2013-	Urology Representative: Clinical Research Workgroup of the Continuous of the Continuous Research Operations Improvement (CROI) Task Force
2015-	Member: Department of Urology Education Committee
2016-	Urology Representative: MGH Research Council
2018	Urology Representative: MGH Frigoletto Committee on Physician Well-Being
2018-	Member: Department of Urology Executive Committee
2019-	Urology Representative: MGH West Ambulatory Operations Committee

2019- Urology Representative: MGH Center for Outcomes and Patient Safety in Surgery (COMPASS)

National

2013- Member: Eastern Cooperative Oncology Group (ECOG) Genitourinary Committee
2012 American Urological Association Representative, Lower Anogenital Squamous Terminology Standardization (LAST) Consensus Conference, 2012
2018, 2019 Member: Braintrust committee. Global Summit on Precision Diagnosis and Treatment for Prostate Cancer. AdMeTech Foundation

Professional Societies

1998- Massachusetts Medical Society, Member
2012-2020 Member: Massachusetts Medical Society Committee on Men's Health
2002- American Urological Association, Member
2018 Moderator at Annual National Meeting
2002- American Urological Association New England, Member
2015, 2016 Member: Scientific Program Committee, Annual Meeting
2017, 2018 Moderator at Annual Meeting
2004- American Association of Clinical Urologists, Member
2009- 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- Ad-Hoc Reviewer, *Journal of Urology*
2010- Ad-Hoc Reviewer, *Urology*
2010- Ad-Hoc Reviewer, *Prostate Cancer and Prostatic Diseases*
2010- Ad-Hoc Reviewer, *Urologic Oncology*
2011- Ad-Hoc Reviewer, *BJU International*
2012- Ad-Hoc Reviewer, *Molecular Cancer Research*
2013- Ad-Hoc Reviewer, *European Urology*
2014- Ad-Hoc Reviewer, *Journal of Endourology*
2015- Ad-Hoc Reviewer, *JAMA*

Editorial Board

2015- Editorial Board Member, BMC Urology
2017- 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
2020	Best Poster - Annual Meeting of the American Urological Association, Virtual
2020	Castle Connolly Top Doctor Award

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, Massachusetts General Hospital, Boston, MA; A Proteomic Approach to Prostate Cancer Biomarker Discovery

- Use proteomic techniques for urine biomarker discovery in men with prostate cancer

- award

2007-2009 P.I. Company – Predictive Biosciences, Lexington, MA; 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, Massachusetts General Hospital, Boston, MA; Active Surveillance for Prostate Cancer: Management Patterns, Outcomes, and Quality of Life

- Funding supports research personnel for data mining and management
- award

2008-2012 P.I. Prostate Cancer Foundation, Santa Monica, CA – 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

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

- 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:

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. 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:
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 form 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

2008-2010 Patient Doctor II

		contact time	*prep time*
Attending	5 Medical Students	8 hours/year for 1 year(s)	none reported

2010, 2015 HMS2 Pathophysiology

		contact time	*prep time*
Attending	25 Medical Students	3 hours/year for 1 year(s)	3 hours

2013-2017 HMS Surgical Clerkship Lecture on Urologic Surgery

		contact time	*prep time*
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 **Surgical Chief's Rounds** - Department of Surgery - Injuries to the Urogenital Tract

		contact time	*prep time*
Lecturer	25 Residents	1 hour	5 hours

2008-2013 Ambulatory Teaching Rounds - Department of Medicine – Uro-oncology for the primary care physician; Management of Small Renal Masses

		contact time	*prep time*
Lecturer	30 Residents	4 hours/year	10 hours/year

2010 General Surgery Teaching Rounds – Department of Surgery – Bladder Cancer Review

		contact time	*prep time*
Lecturer	25 Residents	0.5 hour	3 hours

Clinical Supervisory and Training Responsibilities

2006- Core Clerkship in General Surgery – Average of 3-4 students per year for 2-4 weeks

2-4 hours/week

2006- HMS 4th Year Elective in Urology – Average of 5-10 students per year for 4 weeks

2-4 hours/week

2006- MGH Training Program in General Surgery –

Participate in daily supervision, teaching and evaluation of general surgery residents assigned to Urology service

2006- MGH Training Program in Urology –

Participate in daily supervision, teaching and evaluation of Urology residents – In our 15 resident program, I interact with 2-3 residents daily

2008- MGH Fellowship in Urologic Oncology/Combined Harvard Urologic Oncology Fellowship (Society of Urologic Oncology Accreditation in 2012)

Participate in daily supervision, teaching and evaluation of Urologic Oncology Fellows – 1 fellow per year

In 2013, our fellowship united with BWH/DFHCC to become the Combined Harvard Urologic Oncology Fellowship

Participate in daily supervision, teaching and evaluation of Urologic Oncology Fellows – 1 fellow per year

As of 2015, I became Director of the Combined Harvard Urologic Oncology Fellowship with development of curriculum, faculty, fellows

2008-2012 Acute Care Surgery Fellowship, MGH Department of Surgery 10 hours/year

Sub-specialty Faculty Advisor for the AAST Accredited Fellowship

Laboratory and Other Research Supervisory and Training Responsibilities

2007-present Supervision and mentoring of Research Fellow 8 hours/week

I have trainees who are medical students, Urology residents, Urologic Oncology fellows

Formally Mentored Harvard Medical, Dental and Graduate Students:

Sarah Psutka, BS (HMS IV): 2010 – Research Rotation

- 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

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

- Current position – Urology resident, Massachusetts General Hospital

Yefri Baez (HMS): 2019 – Research Rotation

- Current position – Urology resident, Brigham and Women's Hospital

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
- 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 Fellow 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 Fellow 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 (HMS CME Course): Primary Care Internal Medicine: Principles & Practice – Case Studies in Urology *[Invited Lecture]*
2013	Ft. Lauderdale, FL	Faculty (CME Course): Winter Ongology 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 [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
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 [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
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 Diagnostics/Biomarkers for the Detection of Prostate Cancer
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 Ongology 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 *[Invited Lecture]* Management of Hormone Sensitive Prostate Cancer *[Invited Lecture]*
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 *[Invited Lecture]*
2008	Boston, MA	Prostate Cancer: Diagnosis and Management. Prostate Cancer Support Group, Massachusetts General Hospital *[Invited Lecture]*
2011	Boston, MA	Controversies Around the Management of Small Renal Masses – DF/HCC Kidney Cancer Program *[Invited Lecture]*
2011	Boston, MA	Proteomic Discovery of Novel Biomarkers in Prostate Cancer – Massachusetts General Hospital Department of Urology Centennial Academic Program *[Invited Lecture]*
2011	Cambridge, MA	Management of Small Renal Masses – Harvard University Health Services Grand Rounds *[Invited Lecture]*
2011	Boston, MA	Incidental Radiologic Findings: "Incidental Renal Masses" – Massachusetts General Hospital Medical Grand Rounds *[Invited Lecture]*
2012	Concord, MA	Controversies in the Management of the Small Renal Mass – Emerson Hospital Medical Grand Rounds *[Invited Lecture]*
2014	Boston, MA	Mangement 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 *[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 Ongology 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 *[Invited Lecture]*
2016	Boston, MA	DF/HCC Kidney Cancer Program Retreat - Metabolomic imaging of RCC using MR Spectroscopy: Proposal for a comparative *in vivo* and *ex vivo* 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 Tuberous Sclerosis Complex Symposium – Management of Renal Masses in Tuberous 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 *[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]*
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 *[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	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	5th International Urology Forum – The Potential of Nanoparticle Enhanced Imaging in the Accurate Detection of Lymph Node Metastases *[Invited Lecture]*
2012	Mallorca, Spain	6th International Urology Forum – Renal Mass Biopsy *[Invited Lecture]*
2016	Tel Aviv, Israel	Faculty: Friends of Israel Urology Symposium –
		Nephron sparing surgery for multiple renal tumors *[Invited Lecture]*
		Partial Nephrectomy: How I do it with less than 20 minutes warm Ischemia time *[Invited Lecture]*
		Session Chair: Oligometastases in Prostate Cancer
2017	Hachioji, Japan	Olympus Corporation - Future of Urologic Surgery *[Invited Lecture]*
2018	Santo Domingo, Dominican Republic	Latin America Prostate Cancer Summit –
		Management of Patients post-radical prostatectomy *[Invited Lecture]*
		Management of Hormone Sensitive Prostate Cancer *[Invited Lecture]*
2018	Tel Aviv, Israel	Faculty: Friends of Israel Urology Symposium –
		Active Surveillance for Prostate Cancer in Young Men *[Invited Lecture]*
		Trimodality Therapy for Muscle Invasive Bladder Cancer *[Invited Lecture]*

Report of Clinical Activities and Innovations

Current Licensure and Certification

2002	Diplomate, National Board of Medical Examiners
2004-	Massachusetts Board of Registration in Medicine – Full License
2008-	ABU
date	ABU Recertified

Practice Activities

Urology/Urologic Oncology, Laparoscopy and Endourology	Massachusetts General Hospital
Attending Urologic Surgeon, Polycystic Kidney Disease Clinic	Massachusetts General Hospital
Attending Urologic Surgeon, Herscot TSC center	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 ingestigation 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.
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, Paweletz 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.

32. Mak KS, Smith AB, Eidelman A, Clayman R, Niemierko A, Cheng JS, Matthews J, Drumm MR, Nielsen ME, **Feldman AS,** Lee RJ, Zietman AL, Chen RC, Shipley WU, Milowsky MI, Efstathiou JA. Quality of Life in Long-term Survivors of Muscle-Invasive Bladder Cancer. Int J Radiat Oncol Biol Phys. 2016 Dec 1;96(5):1028-1036.

33. Chen AL, Brown PA, Sweeney BJ, **Feldman AS**, Arellano RS, Tambouret RH. Smears are important for adequate cytologic diagnosis of kidney lesions. Journal of the American Society of Cytopathology. 2017; 6(4):162-9.

34. Krasnow RE, Drumm M, Roberts HJ, Niemierko A, Wu CL, Wu S, Zhang J, Heney NM, Wszolek MF, Blute ML, **Feldman AS,** Lee RJ, Zietman AL, Shipley WU, Efstathiou JA. Clinical Outcomes of Patients with Histologic Variants of Urothelial Cancer Treated with Trimodality Bladder-sparing Therapy. Eur Urol. 2017 Jul;72(1):54-60.

35. Giacalone NJ, Shipley WU, Clayman RH, Niemierko A, Drumm M, Heney NM, Michaelson MD, Lee RJ, Saylor PJ, Wszolek MF, **Feldman AS,** Dahl DM, Zietman AL, Efstathiou JA. Long-term Outcomes After Bladder-preserving Tri-modality Therapy for Patients with Muscle-invasive Bladder Cancer: An Updated Analysis of the Massachusetts General Hospital Experience. Eur Urol. 2017 Jun;71(6):952-960.

36. Dhyani M, Grajo JR, Rodriguez D, Chen Z, **Feldman A**, Tambouret R, Gervais DA, Arellano RS, Hahn PF, Samir AE. Aorta-Lesion-Attenuation-Difference (ALAD) on contrast-enhanced CT: a potential imaging biomarker for differentiating malignant from benign oncocytic neoplasms. Abdom Radiol (NY). 2017 Jun;42(6):1734-1743.

36. Buscariollo DL, Drumm M, Niemierko A, Clayman RH, Galland-Girodet S, Rodin D, **Feldman AS**, M Dahl D, McGovern FJ, F Olumi A, Eidelman A, Shipley WU, Zietman AL, Efstathiou JA. Long-term results of adjuvant versus early salvage postprostatectomy radiation: A large single-institutional experience. Pract Radiat Oncol. 2017 Mar - Apr;7(2):e125-e133.

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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 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.