Fiscal Year:	FY 2006	**Task Last Updated:**	FY 05/31/2006
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		
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Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
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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		
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Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
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No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	End date changed to 3/31/2008 per JSC info update (10/06)		
Key Personnel Changes/Previous PI:	0		
COI Name (Institution):	Cucinotta, Francis (NASA Johnson Space Center) Feiveson, Al (NASA) Wear, Mary (Wyle Labs, NASA) Manuel, F Keith (Space Center Eye Associates) Peterson, Leif (Baylor College of Medicine)		
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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 incidence and progression in the whole population of American astronauts and two control populations – pilots with military aviation experience and 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, measures of nutrition, and general health. The assessment of cataract will use digital images of the lens and validated measures of severity. The study will measure the prevalence, incidence, and progression rates of cortical, nuclear, posterior subcapsular, and mixed cataracts, and it will relate these measures to measures of radiation, nutrition, 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. NASCA contains an initial cross-sectional assessment of prevalence, and a follow-on assessment of progression rates of lens opacification in the populations of astronauts, military pilots, and ground based comparison participants in the Longitudinal Study of Astronaut Health (LSAH). Main goal of cross-sectional study: To determine the prevalence of the three main classes of age-related lens opacification in the complete sample of astronauts and in two control populations: military pilots and ground-based subjects in the LSAH. We will determine the risk of each class of cataract associated with exposure to various components and dosages of radiation during space flight. A secondary goal of the cross-sectional study is to estimate the prevalence of the three main classes of age-related lens opacification and determine the risk of each class of cataract associated with various factors (nutrition, general health, UV radiation, and others) encountered non-space flight. A tertiary goal of the cross-sectional study is to modify the ocular assessment protocol in the astronauts' regular annual medical examination to improve the assessment of the status of the crystalline lens. 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 pilots 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 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 Department of Medicine at Baylor College of Medicine (BCM), Wyle Laboratories, and Space Center Eye Associates are the five centers cooperating in the execution of this study. The epidemiologic team at BCM will recruit astronauts and control subjects. Members of the Flight Medicine Clinic at the JSC will perform ocular and general medical examinations and will obtain blood samples for analysis. They will obtain specialized digital images of the crystalline ocular lens that will enable investigators at The Center for Ophthalmic Research 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 would enable 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 the prevalence 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 prevalence and progressions rates of lens opacification in astronauts to those in pilots 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.
	The progress described in this report was presented as a poster at the annual meeting of the Association for Research and Vision in Ophthalmology, on May 3, 2006. The following paragraph contains the abstract of this poster. POSTER ABSTRACT**: ** PLEASE SEE "RESULTS SECTION" FOR UPDATED FINDINGS WHICH IN SOME CASES DIFFER SIGNIFICANTLY FROM THOSE CITED IN ABSTRACT Purpose: NASCA is a 5-yr study of the risk factors associated with cataract incidence and progression in US astronauts, military pilots, and ground-based controls (GBC). Risk factors studied include: space radiation exposure, nutrition, UV exposure, and age. Methods: Areal extent of cortical (C), and posterior subcapsular (P) opacity and density of nuclear (N) opacity were assessed in Nidek EAS 1000 digital lens images. Nuclear color was graded with LOCS III. We used the Harvard Food Frequency Questionnaire (HFFQ). Lens-specific radiation exposures from space, medical sources, aviation training, and isotopes were incorporated. Statistical analyses used space radiation dose-response modeling of baseline prevalence of C, P, and N adjusted for age, nutrition, and solar exposure. Several dose-response models were considered, choosing the most parsimonious ones that described the data. We modeled distribution of log C area opaque as a skew-normal distribution, discrete levels of the area of P opacification with an ordered logit-regression and N density at three loci with beta distributions. In each case we determined the statistical significance of age, space radiation exposure, and 105 nutritional variables on the distribution of each type of opacity. Results: Complete data from 199 astronauts, 90 pilots, and 95 GBC were available after 1 yr. In our preliminary results

Task Progress:

baseline prevalences of C, N, and P among astronauts and pilots were significantly lower than in GBCs. For astronauts only, age, radiation and sun exposures were statistically significantly associated with worsening, and a- and ß-carotene with amelioration, of C. For N age was the main explanatory variable for all loci. For astronauts only, space radiation had no effect on pixel density of the central N clear zone or the posterior embryonal nucleus, but it did have a small statistically significant effect (worsening) on the pixel density of the N anterior embryonal nucleus. Lutein had a strong protective effect at each of the three N loci. a- and ß-carotene produced similar results. Age was the only variable statistically significantly associated with extent of P.

Conclusions: Age was significantly associated with severity in C, P, and N. For astronauts only, space radiation and UV exposures were significantly associated with worsening C and with opacification of the anterior embryonal nucleus. a- and ß-carotene and lutein had small beneficial effects on C and N opacification, respectively.

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** PLEASE SEE “RESULTS SECTION” FOR UPDATED FINDINGS WHICH IN SOME CASES DIFFER SIGNIFICANTLY FROM THOSE CITED IN ABSTRACT

NARRATIVE PROGRESS REPORT

PROJECT OBJECTIVES:

1. To determine if exposure to space radiation produces more cortical, posterior subcapsular (PSC), or nuclear opacity in astronauts vs. comparison groups after adjustment for age, solar radiation exposure, and possible nutritional effects. 2. To identify nutritional groups that appear likely to be associated with increased or decreased cortical, PSC, or nuclear opacity.

RECRUITMENT STATISTICS AS OF MARCH 23, 2006:

As of March 23, 3006 we have recruited 222 astronauts (188 male/34 female), 94 military pilots (88 male/6 female), and 99 ground-based controls (79 male/20 female).

METHODS:

We gathered demographic data (age, gender, other) with standardized questionnaires. Ocular data were obtained for all subjects (astronauts and controls) from NASA’s standardized, comprehensive, annual, ocular examination that included best-corrected LogMAR Visual Acuity, and contrast sensitivity function. To estimate space radiation doses to the lens we used space dosimetry, and we made a best estimate of the mission and astronaut-specific lens doses, or lens dose equivalents including the individual contributions from trapped radiation and galactic cosmic rays (GCR). We estimated solar UV exposures from validated demographic data and personal histories. We estimated the color of the lens nucleus with the Lens Opacities Classification System (LOCS III) measure of nuclear color. We gathered nutritional data with the validated Harvard Food Frequency Questionnaire (HFFQ).

We used digital images of the lens obtained with a specialized camera (Nidek EAS 1000 Lens imaging system) to assess the type and severity of lens opacification.

STATISTICAL ANALYSIS:

Our basic statistical objectives were to test if exposure to space radiation produces higher cortical, PSC, or nuclear opacification in astronauts vs. comparison groups after adjustment for age, solar radiation exposure, and possible nutritional effects, and to identify nutritional groups that appear likely to be associated with increased or decreased cortical, PSC or nuclear opacity. In this first year of the study, only one observation per subject was available, so no opacity growth models were considered here. Our dependent variables were maximum image area opaque (OD, OS) one observation per subject for the first year, and our independent (explanatory) variables were: subject group, age, annual solar UV exposure, space radiation exposure, and weekly intake of 105 nutrients. Because the distributions of many of the variables were skewed, we used Skew-normal regression modeling.

1. Analysis of PSC data:

The Maximum PSC opacity (OD, OS) measures were grouped into 5 binned ranges. We used ordered logistic regression model to test for effects of explanatory variables on probability of maximum PSC opacity falling into each of the above bins.

2. Analysis of nuclear cataract data:

We used the log of the maximum pixel density (OD, OS) for three locations (nuclear central clear zone, anterior embryonal and posterior embryonal nuclei) and Beta regression to test for effects of explanatory variables on the mean and variance of the distribution of pixel density at each location.

RESULTS:

Cortical opacity tends to increase with age, and with intake of Omega-3-fatty acids. Cortical opacity tends to be lowered by greater intake of A-vitamins and pro-vitamins. There is increased variation in cortical opacities for older subjects and in those exposed to space radiation. There does not appear to be much evidence supporting more variation in cortical opacities for persons with higher sun exposure. There is considerable skewness in the distribution of log cortical opacities.

Posterior Subcapsular (PSC) Opacity: The only explanatory variable that was significantly associated with PSC opacity was age

Nuclear Cataracts: Increased age was shown to be an overwhelming contributor to density of nuclear cataract at all three measurement loci. No other explanatory variable was found to be significantly associated with pixel density.

CONCLUSIONS:

Cortical Cataracts:

1. Age is the most important predictor of cortical opacification. Populations of older people have a higher mean cortical opacity (P<0.001) and a larger spread of opacities (P = 0.012) than do populations of younger people.

2. Astronauts who have not yet flown and non-astronaut pilots appear to have less mean opacity than the ground-based comparison group (P = 0.10) and more clearly have a tighter distribution of cortical opacities (P = 0.017),

3. The population of astronauts who have been exposed to space radiation (i.e. have flown at least one mission) has a significantly increased variation in opacity relative to the other astronauts and pilots (P = 0.007)

4. Astronauts who have flown do not have a discernable difference in mean opacity from those who have not flown. Within the group of astronauts who have flown, there is no relationship between the total amount of space radiation received and the mean or variance of cortical opacity.

5. Solar radiation exposure had no discernable effect on either the mean or variance of cortical opacity.

6. Nutritional Findings: Larger intake of omega fatty acids appears associated with increased cortical opacity (P = 0.012*). Larger intake of A-vitamins and pro-vitamins appears associated with decreased cortical opacity (P = 0.004*)

PSC and Nuclear Cataracts:

1. Increasing age was significantly associated with increasing opacity. No other significant explanatory variables were found. 2. Although no factors other than age appeared to effect PSC and nuclear cataracts across subjects in this cross-sectional study, there may well be effects of radiation (space and/or solar) on the growth rates of these types of cataracts. This question will be addressed when the longitudinal analysis phase begins after the second year of the study.

MANUSCRIPTS IN PREPARATION:

1. We are preparing a manuscript describing the NASCA methodology and recruitment results after the first year. The paper will also have baseline descriptive data on all of the experimental variables assessed in this project. We expect to complete this manuscript and submit it to Archives of Ophthalmology before July, 2006. 2. We are also preparing a second manuscript describing the results of a cross-sectional analysis of the cataractogenic risks of space radiation for astronauts, pilots, and ground-based controls. We will also present the effect of nutritional variables, age, gender, and annual solar UV exposure on these risks. The results of this analysis are described in the annual report (see earlier sections). We also expect to complete this manuscript and submit it to Archives of Ophthalmology before July, 2006.

3. We are analyzing the relationship between the number of loci in the phenotype of posterior subcapsular cataracts and the dose of space radiation. There are significant findings in this analysis, but we have not yet decided if they will be included in Manuscript 2 (above) or in a separate paper. We will make this decision in the next few weeks.

4. As we move into the longitudinal phase of the NASCA project we expect to be able to assess the relationship between dose of space radiation and measures of cataract incidence (new cases of lens opacification) and progression (of existing opacities) and the effects of age, gender, nutrition, and annual solar UV exposure on these progression rates. The manuscripts for these analyses will probably be cataract-specific (separate papers for cortical, nuclear, and posterior subcapsular cataract).

Respectfully submitted,

Leo T. Chylack, Jr., M.D. Principal Investigator of NASCA Project

Bibliography Type:	Description: (Last Updated: 08/21/2012)
Abstracts for Journals and Proceedings	Cucinotta FA, Feiveson AH, Manuel FK, Wear ML, Marak L, Peterson LE, Hardy D, Tung WH, Hernandez E, Chylack LT Jr. "Posterior Subcapsular Cataracts and Space Radiation: Findings from the NASA Study of Cataracts in Astronauts (NASCA)." International Radiation Research Meeting, Moscow, Russia, June 2006. International Radiation Research Meeting, June 2006, NASCA Data Set. , Jun-2006
Papers from Meeting Proceedings	Chylack LT Jr, Feiveson AH, Peterson LE, Manuel FK, Wear ML, Hardy D, Marak L, Tung WH, Hernandez E, Cucinotta F. "The NASA Study of Cataract in Astronauts (NASCA): Year-1 Data." Annual international meeting of the Association for Research and Vision in Ophthalmology (ARVO), the largest eye research meeting in the world, May 2006. Annual international meeting of the Association for Research and Vision in Ophthalmology (ARVO), May 2006. NASCA Data , May-2006