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| <b>Fiscal Year:</b>                               | FY 2010                                                                                                                                                                                                                                                                                                                                                        | <b>Task Last Updated:</b>             | FY 06/30/2010     |
| <b>PI Name:</b>                                   | Chylack, Leo M.D.                                                                                                                                                                                                                                                                                                                                              |                                       |                   |
| <b>Project Title:</b>                             | 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                                                                                                                                         |                                       |                   |
| <b>Division Name:</b>                             | Human Research                                                                                                                                                                                                                                                                                                                                                 |                                       |                   |
| <b>Program/Discipline:</b>                        | HUMAN RESEARCH                                                                                                                                                                                                                                                                                                                                                 |                                       |                   |
| <b>Program/Discipline--Element/Subdiscipline:</b> | HUMAN RESEARCH--Radiation health                                                                                                                                                                                                                                                                                                                               |                                       |                   |
| <b>Joint Agency Name:</b>                         |                                                                                                                                                                                                                                                                                                                                                                | <b>TechPort:</b>                      | No                |
| <b>Human Research Program Elements:</b>           | (1) <b>SR:</b> Space Radiation                                                                                                                                                                                                                                                                                                                                 |                                       |                   |
| <b>Human Research Program Risks:</b>              | (1) <b>Cardiovascular:</b> Risk of Cardiovascular Adaptations Contributing to Adverse Mission Performance and Health Outcomes                                                                                                                                                                                                                                  |                                       |                   |
| <b>Space Biology Element:</b>                     | None                                                                                                                                                                                                                                                                                                                                                           |                                       |                   |
| <b>Space Biology Cross-Element Discipline:</b>    | None                                                                                                                                                                                                                                                                                                                                                           |                                       |                   |
| <b>Space Biology Special Category:</b>            | None                                                                                                                                                                                                                                                                                                                                                           |                                       |                   |
| <b>PI Email:</b>                                  | <a href="mailto:leo@chylackinc.com">leo@chylackinc.com</a>                                                                                                                                                                                                                                                                                                     | <b>Fax:</b>                           | FY 781-934-2747   |
| <b>PI Organization Type:</b>                      | UNIVERSITY                                                                                                                                                                                                                                                                                                                                                     | <b>Phone:</b>                         | 617-732-7355      |
| <b>Organization Name:</b>                         | Harvard Medical School, Brigham & Women's Hospital                                                                                                                                                                                                                                                                                                             |                                       |                   |
| <b>PI Address 1:</b>                              | Center for Ophthalmic Research                                                                                                                                                                                                                                                                                                                                 |                                       |                   |
| <b>PI Address 2:</b>                              | 221 Longwood Ave., EBRC 323                                                                                                                                                                                                                                                                                                                                    |                                       |                   |
| <b>PI Web Page:</b>                               |                                                                                                                                                                                                                                                                                                                                                                |                                       |                   |
| <b>City:</b>                                      | Boston                                                                                                                                                                                                                                                                                                                                                         | <b>State:</b>                         | MA                |
| <b>Zip Code:</b>                                  | 02115                                                                                                                                                                                                                                                                                                                                                          | <b>Congressional District:</b>        | 8                 |
| <b>Comments:</b>                                  | 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]                                                                                                                                                                                                  |                                       |                   |
| <b>Project Type:</b>                              | GROUND                                                                                                                                                                                                                                                                                                                                                         | <b>Solicitation / Funding Source:</b> | Directed Research |
| <b>Start Date:</b>                                | 01/27/2003                                                                                                                                                                                                                                                                                                                                                     | <b>End Date:</b>                      | 12/31/2009        |
| <b>No. of Post Docs:</b>                          | 0                                                                                                                                                                                                                                                                                                                                                              | <b>No. of PhD Degrees:</b>            | 1                 |
| <b>No. of PhD Candidates:</b>                     | 1                                                                                                                                                                                                                                                                                                                                                              | <b>No. of Master' Degrees:</b>        | 0                 |
| <b>No. of Master's Candidates:</b>                | 0                                                                                                                                                                                                                                                                                                                                                              | <b>No. of Bachelor's Degrees:</b>     | 0                 |
| <b>No. of Bachelor's Candidates:</b>              | 0                                                                                                                                                                                                                                                                                                                                                              | <b>Monitoring Center:</b>             | NASA JSC          |
| <b>Contact Monitor:</b>                           | Cucinotta, Francis                                                                                                                                                                                                                                                                                                                                             | <b>Contact Phone:</b>                 | 281-483-0968      |
| <b>Contact Email:</b>                             | <a href="mailto:noaccess@nasa.gov">noaccess@nasa.gov</a>                                                                                                                                                                                                                                                                                                       |                                       |                   |
| <b>Flight Program:</b>                            |                                                                                                                                                                                                                                                                                                                                                                |                                       |                   |
| <b>Flight Assignment:</b>                         | NOTE: Extended to 12/31/2009 per J. Dardano/JSC (8/09)<br>NOTE: Extended to 5/31/2009 (from 11/30/2008) per PI (7/09)<br>NOTE: Received NCE to 11/30/2008 per JSC (8/08)<br>NOTE: Received NCE to 8/31/2008 per JSC (11/07)<br>NOTE: End date changed back to 01/27/2008 per S. Krenek/JSC (8/07)<br>End date changed to 3/31/2008 per JSC info update (10/06) |                                       |                   |

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| Key Personnel Changes/Previous PI: | <p>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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| COI Name (Institution):            | <p>Cucinotta, Francis ( NASA Johnson Space Center )<br/> Feiveson, Al ( NASA )<br/> Wear, Mary ( Wyle Labs, NASA )<br/> Peterson, Leif ( Resigned from Baylor College of Medicine in January 2007. Now at The Methodist Hospital in Houston, TX )</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       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| Grant/Contract No.:                | NAG9-01491                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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| Performance Goal No.:              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Performance Goal Text:             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| Task Description:                  | <p>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). After the completion of the analyses of the cross-sectional baseline data, and the ascertainment that the ground-based comparison subjects differed significantly from astronauts and military aircrew in several ways, it was decided to discontinue the monitoring of this group of comparison subjects and continue the project as a comparison of astronauts who have flown at least one mission in space to astronauts who had not yet flown in space plus military aircrew. Except for exposure to space radiation these to groups of subjects were very similar, and it was possible to use propensity scoring to assess their similarities and then match astronauts with exposure to space radiation to either astronauts who had not flown in space or to military aircrew members. The longitudinal phase of NASCA was completed in the summer of 2009 and the image and nutritional analyses were completed by the end of November 2009. The analysis of the longitudinal data began in early December 2009 and we are now (12/21/09) in the process of completing these analyses and planning a manuscript describing the longitudinal results.</p> <p>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.</p> <p>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).</p> <p>The main goal of the five-year longitudinal study is to determine the progression rates of the three main types of lens opacification in astronaut who have flown at least one mission in space, and a comparison group made up of astronauts who have not yet flown in space and military aircrew members. We will 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.</p> <p>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.”</p> <p>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.</p> <p>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.</p> <p>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</p> |

presumably are not exposed to high altitude or space radiation.

#### Rationale for HRP Directed Research:

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.

**LIMITATIONS OF THE NASCA STUDY:** 1) relatively small sizes of cohorts studied, 2) no perfect comparison group (astronaut who flew in space w/o radiation exposure), 3) combining the two comparison groups (astronauts who did not fly in space + military aircrew), albeit reasonable, was not ideal, 4) NASA's group of ground-based subjects, each of whom was matched to a newly selected astronaut and designated a "control" subject for that astronaut, proved to be very dissimilar to the astronaut group in the NASCA study and had to be dropped from the cross-sectional and longitudinal 5-year data analyses, 5) space radiation exposures were generally on the low side, so the utility of individual dose data was limited, 6) precision of measured doses of space radiation exposure was also limited, 7) distributions of primary end-point variables were non-normal and often skewed requiring highly specialized statistical methods.

#### Research Impact/Earth Benefits:

**STRENGTHS OF THE NASCA STUDY:** 1) well-defined population of astronauts, 2) highly standardized methods used for all measures, 3) sensitive, precise, continuous, and validated measures of cataract severity, 4) these methods clearly detected the age-related changes in each class of lens opacification. Opacities increased slowly with age, as expected, 5) Excellent consistency and concordance of results for cortical opacification among the cross-sectional and longitudinal studies, 6) moderate consistency and concordance of results for PSC opacification among the cross-sectional and longitudinal studies, 7) results of the analyses relating nuclear cataract to space radiation exposure less consistent, 8) the lack of a dose-response relationship between dose of space radiation and rate of progression of lens opacification may be due in part to non-targeted effects (Cucinotta & Chappell, Mutation Res., 2010) in which the RBE at low doses is much higher than previously expected.

**IMPLICATIONS OF THE NASCA STUDY:** 1) Adverse effect of space radiation exposure on the lens (particularly on cortical and PSC) are evident in a five year follow-up study, 2) the adverse effects are greater for cortical and PSC than nuclear opacification, although the cross-sectional data showed an effect on nuclear as well, 3) further study of the relationship between space radiation exposure is needed, but the study will be complicated by the need for longer-term follow-up (>5 years), the lack of ideal or even optimal comparison subjects, and relatively small numbers of astronauts available to study, 4) it may be preferable to study only astronauts who have flown in space and compare cohorts with higher-doses to those with lower-dose exposures, rather than use non-astronaut comparison subjects, 5) increased precision of assessing the doses space radiation exposure by radiation source is needed, 6) it is likely that worsening of lens opacification will manifest itself on prolonged manned space missions (e.g. to Mars), but NASCA data suggest that the consequences to high- and low-contrast visual acuity will be small.

**Purpose:** NASCA is designed to measure the impact of exposure to space radiation on progression rates of cortical (C), nuclear (N), and posterior subcapsular opacification (P) in US astronauts (Ast) who have flown at least one mission in space (AstEx), astronauts who have not flown in space (Ast0Ex), and military aircrew (Mil). The study is complete; we present our analyses of 5-6 years of data. The first section deals with CROSS-SECTIONAL STUDIES OF: 1) BASELINE DATA and 2) FIVE YEARS-WORTH OF DATA.

#### BASELINE CROSS-SECTIONAL ANALYSIS:

In our publication of baseline analyses (Chylack LT Jr. et al. NASA Study of Cataract in Astronauts (NASCA). Report 1: Cross-Sectional study of the relationship of exposure to space radiation and risk of lens opacity. Rad. Res. 2009;172:10-20.), we analyzed baseline data from 171 astronauts who flew at least one mission, 53 astronauts who had not flown in space, 95 military aircrew, and 99 non-aircrew ground-based comparison subjects.

We used continuous measures of severity of lens opacification (C, N, and PSC) that were derived from images obtained with the Nidek EAS 1000 Lens Imaging System. Astronauts who flew at least one mission were matched to comparison subjects with Propensity Scores based on demographic characteristics, medical history stratified by gender and smoking (ever/never). Customized non-normal regression models examining effect of space radiation on each measure of opacity. We found that 1) the median severity and variability in the size of cortical opacities were greater in exposed astronauts ( $p=0.015$ ), 2) galactic cosmic rays (GCR) may be linked to increased PSC area ( $p=0.056$ ) and the number of PSC centers ( $p=0.095$ ), 3) within the astronaut group PSC severity (area) was greater in subjects with higher radiation doses ( $p=0.016$ ).

#### CROSS-SECTIONAL ANALYSIS OF FIVE YEARS-WORTH OF DATA:

After completing the five-year study we examined the relationship between cataract severity and space radiation exposure using a non-parametric, cross-sectional analysis using all five years-worth of data. We used the the median maximum opacity (OD,OS) over all visits as primary outcome variable, and customized regression models to make inferences on possible space radiation effects on severity of C, N, and PSC, also adjusting for confounding variables. Each regression model was chosen to most closely accommodate the distribution of the outcome variable (opacity type) to be studied.

The results of this analysis are as follows by cataract class: (Nuclear, Cortical, and Posterior Subcapsular). For Nuclear we used as measures of cataract severity: 1) the ave. pixel density within oval mask of entire nucleus, 2) the average pixel density in smaller masks in the central clear zone (CCZ) and the anterior embryonic nucleus (AEN) of the nucleus. All measures were statistically significantly ( $p=0.02$ ) linked to exposure to space radiation (yes/no). For Cortical we used as a measure of severity the ave. % area opaque in the digital, binarized image of the lens. The variance (pleomorphic character of the opacity) was linked directly with exposure to space radiation ( $p=0.000$ ) but the mean severity of cataract was not linked to exposure to space radiation ( $p=NS$ ). For posterior subcapsular cataract (PSC) we used the average % area opaque in a digital binarized image and also the # of centers of PSC. Neither of these measures of PSC was linked to exposure to space radiation.

The conclusions from the five-year cross-sectional analysis were: 1) we confirmed the findings of the baseline cross-sectional analysis that there is a direct relationship between the variance in severity, but not the mean severity, of cortical cataract and exposure to space radiation, and 2) the average densities of nuclear opacification in the CCZ, AEN, and entire oval mask were significantly and directly related to exposure to space radiation.

#### LONGITUDINAL ANALYSIS OF NASCA DATA:

In these studies we were examining the relationship of exposure to space radiation and the rates of cataract progression for Nuclear, Cortical and PSC.

Methods: All subjects had eye exams at NASA. Digital lens images (Nidek EAS 1000) were obtained. Nutritional data were derived from standardized questionnaires. Because of high variability and skewness of opacity measures, nonparametric methods were used to test for association between rates of opacification and space radiation exposure. First, median regression was used to obtain robust estimates of slopes of opacity vs. time for each eye of each subject. Next, a partial correlation analogue of Kendall's Tau was used to quantify and test radiation effect on slopes, adjusting for confounding variables age, nutritional and sun-exposure histories, with std. errors adjusted for repeated observations on each eye for each subject. The dose of exposure to space radiation of the lens was estimated using recorded personal dosimetry from each space mission, adjusted by radiation quality factor, and quantified in terms of dose equivalent and dose equivalent latency for total & galactic cosmic radiation. For Ast0Ex and Mil, radiation exposure was set = zero. In addition to the analysis of growth rates, we similarly analyzed median values of max (OD,OS) opacity over the multiple visits for each subject. In these longitudinal analysis of the relationship between cataract progression rates and exposure to the space radiation we observed the following trends: 1) estimates of progression rates exhibited high variability and skewed distributions, and 2) regression models assuming normally distributed errors were deemed inappropriate. Consequently, we used a two-step approach: as a first step we used median regression to estimate slope (opacity change/yr.); and as a second step we used PC-tau, a partial correlation analog of Kendall's Tau, to quantify association between opacity growth and various measures of space radiation. We adjusted for age, sun exposure, nutrition and other confounding factors. PC-taus were calculated considering all possible between-subject comparisons, keeping in mind that most subjects had two opacity slopes (OD and OS), and then inferences on the effect of radiation were then made on the basis of PC-Tau, relative to its standard error.

#### Task Progress:

#### RESULTS OF LONGITUDINAL STUDY:

(Visual Acuity): In these partial tau analyses the effects of age, pilots, two nutritional variables, and smoking have been removed. Obese astronauts removed. We found no apparent relationship between space radiation exposure and change in high or low contrast measures of visual acuity.

(Cataract): The major conclusions are as follows: 1) Space radiation exposure (yes/no) has a statistically significant relationships with faster rates of progression of cortical opacification ( $p=0.02$ ) and increased numbers of loci of posterior subcapsular opacification ( $p=0.04$ ), 2) Space radiation exposure (yes/no) has no statistically significant relationships with faster rates of progression of either nuclear or posterior subcapsular opacification.

SUMMARY OF NASCA FINDINGS from the Cross-Sectional Study (severity of cataract vs. space radiation exposure), and the Longitudinal Study (progression rate of cataract vs. space radiation exposure):

FINDINGS OF CROSS-SECTIONAL BASELINE STUDY: 1) The median size and variance of cortical opacities were greater in exposed astronauts ( $p=0.015$ ), 2) Within astronaut group PSC severity (area) was greater in subjects with higher radiation doses ( $p=0.016$ ). Galactic cosmic rays (GCR) may be linked to increased PSC area ( $p=0.056$ ) and the number of PSC centers ( $p=0.095$ ), 3) No relationship between severity of nuclear opacification and space radiation exposure.

FINDINGS OF CROSS-SECTIONAL STUDY OF 5-YEARS-WORTH OF DATA: 1) The variance in size, but not the mean size, of cortical opacities was greater in exposed astronauts ( $p=0.000$ ), 2) Neither size nor number of centers of PSC was linked to space radiation exposure (yes/no), 3) The average density of nuclear opacification in the CCZ, AEN, and entire oval mask was significantly related to exposure to space radiation (yes/no) ( $p=0.02$ ).

FINDINGS OF LONGITUDINAL STUDY OF 5-YEARS-WORTH OF DATA: 1) The rate of progression of cortical opacification was significantly higher in exposed astronauts ( $p=0.02$ ), 2) The increase in numbers of centers, but not the change in area, of posterior subcapsular opacification was significantly higher ( $p=0.04$ ) in astronauts exposed to space radiation (yes/no), 3) Space radiation exposure (yes/no) had no statistically significant relationships with faster rates of nuclear opacification.

LIMITATIONS OF THE NASCA STUDY: 1) relatively small sizes of cohorts studied, 2) no perfect comparison group (astronaut who flew in space w/o radiation exposure), 3) combining the two comparison groups (astronauts who did not fly in space + military aircrew), albeit reasonable, was not ideal, 4) NASA's group of ground-based subjects, each of whom was matched to a newly selected astronaut and designated a "control" subject for that astronaut, proved to be very dissimilar to the astronaut group in the NASCA study and had to be dropped from the cross-sectional and longitudinal 5-year data analyses, 5) space radiation exposures were generally on the low side, so the utility of individual dose data was limited, 6) precision of measured doses of space radiation exposure was also limited, 7) distributions of primary end-point variables were non-normal and often skewed requiring highly specialized statistical methods.

STRENGTHS OF THE NASCA STUDY: 1) well-defined population of astronauts, 2) highly standardized methods used for all measures, 3) sensitive, precise, continuous, and validated measures of cataract severity, 4) these methods clearly detected the age-related changes in each class of lens opacification. Opacities increased slowly with age, as expected, 5) excellent consistency and concordance of results for cortical opacification among the cross-sectional and longitudinal studies, 6) moderate consistency and concordance of results for PSC opacification among the cross-sectional and longitudinal studies, 7) results of the analyses relating nuclear cataract to space radiation exposure less consistent, 8) the lack of a dose-response relationship between dose of space radiation and rate of progression of lens opacification may be due in part to non-targeted effects (Cucinotta & Chappell, Mutation Res., 2010) in which the RBE at low doses is much higher than previously expected.

IMPLICATIONS OF THE NASCA STUDY: 1) Adverse effect of space radiation exposure on the lens (particularly on cortical and PSC) are evident in a five year follow-up study, 2) the adverse effects are greater for cortical and PSC than nuclear opacification, although the cross-sectional data showed an effect on nuclear as well, 3) further study of the

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|                                           | relationship between space radiation exposure is needed, but the study will be complicated by the need for longer-term follow-up (>5 years), the lack of ideal or even optimal comparison subjects, and relatively small numbers of astronauts available to study, 4) it may be preferable to study only astronauts who have flown in space and compare cohorts with higher-doses to those with lower-dose exposures, rather than use non-astronaut comparison subjects, 5) increased precision of assessing the doses space radiation exposure by radiation source is needed, 6) it is likely that worsening of lens opacification will manifest itself on prolonged manned space missions (e.g. to Mars), but NASCA data suggest that the consequences to high- and low-contrast visual acuity will be small. |
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