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PRINCIPAL INVESTIGATOR: Avrum E. Spira, MD

CONTRACTING ORGANIZATION: Boston University
Boston, MA 02118

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Avrum E. Spira, MD
Ehab Billatos, MD
Elizabeth Moses, PhD

E-Mail: emoses@bu.edu

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Trustees of Boston University, 85 East Newton St, M-921,
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14. ABSTRACT

The purpose of this work is to develop and validate molecular biomarkers found in blood, tissues, or other bodily fluids, which may be used for the early detection of lung cancer among military personnel and veterans. Over the course of the seventh year of this award, we have made significant progress towards enrollment in both clinical trials. We have recruited ~85% of the 500 total subjects in the indeterminate pulmonary nodule study (Protocol 1), and ~66% of the 800 total subjects in the longitudinal screening study (Protocol 2). We also held an in-person meeting in order to facilitate recruitment, brainstorm new scientific directions, and discuss potential avenues for ensuring DECAMP's longevity. The Leadership, Steering, Adjudication, Biostatistics, Imaging and Biomarker Committees continue to meet regularly. Most notably, significant progress has been made in adjudication of cases and controls within DECAMP-1 which will facilitate the validation of our cancer biomarkers. We have also begun to explore potential new assays and sequencing platforms in support of our scientific aims. Lastly, we have secured additional funding for the DECAMP consortium through July 2022, to ensure the completion of our enrollment goals and study aims.

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Introduction:

The purpose of this work is to develop and validate molecular biomarkers that may be used for the early detection of lung cancer. By recruiting approximately 500 patients with indeterminate pulmonary nodules from Military Treatment Facilities and Veteran's Administration Hospitals, DECAMP plans to identify 75 patients with lung cancer for our molecular studies. For the study to develop tests that can identify the patients at highest risk for having or developing lung cancer, DECAMP will recruit approximately 800 high-risk current and former smokers from these same hospitals, determine whether they have lung cancer now and then follow them annually for up to four years to determine if they develop lung cancer. We expect to identify 50 patients who did not have cancer when they join the study, but develop lung cancer while they are being monitored. The clinical applications of this study will come from the development of tests to more accurately diagnose disease at an early potentially curable stage but also predict the occurrence of lung cancer in the future. Additionally, these biomarkers found in blood, other body fluids, or tissues will be collected more easily and are less invasive than surgery. Non-invasive collection of biological samples will be less painful for the patient and allow easier and more frequent monitoring of disease. The intent of this research is to develop early detection strategies that will ultimately decrease lung cancer deaths. This will improve the health and welfare of the military, and the American public as a whole.

Body:

During the seventh year of the DECAMP consortium, we have made significant progress toward the Specific Aims of the grant. Specifically, recruitment of subjects into both clinical trials has continued to progress (see Tables 1-4 for cumulative and yearly accrual by site, for DECAMP-1 and -2; see Figures 1-4 for cumulative and yearly accrual by month, for DECAMP-1 and -2). As would be expected in a multicenter trial, these tables demonstrate that there is heterogeneous recruitment between the sites. Cumulatively, 428 subjects have now been enrolled in DECAMP-1, and 524 subjects in DECAMP-2. Demographic information on these subjects is shown in Tables 7-8, and indicate an older, mostly Caucasian male cohort, as one would expect in a military population. The RA team continues to meet biweekly to discuss recruitment, including any changes or revisions to sample collection or inclusion criteria, and to share patient recruitment and screening strategies.

A major accomplishment of this year was our DECAMP in-person meeting in February 2018. We brought together over 40 of our talented DECAMP investigators and staff to discuss successful recruitment strategies, new scientific aims and future collaborations. We hope to continue to hold these meetings annually as they are excellent opportunities to advance DECAMP and have informative discussions. In addition, we look forward to our final External Advisory Board meeting next month in order to get the final feedback and suggestions from our talented EAB. In all, we have aimed to utilize this seventh year to put practices in place and establish partnerships that will ensure DECAMP's longevity beyond the no cost extension. As an example, biospecimen tracking is a key responsibility of the consortium to ensure specimens are properly selected for analysis and remaining sample volumes are accurately recorded. Given the oversight necessary for these tasks, we decided in this year to move the DECAMP biorepository from the Pathology department at Boston University to our lab, under Dr. Spira. In this manner, we will have more direct oversight of the biospecimen tracking and can dedicate a clinical biorepository manager to carry out these responsibilities.

Along with our progress towards patient enrollment, we have continued to evaluate the data and biospecimens collected from the clinical sites. Currently, there are a total of 25,429 samples banked at the Biorepository of Boston University and there are additional samples pending shipment from individual sites (Tables 12 and 13). In addition, a total of 1,570 tissue specimens are currently banked at MD Anderson and have been reviewed by consortium pathologists (Table 14). Of the evaluated biopsies, the majority are normal epithelium (570/878 in DECAMP 1 and 404/692 in DECAMP 2), in addition to many denuded epithelium, basal cell hyperplasia, squamous metaplasia, mild dysplasia and moderate dysplasia samples. Additionally, we continue to process and sequence samples for our biomarker work, including bronchial brushings (n=484), nasal brushings (n=303) and bronchial biopsies (n=125). For these samples we also have continued to evaluate the quality and quantity of RNA isolated, for each site (Table 9). In those sites with lower yields and poor quality, we provided feedback and reviewed the protocol for sample collection. Finally, our team has also made significant strides in quality control of the images submitted to DECAMP (Tables 5-6), and continues to track site compliance with image submission. Over the past 12 months, in those sites with low imaging compliance, we have provided feedback to ensure that they continue to submit CT images in a timely fashion. In addition, we have recently made a large push to ensure follow-up images, particularly on DECAMP-2 subjects, are being submitted to ACRIN. We have seen a significant increase in

submitted images following our study staff reaching out to each site to discuss their outstanding images. In all, collection of this data is tracked and stored in our clinical database, and the current database is summarized in Table 10.

One of the major milestones achieved over the past 12 months is the adjudication of 370 total cases and controls in DECAMP-1, with a total adjudication rate of 90%. Of these 370 subjects, 235 have been confirmed to have a lung cancer diagnosis, 128 as benign samples and 7 as metastatic cancer. The increase in adjudicated patients in DECAMP-1 has allowed us to further accelerate our biomarker validation work. In addition, through extensive discussion of the data access committee, our three main biomarkers have transitioned to novel platforms and assays for a second phase of validation in order to improve biomarker performance. The plasma protein biomarker will be evaluated in an additional 200 subjects (following a first phase validation in 91 subjects), using a novel assay which incorporates radiomics into the biomarker performance. The bronchial airway gene expression biomarker is currently being validated in an additional 266 subjects (following a first phase validation in 91 subjects), on a new CLIA-based assay at Veracyte. The plasma exosomal miRNA biomarker (previously measured on 24 subjects), has transitioned to a new circulating miRNA platform at MiRXES which shows greater promise for validation (191 subjects). Our partners at the NCI continue to validate a urinary metabolomics biomarker, and have found four metabolites capable of distinguishing patients with malignant and benign nodules. Previous profiling was performed on 78 subjects, 54 cancers and 24 controls, and they are currently profiling an additional 225 subjects, 144 cancers and 81 controls. Finally, our partners at the Mayo Clinic have developed a CT-base radiomic classifier based on the NSLT cohort and have preliminarily validated this classifier on 293 DECAMP-1 subjects.

In addition, we have made significant progress towards our scientific discovery aims. Prior work from BU has identified alterations in bronchial and nasal epithelial cell gene-expression associated with lung cancer. Using specimens from DECAMP-1 (50 lung cancer patients and 47 benign), we have sought to evaluate the ability of nasal epithelial gene-expression to identify patients with lung cancer among ever smokers with indeterminate pulmonary nodules. We identified 37 differentially expressed genes from the nasal epithelium associated with lung cancer status (FDR $q<0.05$), and concordant enrichment of the nasal signature was observed by Gene Set Enrichment Analysis in patients with indeterminate pulmonary nodules from a screening cohort at Lahey Hospital Medical Center (19 lung cancer patients and 19 benign). Additional samples (n=143) are currently being profiled in order to build a biomarker for early detection of lung cancer in high-risk smokers with indeterminate pulmonary nodules. In addition, we have begun to interrogate the microbiome environment of the nasal airway, as our bulk RNA sequencing also provides bacterial gene expression data. In the 67 subjects analyzed (39 lung cancer patients and 28 benign), we found significant differences in the bacterial species present in the nasal airway of lung cancer and non-lung cancer patients, suggesting that we may be able to develop a secondary nasal microbiome biomarker in addition to our nasal epithelium biomarker. Second, we have leveraged the unique collection of bronchial biopsies from DECAMP-1 in order to identify differences in gene expression pathways between smokers with and without lung cancer. Given that airway biopsies contain a mixture of lung cell types, these samples provide an unprecedented opportunity to characterize both the airway immune and epithelial responses in smokers who develop lung cancer. We found that the airway transcriptome in subjects with lung cancer is altered compared to subjects with benign nodules

(20 patients with malignant nodules, 18 benign; 22 genes differentially expressed with cancer status, FDR q<0.25). Down-regulated genes in cancer subjects were strongly associated with functions of the immune response and a decrease in airway leukocyte content, suggesting that the immune microenvironment of the airway "field of injury" may be altered among ever smokers who develop lung cancer. We are currently expanding our analysis to an additional 50 subjects (25 patients with malignant nodules, 25 benign) and will next validate gene expression changes using immunohistochemistry on the corresponding paraffin-embedded biopsies. Finally, given our increasing numbers of submitted DECAMP-1 images, we continue to work to develop semantic and quantitative imaging biomarkers for lung cancer diagnosis. This includes geospatial modeling techniques, examining the influence of the surrounding normal, and deep learning techniques to develop an artificial intelligence system that takes into account global and local systemic risk, to perform lung cancer prediction.

We have also made major progress in securing additional funding for the DECAMP consortium. In addition to our substantial Janssen funding through November 2020, we have also initiated a partnership with Novartis, as part of a four-year contract to support gene expression and protein biomarkers in DECAMP-2, through July 2022. The consortium will also play a significant role in the Stand Up to Cancer Lung Cancer Interception Dream Team, with Dr. Avrum Spira as the principal investigator on this proposal. DECAMP will serve as a crucial cohort in this study, providing an opportunity to develop novel imaging, ctDNA and single-cell nasal gene-expression biomarkers for lung cancer detection. Finally, we look forward to expanding DECAMP's impact with a new cohort, DECAMP-1 PLUS, a non-bronchoscopy based cohort for lung cancer detection, in early 2019. Together, this scientific and financial progress ensures DECAMP's longevity beyond this final year of Department of Defense support.

Additional accomplishments in the past 12 months are included in the summary of our progress related to each of the tasks in our SOW as specifically outlined below.

Task 1 Clinical Trial Accrual

Project 1 – Accrual Target 500 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies
Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine
Current Accrual: See Tables 1-2 and Figures 1-2

Project 2 – Accrual Target 800 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies
Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine
Current Accrual: See Tables 3-4 and Figures 3-4

1a. Clinical site Accrual: Based on accrual rates, the projected accrual over the 18 month No-Cost Extension is outlined in the graph below.

Site	DECAMP-1	DECAMP-2
Boston VA	25	29
Boston University Medical Center*	30	0
Dallas VA	7	2
Denver VA	4	16
LA VA/UCLA*	9	38
Nashville VA Medical Center	7	20
Philadelphia VA/UPenn	30	5
Pittsburgh VA	7	0
Roswell Park Cancer Center	0	4
Brooke Army Medical Center	3	0
Naval Medical Center Portsmouth	9	23
Naval Medical Center San Diego	18	38
Walter Reed National Military Medical Center	27	56
Total	**182**	**231**

**Note that funding for patient recruitment at BUMC and UCLA is provided by the NIH/NCI.*

1b. Samples collected:

Biosamples	Quantity	Analytes	Project 1 Diagnostic	Project 2 Screening
Blood*	50 mL	Protein/RNA/DNA	Plasma Protein	-------
Blood*	50 mL	RNA	Exosomal miRNA	-------
Endobronchial Biopsies via Bronchoscopy	6 biopsies**	Protein/RNA/DNA	-------	-------
Endobronchial Brushings via Bronhcoscopy	1 brush	RNA	23 Gene Expression Marker	-------
	1 brush	Protein	-------	-------
	1 brush	DNA	-------	-------
Nasal Brushings	2 brushes	RNA	-------	Gene expression profiling
Buccal Scrapings	1 brush	RNA	-------	-------
Sputum	-------	DNA	-------	-------
Urine	25 mL	Metabolomics	4 Metabolite Marker	-------
Tumor Tissue***	-------	DNA/RNA	-------	-------

* **Plasma, Serum, PAXGene, Streck**

** **2 biopsies are obtained from three subsegmental carinas (RUL, LUL, RML)**

*** **Paraffin and fresh frozen tissue where available**

1c. Core Labs

- **Biorepository:** The Biorepository Core has transitioned to the lab of Dr. Spira. It receives, stores, and tracks all biospecimens in the DECAMP Consortium. The clinically biospecimen coordinator provides Dr. Moses with a spreadsheet, updated quarterly, of all specimens being housed in and pulled from the Biorepository Core at BU.
  Please see Table 13 for updated sample numbers.
- **Pathology:** The Pathology Core at MD Anderson will continue to store all ambient samples provided by clinical sites of bronchial biopsy and surgical tissue. MD Anderson will also continue to process formalin-fixed samples.
  MD Anderson continues to provide a spreadsheet, updated monthly. Please see Table 14 for updated sample numbers.
- **Biostatistics:** The Biostatistics Core at Brown University will continue to maintain the database and provide support for biomarker analysis.
  The Biostatistics Core at Brown holds biweekly biomarker analysis meetings to update progress on biomarker analysis and manuscript writing.

Task 2 Biomarkers

2a Validation

- Bronchial Airway gene-expression Biomarker: We have successfully validated a 23 gene airway biomarker in 91 DECAMP-1 subjects to date from (phase 1). We are currently performing additional validation on 266 subjects from DECAMP-1 on a CLIA-based platform (phase 2).
  The results of the phase 1 bronchial airway gene-expression biomarker validation were presented at the July 2017 EAB meeting. During FY7 we have begun phase II validation.
- Plasma Protein Biomarker: We have attempted to validate three protein markers in the serum of the same 91 subjects: C4d , CRP and CYFRA21. Using a new assay, we are validating these proteins on an additional 200 subjects (phase 2).
  The results of the phase 1 plasma protein biomarker validation were presented at the July 2017 EAB meeting. During FY7 we have approved a request for additional validation and anticipate phase 2 to begin in early 2019.
- Plasma miRNA Biomarker: We have attempted to validate ten microRNAs generated from a discovery set in DECAMP-1, in the blood of 24 subjects. We are currently assessing a novel circulating miRNA platform on an additional 191 subjects.

The results of the phase 1 plasma miRNA biomarker validation were presented at the July 2017 EAB meeting. During FY7 we initiated a phase 2 validation on a novel, circulating miRNA platform.

- Urinary Metabolomics Biomarker: We have successfully validated a biomarker comprised of four different urinary metabolites in 78 DECAMP-1 subjects (phase 1). We are currently performing additional validation on 225 subjects.
  The results of the phase 1 urinary metabolomics biomarker validation were presented at the January 2018 EAB meeting. During FY7 we initiated a phase 2 validation.
- CT-based Radiomic Classifier: We have begun preliminary validation of radiomic classifier from NLST in 293 DECAMP-1 subjects (phase 1).
  During FY7 we initiated a phase 1 validation.

2b Biomarker Discovery

- Bronchial Biopsies: We have sequenced mRNA from the endobronchial biopsies of 100 subjects in DECAMP-1 to immunophenotype the airway 'field of injury" in smokers with lung cancer.
  Data from the second batch of 50 subjects is currently being analyzed.
- Nasal Airway Biomarker: We have sequenced mRNA from the nasal epithelium of 84 subjects in DECAMP-1 to refine an existing nasal gene-expression biomarker for lung cancer diagnosis in Spring 2017. We are currently sequencing additional nasal epithelium samples from 143 subjects from DECAMP-1 to evaluate a potential biomarker of risk. The second batch of nasal epithelial brushings (n=143) are currently being sequenced.
- Semantic and Quantitative Imaging: We are developing imaging biomarker for lung cancer diagnosis in DECAMP-1. 360 cases and controls from DECAMP-1 have been analyzed using geospatial modeling and deep learning methods.
  These analyses continue to be supported by additional DECAMP-1 images uploaded daily.

Task 3 DECAMP Committees

- Leadership/Publications Committee: meets monthly; continues to meet monthly
- Steering Committee: meets monthly; continues to meet monthly
- Adjudication Committee: meets as needed; continuous adjudication being processed; currently 370 subjects adjudicated. The committee will meet again in Spring 2019.
- Data Access Committee: meets as needed depending on when biomarkers or data access requests are being proposed; the committee continues to meet as needed
- Biostatistics Committee: meets biweekly; led by the Biostatistics core at Brown. Continues to meet biweekly
- Imaging Working Group: meets monthly; led by Dr. Denise Aberle and Dr. Caroline Chiles. Continues to meet monthly

DECAMP-1 (ACRIN 4703)

Table 1: DECAMP 1 Cumulative Accrual by Submitting Institution (Jan 2013-Sep 2018)

Institution	N
Walter Reed National Military Medical Center	75
VA Boston Healthcare System	59
Naval Medical Center San Diego	56
Philadelphia VA Medical Center	43
Brooke Army Medical Center	35
VA Greater Los Angeles Health Care System	29
Hospital of the University of Pennsylvania	29
Nashville VA Medical Center	25
Boston University Medical Campus	22
Naval Medical Center Portsmouth	20
VA North Texas Health Care System	15
VA Pittsburgh Healthcare System	12
VA Eastern Colorado Health Care System	6
University of California Los Angeles	2
Total	**428**

Figure 1: DECAMP 1 Cumulative Accrual: January 2013 - September 2018

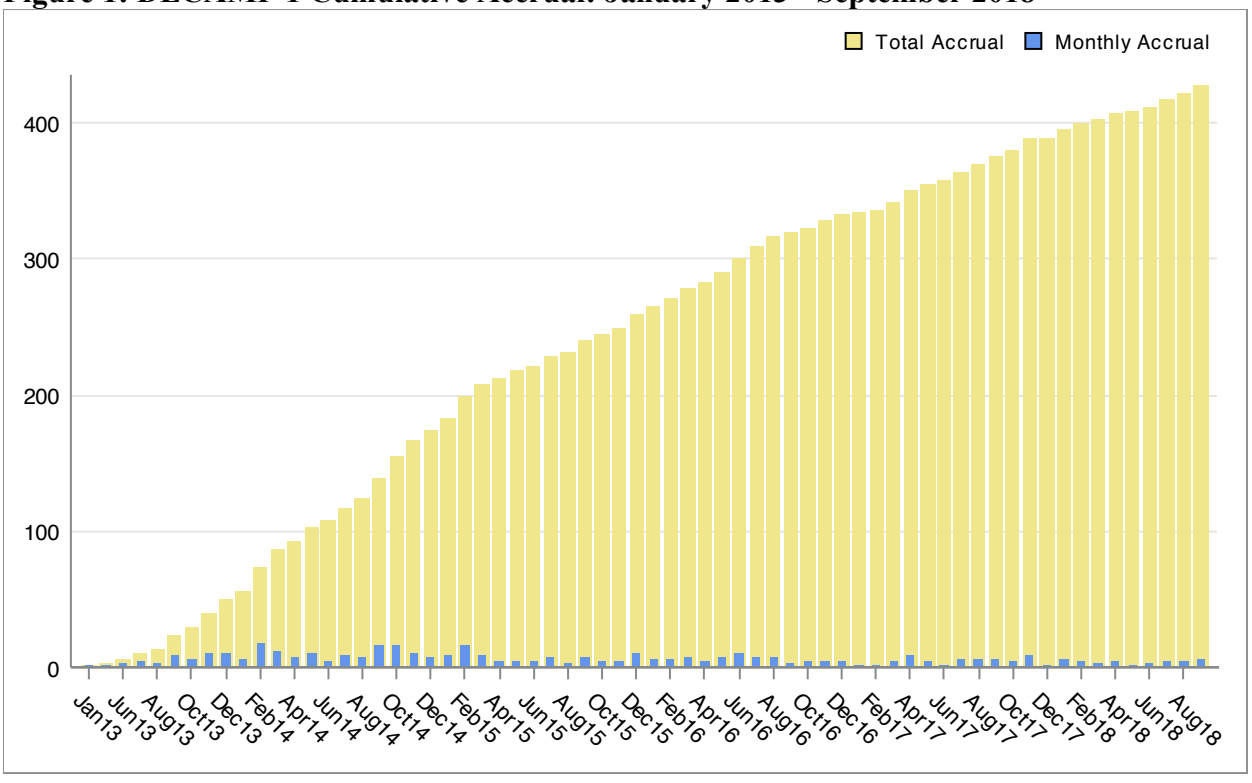
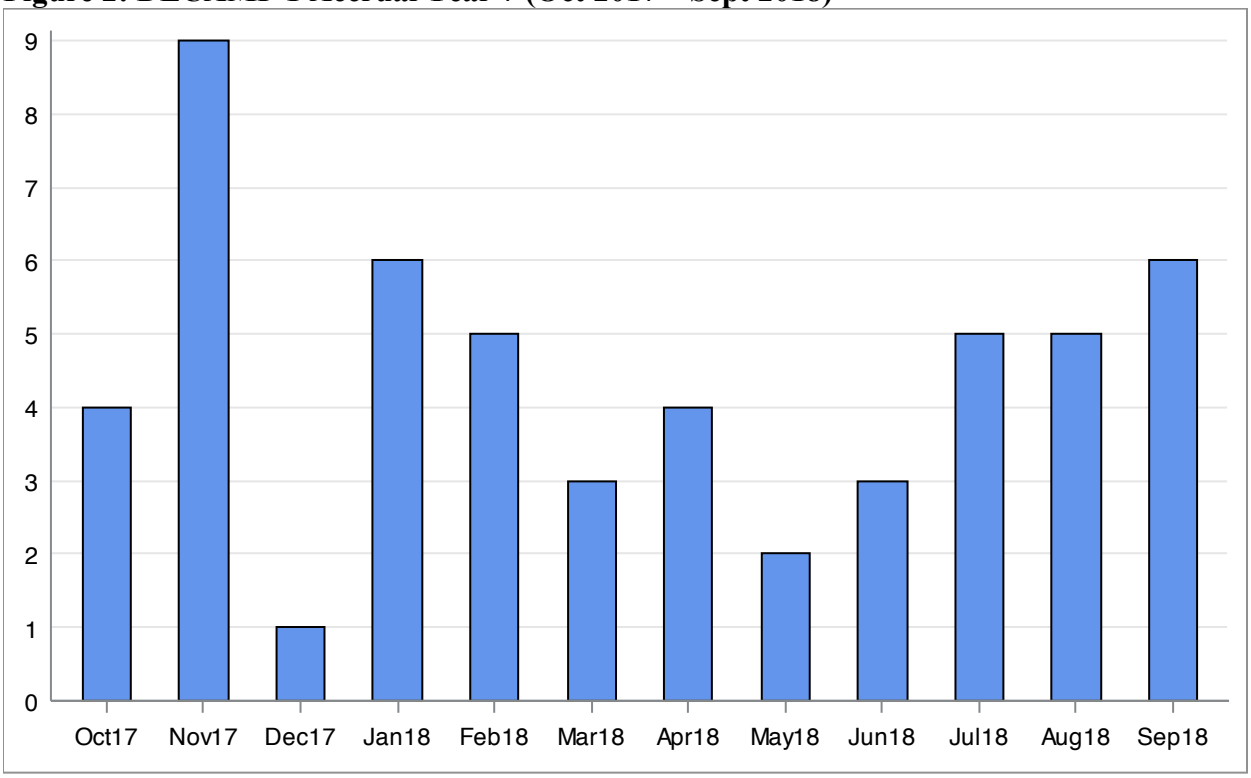


Table 2: DECAMP 1 Accrual Year 7 (Oct 2017 – Sept 2018)

Institution	N
Boston University Medical Campus	15
Walter Reed National Military Medical Center	10
Naval Medical Center San Diego	6
VA Greater Los Angeles Health Care System	6
Nashville VA Medical Center	6
Philadelphia VA Medical Center	4
VA Boston Healthcare System	2
University of California Los Angeles	2
Naval Medical Center Portsmouth	2
Total	**53**

Figure 2: DECAMP 1 Accrual Year 7 (Oct 2017 – Sept 2018)



DECAMP 2 (ACRIN 4704)

Table 3: DECAMP 2 Cumulative Accrual Yr 2 through Yr 7 (Nov 2013 – Sept 2018)

Institution	N
Naval Medical Center San Diego	118
Walter Reed National Military Medical Center	104
VA Greater Los Angeles Health Care System	83
Naval Medical Center Portsmouth	52
VA Eastern Colorado Health Care System	51
VA Boston Healthcare System	48
Nashville VA Medical Center	39
Brooke Army Medical Center	9
Hospital of the University of Pennsylvania	7
VA Pittsburgh Healthcare System	6
Roswell Park Cancer Institute	4
Boston University Medical Campus	2
VA North Texas Health Care System	1
Total	**524**

Figure 3: DECAMP 2 Cumulative Accrual: November 2013 - September 2018

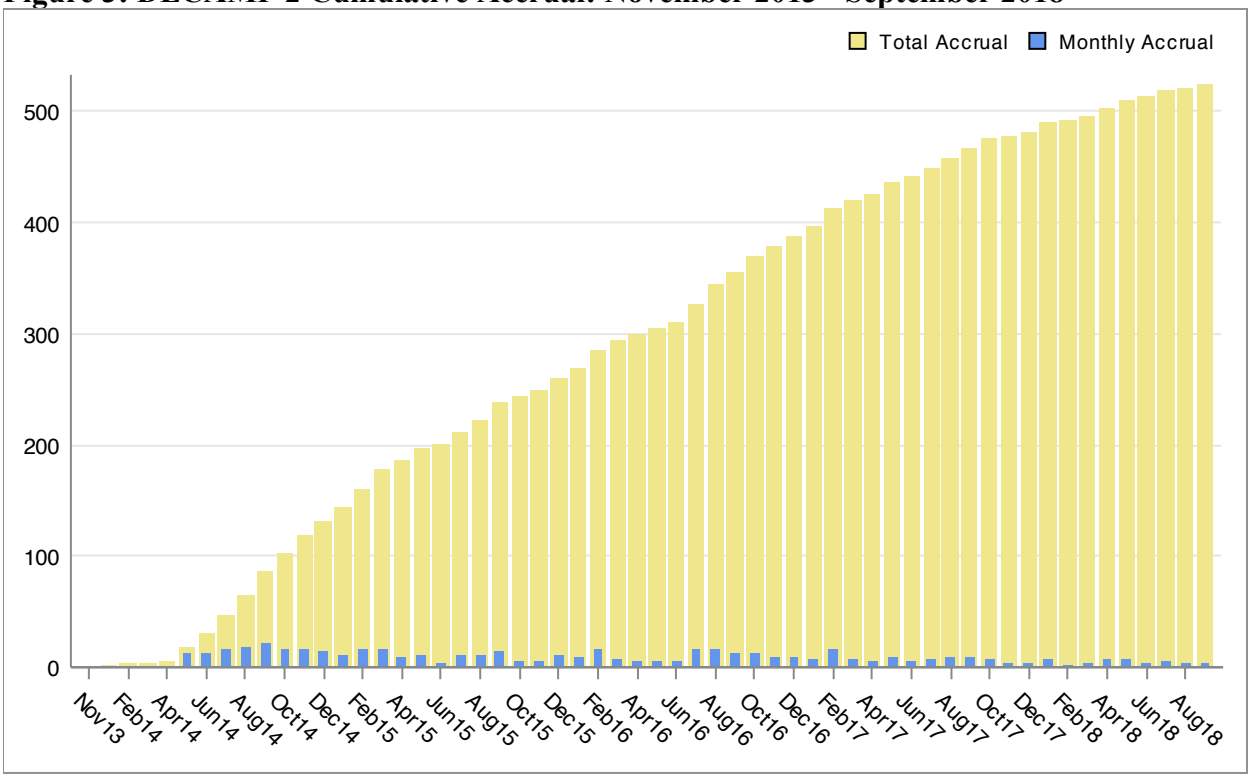


Table 4: DECAMP 2 Accrual Year 7 (Oct 2017 – Sept 2018)

Institution	N
Naval Medical Center San Diego	21
Naval Medical Center Portsmouth	12
VA Eastern Colorado Health Care System	5
Walter Reed National Military Medical Center	5
VA Pittsburgh Healthcare System	5
VA Greater Los Angeles Health Care System	5
Boston University Medical Campus	2
VA Boston Healthcare System	1
Nashville VA Medical Center	1
Total	**57**

Figure 4: DECAMP-2 Accrual: Year 7 (Oct 2017 – Sept 2018)

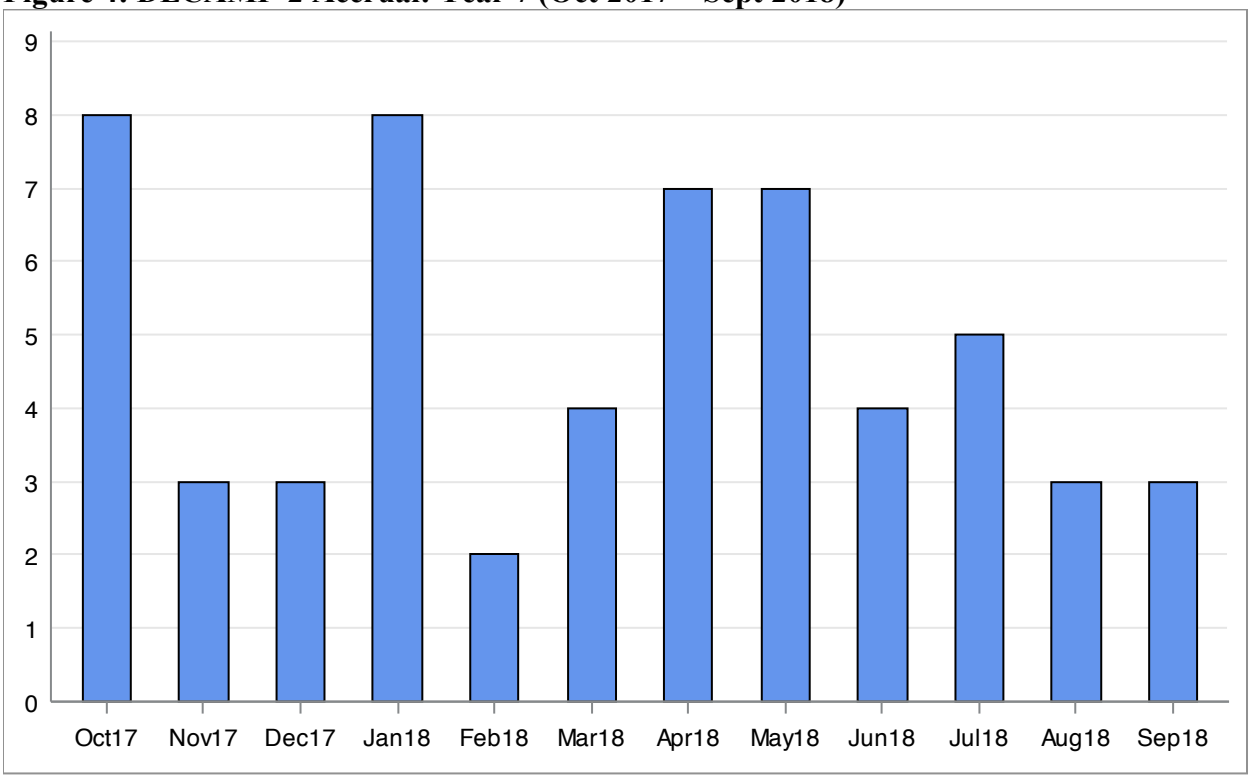


Table 5: DECAMP-1 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	27	27	26	1
4238	Brooke Army Medical Center	130	128	35	93
4278	Roswell Park Cancer Institute	0	0	0	0
4438	VA Los Angeles Healthcare	27	25	23	2
4714	VA Philadelphia	30	30	27	2
4790	VA Boston Healthcare	70	70	59	11
4791	VA North Texas Healthcare	17	17	13	4
4792	VA Eastern Colorado	11	11	6	5
4793	VA Nashville Medical Center	25	22	18	4
4794	VA Pittsburgh Healthcare	53	53	12	41
4795	Walter Reed National Military MC	71	66	60	7
4796	Naval Medical Center San Diego	127	123	56	67
4797	Naval Medical Center Portsmouth	38	38	19	19
4798	Boston Medical Center	17	16	16	0
4494	UCLA Medical Center	0	0	0	0
Total		**643**	**626**	**370**	**256**

Table 6: DECAMP-2 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	12	12	7	5
4238	Brooke Army Medical Center	12	12	8	4
4278	Roswell Park Cancer Institute	13	12	3	6
4438	VA Los Angeles Healthcare	139	136	68	63
4790	VA Boston Healthcare	115	113	48	62
4791	VA North Texas Healthcare	1	1	1	0
4792	VA Eastern Colorado	77	76	44	30
4793	VA Nashville Medical Center	92	84	37	40
4794	VA Pittsburgh Healthcare	1	1	1	0
4795	Walter Reed National Military MC	76	65	62	3
4796	Naval Medical Center San Diego	246	229	114	95
4797	Naval Medical Center Portsmouth	115	112	50	51
4798	Boston Medical Center	1	0	0	0
Total		**900**	**853**	**443**	**361**

Table 7: DECAMP-1 Table 1

Demographics Information for DECAMP 1 (n=428)		
Nodule Size	Mean	1.5
	Range	0.7-3.0
Age	Mean	68.0
	Range	46.0-89.0
Gender	Male	330
	Female	98
Smoking Status	Current	171
	Former	189
	Missing	68
Pack Years	Mean	51.6
	Range	20.0-185.0
	Missing	1
COPD (lln)	No	187
	Yes	163
	Missing	78
FEV1%	Mean	75.7
	Range	24.0-130.0
	Missing	76

Table 8: DECAMP-2 Table 1

Demographics Information for DECAMP 2 (n=524)		
Age	Mean	63.8
	Range	50.0-79.0
Gender	Male	417
	Female	107
Smoking Status	Current	209
	Former	315
Pack Years	Mean	44.3
	Range	2.1-160.0
	Missing	39
COPD (lln)	No	204
	Yes	253
	Missing	67
FEV1%	Mean	70.9
	Range	20.0-121.0
	Missing	67

Table 9: Biosample Quality and Quantity

Site	Nasal							Bronch Brush							Bronch Biopsy						
	Sample Count	RIN			Yield (ug)			Sample Count	RIN			Yield (ug)			Sample Count	RIN			Yield (ug)		
		Avg	Min	Max	Avg	Min	Max		Avg	Min	Max	Avg	Min	Max		Avg	Min	Max	Avg	Min	Max
4202	16	3.8	2.3	7.1	5.08	0.02	15.3	24	6.71	3.7	8.6	4.06	0.73	13.6	14	6.3	2.4	8.6	0.99	0.06	2.43
4238	9	3.9	2.5	10	0.83	0.16	3.56	27	6.59	2.3	9.2	1.69	0.25	4.19	0						
4278	2	3.5	3.1	3.9	4.63	0.41	8.86	3	5.93	3.1	8.2	2.97	1.19	6.03	0						
4438	32	5.4	2.5	8.5	1.92	0.21	9.63	54	6.91	2.1	8.8	1.55	0.16	4.72	16	5.7	2.7	8.2	0.85	0.21	1.95
4714	11	4.1	2.6	7.1	5.99	1.28	15.5	10	6.52	2.7	9.1	4.08	1.35	8.31	6	4.1	2.2	7.2	1.40	0.46	2.85
4790	59	5.1	2.0	8.3	2.32	0.19	11.0	70	7.21	3.5	9.2	3.1	0.36	10.4	19	6.0	1.1	8.6	1.35	0.19	2.97
4791	7	3.3	2.5	5.8	0.7	0.24	2.6	6	5.12	2.6	6.9	2.01	0.07	4.54	6	6.3	2.5	8.6	1.79	0.39	5.73
4792	13	5.9	2.9	7.7	2.77	0.18	14.4	19	7.51	5.8	8.9	2.34	0.41	7.07	5	4.5	2.9	6.6	1.53	0.27	4.09
4793	20	4.9	2.5	7.1	1.16	0.14	4.8	32	6.24	2.2	8.9	2.47	0.55	6.46	7	4.2	2.2	9.0	1.30	0.30	2.77
4794	2	4.0	3.3	4.7	3.52	1.93	5.12	2	7.3	6.6	8.0	4.37	4.34	4.39	6	3.5	2.6	5.2	0.51	0.06	1.31
4795	46	5.6	1.7	9.0	7.18	0.65	22.9	91	6.65	2.3	9.4	2.57	0.24	15.4	10	5.7	2.4	9.1	0.91	0.25	1.81
4796	45	4.6	2.0	8.6	1.63	0.17	7.85	111	6.6	2.5	8.8	2.35	0.18	7.64	23	4.9	2.3	8.4	0.88	0.20	2.23
4797	29	3.4	2.0	7.1	1.89	0.26	7.14	35	6.31	2.2	8.7	3.37	1.01	7.28	10	4.5	2.4	8.3	0.85	0.17	2.15
4798	12	3.1	1.8	7.0	0.22	0.15	0.5	0													
All Sites	**291**	**4.7**	**1.7**	**10**	**2.95**	**0.02**	**22.9**	**484**	**6.7**	**2.1**	**9.4**	**2.58**	**0.07**	**15.4**	**122**	**5.3**	**1.1**	**9.1**	**1**	**0.06**	**5.73**

Table 10: Data Quality

Current Database Build Stats

	# of Unique Folders (Timepoints)	# Unique Forms	# Unique Fields	# of Automatic Validations Programmed	# Updates to DB (since activation of trial)
DECAMP 1	24	92	1171	1462	25
DECAMP 2	35	109	1633	1555	15

Table 11: Study Procedures Performed

	Total	D1 Baseline	D1 Post Cancer	D2 Baseline	D2 Year 1	D2 Year 2	D2 Year 3	D2 Year 4
PFT	**1484**	392	N/A	478	338	193	74	9
Bronchoscopy	**910**	389	N/A	405	N/A	116	N/A	N/A
CT Image	**1490**	509	N/A	476	297	206	N/A	2
Blood	**1333**	381	17	452	296	187	N/A	N/A
Nasal	**1248**	365	15	428	257	183	N/A	N/A
Buccal	**1116**	356	14	428	156	162	N/A	N/A
Urine	**1052**	294	14	362	236	146	N/A	N/A

Table 12: Total Biospecimens Collected

Study	Nasal	Bronch	Buccal	Urine	Biopsy	Plasma	Serum	Pax Gene	TOTAL
DECAMP 1	711	1,800	370	1,685	882	2,273	2,154	745	**10,620**
DECAMP 2	1482	2,849	842	4,078	1,353	4,903	4,570	1,633	**21,710**

Table 13: Total Biospecimens Received at Biorepository Core

Study	Nasal	Bronch	Buccal	Urine	Sputum	Biopsy	Plasma	Serum	Pax Gene	TOTAL
DECAMP 1	627	1,115	318	1,533	393	775	1,924	1,903	608	*9,196*
Percent of Collected	*88%*	*62%*	*86%*	*91%*	*n/a*	*88%*	*85%*	*88%*	*82%*	*83%*
DECAMP 2	1,221	1,483	612	3,319	196	1,195	3,593	3,447	1,167	*16,233*
Percent of Collected	*82%*	*62%*	*86%*	*81%*	*n/a*	*88%*	*85%*	*88%*	*82%*	*74%*

Table 14: Summary of Reviewed Biopsy Histology

Biopsy Histology	DECAMP 1	DECAMP 2
Normal Epithelium	570	404
Basal Cell Hyperplasia	66	49
Squamous Metaplasia	27	34
Mild Dysplasia	13	10
Moderate Dysplasia	4	8
Denuded epithelium	198	187
TOTAL	**878**	**692**

Key Research Accomplishments:

Publications:
Silvestri, G. A., et al. (2015). A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer. *N Engl J Med,* 373, 243-51.

Oral Presentations:
Julian Lel, Ehab Billatos, Elizabeth Moses, Christopher Stevenson, Matthew Lorenzi, Gang Liu, Joshua Campbell, Yusuke Koga, Jiarui Zhang, Fenghai Duan, Helga Marques, A Maoz, Marc Lenburg, Avrum Spira, Jennifer Beane, DECAMP Consortium. (2018, May). *Immune alterations in the airway transcriptome of lung cancer patients.* Presented at The American Thoracic Society Annual Meeting, San Diego, CA.

Billatos, E., Muse, M., Jiwani, A., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning, R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M., Parrish, J.S., Reid, M., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D., Wistuba, I.I., Schnall, M., Vachani, A., Spira, A. (2016, May). *Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium.* Presented at the American Thoracic Society Annual Meeting, San Francisco, CA.

Poster Presentations:
Xingyi Shi, Ehab Billatos, Jiarui Zhang, Jennifer Beane, Elizabeth Moses, Gang Liu, Christopher Stevenson, Marc E Lenburg, Avrum Spira. (2018, April). *Diagnostic evaluation of indeterminate pulmonary nodules via rna-seq of bronchial epithelium.* Presented at The American Association for Cancer Research Annual Meeting, Chicago, IL.

Jiarui Zhang, Ehab Billatos, Elizabeth Moses, Gang Liu, Katie Steiling, Chris Stevenson, Matt Lorenzi, J Sands, T Sullivan, Carla Lamb, B McKee, P Hesketh, Kimberly Christ, Marc Lenburg, Avrum Spira. (2018, May). *Nasal Gene Expression for the Diagnostic Evaluation of Indeterminate Pulmonary Nodules Within the DECAMP Consortium*. Presented at The American Thoracic Society Annual Meeting, San Diego, CA.

Ehab Billatos, Elizabeth Moses, Fenghai Duan, Helga Marques, Chris Stevenson, Matt Lorenzi, Marc Lenburg, Avrum Spira, George Washko, DECAMP Consortium. (2018, May). *Quantitative Imaging of the Indeterminate Pulmonary Nodule and Surrounding Parenchyma for Lung Cancer Diagnosis Within the DECAMP Consortium.* Presented at The American Thoracic Society Annual Meeting, San Diego, CA.

Stevenson, C., Billatos, B., Beane-Ebel, J., Campbell, J., Lel, J., Zhang, J., Lenburg, M., Moy, C., Lorenzi, M., Wiegand, B.C., Spira, A.; On behalf of the DECAMP Consortium. (2017, August). *Airway Gene Expression Signatures for the Early Detection and Interception of Lung Cancer via the DECAMP Cohort*. Presented at the 2017 Johnson and Johnson Symposium, Los Angeles, CA.

Wilkerson, M., Campbell, J., Dalgard, C.L., Billatos, E., Pollard, H.B., Browning, R., Stevenson, C., DECAMP Consortium, Spira, A. (2017, August). *RNA sequencing of the bronchial airway identifies molecular subtypes of COPD within the DECAMP consortium.* Presented at the 2017 Military Health System Research Symposium, Kissimmee, FL.

Radin, G., Billatos, E., Snyder, B., Stevenson, C., Duan, F., Gatsonis, C., O'Connor, G., Lenburg, M., Washko, G., Spira, A. (2017, May). *Characterizing clinical and imaging phenotypes of COPD within the DECAMP consortium*. Presented at the American Thoracic Society Annual Meeting, Washington, DC.

Billatos, E., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning, R., Garshick, E., Goldstein, R.H., Vachani, A., Keith, R.L., More, K., Morris, M., Parrish, J.S., Reid, M., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P, Remick, D., Wistuba, I.I., Schnall, M., Spira, A. (2016, October). *Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium*. Presented at Evans Day, Boston University, Boston, MA.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2015, May).
Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium. Presented at the American Thoracic Society Conference, Denver, Colorado.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2014, October). *Airway gene-expression in the DECAMP consortium as a molecular window into COPD and lung cancer.* Presented at American Association of Bronchology and Interventional Pulmonology Research Symposium, Austin, TX.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2014, October). *Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium.* Presented at American College of Chest Physicians Conference, Austin, TX.

Reportable Outcomes:
n/a

Conclusion:

Overall, we have made significant progress towards the goals of this consortium over the past 12 months, including in our biomarker validation and discovery aims, laying the groundwork for the development of new diagnostic biomarkers for lung cancer. As we come to the end of the no cost extension, we feel confident that we have taken the necessary steps to ensure DECAMP's impact and longevity beyond our partnership with the Department of Defense. This includes securing additional funding from the NCI, Johnson and Johnson, and Novartis to sustain DECAMP-1 and -2 through mid-2022 and the creation of a new cohort, DECAMP-1 PLUS, in partnership with Johnson and Johnson. In addition, we are exploring a potential relationship with the Murtha Cancer Center in order to ensure that DECAMP has a continued presence in the Department of Defense and can continue to benefit our service men and women battling lung cancer. In all, we look forward to sharing the results, data, and lessons learned from DECAMP with the scientific community in the coming years.