Fiscal Year:	FY 2008	**Task Last Updated:**	FY 01/30/2008
PI Name:	Chylack, Leo M.D.		
Project Title:	Precise Assessment of Prevalence and Progression of Lens Opacities in Astronauts as a Function of Radiation Exposure During Space Flight and Development of Improved Routine Clinical Assessment of Ocular Lens Status		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **Cardiovascular**:Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	leo@chylackinc.com	**Fax:**	FY 781-934-2747
PI Organization Type:	UNIVERSITY	**Phone:**	617-732-7355
Organization Name:	Harvard Medical School, Brigham & Women's Hospital		
PI Address 1:	Center for Opthalmic Research		
PI Address 2:	221 Longwood Ave., EBRC 323		
PI Web Page:			
City:	Boston	**State:**	MA
Zip Code:	02115	**Congressional District:**	8
Comments:	If I am not available at 617-732-7355, my office number, please call 781-934-5052, my home number. [Ed. note: email changed to leo@chylackinc.com on 8/23/12]		
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	01/27/2003	**End Date:**	12/31/2009
No. of Post Docs:	0	**No. of PhD Degrees:**	1
No. of PhD Candidates:	1	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: Extended to 12/31/2009 per J. Dardano/JSC (8/09) NOTE: Extended to 5/31/2009 (from 11/30/2008) per PI (7/09) NOTE: Received NCE to 11/30/2008 per JSC (8/08) NOTE: Received NCE to 8/31/2008 per JSC (11/07) NOTE: End date changed back to 01/27/2008 per S. Krenek/JSC (8/07) End date changed to 3/31/2008 per JSC info update (10/06)		

Key Personnel Changes/Previous PI:	In July, 2006 after providing excellent optometric backup to the NASCA study the optometrists in Space Center Eye Associates left the project and were replaced by two new optometrists, Robert Gibson, O.D. and Jung Choi, O.D. The transition was a smooth one. Training in the standardized techniques of the routine eye examination for astronauts was provided, and training and certification in HIPAA and LOCS III classification were provided. The new optometrists have maintained the pace of the project. In the fall of 2006 for three months Cynthia Bell, M.S assisted Alan H. Feiveson, Ph.D. in the statistical analyses for the two NASCA manuscripts submitted to Archives of Ophthalmology in December, 2006. She then went onto a faculty position in academe. NASCA Administrative Assistant, Ms. Evelyn Hernandez left the BWH and the project in mid-2006 and was replaced by Ms. Nancy Leslie. This transition was also smooth and non-disruptive. As of January, 2008, the personnel on this project remains the same as outlined above. There have been no new additions or deletions.
COI Name (Institution):	Cucinotta, Francis (NASA Johnson Space Center) Feiveson, Al (NASA) Wear, Mary (Wyle Labs, NASA) Peterson, Leif (Resigned from Baylor College of Medicine in January 2007. Now at The Methodist Hospital in Houston, TX)
Grant/Contract No.:	NAG9-01491
Performance Goal No.:	
Performance Goal Text:	
Task Description:	The NASA Study of Cataract in Astronauts (NASCA) is a cross-sectional and longitudinal five-year epidemiological study of the risk factors associated with cataract severity and progression in the whole population of American astronauts and two control populations – aircrew with military aviation experience and ground-based participants in the Longitudinal Study of Astronaut Health (LSAH). The study of risk factors focuses on the types and doses of radiation exposure in space flight, on measures of terrestrial solar UV radiation exposure, measures of nutrition, smoking, and general health. The assessment of cataract will use standardized digital images of the lens and validated measures of severity. The study will measure the severity and progression rates of cortical, nuclear, posterior subcapsular, and mixed cataracts, and it will relate these measures to measures of UV and ionizing radiation, nutrition, smoking, and general health. A secondary goal of this project will be to improve the routine annual clinical assessment of the ocular lens by including Nidek EAS 1000 digital imaging of the lens in the annual ocular examination protocol for astronauts. NASCA contains an initial cross-sectional assessment of the severity of the three types of lens opacification, and a follow-on assessment of progression rates of the three classes lens opacification in the populations of astronauts, military aircrew, and ground based comparison participants in the Longitudinal Study of Astronaut Health (LSAH). The main goal of the five-year longitudinal study is to determine the progression rates of the three main types of lens opacification in the complete sample of astronauts, the control populations of military aircrew and ground-based subjects in the LSAH, and then determine the risk factors associated with cataract progression with a specific focus on the components and doses of radiation exposure during space flight. Specifically, total radiation lens dose, space radiation lens dose, and individual contributions from space galactic cosmic ray and trapped proton lens dose will be assessed. NASA is also concerned about identifying and ultimately mitigating the risks to astronaut health of exposure to radiation in space. Several avenues of research now suggest that increased risk of lens opacification may be one of these adverse health effects. In order to address this issue, NASA has approved and funded this five-year, multi-centered research proposal entitled “The Precise Assessment of Prevalence and Progression of Lens Opacities in Astronauts as a Function of Radiation Exposure During Space Flight.” The Brigham and Women’s Hospital (BWH), the Johnson Space Center (JSC), the Departments of Medicine at Baylor College of Medicine (BCM) and The Methodist Hospital (TMH) both in Houston, Wyle Laboratories, and Space Center Eye Associates are the six centers cooperating in the execution of this study. The epidemiologic team at BCM and TMH will recruit astronauts and control subjects. Members of the Flight Medicine Clinic at the JSC and will perform ocular and general medical examinations. They will obtain specialized digital images of the crystalline ocular lens that will enable investigators at The Center for Ophthalmic Research (COR) at the BWH to derive measures of the severity for each class of cataract. Wyle Laboratories personnel at JSC will create and maintain the main data set of this project, and members of the Radiation Safety Office and the Statistical Branch of the JSC will work with Dr. Chylack, the PI of this project, and the other Co-Investigators to analyze of the data from this project and prepare regular reports and manuscripts. Leo T. Chylack, Jr., M.D. (BWH) originally submitted the proposal as a Supplemental Medical Objective (SMO). The goal of the proposal was to supplement the current annual ocular examination with new measurements that would allow an objective and more quantitative routine assessment of the status of the crystalline lens in astronauts. This supplementary methodology has enabled NASA to obtain objective assessments of the clarity of the lens, quantitative, continuous measures of the severity of lens opacification, and, over time, cataract type-specific progression rates. The SMO has undergone review by several intramural boards and a non-advocate peer review (NAR) panel. As a result of this review, the NAR recommended 1) a major expansion of the project to enable measures of severity and progression rates of various forms of lens opacification, and 2) modifications of the number and composition of the control groups to provide comparisons of severity and progressions rates of lens opacification in astronauts to those in military exposed to the cataractogenic risks of high altitude (but not space) flight and to those in LSAH subjects, who presumably are not exposed to high altitude or space radiation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Expanding our understanding of the mechanisms of space-radiation-induced cataract may suggest means of reducing the risk of radiation-induced cataract on earth among individuals employed in jobs in which radiation constitutes an occupational hazard. Also, it may suggest improved means of shielding the eyes of patients undergoing radiation therapy. Information about the mechanisms of cataracts in astronauts may suggest additional research into the causes of age-related cataract, the world’s leading cause of blindness. Lastly, the longitudinal phase of the study which links nutritional data to the risk of cataract progression may suggest nutritional means of ameliorating the risk of cataract.

Task Progress:

January 26, 2008 is the official end of the Project Period for the NASCA project. From January 27th through August 31st NASCA will be functioning under a No-Cost-Extension (NCE) from NASA. This is possible because the Brigham and Women's Hospital (BWH) has underspent its budget for the project. This Taskbook Report and the Annual Report (included herein) will present our assessment of the progress of NASCA since its inception and our plans for the project during the NCE. These plans depart somewhat from those originally approved, but they seem reasonable in light of some of the problems we face.
Since January 2007, the project has proceeded apace. There have been no significant delays in seeing subjects, and we anticipate that our three cohorts will complete two full years of follow-up between December 2007 and May, 2008. The last ground-based control subject completed two full years of follow-up on December 14, 2007; the last military aircrew will complete two years of follow-up on March 16, 2008, and the last astronaut to complete two full years of follow-up will be seen on or about May 25, 2008. I emphasize this two-year follow-up interval, because the Non-Advocate Review (NAR) Panel which was convened in April, 2007 recommended that we assess the longitudinal data from NASCA after all subjects had completed two full years of follow-up. This recommendation originated in discussions of the need to ascertain the existence of a longitudinal signal and the need to estimate the power of the study to detect a relationship in five years between space radiation exposure and lens opacity progression rates.

Because we will not be able to complete a longitudinal analysis of the complete two-year data set until late fall 2008, we have decided to conduct preliminary statistical analysis of completed longitudinal data sets in February 2008. We hope to identify any longitudinal trends relating the dose of space radiation exposure to progression rates of C, N, and PSC opacification. The complete NASCA data set will not be proofread and analyzed before the end of the year. We hope that the preliminary analysis, if positive, will allow us to seek extended funding for the project without losing momentum. If the preliminary analyses are inconclusive, we will have to wait until the fall to conduct an analysis of the entire two-year data set. As explained above, it is not clear how we are going to proceed beyond the end of the NCE without funding. Notwithstanding the above, we are on track to complete these tasks on this timeline.

There has been an important change in the manner in which we are approaching the statistical analyses of the data. In our report last year we compared astronauts to controls, regardless of whether or not the astronaut had flown in space. We were concerned that by including astronauts who had not flown in space, we might be reducing our chance to see the relationships we were investigating. Now we are using propensity scores to match astronauts who have flown in space to those controls without space flight experience (astronauts who have not flown, military aircrew, and ground-based controls). Exposed astronauts were matched to an equal number of non-exposed control subjects using a propensity score based on demographic characteristics and medical history, stratified by gender and whether or not the subject ever smoked. For each stratum, the propensity score was a linear combination of the five best predictors of exposure with coefficients estimated from a logistic regression model. Using the body mass index (BMI) in the propensity model, even with height and weight as separate terms, significantly improved the overall fit in characterizing exposed subjects. This is possible because BMI is a nonlinear function of height and weight. Age was not included as a propensity score variable, because exposed astronauts tended to be older than non-exposed astronauts, and we considered it important that all astronauts be in the matched sample. Adjustments for age differences were made in the regression models. For each of the four strata defined by gender and smoking history, each of the 171 exposed astronauts were then matched with the available (i.e. not already matched) subject; having the closest possible propensity score. An exception to this rule was made to ensure that all 53 members of the astronaut corps who hadn't yet flown were matched with an exposed astronaut.

We have also modified out analysis methodologies: opacity data were highly skewed and/or were partially discrete, which obviated use of models with normally distributed errors for making inference on the effect of space radiation on lens opacification. Instead, we used customized non-normal regression models with parameters (or transformed parameters) modeled as linear combinations of explanatory variables to test if exposure to space radiation was associated with higher N, C, or PSC opacification after adjustment for age, sun exposure, occupational group (astronaut, aircrew, or ground), baseline differences, and nutritional intake. More specifically, we used beta regression for scaled N mask density, skew-normal regression for log-transformed C opacity, and ordered logit regression for PSC opacity and counts of PSC centers. Dependent variables for all analyses were the maximum measure of opacity between the right (OD) and left (OS) eyes. Maximum N mask density was scaled from 0 to 1 (instead of the original pixel count ranging from 0 to 255), maximum C opacity was log-transformed to fit the skew-normal model, while maximum PSC opacity (% opaque) , because of its discrete character, large quantities of zeros and extreme skewness, was grouped into five bins: #1 (0) #2 (.01 - .03), #3 (0.04 – 0.06), #4 (0.07 – 0.16) and #5 (> 0.16). These bins were chosen to make the overall proportion of observations in each bin as close as possible to each other. PSC center data was in the form of total counts of opacity islands per eye. Analyses were run only on data from exposed and matched subjects. Remaining subjects were considered too unlike the exposed group, and were thus not included in these cross-sectional analyses because of potential for biasing the results. However some or all of these subjects could be included in future analyses of longitudinal data.

A secondary objective of these analyses was to identify nutritional covariates that appeared to ameliorate or exacerbate opacification. Therefore, in the beta regression model for nuclear opacity, alpha-carotene, beta carotene, lutein + zeaxanthin, and poly-unsaturated fats were included as possible explanatory variables. In the skew-normal regression model for C opacity, alpha-carotene, other carotenoids, and vitamin A were incorporated. Lastly, in the ordered logit regression model for PSC opacity, only lycopene was incorporated with other covariates.

In January 2008 we submitted to Investigative Ophthalmology and Visual Science (IOVS) a manuscript with results of an analysis of our baseline data. We found that the variability and median area of C cataract were significantly higher for exposed astronauts than for a hypothetical group of non-exposed astronauts with similar ages (P = 0.015), and galactic-cosmic space radiation may be linked to increased PSC area (P = 0.056) and the number of PSC centers (P = 0.095). No association was found between space radiation and increased N. We concluded that the cross-sectional data analysis revealed a small deleterious effect of space radiation for C and possibly for PSC at smaller radiation doses than had been reported previously.

There were also statistically significant relationships between certain nutrients and lens opacification. Nutritional information collected in NASCA may also unravel uncertainties surrounding the role of various nutrients on the progression of opacities. Our results for N opacification suggest a protective effect of beta-carotene. Our findings also suggest a significant protective effect of lycopene intake on PSC density and centers.

Bibliography Type:	Description: (Last Updated: 08/21/2012)
Abstracts for Journals and Proceedings	Chylack LT Jr, Feiveson AH, Peterson LE, Manuel FK, Wear ML, Tung WH, Hardy DS, Marak LJ, Bell C, Cucinotta FA. "The NASCA Study: Cross-sectional analyses of exposure to radiation in space and risk of lens opacification." The Human Space Radiation Research Workshop - League City, TX, February 12-14, 2007. Human Space Radiation Research Workshop Program Document, 2007. , Feb-2007
Abstracts for Journals and Proceedings	Chylack LT Jr, Feiveson AH, Peterson LE, Manuel FK, Wear ML, Yung WH, Hardy DS, Marak LJ, Bell C, Cucinotta FA. "The NASCA Study - Report 3: Cross-sectional analysis of exposure to radiation in space and risk of lens opacification." Poster B700, Session #525, Annual Meeting of the Association for Research and Vision in Ophthalmology (ARVO), May 10, 2007. Invest Ophthalmol Vis Sci. 2007;48:E-Abstract 5454 . , May-2007
Abstracts for Journals and Proceedings	Chylack LT Jr, Feiveson AH, Peterson LE, Manuel FK, Wear ML, Tung WH, Hardy DS, Marak LJ, Bell C, Cucinotta FC. "The NASCA Study: Cross-sectional analysis of exposure to radiation in space and risk of lens opacification." 18th Annual NASA Space Radiation Investigators' Workshop, Rohnert Park, CA, July 13-15, 2007. 18th Annual NASA Space Radiation Investigators' Workshop, Abstract Booklet, p 148, 2007. , Jul-2007