A. COVER PAGE

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.

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3. Grant Number: COOPERATIVE AGREEMENT NUMBER: NAG9-1491

4. SUPPLEMENT NUMBER: Basic
5. EFFECTIVE DATE: January 14, 2003
6. COMPLETION DATE: January 27, 2008
7. ISSUED TO:
   Brigham and Women’s Hospital
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8. ISSUED BY: NASA Johnson Space Center
   Attn. Jessica Brooks / BL
   2101 NASA Rd. 1
   Houston, TX 77508

9. TAXPAYER IDENTIFICATION NO. (TIN): 042312909

a) Administrative Overview: The principal grantee institution is the Brigham and
   Women’s Hospital (BWH). Drs. Cucinotta and Feiveson are employees of NASA
   and as such receive no direct financial support through the BWH, but instead
   through NASA. Dr. Cucinotta is the lead in Houston and will be responsible for
   organizing efforts at the institutions in Houston (NASA, JSC, BCM, Wyle Labs,
   and Space Center Eye Associates).

b) The BWH has subcontracted with:
   i) Baylor College of Medicine for epidemiological services (recruitment,
      enrollment) of Dr. Leif Peterson and his staff. Dr. Peterson’s project
      coordinator/interviewer will obtain informed consent from all non-astronaut
      subjects upon arrival at the NASA/JSC Eye Clinic for a scheduled interview
      and eye exam
   ii) Wyle Laboratories for the data management services of Dr. Mary Wear, and
   iii) Space Center Eye Associates (SCEA) for the clinical services of Francis
        Keith Manuel, O.D. Dr. Manuel and his associates, Dr. Geoff Izsard and Dr.
        Lisa Maxwell will obtain informed consent from all astronauts and NASA AOD
        pilots at the time of their examination at the Flight Medicine Clinic (FMC) at
        the JSC/NASA/ Houston, TX.
   iv) Drs. Manuel, Izsard, and Maxwell will see all LSAH subjects and military
       pilots in the Flight Medicine Clinic or a similar clinic at JSC or at Dr. Manuel’s
       office in the SCEA.

c) Most data will be electronic as part of the Electronic Medical Record (EMR) and
   will be entered into the study’s master data file by Dr. Wear and her staff. The
   interview form “FORM-A, DEMOGRAPHICS, HEALTH, AND SUNLIGHT
   EXPOSURE QUESTIONNAIRE” and data recorded on hard copy will be input
   into a NASCA computer database by Dr. Wear’s staff. Completed Harvard
   University Food Frequency Questionnaires (HUFFQ 88GP) will be shipped in
   batches to Channing Laboratory (Boston, MA) for scanning and generation of
   nutrient intake estimates, which will be returned to Dr. Peterson at Baylor for
   analysis.

d) All image data will be sent to the Center for Ophthalmic Research (COR) in
   Boston and Dr. Chylack and William H. Tung will do the image analyses.

e) The BWH will administer the project.
B. INTRODUCTION:

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.

1. PROJECT AIMS, OBJECTIVES, OR HYPOTHESES:

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).

a. 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.

b. Secondary goal of the cross-sectional study: 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.

c. Tertiary goal of the cross-sectional study: To modify the ocular assessment protocol in the astronauts’ regular annual medical examination to improve the assessment of the status of the crystalline lens.

d. Main goal of the five-year longitudinal study: 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.
2. SIGNIFICANCE OF NASCA PROJECT TO THE CRITICAL PATH ROADMAP (CPR)

The NASCA project fits within the Bioastronautics Roadmap as follows:

a. Risk 30: Chronic and Degenerative Tissue Risks
b. Crosscutting Area: Radiation Health
c. Risk Number: 30
d. Risk Description: Radiation exposure may result in degenerative tissue diseases (non-cancer or non-CNS) such as cardiac, circulatory, or digestive diseases, as well as cataracts. Occupational radiation exposure or the combined effects of radiation and other space flight factors may cause these degenerative conditions.

3. THE NASCA PROJECT WILL ADDRESS THE FOLLOWING SPECIFIC CPR QUESTIONS:

30a: What are the probabilities for degenerative tissue risks from protons and HZE ions as a function of NASA's operational parameters (age at exposure, age and time after exposure, gender, tissue, mission, radiation quality, dose rate)?

30b: What are the mechanisms of degenerative tissues risks in the heart, circulatory, endocrine, digestive, lens and other tissue systems?

30c: How can the latency period for degenerative tissue risks, including sub-clinical diseases, following space radiation exposures be estimated?

30e: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict degenerative tissue risks in astronauts? How can human epidemiology data best support these procedures of models?

4. INDICATE SPECIFICALLY HOW THE RESEARCH CONTRIBUTES TO ANSWERING THE ABOVE CPR QUESTIONS.

a. 30a: What are the probabilities for degenerative tissue risks from protons and HZE ions as a function of NASA's operational parameters (age at exposure, age and time after exposure, gender, tissue, mission, radiation quality, dose rate)?

In the NASCA study the tissue studied is the lens of the eye (the crystalline lens), and the degenerative tissue risk to the lens is incident cataract or accelerated cataract progression. We are employing state-of-the-art technology to capture digital images of the lens in vivo from all of our male and female subjects, and from these images with validated image analyses we will be able to define the type of cataract present, the severity of each type, and in the longitudinal phase of the study (years 1-5) the rate of cataract progression in each lens of each subject. We will have two
control groups: 1) pilots with a history of military aviation and 2) ground-based LSAH subjects who have been matched for each astronaut. We will also have the radiation exposure data that NASA gathers on all of its astronauts and on all flights and from these data we will be able to calculate the tissue dose in the lens for protons and HZE ions (as well as other forms of space radiation). From these data we will define the statistical significance (probabilities) of any relationships between specific radiations and specific types and severities of cataract. After the completion of the longitudinal study, we will be able to define these relationships for rates of progression in each class of cataract.

We will also be able to define any unusual types of cataract that are seen in this population – unusual in that their phenotype differs from those of age-related cataracts.

A possible confounding factor is UV radiation, a known cataractogenic risk. We believe that the inclusion of a control group of military pilots will allow us to control for UV radiation exposure. They have increased UV exposures during high altitude flights, but they do not have exposure to the high levels of space radiation. The LSAH subjects will help us control for other factors in the NASA environment. We will be able to address all of the other issues in Question 30a (age at exposure, age and time after exposure, gender, tissue, mission, radiation quality, dose rate) from data that is gathered routinely at NASA.

b) 30b: What are the mechanisms of degenerative tissues risks in the heart, circulatory, endocrine, digestive, lens and other tissue systems?

The NASCA study, albeit an epidemiological study, offers us an exciting opportunity to ascertain if there is more than one mechanism of radiation cataract.

In classical studies of the mechanisms of radiation-induced cataract, x-irradiation was believed to cause nuclear DNA breaks and subsequent disorders of cell growth, differentiation and maturation. It was a “maturation arrest" that was believed to be responsible for the breakdown in the orderly transition between the lens epithelial cell and the cortical/nuclear fiber cell. These abnormal cells migrated posteriorly in the lens to accumulate at the posterior pole causing the classical radiation-induced posterior subcapsular (PSC) cataracts. There are many studies of PSCs complicating therapeutic radiation in and around the eye, atomic bomb exposure, and industrial exposures to high levels of x-irradiation. In a recent publication by Cucinotta, F. K. Manuel, J.A. Jones, T.G. Izsard, J.D. Murray, B.M. Dojonegoro and M.L. Wear, (Radiation Research. 2001;156:577-583) not only was there nearly an eight-fold increase in the risk of PSC, but there was also an increase in risk of nuclear cataract among astronauts in the high-space-radiation-exposure group. The increased risk of PSC was expected, but the increased risk of nuclear cataract was not. The finding increased risk of nuclear cataract needs to be confirmed, and in the NASCA study we will be able to precisely define the relationship between each component of space radiation and each type of nuclear change (increased opacification and increased brunescence (browning)). We will also be able to confirm the risk of PSC from each form of space radiation.
Should we be able to confirm that space radiation increases the risk of nuclear opacification or brunescence, we must implicate mechanisms of opacification other than nuclear DNA damage, because the deep cortical and nuclear cells of the lens are anucleate. Confirming an increased risk of nuclear opacification and/or brunescence would imply that there are direct adverse effects of radiation on the nuclear proteins of the nucleus. Such changes are likely to be oxidative in nature and such change could lead to both increased pigmentation and increased protein aggregation (opacification). While the NASCA study is not designed to explore the mechanisms of these radiation effects on nuclear protein, it will be able to point the way for basic studies of this process.

c) 30c: How can the latency period for degenerative tissue risks, including subclinical diseases, following space radiation exposures be estimated?

The NASCA study offers unique opportunities to measure rates of “incident” cataract (when a clear lens develops an early opacity), the rates of cataract “progression” (when an extant cataract gets worse) by cataract type (cortical, nuclear, and PSC) as a function of space radiation exposure. We will also know from our control groups these rates in comparable individuals not exposed to space radiation. From these sets of data we will be able to calculate the difference in rates that will be due to space radiation exposure. Since we will have lens-specific-dose data on each astronaut we will be able to relate these measures to the rates of incident or progressive cataract and thereby develop a profile of the relationship between space radiation dose and the rate of incident or progressive cataract.

A “latency period” in the context of human cataract has two connotations: 1) there is a latency period between the time of exposure of a clear lens to space radiation and the appearance of a cataract, and 2) there is a latency period defined as the time needed to change a clinically (visually) insignificant cataract into a clinically significant cataract. These latency periods may vary by cataract class with PSC incidence and progression anticipated to be much more rapid than those for cortical cataract. The NASCA study will afford us the opportunity to define these latency periods if they are short enough to fall within the five-year life span of the NASCA study.

With some forms of cataract (mostly cortical) there is a long period during which significant amounts of opacification can exist without visual sequelae. This would be the “subclinical” phase of this cataract’s life span. Other forms of cataract, however, (e.g. nuclear and PSC) cause clinical symptoms much earlier in their natural history, and consequently the subclinical phases would be much shorter. From data gathered in the NASCA study we will define these subclinical phases for each cataract class.

d) 30e: What quantitative procedures or theoretical models are needed to extrapolate molecular, cellular, or animal results to predict degenerative tissue risks in astronauts? How can human epidemiology data best support these procedures of models?

In the case of the NASCA study, we are gathering data directly from humans, and an animal-human extrapolation is not needed. This is not to say that animal or human
cell or tissue culture work is not relevant to the study of the cataractogenic effects of space radiation. It is fortunate in the case of the ocular lens that sufficiently sensitive and specific methodologies exist for the assessment of the human lens, and well-designed epidemiological studies will provide direct answers to many questions about the effects of space radiation on the human lens.

Although we have no evidence at present that the NASCA epidemiological study lacks sufficient statistical power to definitively rule in or rule out specific cataractogenic risks of space radiation, it is possible that some of our questions may not be answered by the NASCA study due to the relatively small sizes of the cohorts under study. Should the NASCA study not answer definitively questions that NASA believes to be important, it may be advisable for NASA and space agencies in Russia and other countries to collaborate in a larger NASCA-like study. The increased power of a collaborative effort of this type might afford the statistical power to answer the questions that were unanswered by NASCA. Dr. Cucinotta and I have explored in the most preliminary manner the feasibility of such a collaborative effort, and we believe that at this time there is not sufficient interest in or importance given to such a study to justify planning such a collaboration at this time.

2) **INDICATE ANY NEW CRITICAL PATH QUESTIONS THAT MAY HAVE RESULTED FROM THE NASCA STUDY**

Although it may be premature to raise this question, it may be advisable at this time to explore the feasibility of designing a collaborative NASCA-type study involving the space agencies of other countries. It is already clear that the inclusion of Cosmonauts and astronauts from other countries would increase the scientific yield of a NASCA-type study, specifically by increasing the number of subjects in each cohort and the likelihood of seeing statistically significant results from the analyses. As the PI of this project, and as a non-NASA “insider”, it is not clear to me why this kind of collaboration would not be possible. It would be worthwhile for me to better understand the actual and/or potential roadblocks to an international collaboration of this type. I would be interested in working with NASA personnel to better define the opportunities to pursue this.

From my point of view as a lens researcher, the expansion of the NASCA study would be feasible, because the technology needed to assess the lens, the nutritional status of the various subjects, and the component parts of the ocular examination are readily available and ideally suited to a study in which most of the subjects are in one locale. There may be substantial reasons why such a study could not take place, but it is my recommendation that we at least consider the feasibility of such a study.

3) **SUMMARY OF BACKGROUND MATERIAL:**

a) **Likelihood of radiation exposures with various types of space missions.**

The first issue in determining the scientific rationale was to determine if significant exposure to radiation occurs in space travel. The likelihood of radiation exposure depends on several mission factors including onboard shielding mass and composition, the altitude and inclination of the space vehicle, solar activity, dose rate,
and duration or number of missions. The average lens dose calculated from flight dosimetry ranged from 1.7 mSv on the shuttle at 28.5° and <400 km to 91 mSv on NASA-Mir. The results of preliminary studies (1-3) suggest that radiation exposures that include high-LET radiations may be associated with earlier onset and more rapidly progressive cataract formation.

b) **Cell biology/animal models:**

Numerous studies have demonstrated a link between exposure to ionizing radiation (from gamma-rays to heavy ions) and the development of cataracts in animals (4-11). These studies have shown that the primary radiation targets are the actively dividing cells in the “germinative zone” of the lens epithelium, near the lens equator. The mitotically quiescent central epithelial cells and the postmitotic fiber cells are relatively radio-resistant. Germinative zone cells in the S-phase of the cell cycle at the time of radiation exposure often die. Their loss is manifested as a transient decrease in mitotic activity. This decrease is followed by an “overshoot” in the rate of cell division. In general, lenses of younger animals and species that have higher mitotic rates develop cataracts more rapidly than older animals and species with more slowly growing lenses. Cataracts are prevented if mitosis can be suppressed before the lens is irradiated.

The lens fiber cells that differentiate from damaged germinative zone cells first show defects in cell shape weeks to months after radiation exposure. These damaged cells often collect at the posterior pole of the lens, leading to the formation of a posterior subcapsular cataract. Opacification of the lens cortex and, finally, the lens equator often follows. Cataract formation follows the loss of ion homeostasis, a decrease in antioxidant defenses in the affected fiber cells, modulation of lens cell adhesion molecules, and formation of intra-cytoplasmic high molecular weight protein aggregates (12, 13).

The mechanisms that lead to abnormal fiber cell differentiation after radiation exposure are not known. It is not clear whether fiber cell defects are caused by the accumulation of increased numbers of mutations in the remaining lens epithelial cells, by other kinds of genotoxic damage, or by defects in fiber cell differentiation caused by disruption of the organization of cells at the lens equator. Whatever the mechanism, cataract formation has become a convenient way to monitor radiation damage in experimental animals. The effects of ionizing radiation on the lenses of experimental animals have generally been similar to radiation effects in human lenses, but a variety of cataract scoring methods and species-specific latencies exist in the animal radiation cataractogenesis literature. Larger animals such as dogs, goats, and monkeys are less sensitive than smaller species, and appear to be more similar to humans.

c) **Human clinical/epidemiology data:**

Human lens epithelial cell death has been linked to cataract formation (14). The epidemiological data linking lens opacification to radiation exposure, with the exception of UVB radiation, is sparse. X-rays are known to induce cataracts, and x-ray-induced cataract in animals is a widely used model of cataractogenesis. Studies in patients undergoing radiotherapy for cancer or bone marrow transplantation (where dosimetry is well documented) have shown that with increasing doses, many
patients develop cataract (15-21). In these studies, the latency period is related to radiation dose and the volume of lens in the radiation field. Research on the atomic bomb survivors in Japan (18,19) who received mixed gamma-ray and neutron radiation exposures showed excess lens opacification in those exposed to single, acute doses of 1.5 Sv or greater, compared to those exposed to a lesser dose. The assessment of cataract in these studies was not always uniform, and in some cases, not carried out through dilated pupils. Assessing lens opacification through undilated pupils can lead to severe under ascertainment of presence/absence and severity. Some recent theoretical modeling of the atomic bomb survivor data suggests no dose threshold for radiation-induced cataract (18).

Since the 1980s, epidemiological studies of cataract have focused on three main classes of age-related cataract: nuclear, cortical, and posterior subcapsular. These cataracts have different anatomical locations and risk factor profiles, so in any epidemiological study it is important Such assessments are now objective and capable of providing accurate, sensitive, and often continuous measures of severity of each type of lens opacification (22-30). Application of these new methods in cross-sectional and longitudinal studies of age-related cataract has afforded opportunities to validate many of these methods (31-37). Now there are several validated subjective and objective (e.g. photographic) techniques to document severity and to measure progression of cataractous change.

Data from Cucinotta et al. (1) provide intriguing information about a potential link between radiation exposure in astronauts and the development of cataract. The dosimetry was very precise. It is of interest that Cucinotta et al. detected increased numbers of nuclear cataracts in astronauts. Earlier studies of radiation cataracts in humans had not identified ionizing radiation as a risk factor for nuclear cataracts. Cucinotta’s observation raises the possibility that other risk factors associated with space flight or astronaut training might contribute to cataract formation. Although the radiation dosimetry in Cucinotta’s study was very precise, the data on cataract type and severity were not as robust. Cataract classification data were abstracted from clinical records and the original clinical designations about type and severity of cataract were not based on standardized or validated methodologies. Studies by Klein et al. (20,21) suggested that x-ray exposure may be correlated with PSG and nuclear cataract, but precise radiation dosimetry in that study was not available.

Numerous studies have demonstrated a link between cortical cataract and cumulative lifetime ocular exposure to ambient ultraviolet B radiation (38-41). Nuclear cataract has also been found to be associated with exposure to UVB (41).

In a recent study of commercial pilots, there was a suggestion of a relationship between flight time and cataract prevalence (42). This study and the abstract below suggest that pilots are subjected to cosmic radiation, as well as UV radiation, although the dose of the former is likely to be considerably less than that found in astronauts in space. The data in reference (42) were retrospectively collected based on self-reports, and cataract assessment was not made in a standardized manner. In an abstract (43) presented at the 2004 meeting of the Committee on Space Research (COSPAR), Rafnsson et al. presented additional data linking cataract in airline pilots with radiation. The odds ratio from logistic regression of nuclear cataracts risk among cases and controls was 3.02 (95% CI 1.44 – 6.35), and the odds ratio for nuclear cataracts associated with cumulative radiation dose to 40
years of age, adjusted for age, smoking, and sunbathing habits was 1.06 (95% CI 1.02 – 1.10). In this study, cataracts were classified with the WHO Simplified Cataract Grading System.

d) Rationale:

In summary, there is good reason to suspect that astronauts have a greater risk of developing lens opacification than non-astronauts, and that this risk is dose dependent. Further assessment of the relevance of known risk factors to lens opacification in astronauts is warranted. In particular, objective measurement of the severity of each class of opacity must be undertaken with standardized, validated techniques. Digital images of the lens afford the opportunity to do this, and they also offer the opportunity to document unusual, non-age-typical cataract phenotypes. Analyses of these images can be masked as to the participant’s radiation status and will yield continuous measures of nuclear, cortical, and posterior subcapsular cataract formation. Data on the radiation-associated and other space environment-associated risks are available. These data, together with a reliable, accurate measure of cataract severity, will make it possible to ascertain the contribution of space radiation to the incidence and progression of cataracts in astronauts. It is hoped that such information will enable NASA to modify, and thereby reduce, these risks and increase the overall safety of space flight.

e) REFERENCES

C. MATERIALS AND METHODS:

a) Populations studied:

We will study three populations in the NASCA study; 1) the entire population of American astronauts (both active and retired), 2) a control population of pilots in the Houston area with a history of military aviation activity, and 3) a second control populations of ground-based NASA staff participating in the LSAH. See the recruitment section for more information on these populations.

b) Recruitment / Interviews: The following provides detail regarding the recruiting activities in this project.

a. NASA/LSAH - Astronauts/Retired Astronauts (NASA):

   i. Consent, NASA Layman summary, Study Invitation letter, FFQ and Form A to be mailed to astronauts (active and retired) one month prior to scheduled
appointment. An instruction sheet is included with packet, asking subjects to bring completed paperwork to appointment.

ii. Wyle Data Coordinator will send a reminder e-mail to subject (if current e-mail is captured at time of physical exam scheduling) asking that the paperwork is completed and brought to the clinic on the day of the eye exam

1. At the time of the vision exam, the study is explained in full by optometry staff.
2. All completed forms will be given to Wyle Data Coordinator for inclusion into study specific folder.
3. Wyle Data Coordinator will coordinate data entry of Form A (Demographics, Health, and Sunlight Exposure Questionnaire) into the electronic medical record.

b. NASA/LSAH Participants (Military aviators / Non-military controls):

i. Consent, NASA Layman summary, Study Invitation letter mailed to LSAH participants in bulk to those with known aviation experience (military and civilian), as well as subjects without aviation experience (military or civilian), based on birth month. Participants requested to return signed consent form if interested in participating in the study.

ii. Once consent form is returned, Wyle Data Coordinator or designee will contact subject to review exclusion criteria form for eligibility. If subject is eligible, Wyle Data Coordinator will schedule appointment into the electronic medical record.

iii. Wyle Data Coordinator will send confirmation of appointment made, and FFQ and Form A will be mailed to the subject, along with an instruction sheet to aid with form completion. Wyle Data Coordinator will send appointment reminder 2-4 days prior to exam via e-mail, and will print both confirmation/reminder correspondence for chart completion.

iv. All completed forms will be given to Wyle Data Coordinator (by Baylor representative) for inclusion into study specific folder.

v. Wyle Data Coordinator will coordinate data entry of Form A (Demographics, Health, and Sunlight Exposure Questionnaire) into the electronic medical record.

vi. All Study subject folders will be kept in Ste. 229B.

vii. Each folder will contain: Signed consent form (original or copy); Form A (will be documented in the EMR); FFQ; Logmar acuity documentation; and any correspondence with the subject during the process.

viii. All FFQ's will be delivered to Baylor representative for proper handling.

c) Baylor College of Medicine Participants - Baylor Participants (Military aviators / Non-military controls):

i) Subject with military aviation experience, as well as subjects without aviation experience responds to advertisement to NASA point of contact to be a participant in study.

ii) Baylor research associate will contact subject to review exclusion criteria form for eligibility.

iii) If subject is eligible, Wyle Data Coordinator will call subject and will schedule appointment into the electronic medical record.

iv) Baylor's Study Invitation letter, consent form, Form A and FFQ along with an instruction sheet to aid with form completion are mailed to subject.
v) Wyle Data Coordinator will send confirmation of appointment made.

vi) Wyle Data Coordinator will send appointment reminder 2-4 days prior to exam via e-mail, and will print both confirmation/reminder correspondence for chart completion. Form A on completion will be given to Wyle Data Coordinator (by Baylor representative) for inclusion into study specific folder.

vii) Wyle Data Coordinator will coordinate data entry of Form A (Demographics, Health, and Sunlight Exposure Questionnaire) into the electronic medical record.

viii) All Study subject folders will be kept by Baylor research associate.

ix) Each folder will contain: FFQ, Signed consent form (original), and any correspondence with the subject during the process.

x) All completed FFQs will be batched to be sent off to Channing Labs at Harvard School of Public Health for later processing.

d) Baylor College of Medicine Participants (AOD Military aviators / Non-military controls):

i) Baylor’s Study Invitation letter and consent form are mailed to AOD participants with known military aviation experience, as well as subjects without aviation experience. Participants are requested to return signed consent form if interested in participating in the study.

ii) Once consent form is returned, Baylor research associate will contact subject to review exclusion criteria form for eligibility. If subject is eligible, Form A and FFQ will be mail to the AOD along with the instruction sheet to aid with forms completion.

iii) Wyle Data Coordinator will schedule appointment into the electronic medical record.

iv) Wyle Data Coordinator will send confirmation of appointment made.

v) Wyle Data Coordinator will send appointment reminder 2-4 days prior to exam via e-mail, and will print both confirmation/reminder correspondence for chart completion.

vi) At the eye exam appointment, all completed forms will be given to Baylor research associate for inclusion into study specific folder.

vii) Copies of consent form and completed exclusion criteria form will be given to Wyle Data Coordinator.

viii) Wyle Data Coordinator will coordinate data entry of Form A (Demographics, Health, and Sunlight Exposure Questionnaire) into the electronic medical record.

ix) All completed FFQs will be delivered to Baylor research associate for proper handling.

e) Harvard Food Frequency Questionnaires:

The Harvard Food Frequency Questionnaire (FFQ) is a validated, questionnaire used widely throughout the world to gather standardized information about nutritional intake. It is particularly useful in gathering data on antioxidant intake. We are asking all NASCA subjects to complete the questionnaire at the initial and each subsequent visit. The data forms are sent to the Channing Laboratory at Harvard Medical School (Brigham and Women’s Hospital) for scanning and a computerized record of the results for each patient is returned to NASA for incorporation into the NASCA main database. With these nutritional data we will
be able to control our regression models for anti-oxidant nutrient intake and any other intake that we believe to be relevant.

At the time of the 2004 Annual Report, the NASCA team had not selected the format for gathering nutritional data. The indecision was due partly to the uncertainty about the feasibility of using blood to assess the nutritional status of astronauts and controls. We were particularly interested in assessing the antioxidant status of individuals in all groups using anti-oxidant indices. Two factors helped us make the decision against using blood data to assess nutritional status: 1) the cost of these analyses would be prohibitively high even if some of them were done “in house” at NASA, and 2) there were respected peer review publications suggesting that blood levels accurately reflect recent nutritional intake but are not as robust as indicators of chronic or long-term nutritional patterns. Having made the decision not to use blood analyses to determine anti-oxidant status, we decided to evaluate nutritional questionnaires as alternative methodologies. The Harvard Food Frequency Questionnaire (HFFQ) proved to be a validated instrument that was reasonably efficient to use in the setting of the NASCA study. Accordingly we obtained HSC approval to use the HFFQ and began using this at the outset of the study. Dale Hardy, our Patient Recruiter is administering these questionnaires in a standardized manner and the Channing Laboratory at the Brigham and Women’s Hospital is doing the automated assessment of the nutritional information. Data in electronic form will be sent to Dr. Wear for entry into the NASCA database.

We have completed an analysis of those nutrients that have been identified as risk factors for age-related cataract (ARC), and we will look first at the relevance of these nutrients to the risk of cataract in the NASCA cohorts. Due to the relatively small size of our NASCA cohorts, we will not be able to include more than 1-2 of these nutrients in regression models in which age, lens-specific radiation dose, and gender will be included as independent variables. We will be able to test each of the nutrient values of interest and which have relevance to ARC. From these data we hope to find nutritional factors that ameliorate the risk of radiation-induced cataract. Such findings might form the basis for an interventional study of efficacy of one or more nutrients as anti-cataract treatments.

f) Ocular examination and LogMAR acuity measurement

The ocular examination protocol in the NASCA study is identical to the routine ocular examination at the Johnson Space Center (NASA) used for the annual astronaut examination with the addition of: a test of LogMAR acuity with the Early Treatment Diabetic Retinopathy Study (ETDRS) standardized charts, Nidek EAS 1000 lens imaging, (see below), and LOCS III grading of nuclear brunescence (nuclear color). “LOCS” is the acronym for the Lens Opacities Classification System, Version III, a widely used, validated subjective means of grading lens opacification and nuclear color at the slitlamp. We are grading nuclear color as a means of decreasing the variability of our measurements of nuclear opacification.

g) Nidek EAS 1000 Lens Imaging
The Nidek EAS 1000 lens imaging system is a widely used, validated means of gathering high quality digital slit and retroillumination images of the lens in vivo. Each NASCA subject will have three such photos taken of each eye. The slit image will be used to assess nuclear opacification, and the two retroillumination images will be used to assess cortical and posterior subcapsular opacification. All images will yield continuous measures of cataract severity. In the case of nuclear cataract we will use pixel density - a measure of the intensity of light scattered from the nucleus, and in the case of cortical and posterior subcapsular cataract we will use “% area opaque”. Each of these measures will be derived from standardized image analysis protocols that have been described in detail in the application and the Manual of Operations. Since the Nidek EAS 1000 Lens Imaging system is a very sensitive means of recording the severity of lens opacification, these images will enable us to assess progression of cataract over time in addition to the assessment of severity of cataract at any given point in time.

h) Image analysis:

William H Tung and Leo T. Chylack, Jr., M.D. do the image analyses, M.D. at the Center for Ophthalmic Research (COR) at the BWH. The analytical protocols have been standardized and are spelled out in detail in the Manual of Operations.

Briefly, the Nidek slit image yields biometric data on the thickness of the cornea, depth of the anterior chamber, thickness of the axial portion of the lens and the pixel density at three specified loci in the mid nucleus. The biometric data is read out as distances in mm., and the pixel density is read out as pixel density units (pdu) on a scale of 1-255. The location of the loci at which pixel density is measured is specified for each image so that at each visit the analyst can revisit these same loci for repeat measures of pixel density. It is likely the pdu at one of the three loci will be used as a primary endpoint. The pixel density at the three loci are highly correlated in the normal lens and in the ARC, and only if there is an anomalous phenotype of nuclear change in the astronaut population will all three loci be used.

There are two retroillumination images/eye in the NASCA protocol, one focused at the plane of the anterior capsule and the second focused at the plane of the posterior capsule. The former will be used to assess the area of cortical cataract and the latter will be used to assess the area of posterior subcapsular cataract. In the case of mixed opacification (both cortical and PSC) in most cases the areas of the two classes of cataract can be assessed and reported separately.

We have completed the image analyses of 250 subjects who have been through the ocular examination protocol to date. We have encountered no unanticipated difficulties in the image analyses. The images have been of unusually high quality. We expect to receive another 90 subjects-worth of image data on 05/01 and we will have all of these image analyses completed before the end of July 2005 when we will begin the cross-sectional analyses of the NASCA data.

i) Radiation exposure dose estimation
**Radiation Data:** A database of radiation doses received by astronauts from all known sources will be used in the NASCA study. The database includes astronaut radiation exposures from medical, aviation training, isotopes, and space radiation. Computer models are used to estimate the lens dose based on available dosimetry for each exposure. Here differences in radiation attenuation at the lens compared to a dosimeter location are calculated. Conventional risk assessment uses dose-based concepts to relate the macroscopic dose and the rate of energy loss per unit path-length (LET) of a particle to human risk through a LET dependent weighting factors and a tissue specific risk coefficient. For space doses, we consider the matrix of doses behind aluminum shielding of depth $x$, and tissue shielding of depth, $y$. The dose and dose equivalent for a component of fluence, $F$ and LET, $L$ are

$$D(x,y) = F(x,y) \cdot L$$

and

$$H(x,y) = F(x,y) \cdot L \cdot Q(L)$$

respectively, where $Q$ is the quality factor. For a mixed radiation fields the equivalent dose is found by summing over particle types, $j$ as

$$H(x,y) = \sum_j \int dE \cdot \phi(x, y, E) \cdot L(E) \cdot Q[L(E)]$$

with a similar expression for the dose. The organ dose is found by summing over the tissue shielding distribution provided by the computerized anatomical CAM/CAF model

$$H_T(x) = \sum_y a_y \sum_j \int dE \cdot \phi(x, y, E) \cdot L(E) \cdot Q[L(E)]$$

where $a_y$ is the shielding segment derived from the spacecraft geometry. Since an astronaut's location is not precisely known during the mission, we make comparisons of dose values at fixed dosimeter locations to understand systematic behavior. The dose equivalent at a specific dosimeter location, $β$ is given in terms of the spacecraft shielding model as

$$H_{T,β} = \sum_x b_x \cdot H_T(x)$$

A normalization procedure is followed to scale transport results to crew personnel and area dosimetry. The procedure assumes that the error in the baseline model and measurement is dominated by inaccuracies in the AP8 Model of the trapped protons. Using the point-dose corrected for APD shielding we choose a normalization constant, $α_A$, that minimizes $χ^2$

$$χ^2 = \sum_β [D^{TLD}_β - (α_A D_β^{APD} + D_β^{GCR})]^2$$

where $D_β^{APD}$ and $D_β^{GCR}$ are the doses from the baseline model evaluated at the TLD location. In comparing to data from TLD’s, we correct for the efficiency of the TLD using a response function determined from accelerator measurements.
For the purpose of this study the AREDB will be coded with a non-identifiable numerical provide by the Epidemiology Group at NASA JSC. The age-specific lens dose or biological dose equivalent from each radiation exposure type will thus be available for data analysis to study possible associations radiation and cataracts.

j) **Statistical models:**

**Statistical Analysis:** Dr. AI Feiveson is currently reviewing the data sets with a goal of developing appropriate statistical models for the initial cross-sectional analyses of the risk factors for cataract prevalence. The general approach to be taken is outlined below:

**Statistical Analysis.**
Various statistical models, customized for each dependent measure, will be used to determine if differences between astronauts and control subjects are greater than what would be expected by chance after adjusting for differences in age, climate, food intake and solar exposure on the ground. As an example, the following model applies to pixel density, a measure of percent occlusion of the lens.

\[
\logit(y_{ikt}/100) = \mu + a_i + \beta_1 X_{1it} + \beta_2 X_{2it} + \beta_3 (age) + e_{ik}
\]

where:
- \(y_{ikt}\) is the percent occlusion for the \(k\)-th eye of the \(i\)-th subject at the \(t\)-th study year of observation, \((k = 1, 2), (i = 1, \ldots, N), (t = 1, \ldots, 5)\)
- \(X_1\) = accumulated space dose - for astronauts, starts at age of first exposure = 0 for non-astronauts
- \(X_2\) = time in years since start of accelerated cataract growth
- accelerated cataract growth starts at age = \(A_0\)
- \(A_0\) varies randomly between subjects following a gamma distribution
- \(a_i\) and \(e_{ik}\) are random error terms, between and within subjects, respectively

D. **RESULTS:**

1. **General:**

Since the initiation of recruitment in July, 2004 we have made considerable progress in the development of protocols to be used in recruitment, assessing nutrient intake, acquiring ocular and lens image data, performing the image analyses, specifying the radiation exposure parameters, developing appropriate statistical models and recruiting subjects of the NASCA study. The development of the various methodologies has been described in the section above and the recruitment statistics are presented in the sections below.

2. **Recruitment statistics:**
In summary out of the 288 astronauts and 200 control subjects (488 total subjects) as of 04/16/05 we have recruited and consented 68% of our targeted population. We are on track to complete recruitment in the next three months.

<table>
<thead>
<tr>
<th></th>
<th>Subjects Enrolled and Consented</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>Astronauts</td>
<td>131</td>
</tr>
<tr>
<td>Military pilots</td>
<td>73</td>
</tr>
<tr>
<td>LSAH</td>
<td>79</td>
</tr>
<tr>
<td>TOTAL</td>
<td>283</td>
</tr>
</tbody>
</table>

Other components of our progress are as follows:

a. Completed the Human Subjects Committee (HSC) applications and secured approval from the HSCs at the Brigham and Women's Hospital, Baylor College of Medicine, and NASA/JSC.


c. NASCA Website: At the BWH we have established a secure NASCA-specific server, and we are now uploading administrative information (Manual of Operations, award statements, policies, teleconference minutes, etc.), image data, recruitment statistics, relevant references, and many other study-related materials. The server will also hold a copy of the main NASCA data file prepared by Dr. Wear at Wyle Labs.
RECRUITMENT: DURING THE PAST CALENDAR YEAR, 2004, THE NASCA TEAM HAS ACCOMPLISHED THE FOLLOWING IN TERMS OF RECRUITMENT:

AGE DISTRIBUTION TABLES – ASTRONAUTS
AS OF 4-6-05

General statistics:
US Astronauts: 323 (288 living, 35 deceased); Women: 45 (41 living, 4 deceased)
Men: 278 (247 living, 31 deceased); All statistics are based on US Astronauts alive as of August 1, 2004;
*Percent includes only those who have consented*

WOMEN:

<table>
<thead>
<tr>
<th>Age</th>
<th>Total</th>
<th>Total Consented/ Data Complete</th>
<th>Total Consented/ Data incomplete</th>
<th>Awaiting consents/ data</th>
<th>Percent Recruited For Age</th>
<th>Total Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>30-34</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>35-39</td>
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<td>0</td>
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</tr>
<tr>
<td>40-44</td>
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<td>0</td>
<td>89%</td>
<td></td>
</tr>
<tr>
<td>45-49</td>
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<td>0</td>
<td>58%</td>
<td></td>
</tr>
<tr>
<td>50-54</td>
<td>8</td>
<td>5</td>
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<td>0</td>
<td>63%</td>
<td>1</td>
</tr>
<tr>
<td>55-59</td>
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<td>0</td>
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</tr>
<tr>
<td>60-64</td>
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<td>0</td>
<td>100%</td>
<td></td>
</tr>
<tr>
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<td>0</td>
<td>0%</td>
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<td>0</td>
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</tr>
<tr>
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<td>0%</td>
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</tr>
<tr>
<td>TOTALS</td>
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<td>23</td>
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<td>0</td>
<td>63%</td>
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***Women - 18 Active / 8 Retired***

MEN:

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<tr>
<th>Age</th>
<th>Total</th>
<th>Total Consented/ Data Complete</th>
<th>Total Consented/ Data incomplete</th>
<th>Awaiting consents/ data</th>
<th>Percent Recruited For Age</th>
<th>Total Declined</th>
</tr>
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<tr>
<td>30-34</td>
<td>1</td>
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<td>0</td>
<td>100%</td>
<td>1</td>
</tr>
<tr>
<td>35-39</td>
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<td>0</td>
<td>50%</td>
<td>1</td>
</tr>
<tr>
<td>40-44</td>
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<td>24</td>
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<td>0</td>
<td>72%</td>
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</tr>
<tr>
<td>45-49</td>
<td>50</td>
<td>27</td>
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<td>1</td>
<td>58%</td>
<td>1</td>
</tr>
<tr>
<td>50-54</td>
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<td>20</td>
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<td>0</td>
<td>55%</td>
<td></td>
</tr>
<tr>
<td>55-59</td>
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<td>59%</td>
<td></td>
</tr>
<tr>
<td>60-64</td>
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<td>1</td>
<td>0</td>
<td>37%</td>
<td></td>
</tr>
<tr>
<td>65-69</td>
<td>18</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>70-74</td>
<td>26</td>
<td>8</td>
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<td>0</td>
<td>35%</td>
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</tr>
<tr>
<td>75-79</td>
<td>9</td>
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<td>0</td>
<td>11%</td>
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</tr>
<tr>
<td>80+</td>
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<td>0</td>
<td>0%</td>
<td></td>
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<tr>
<td>TOTALS</td>
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<td>118</td>
<td>12</td>
<td>1</td>
<td>53%</td>
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</table>

**Men - 62 Active / 68 Retired**
Age Distribution Tables as of 4-6-05
For Military Aviation Control Group
(AOD's, LSAH, Baylor)
Target Population: 105

**WOMEN:**

<table>
<thead>
<tr>
<th>Age</th>
<th>Total Needed</th>
<th>Rounded Total Needed</th>
<th>Total Consented/Data Complete</th>
<th>Total Consented/Waiting Exam</th>
<th>Total Consented/ Data Incomplete</th>
<th>Percent Recruited For Age</th>
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<tbody>
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<td>25-29</td>
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<td>0</td>
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</tr>
<tr>
<td>30-34</td>
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</tr>
<tr>
<td>35-39</td>
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<td>0%</td>
</tr>
<tr>
<td>40-44</td>
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<td>33%</td>
</tr>
<tr>
<td>45-49</td>
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<td>1</td>
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<td>25%</td>
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<tr>
<td>50-54</td>
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<td>0%</td>
</tr>
<tr>
<td>55-59</td>
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</tr>
<tr>
<td>60-64</td>
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</tr>
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<td>65-69</td>
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<td>0</td>
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<td>0%</td>
</tr>
<tr>
<td>70-74</td>
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<td>0</td>
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<td>0%</td>
</tr>
<tr>
<td>75-79</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>TOTALS</td>
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<td>17</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>24%</td>
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</table>

**MEN:**

<table>
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<tr>
<th>Age</th>
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<th>Rounded Total Needed</th>
<th>Total Consented/Data Complete</th>
<th>Total Consented/Waiting Exam</th>
<th>Total Consented/ Data Incomplete</th>
<th>Percent Recruited For Age</th>
</tr>
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<tbody>
<tr>
<td>30-34</td>
<td>0.4</td>
<td>1</td>
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<td>35-39</td>
<td>5.8</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>40-44</td>
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<td>1</td>
<td>43%</td>
</tr>
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<td>67%</td>
</tr>
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<td>50-54</td>
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<td>14</td>
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<td>100%</td>
</tr>
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<td>60-64</td>
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<td>86%</td>
</tr>
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<td>65-69</td>
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<td>2</td>
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<td>1</td>
<td>43%</td>
</tr>
<tr>
<td>70-74</td>
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<td>10</td>
<td>10</td>
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<td>100%</td>
</tr>
<tr>
<td>75-79</td>
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<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>TOTALS</td>
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<td>91</td>
<td>72</td>
<td>1</td>
<td>3</td>
<td>84%</td>
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### Age Distribution Tables as of 4-6-05
For Non-Military Aviation Control Group
(LSAH, Baylor)
Target Population: 105

#### WOMEN:

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<tr>
<th>Age</th>
<th>Total Needed</th>
<th>Rounded Total Needed</th>
<th>Total Consented/Exam Completed</th>
<th>Total Consented/Awaiting Exam</th>
<th>Percent Recruited For Age</th>
</tr>
</thead>
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<tr>
<td>25-29</td>
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<td>1</td>
<td>1</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>30-34</td>
<td>0.4</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>35-39</td>
<td>1.8</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>40-44</td>
<td>3.3</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>100%</td>
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<td>45-49</td>
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</tr>
<tr>
<td>50-54</td>
<td>2.9</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>100%</td>
</tr>
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<td>55-59</td>
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<td>0</td>
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<td>60-64</td>
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<td>1</td>
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<td>TOTALS</td>
<td>15.6%</td>
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<td>18</td>
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#### MEN:

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<th>Total Consented/Exam Completed</th>
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<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>35-39</td>
<td>5.8</td>
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<td>100%</td>
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<td>40-44</td>
<td>14.2</td>
<td>14</td>
<td>13</td>
<td>1</td>
<td>93%</td>
</tr>
<tr>
<td>45-49</td>
<td>18.2</td>
<td>18</td>
<td>15</td>
<td>1</td>
<td>88%</td>
</tr>
<tr>
<td>50-54</td>
<td>13.9</td>
<td>14</td>
<td>13</td>
<td>0</td>
<td>93%</td>
</tr>
<tr>
<td>55-59</td>
<td>10.6</td>
<td>11</td>
<td>7</td>
<td>0</td>
<td>64%</td>
</tr>
<tr>
<td>60-64</td>
<td>6.9</td>
<td>7</td>
<td>7</td>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>65-69</td>
<td>6.6</td>
<td>7</td>
<td>6</td>
<td>0</td>
<td>86%</td>
</tr>
<tr>
<td>70-74</td>
<td>9.5</td>
<td>10</td>
<td>6</td>
<td>2</td>
<td>80%</td>
</tr>
<tr>
<td>75-79</td>
<td>3.3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>TOTALS</td>
<td>89.4</td>
<td>91</td>
<td>75</td>
<td>4</td>
<td>87%</td>
</tr>
</tbody>
</table>

2. **Summary of Recruitment:**

Recruitment is proceeding apace for all groups except female pilots and retired astronauts. The lack of any women pilots in the military air forces until recently constitutes an insurmountable problem. We may not be able to recruit more women pilots in the older age groups, simply because there are none to recruit.

The lower than expected participation by retired astronauts has been addressed in several ways including ads in local news papers, direct recruiting at air bases (U.S. Air Force, U.S. Coast Guard, and others) around Houston, contacting all of the local
airlines, and finally an appeal to the retired astronaut group by Dr. Jeffreys. We remain optimistic that we will be able to enroll additional retired astronauts so that we have not only subjects in the older age groups but subjects in the higher radiation-exposure groups.

3. Data Management: Dr. Mary Wear and her staff at Wyle labs are compiling the data sent from the various study sites (ocular and general medical examinations, data from analysis of digitized lens images, radiation exposure statistics, nutritional Food Frequency Questionnaires, demographic data, and routine blood data. The team is about to begin the process of assessing the univariate characteristics of each variable as the initial step in assessing the quality of the data. The number of variables will be reduced to those with direct primary relevance to the study’s objectives.

4. Lens/Cataract Image Analysis: As of 04/27/05 we have completed the analyses of lens images (slit and retroillumination) from both eyes of 250 subjects (approximately 1500 image analyses). We anticipate receiving from NASA another 90-subjects-worth of image data on 05/01/05. All of this image-derived data has been transferred to NASA for inclusion in the master data file.

5. Food Frequency Questionnaires (FFQs): We have gathered completed FFQs from all but about 20 subjects. We are attempting to gather these outstanding data now. Two large batches of FFQ forms have been scanned and reported to us by The Channing Laboratory and are ready to be incorporated into the NASCA data base.

E. DISCUSSION:

F. OTHER INFORMATION AND MATERIALS:

i) Complete listing of all presentations this grant supports:

   a. A poster entitled “The NASCA Study – The NASA Study of Cataract in Astronauts” was presented by Leo T. Chylack, Jr., M.D. at the 2005 Bioastronautics Workshop in Galveston, TX on January 10-12, 2005.


ii) Complete listing of all published abstracts

   a) There were abstracts for each of the above-referenced presentations

iii) Complete listing of all published articles:

   a) None to date

iv) Complete listing of all other published materials (books, chapters, newspaper releases):

   a) Newspaper releases are planned for the immediate future for the following local papers:
A new multicenter study on cataracts and space radiation (NASCA) is looking for healthy individuals aged 30+ with a history of military aviation to participate in a 5-year study on cataracts and space radiation exposure. The NASCA study is a multicentered project involving investigators at Harvard Medical School, the Brigham and Women's Hospital, Baylor College of Medicine, Wyle Laboratories, Space Center Eye Associates, and NASA. NASCA will assess the role of space radiation, solar ultraviolet-B, diabetes, smoking, and nutrition in the presence and development of cataracts among astronauts and comparison subjects. The long term goal of this project is to improve the ocular safety for astronauts during space flight. In the first year, participants will complete two short questionnaires general health, sunlight exposure, and consumption of various foods. The interview will be followed by a standard flight medicine eye exam with additional imaging. Completion of an eye exam and food consumption questionnaire is also required annually during years 2-5 of the study. Volunteers will not be compensated for their time. At present, subjects with and without a history of military aviation in specific age categories are needed. Subjects would also need to undergo an annual eye exam at the NASA Lyndon B. Johnson Space Center, in Houston. For more information, please contact Dr. Leif Peterson at Baylor College of Medicine, Telephone (713) 798-5385, E-mail: peterson@bcm.tmc.edu.

Announcement in Brooks Air Force Base (San Antonio) Newspaper:

NASA Cataract Study Under Way

Is exposure to space radiation during manned space flight associated with development of cataracts? Is the development of space radiation-induced cataract modified by lifetime exposure to solar ultraviolet B (UV-B) radiation or consumption of certain nutrients in the diet? To answer these questions, NASA has recently funded a five-year multi-center research study to assess the prevalence and progression of lens opacities (cataracts) in astronauts exposed to radiation during space flight. Collaborating institutions involved in the study include the Brigham and Woman's Hospital in Boston, Baylor College of Medicine, Space Center Eye Associates, and Wyle Laboratories.

Historically, numerous laboratory animal studies have demonstrated a link between exposure to ionizing radiation (x- or gamma rays, heavy charged particles, etc.) and the development of cataracts. In fact, cataract formation has become a convenient way to monitor radiation damage in experimental animals.
involved in radiation effects research. In general, younger animals and species that have a higher cellular growth rates in the lens develop cataracts more rapidly than older animals and species with slower growing lens. Larger animals such as dogs, goats, and monkeys are less sensitive than smaller species. A similar pattern has been observed among humans, where younger and naturally smaller subjects are more prone to develop cataracts than larger and older persons. In addition, the effects of ionizing radiation on the lens of experimental animals have generally been similar to radiation effects in human lens.

While human studies on space radiation and cataract formation are limited, there is a large body of information from ground-based medical research. Patients exposed to increasing doses of radiotherapy for cancer or bone marrow transplantation have been shown to develop cataract. Atomic bomb survivors in Japan have also developed cataracts from single acute doses of 1.5 Sv and greater. Another study conducted with commercial pilots using a form of unstandardized cataract assessment showed an association between flight time and cataract prevalence. Most of the evidence suggests a causal role of lifetime exposure to ultraviolet-B radiation for development of “cortical” cataracts, while exposure to ionizing radiation in the form of x-rays is more likely to produce “nuclear” cataract. Recently, a team of investigators in JSC’s Space and Life Sciences Directorate led by Dr. Frank Cucinotta reported that cataract prevalence was dose dependent in astronauts and greater when compared with non-astronauts. This has raised questions concerning the likelihood that astronauts are at increased risk when compared with ground-based controls and that other risk factors associated with space flight and astronaut training could possibly contribute to cataract formation.

In addition to astronaut participation, two civilian “control” groups are being recruited for participation. The first control group includes civilians with a history of military aviation, whereas the second group consists of civilians with essentially no history of military, commercial, or private aviation. Both control groups are matched to the astronaut population according to age and gender composition. During the first year of the study, astronauts and controls fill out a short questionnaire on general health history and sunlight exposure, complete a food frequency questionnaire, and undergo an eye exam in the Optometry Clinic at the Lyndon B. Johnson Space Center. The annual eye exam involves specialized imaging of the lens in order to assess early development of cataract. During years 2-5, participants are required to complete the same food frequency questionnaire annually and take an annual eye exam.

Using information collected from research subjects, the primary goals of the study are to determine the prevalence and progression of the three main types of age-related lens opacities in the entire astronaut population and determine the risk associated with radiation exposure during space flight. A secondary goal of the project is to improve the routine assessment of lens status in astronauts by objectively assessing the incidence of cataract and their progression as a function of radiation exposure during space flight. The third goal is to develop means of assessing agents that might slow the incidence and/or progression of cataracts. The data analysis stage will compare results from astronauts with results from controls to determine the association between space radiation,
lifetime sunlight exposure, cumulative flight time, and consumption of various foods with the presence of cataracts, while controlling for age and gender.

Information obtained from the study will provide new insights into the role of various components of space radiation (geomagnetically trapped protons, heavy charged particles, etc.) in cataract development, and establish new leads for future research. Moreover, the knowledge gained will be invaluable for NASA and its population of astronauts, improving radiation shielding in space vehicles, and future prevention studies on cataract development. Overall, this study will make a significant contribution to flight safety in manned space activities. At present, subjects with and without a history of military aviation in specific age categories are needed. For more information about the study, or information on participating in the study, please contact Dr. Leif Peterson, Associate Professor of Medicine, Baylor College of Medicine, at (713) 798-2062.