Award Number: W81XWH-11-2-0161

TITLE: Detection of Early Lung Cancer among Military Personnel (DECAMP)

PRINCIPAL INVESTIGATOR: Avrum E. Spira, MD

CONTRACTING ORGANIZATION: Boston University

Boston, MA

REPORT DATE: JUNE 2019

TYPE OF REPORT: FINAL

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
JUNE 2019	FINAL	30Sept 2011 - 29 MAR 2019

4. TITLE AND SUBTITLE

Detection of Early Lung Cancer among Military Personnel (DECAMP)

5a. CONTRACT NUMBER
W81XWH-11-2-0161

5b. GRANT NUMBER
W81XWH-11-2-0161

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

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

E-Mail: emoses@bu.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Trustees of Boston University, 85 East Newton St, M-921,
Boston, MA, 02118

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

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 last year of this award, we have made significant progress towards enrollment in both clinical trials. We have recruited ~92% of the 500 total subjects in the indeterminate pulmonary nodule study (Protocol 1), and ~69% of the 800 total subjects in the longitudinal screening study (Protocol 2). The Leadership, Steering, Adjudication, Biostatistics, Imaging and Biomarker Committees continue to meet regularly. Most notably, significant progress has been made in collection and profiling of biospecimens from both cohorts, which will facilitate the validation of our cancer biomarkers. We have secured additional funding for the DECAMP consortium through July 2022, to ensure the completion of our enrollment goals and study aims. Lastly, we are finalizing discussions regarding dissemination and sharing of DECAMP data in the coming years.

15. SUBJECT TERMS; NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	25	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

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 150 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 this past 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. Recruitment into the DECAMP-2 cohort has continued to slow down and we plan to explore over the next few months, the implications of closing this cohort to new recruitment. Cumulatively, 462 subjects have now been enrolled in DECAMP-1, and 548 subjects in DECAMP-2. Demographic information on these subjects is shown in Tables 7-8. 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.

We have utilized this past year to put practices in place and establish partnerships that will ensure DECAMP's longevity beyond the no cost extension. We continue to meet regularly with the DECAMP Executive and Data Access Committees in order to finalize a plan for data sharing in DECAMP once the cohorts close to recruitment. We are currently exploring a web-based system for data access submissions and to disseminate available data. We aim to finalize this plan at our upcoming DECAMP in-person meeting, in November, 2019.

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 37,009 samples banked at the Biorepository of Boston University and there are additional samples pending shipment from individual sites (Tables 12 and 13). This a significant increase from previous reports, largely due to the addition of a dedicated, Clinical Biospecimen Coordinator at Boston University, who is actively working with the sites to ensure biospecimens are submitted to the biorepository in a timely fashion. Currently, we have 90% of all collected samples in hand, which has greatly facilitated our ability to batch and profile biospecimens for our biomarker analyses. In addition, a total of 2,201 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 (675/1,032 in DECAMP 1 and 712/1,169 in DECAMP 2) or denuded epithelium (243 and 338 respectively), in addition to some basal cell hyperplasia, squamous metaplasia, mild dysplasia and moderate dysplasia samples. We plan in the next few months to begin histological evaluation of collected tumor tissue as well. Additionally, we continue to process and sequence samples for our biomarker work, including bronchial brushings (n=722), nasal brushings (n=858) and bronchial biopsies (n=115). 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. The number of profiled samples has increased significantly from previous reports, largely due to our focused efforts on sequencing for biomarker analyses. As DECAMP-1 nears completion, we intend in the next quarter to begin profiling collected tumor tissue via immunohistochemistry, RNA-seq and whole exome seq. We have been previously unable to profile tumor tissue due to a limited sample size, however we now have tissue from 50 DECAMP-1 cases, in hand. Finally, our team has also made significant strides in quality control of the images submitted to DECAMP (Tables 5-6), and in particular, we have greatly increased

the number of follow-up exams submitted in DECAMP-2, in the past 6 months. In all, collection of this data is tracked and stored in our clinical database, and the current database is summarized in Table 10.

We continue to make efforts to increase adjudication in DECAMP-1, with 392 total cases and controls adjudicated in DECAMP-1, with a total adjudication rate of 87%. Of these 392 subjects, 251 have been confirmed to have a lung cancer diagnosis, 134 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 is currently being 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. Data was received in May and is currently being analyzed. 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). This data is forthcoming this summer. 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 in 222 DECAMP-1 subjects. They are currently pursuing whether these metabolites show promise as a biomarker for early stage (IA and IB) lung cancer and we are identifying additional urine and serum samples from early stage DECAMP-1 subjects to send to the NCI to increase sample size. 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=144) are currently being analyzed 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. We will validate this microbiome biomarker on the newly sequenced 144 nasal samples, this summer. 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 previously 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.

While our DoD Funding has now ended, the DECAMP consortium continues to be industry funded. In addition to our substantial Janssen funding through December 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 also plays 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 serves 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 Fall 2019. Together, this scientific and financial progress ensures DECAMP's longevity in the coming years.

Additional accomplishments and plans for beyond the no cost extension 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

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 clinical 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 this year we continued with 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 this year we have begun phase II validation.
- 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 this year we continued 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 this year we completed a phase 2 validation and are working to acquire additional samples.
- CT-based Radiomic Classifier: We have begun preliminary validation of radiomic classifier from NLST in 293 DECAMP-1 subjects (phase 1).
  During this year we continued 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 and selected

markers for IHC are being finalized.

- 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=144) are currently being analyzed.
- 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; will continue to meet monthly until both cohorts close to recruitment.
- Steering Committee: meets monthly; will continue to meet monthly until both cohorts close to recruitment.
- Adjudication Committee: meets as needed; continuous adjudication being processed; currently 385 subjects adjudicated in DECAMP-1. The committee will meet again in Fall 2019, and will continue to meet as needed until all DECAMP patients have an adjudicated diagnosis.
- Data Access Committee: meets as needed depending on when biomarkers or data access requests are being proposed; the committee will continue to meet as needed, when sample and data access requests are received. The committee will continue to meet beyond closure of the cohorts to recruitment.
- Biostatistics Committee: meets biweekly; led by the Biostatistics core at Brown. Will continue to meet monthly until both cohorts close to recruitment.
- Imaging Working Group: meets monthly; led by Dr. Denise Aberle and Dr. Caroline Chiles. Will continue to meet monthly until both cohorts close to recruitment.

DECAMP-1 (ACRIN 4703)

Table 1: DECAMP 1 Cumulative Accrual by Submitting Institution (Jan 2013-May 2019)

Institution	N
Walter Reed National Military Medical Center	85
VA Boston Healthcare System	62
Naval Medical Center San Diego	58
Philadelphia VA Medical Center	43
Brooke Army Medical Center	35
Nashville VA Medical Center	32
Boston University Medical Campus	32
VA Greater Los Angeles Health Care System	29
Hospital of the University of Pennsylvania	29
Naval Medical Center Portsmouth	22
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	**462**

Figure 1: DECAMP 1 Cumulative Accrual: January 2013 - May 2019

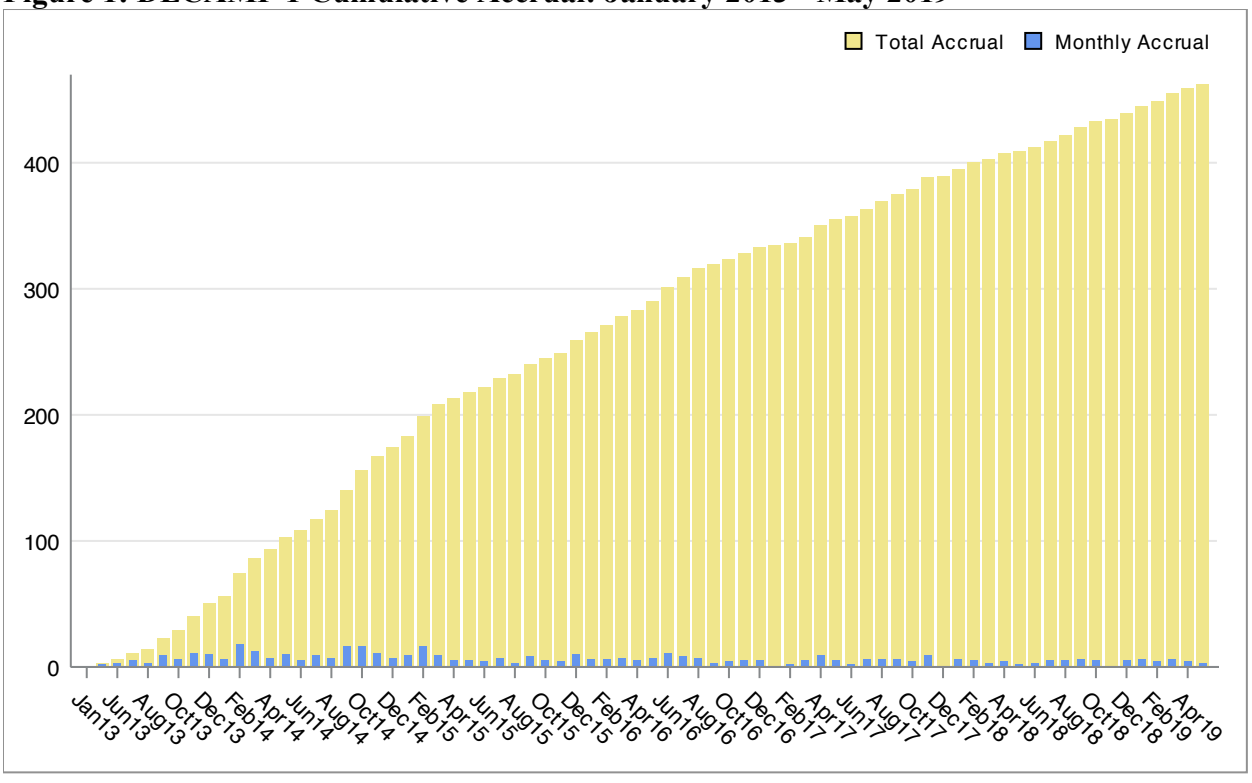
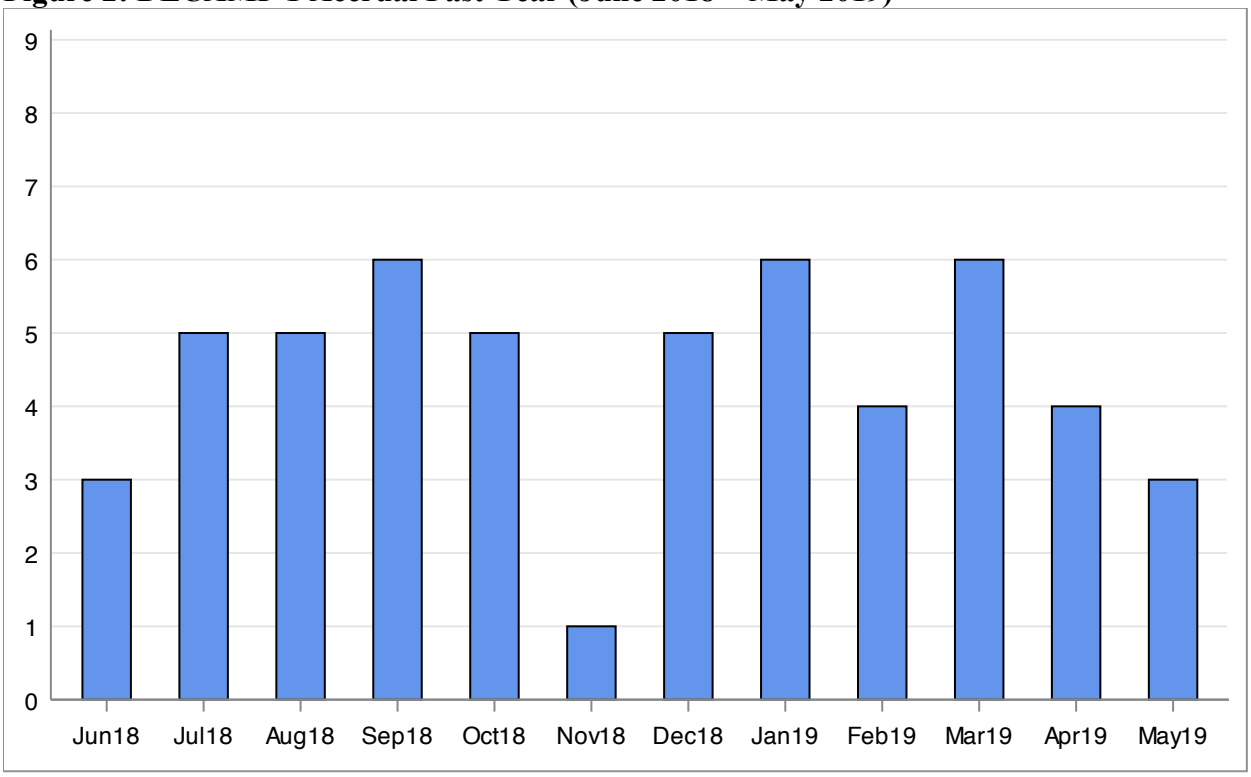


Table 2: DECAMP 1 Accrual Past Year (June 2018 – May 2019)

Institution	N
Boston University Medical Campus	14
Walter Reed National Military Medical Center	14
Nashville VA Medical Center	12
VA Greater Los Angeles Health Care System	4
Naval Medical Center Portsmouth	3
Naval Medical Center San Diego	3
VA Boston Healthcare System	3
Total	**53**

Figure 2: DECAMP 1 Accrual Past Year (June 2018 – May 2019)



DECAMP 2 (ACRIN 4704)

Table 3: DECAMP 2 Cumulative Accrual by Submitting Institution (Nov 2013 – May 2019)

Institution	N
Naval Medical Center San Diego	120
Walter Reed National Military Medical Center	108
VA Greater Los Angeles Health Care System	87
Naval Medical Center Portsmouth	57
VA Eastern Colorado Health Care System	53
VA Boston Healthcare System	49
Nashville VA Medical Center	42
Brooke Army Medical Center	9
Hospital of the University of Pennsylvania	7
VA Pittsburgh Healthcare System	7
Roswell Park Cancer Institute	4
Boston University Medical Campus	4
VA North Texas Health Care System	1
Total	**548**

Figure 3: DECAMP 2 Cumulative Accrual: November 2013 – May 2019

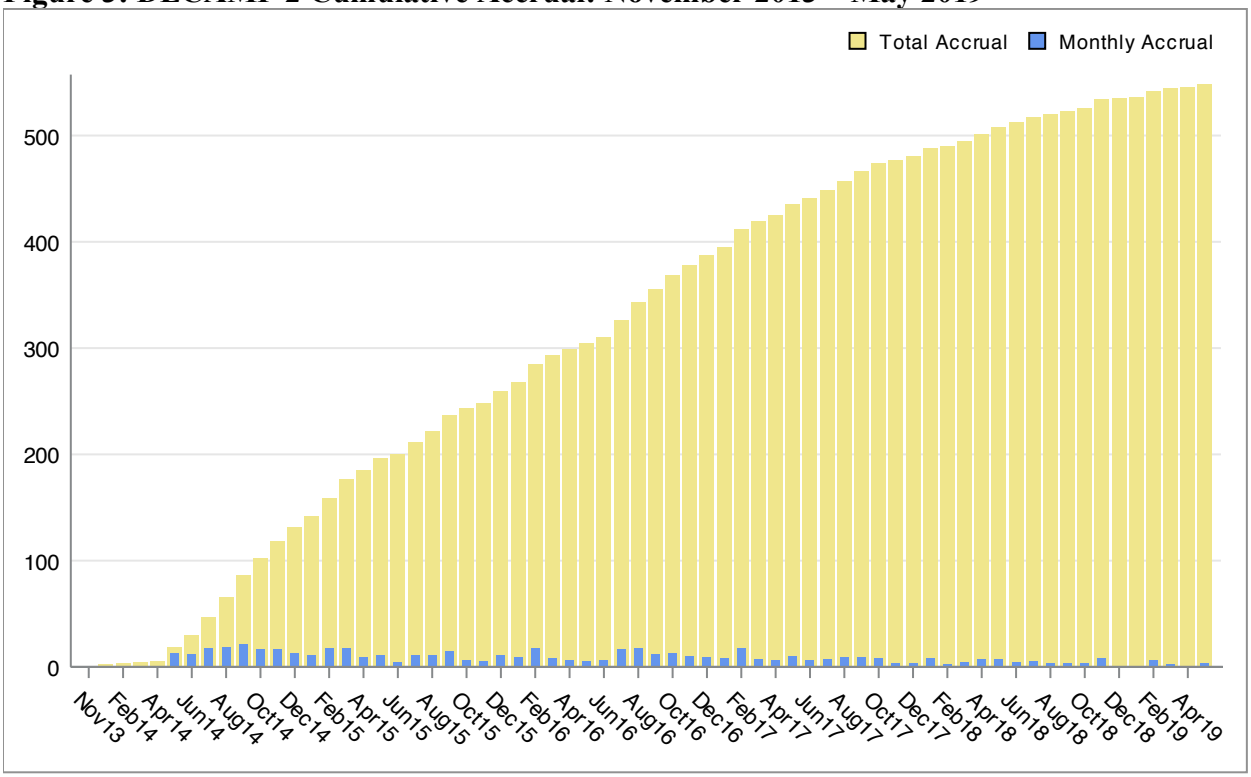


Table 4: DECAMP 2 Accrual Past Year (June 2018 – May 2019)

Institution	N
Naval Medical Center Portsmouth	8
Naval Medical Center San Diego	8
VA Greater Los Angeles Health Care System	7
Walter Reed National Military Medical Center	5
VA Eastern Colorado Health Care System	4
Nashville VA Medical Center	3
VA Pittsburgh Healthcare System	2
Boston University Medical Campus	2
VA Boston Healthcare System	1
Total	40

Figure 4: DECAMP-2 Accrual Past Year (Oct 2017 – May 2019)

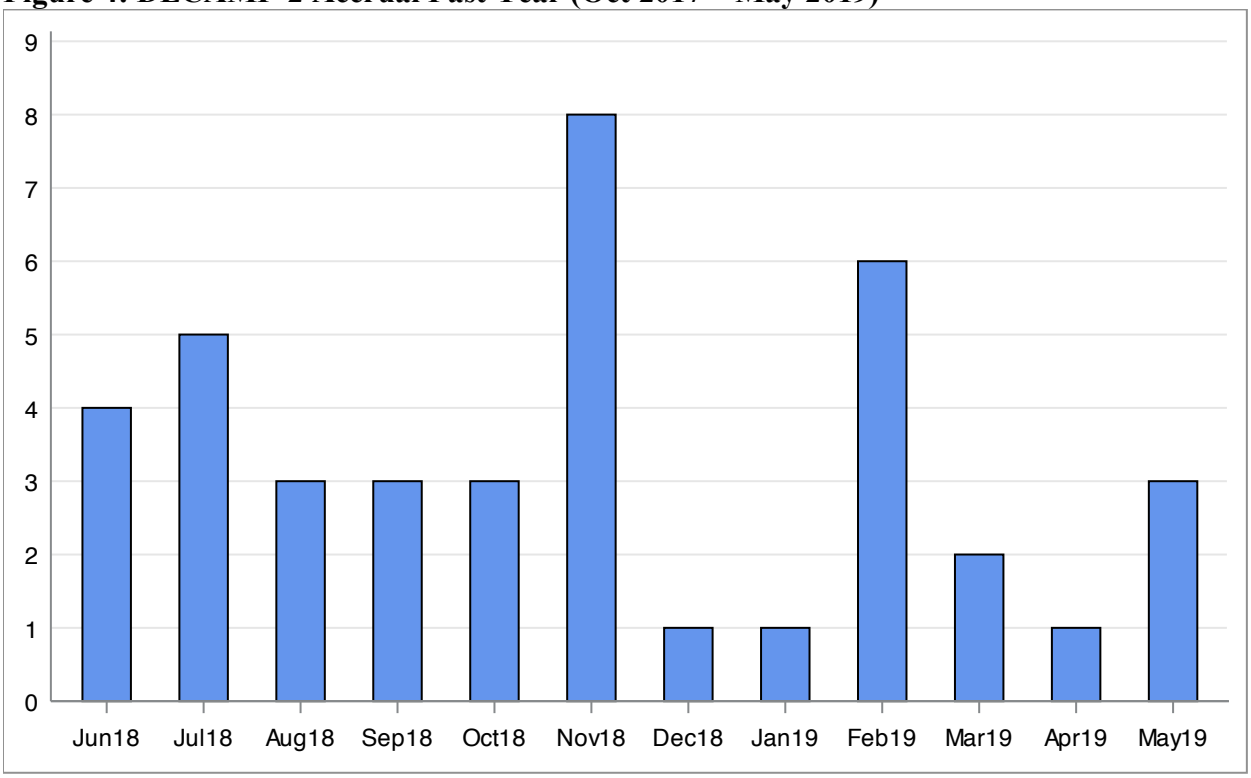


Table 5: DECAMP-1 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	30	30	29	1
4238	Brooke Army Medical Center	130	129	35	94
4278	Roswell Park Cancer Institute	0	0	0	0
4438	VA Los Angeles Healthcare	33	33	29	4
4714	VA Philadelphia	30	30	27	2
4790	VA Boston Healthcare	72	72	61	11
4791	VA North Texas Healthcare	19	19	15	4
4792	VA Eastern Colorado	11	11	6	5
4793	VA Nashville Medical Center	34	34	28	6
4794	VA Pittsburgh Healthcare	53	53	12	41
4795	Walter Reed National Military MC	84	82	76	6
4796	Naval Medical Center San Diego	132	132	57	75
4797	Naval Medical Center Portsmouth	49	49	22	27
4798	Boston Medical Center	25	23	23	0
4494	UCLA Medical Center	0	0	0	0
Total		**702**	**697**	**420**	**276**

Table 6: DECAMP-2 Imaging QC

	Site	Submitted	QC'd	Baseline Exams	Follow-Up Exams
4202	Hospital of the University of Penn	16	15	7	8
4238	Brooke Army Medical Center	12	12	8	4
4278	Roswell Park Cancer Institute	13	13	3	6
4438	VA Los Angeles Healthcare	153	149	73	72
4790	VA Boston Healthcare	130	129	49	72
4791	VA North Texas Healthcare	1	1	1	0
4792	VA Eastern Colorado	85	85	46	36
4793	VA Nashville Medical Center	107	107	40	60
4794	VA Pittsburgh Healthcare	1	1	1	0
4795	Walter Reed National Military MC	137	113	65	48
4796	Naval Medical Center San Diego	295	287	115	127
4797	Naval Medical Center Portsmouth	144	144	56	63
4798	Boston Medical Center	2	2	2	0
Total		**1096**	**1058**	**466**	**496**

Table 7: DECAMP-1 Table 1

Demographics Information for DECAMP 1 (n=462)		
Nodule Size	Mean	1.5
	Range	0.7-3.0
Age	Mean	67.8
	Range	46.0-89.0
Gender	Male	355
	Female	107
Smoking Status	Current	186
	Former	201
	Missing	75
Pack Years	Mean	51.5
	Range	20.0-185.0
COPD (lln)	No	210
	Yes	177
	Missing	75
FEV1%	Mean	75.9
	Range	24.0-130.0
	Missing	73

Table 8: DECAMP-2 Table 1

Demographics Information for DECAMP 2 (n=548)		
Age	Mean	63.7
	Range	50.0-79.0
Gender	Male	433
	Female	115
Smoking Status	Current	217
	Former	331
Pack Years	Mean	44.3
	Range	2.1-160.0
	Missing	41
COPD (lln)	No	219
	Yes	275
	Missing	54
FEV1%	Mean	71.1
	Range	20.0-121.0
	Missing	54

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	37	3.9	2.1	7.1	5.25	0.02	15.97	35	6.9	3.7	8.6	4.03	0.73	13.62	14	6.0	2.4	8.6	0.99	0.06	2.43
4238	15	4.6	2.5	10	0.8	0.16	3.83	30	6.6	2.3	9.2	1.24	0.25	2.93	0						
4278	2	3.5	3.1	3.9	4.63	0.41	8.86	3	5.9	3.1	8.2	2.97	1.19	6.03	0						
4438	95	4.6	1.6	8.5	2.62	0.02	17.4	72	6.9	2.1	8.8	1.65	0.16	5.82	14	5.5	2.7	8.2	0.70	0.21	1.43
4714	35	3.8	2.2	7.8	7.48	1.28	17.18	24	5.8	2.4	9.1	3.78	1.35	8.31	6	4.1	2.2	7.2	1.40	0.46	2.85
4790	125	4.6	1	29	2.35	0.01	22.36	86	7.2	3.5	9.2	2.79	0.36	6.95	19	5.6	1.1	8.6	1.26	0.19	2.97
4791	17	3	2.1	5.8	0.64	0.18	2.6	14	4.9	2.4	7.9	1.66	0.07	4.54	6	6.3	2.5	8.6	1.79	0.39	5.73
4792	38	5.3	1.6	8.5	2.03	0.1	14.35	31	7.4	5.8	8.9	2	0.08	7.07	5	4.5	2.9	6.6	1.53	0.27	4.09
4793	50	5.2	1.6	8.3	1.92	0.01	12.1	50	6.4	2.5	8.9	2.27	0.16	9.9	6	3.7	2.2	9.0	1.18	0.30	2.77
4794	12	4.5	2.2	6.6	3.45	0.86	9.61	10	6.7	1.2	8.3	1.76	0.41	4.34	6	3.1	2.6	5.2	0.51	0.06	1.31
4795	148	5.6	2.3	9	8.33	0.37	33.91	123	6.8	2.3	9.4	2.48	0.11	15.36	8	6.1	2.4	9.1	0.69	0.25	1.07
4796	176	4.7	1	9.4	1.4	0.02	12.13	175	6.8	2.5	9.1	2.06	0.11	7.64	21	4.1	2.3	7.9	0.78	0.20	2.23
4797	73	3.2	1.1	7.3	1.67	0.02	9.78	51	6.8	2.2	9.3	3.07	0.32	8.24	10	4.5	2.4	8.3	0.84	0.17	2.15
4798	35	4.1	1.2	7.8	0.49	0.17	2.44	18	5.1	2.6	7.3	2.3	0.38	5.36	0						
All Sites	**858**	**4.33**	**1.83**	**9.21**	**3.08**	**0.26**	**13.04**	**722**	**6.44**	**2.76**	**8.73**	**2.43**	**0.41**	**7.58**	**115**	**4.9**	**2.3**	**7.9**	**1.1**	**0.2**	**2.6**

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	91	1159	1461	25
DECAMP 2	35	110	1657	1563	16

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	D2 Post Cancer
PFT	1510	396	N/A	497	294	205	93	25	N/A
Bronch-oscopy	999	431	N/A	428	N/A	140	N/A	N/A	N/A
CT Image	1516	436	N/A	509	332	223	N/A	16	N/A
Blood	1396	421	22	460	284	206	N/A	N/A	3
Nasal	1382	407	24	458	286	204	N/A	N/A	3
Buccal	1367	398	23	457	281	205	N/A	N/A	3
Urine	1241	328	24	427	270	189	N/A	N/A	3

Table 12: Total Biospecimens Collected

Study	Nasal	Bronch	Buccal	Urine	Biopsy	Plasma	Serum	Pax Gene	TOTAL
DECAMP 1	855	2,042	419	2,043	1,041	2,572	2,309	840	**12,121**
DECAMP 2	1,764	3,130	945	5,189	1,554	5,528	4,931	1,847	**24,888**

Table 13: Total Biospecimens Received at Biorepository Core

Study	Nasal	Bronch	Buccal	Urine	Sputum	Biopsy	Plasma	Serum	Pax Gene	TOTAL
DECAMP 1	790	1,358	403	1,957	194	836	2,422	2,241	789	10,990
Percent of Collected	*92%*	*67%*	*96%*	*96%*	*n/a*	*80%*	*94%*	*97%*	*94%*	*91%*
DECAMP 2	1,391	1,851	908	4,993	443	1.547	5.285	4.712	1.763	22,893
Percent of Collected	*79%*	*59%*	*96%*	*96%*	*n/a*	*100%*	*96%*	*96%*	*95%*	*92%*

Table 14: Summary of Reviewed Biopsy Histology

Biopsy Histology	DECAMP 1	DECAMP 2
Normal Epithelium	675	712
Basal Cell Hyperplasia	68	58
Squamous Metaplasia	29	43
Mild Dysplasia	13	10
Moderate Dysplasia	4	8
Denuded epithelium	243	338
TOTAL	**1,032**	**1,169**

Key Research Accomplishments:

Publications:

Ehab Billatos, Samuel Ash, Fenghai Duan, Justin Romanoff, Helga Marques, Elizabeth Moses, Meilan Han, Elizabeth Regan, Russell Bowler, Stefanie E Mason, Tracy J Doyle, Ruben San Jose Estepar, Ivan O Rosas, James C Ross, Xiaohui Xiao, Hanqiao Liu, Gang Liu, Gauthaman Sukumar, Matthew Wilkerson, Clifton Dalgard, Chris Stevenson, Denise Aberle, Avrum Spira, Raul San Jose Estepar, Marc E Lenburg, George R Washko. Distinguishing smoking related lung disease phenotypes via imaging and molecular features. *ERJ. Under Review.*

Billatos E, Duan F, Moses E, Marques H, Mahon I, Dymond L, Apgar C, Aberle D, Washko G, Spira A; DECAMP investigators. Detection of early lung cancer among military personnel (DECAMP) consortium: study protocols. *BMC Pulm Med*. 2019 Mar 7;19(1):59. doi: 10.1186/s12890-019-0825-7. PMID:30845938

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:

Ke Xu, Ehab Billatos, Fenghai Duan, Helga Marques, Justin Romanoff, Elizabeth Moses, Christopher Stevenson, Avrum Spira, Samuel Ash, George Washko, Marc E Lenburg. (2019, May). *Gene Expression Alterations associated with Computed Tomography Imaging Clusters of Patients with Chronic Obstructive Pulmonary Disease.* Presented at the American Thoracic Society Annual Meeting, Dallas, TX.

Kahkeshan Hijazi, Julian Lel, Ehab Billatos, Elizabeth Moses, Christopher Stevenson, Matthew Lorenzi, Gang Liu, Joshua Campbell, Yusuke Koga, Jiarui Zhang, Fenghai Duan, Helga Marques, Marc Lenburg, Avrum Spira, Jennifer Beane. (2019, April). *Altered immune response in the transcriptome of patients with lung cancer.* Presented at The American Thoracic Society Annual Meeting, Atlanta, GA.

Ke Xu, Ehab Billatos, Elizabeth Moses, George Washko, Christopher Stevenson, Avrum Spira, Marc E Lenburg. (2018, October). *Gene Expression Perturbations associated with Computed Tomography Imaging Clusters of Patients with Chronic Obstructive Pulmonary Disease.* Presented at Evans Day, Boston University, Boston, MA.

Xingyi Shi, Ehab Billatos, Jiarui Zhang, Jennifer Beane, Elizabeth Moses, Gang Liu, Christopher Stevenson, Marc E Lenburg, Avrum Spira. (2018, October). *Diagnostic evaluation of indeterminate pulmonary nodules via rna-seq of bronchial epithelium.* Presented at Evans Day, Boston University, Boston, MA.

DECAMP Consortium. (2018, October). *Quantitative Imaging of the Indeterminate Pulmonary Nodule and Surrounding Parenchyma for Lung Cancer Diagnosis.* Presented at Evans Day, Boston University, Boston, MA.

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 year, including biospecimen collection and profiling in support of 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. 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. We will focus our efforts over the next few years on: (1) completion of enrollment into the DECAMP cohorts; (2) validation of our lung cancer biomarkers; (3) publication of our biomarkers and scientific work; (4) finalizing the plan for data sharing and dissemination. In all, we look forward to sharing the results, data, and lessons learned from DECAMP with the scientific community in the coming years.