NASA/TM—2000-210041

Monitoring Astronaut Health at the Nanoscale Cellular Level Through the Eye

Rafat R. Ansari
National Center for Microgravity Research, Cleveland, Ohio

Bhim S. Singh
Glenn Research Center, Cleveland, Ohio

Luigi Rovati and Franco Docchio
University of Brescia, Brescia, Italy

Jerry Sebag
Doheny Eye Institute, University of Southern California Medical School,
Los Angeles, California

April 2000

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Prepared for the
Third Annual International Conference on Integrated Nano/Microtechnology
for Space Applications
sponsored by the Institute for Advanced Interdisciplinary Research
Houston, Texas, January 23–28, 2000

National Aeronautics and
Space Administration

Glenn Research Center

April 2000

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MONITORING ASTRONAUT HEALTH AT THE NANOSCALE CELLULAR LEVEL THROUGH THE EYE

Rafat R. Ansari
National Center for Microgravity Research
Cleveland, Ohio
Phone: (216) 433–5008, Fax: (216) 977–7138
E-mail: rafat.r.ansari@grc.nasa.gov

Bhim S. Singh
National Aeronautics and Space Administration
Glenn Research Center
Cleveland, Ohio

Luigi Rovati and Franco Docchio
University of Brescia
Brescia, Italy

Jerry Sebag
Doheny Eye Institute
University of Southern California School of Medicine
Los Angeles, California

ABSTRACT

A user friendly goggles-like head-mounted device equipped with a suite of instruments for several non-invasive and quantitative medical evaluation of the eye, skin, and brain is desired for monitoring the health of astronauts during space travel and exploration of neighboring and distant planets. Real-time non-invasive evaluation of the different structures within the above organs can provide indices of the health of not just these organs, but the entire body. The techniques such as dynamic light scattering (for the early detection of uveitis, cholesterol levels, cataract, changes in the vitreous and possibly Alzheimer's disease.), corneal autofluorescence (to assess extracellular matrix biology e.g., in diabetes), optical activity measurements (of anterior ocular fluid to evaluate blood-glucose levels), laser Doppler velocimetry (to assess retinal, optic nerve, and choroidal blood flow), reflectometry/oximetry (for assessing ocular and central nervous system oxygen metabolism), optical coherence tomography (to determine retinal tissue microstructure) and possibly scanning laser technology (for intraocular tissue imaging and scanning) will be integrated into this compact device. Skin sensors will also be mounted on the portion of the device in contact with the periocular region. This will enable monitoring of body temperature, EEG, and electrolyte status. This device will monitor astronaut health during long-duration space travel by detecting aberrations from pre-established "norms", enabling prompt diagnosis and possibly the initiation of early preventative/curative therapy. The non-invasive nature of the device technologies permits frequent repetition of tests, enabling real-time complete crew health monitoring. This device may ultimately be useful in tele-medicine to bring modern healthcare to under-served areas on Earth as well as in so-called "advanced" care settings (e.g. diabetes in the USA).

INTRODUCTION

The motivation for this paper comes from the human experience and achievements in space flight. In less than 50 years the human-kind has launched rockets into space, gone to the moon and returned safely back to Earth, learned how to live and work in space environment, sent probes and robots to distant planets and obtained detailed images of geological features, repaired orbiting telescopes and satellites, and constructed complex permanent structures in space. The people from ancient Greeks to modern day civilizations have asked the question: is there life on Mars? We do not know the answer to this important age-old question, but as space faring people we can safely say that some day there will be life on Mars. This paper is offered in anticipation of and preparation for that day when humans will land on Mars. With this project we will be ready to monitor their health remotely, safely, non-invasively, and quantitatively to guarantee their safe and healthy return back to Earth. Furthermore, early diagnosis and prevention of diseases is a critical direction of medicine in the 21st century. It is possible that our compact and non-invasive multi-purpose diagnostics device will also be used by today's health conscious consumers for regular health monitoring in settings of their choice such as homes, offices, gymnasiums, drive-thru's, and shopping malls. Governments and healthcare agencies may further find useful applications in using such a device to extend healthcare to under-served areas. The advanced technologies available today could enable the realization of these objectives.

BACKGROUND

The microgravity environment of space flight can affect human physiology. Immediately upon entering this environment astronauts experience shifts in blood flow to upper parts of the body and elimination of weight-bearing forces. The long-term effects hitherto unknown may also include changes at the cellular level due to exposure to cosmic radiation. Thus, important systems such as vestibular, cardiovascular, renal, bone, muscle, brain, and eye could be affected. In the absence of effective counter measures, changes could accelerate the normal aging process.

The eye is built like a camera. The structures in the front of the eye (cornea and lens) focus light onto the tissue that lines the inside of the back of the eye (retina). The retina works like the film in a camera, creating an "image" in the form of nerve signals that are conducted along the optic nerve to the occipital lobe of the brain where the visual process of vision is completed. The path of light from outside the eye to the retina traverses structures that are representative of nearly every tissue type in the body. For example, the cornea is a typical extra- cellular matrix composed primarily of collagen. Aqueous is an ultrafiltrate of blood, containing most of the molecules found in serum at concentrations that are reflective of serum levels. The lens is a highly organized array of crystalline proteins. Vitreous is very similar in nature to the articular cartilage and synovial fluid found in joints. The retina and optic nerves are in fact part of the central nervous system. Within these two structures are blood vessels that can be directly visualized, the only place in the body where this can be done. Thus, circulatory physiology (blood flow, oxygenation, etc.) can be evaluated non-invasively through the eye. Because of these unique features, the eye can be considered a "*microcosm of the body*". Furthermore, since the eye is easily accessed by light, advanced optical technologies can be used for the evaluation of structure and physiology in health, aging, and disease. The use of noninvasive technologies permits frequent repetition of tests enabling real time monitoring. Technologies and approaches that are found to be useful in monitoring astronaut health in space (*celestial tele-medicine*) may have even greater utility and value on earth as a means of bringing advanced health care to under-served people in inner cities, rural America, and the developing countries of our blue planet. Thus celestial tele-medicine will help monitor astronaut health during deep space exploration, so as to detect aberrations from pre-established "norms", enabling prompt initiation of early preventative/curative therapy. The terrestrial tele-medicine will provide a device for use in diseases not adequately diagnosed and/or treated in under-served areas on earth as well as in so-called "advanced" care settings (e.g. diabetes in the USA). This is presented in figure 1.

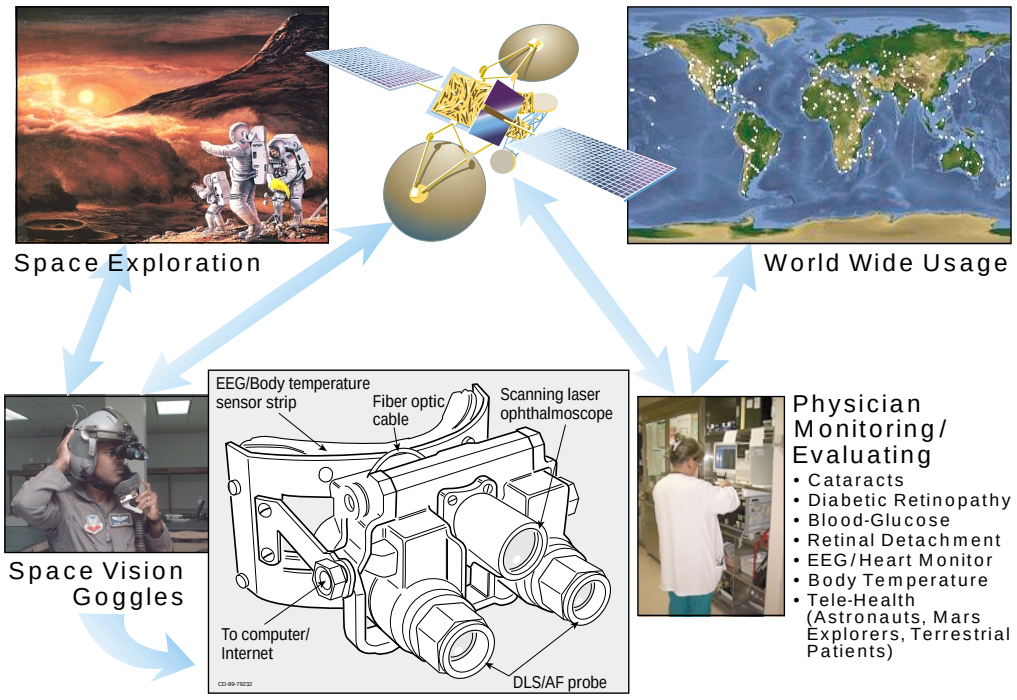


Figure 1.—Ophthalmic Tele-Health for Celestial and Terrestrial environments.

DEVICE DESIGN

We plan to build an easy to use head-mounted apparatus equipped with several powerful optical diagnostic technologies, as well as technologies based upon contact with skin and proximity to the brain. The findings will be downloaded to a center on Earth where the results will enable evaluation of extracellular matrix biology, neuromuscular and neuronal function, and vision. Skin sensors mounted on the portion of the device in contact with periocular tissues will enable monitoring of body temperature and heart rate, pulse oximetry for measurements of oxygen saturation in blood capillaries, electroencephalographs (EEG), and others health indices. These off-the-shelf bio-sensors are frequently used in exercise equipment such as treadmills, bikes, etc. and therefore will not be discussed further. More advanced skin sensors are used in clinical neurology and anesthesiology. Our preliminary prototype design employs a helmet purchased at a cost of $30.00 from a general merchandizing store (Target). The helmet is a replica of Anakin's pod helmet from the 1999 motion picture STARWARS. The helmet is equipped with a flip-up/flip-down eye glasses (see figure 2).

These will be used to house aligning optics and miniaturized fiber optic probes. The interior is covered with a soft cloth lining which is attached with Velcro and can easily be removed/replaced to install optical fibers. The space in the ear-muffs can be used to interface low-power lasers and computer and internet connectors. One unique feature of this design is to combine basic systems (lasers, detectors, correlator, spectrum analyzer) common for various technologies into a single unit that will subserve the technical requirements of all the different technologies. Several noninvasive optical technologies are being considered for integration into this design. A number of optical phenomena such as fluorescence, diffusion, absorption, interference, Doppler shift, rotation of the plane of the polarization of light, and Raman scattering can be exploited as ophthalmic clinical tools. The role and status of these constituent technologies is described below. Our modular approach will utilize these multiple technologies both in a helmet and in a diagnostic module (similar to night-vision goggles) which can be mounted in front of the helmet.

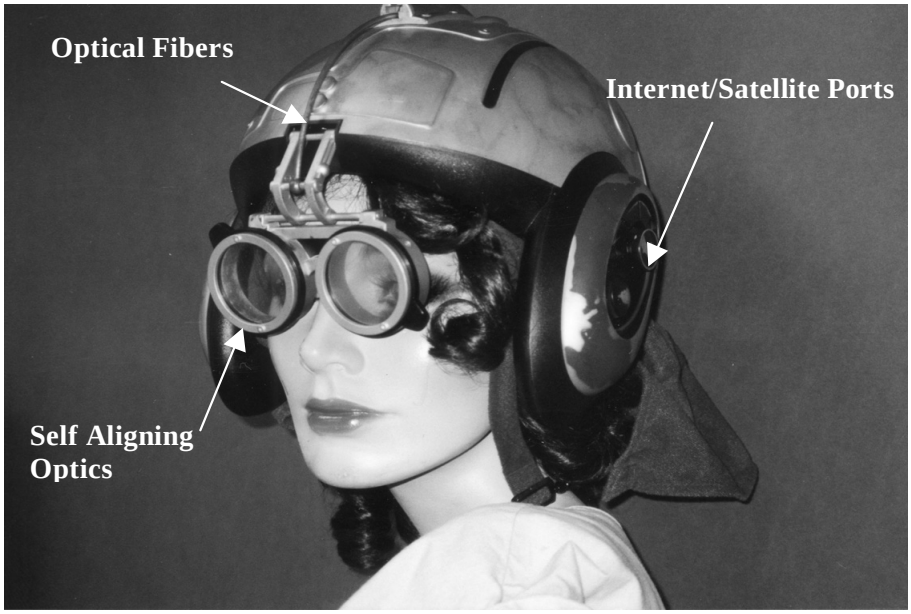


Figure 2.—Health Monitoring Helmet.

Constituent Technologies

Dynamic Light Scattering (DLS):

During a trip to Mars and other extraterrestrial destinations the astronauts will travel through high levels of almost all of the wavelengths (γ-rays, x-rays, UV, visible, IR) found in the electromagnetic spectrum. The radiation exposure can lead to formation of cataracts. Datiles and Magno[1] cites a latent period of 9 to 12 months that exists between ionizing radiation exposure and the onset of cataract in laboratory settings. We believe that a cataract develops much earlier but it cannot be detected before 9-12 months with the conventional ophthalmic instruments in clinical use today. Indeed, studies performed by Ansari and Datiles[2] have shown that DLS is far superior to the most advanced available technology as a way to detect the earliest changes in cataract formation. Here on Earth, cataract is the major cause of blindness affecting about 50 million people each year worldwide. It is estimated that over $5 billion will be spent this year in treating cataract patients in the United States alone. There is no medical treatment to prevent or halt the progression of a cataract; nor is there any way to reverse a cataract once it has formed. The only known treatment is surgical. However, a medical treatment could be possible if we understand how a cataract forms and what makes it grow. In order to find a medical treatment for cataracts, first, we must be able to detect a growing cataract in its incipient stage. Such powerful detection capability will be useful in patient monitoring and in the development and testing of possible "anticataract" drugs or "diet" therapies. Most recently Sardi[3] has strongly argued in favor of using multivitamins, antioxidants, and nutritional supplements in eradicating cataracts. We can perhaps prevent progression of cataracts thus prevent vision loss without surgery. Our DLS methodology has also been used to better understand cataract mechanism at the biochemical and biophysical level.[4] We expect our approach to be helpful in screening the efficacy of such methods. Our device is being used in laboratory and in clinical settings at the National Eye Institute (NEI) of the National Institutes of Health (NIH).[5]

The technique of DLS can be used to diagnose cataracts at the molecular level. Recently new DLS fiber-optic probes were developed by Ansari et al.[6], at NASA GRC for non-contact, accurate, and extremely sensitive particle sizing measurements in fluid dispersions and suspensions for microgravity experiments on-board the space shuttle and space station orbiters. These

probes are shown in figure 3. They can also be used in imaging applications, laser Doppler velocimetry, and Raman spectroscopic measurements. They are compact, portable, rugged, are free of optical alignment requirements, and offer point and shoot operation for various on-line field applications under various challenging environments. The probes are also extremely flexible in regards to sample container sizes, materials, and shapes. No external vibration isolation and no index matching are required. The DLS probe is capable of measuring the size of particles as small as 1 nm to as large as few microns in a wide concentration range from very dilute (water-like) dispersions to very turbid (milk-like) suspensions[7]. It is safe and fast to use as it only requires very low laser power with very short data acquisition times (5 seconds).

A fiber optic probe comprising two monomode optical fibers and two GRIN micro lenses, as illustrated in figure 4, provides a compact and remote means of studying the dynamical characteristics of the macromolecules in the eye. The probe is non-invasive and is conveniently positioned in front of the eye (cornea), but has no physical contact with any part of the eye. The laser light out of a laser/detector module is transmitted by a compact backscatter fiber optic probe to the eye. In our experiments, visible light of 665 nm wavelength from a laser diode is focused into a spot (20μm diameter) inside the eye. The detected signal is processed via a digital correlator to yield a time autocorrelation function (TCF). For dilute dispersions of spherical particles the slope of the (TCF) provides a quick and accurate determination of the particle's translation diffusion coefficient, which can be related to its size via a Stokes-Einstein equation, provided the viscosity of the suspending fluid, its temperature, and its refractive index are known. Depending upon the position of the scattering volume, Brownian motion of the particles in the aqueous humor, protein crystallines inside the lens and the macromolecules in the vitreous humor are monitored. The major proteins that can scatter light in a human eye lens are α, β, and γ crystallines. Since α-crystallines are the largest molecules (molecular wt. ~ 10^6 Daltons), they induce the greatest amount of scattering of laser radiation in a DLS measurements. When these protein molecules are agglomerated, they give rise to lens opacities. The lens gradually becomes cloudy hindering the light transmission and the ability to focus a sharp image on the retina at the back of the eye.

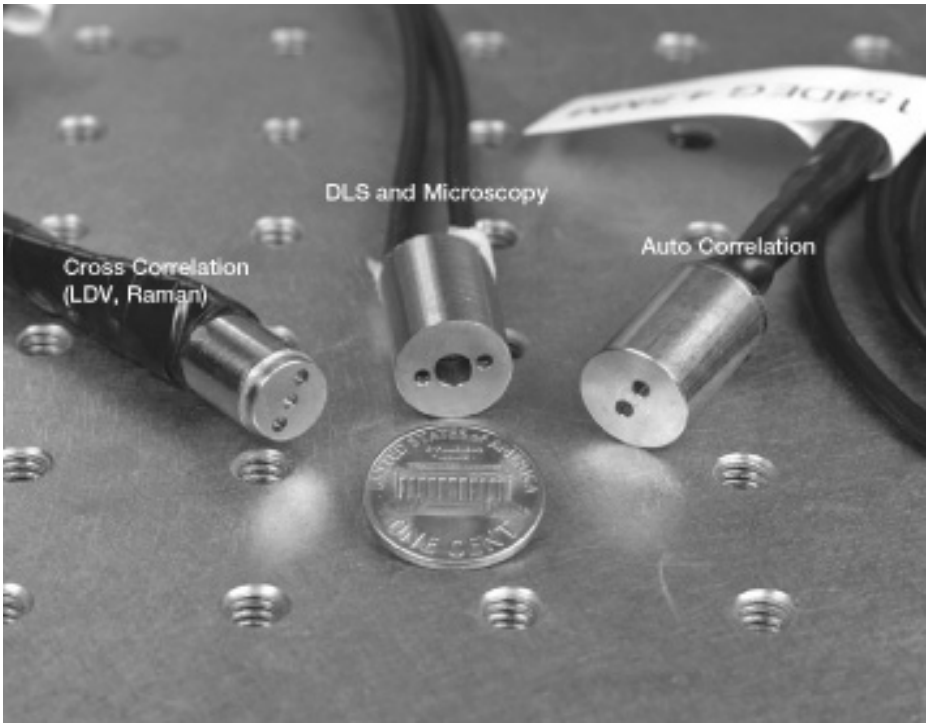


Figure 3.—Fiber Optic Probes.

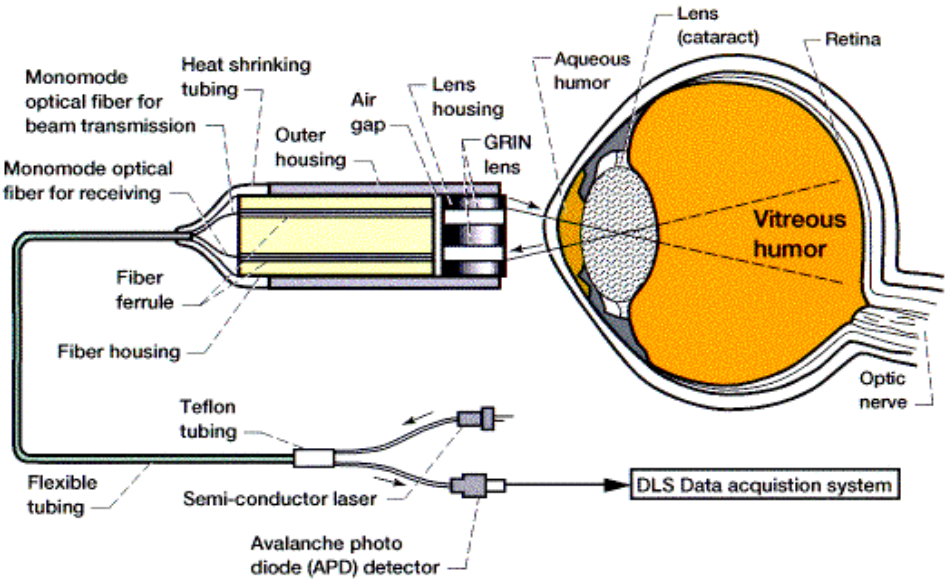


Figure 4.—Schematic of a Dynamic Light Scattering (DLS) probe.

The new DLS probe has been applied to characterize protein solutions and protein crystallization processes in NASA's flight hardware. It is quickly adaptable to various state-of-the-art ophthalmic instruments (e.g., slit-lamp and Scheimpflug imaging) presently in use at NEI/NIH. This modification pushes the envelope of cataract diagnosis from visual and photographic observations, to one that can be studied at the molecular level[2]. In diseases such as diabetes, early detection of lens changes may enable the identification of diabetes in several million people worldwide including several million Americans with undiagnosed diabetes. DLS also detects and quantifies the early changes associated with diabetes in the vitreous (a fluid in the back of the eye that occupies 80 percent volume of the eye globe). An inflammatory disease (uveitis) of the anterior chamber can be easily detected and quantified with DLS. This is an autoimmune disease like asthma, rheumatoid arthritis, chronic hepatitis, drying eye syndrome, and thyoriditis. Uveitis produces a higher number of protein particles in the anterior chamber (aqueous humor). This increase in concentration gives rise to increased scattered light intensity, that is easily quantified by the DLS probe.

Approximately 16 million Americans have diabetes mellitus (DM). DM causes severe visual impairment due to cataract formation (cataracts are 1.6 times more common in people with diabetes than those without diabetes), diabetic retinopathy (the most common cause of blindness in Americans aged 20 to 74 years), and glaucoma. Cataracts are 1.6 times more common in people with diabetes than in those without diabetes. In many cases, diabetes-related ocular pathologies go undiagnosed until visual function is compromised. In a joint project with FDA we are studying the progression of diabetes in a unique animal model by monitoring the changes in the lens using the DLS probe. The animals used in this study at FDA were desert rodents, commonly called the sand rat. The animal is unique in that it develops diabetes in a manner similar to humans. Thus far the results in the eye lens for a group of control animal and diabetic animal over a 3 month time period are very encouraging[8]. The DLS probe is able to discern subtle and diffusive changes in the lens. The shift in the size of the proteins can be seen in the lens during the initial stages of progression of diabetes in this animal model. Our preliminary results have also demonstrated subtle changes in the lens of the diabetic sand rats during the two months on diabetogenic diet. The minor changes over time seen in the control animals are attributed to age and instrument conditions are considered insignificant.

The deleterious effects of diabetes are not only limited to lens. Diabetes induces pathology throughout the human body via nonenzymatic glycation of proteins. We can study earlier changes through the vitreous. Vitreous is the largest structure within the eye occupying ~80 percent of the total ocular volume. Vitreous is 98 percent water, and contains the structural molecules hyaluronan and collagen. The subject of vitreous is covered in detail by Sebag[9]. Significant changes take place in

the diabetic vitreous at the molecular level. Rovati et al.[10], and Sebag et al.[11], have shown that detection of collagen cross-linking and aggregation using DLS provides useful insights into the diabetic eye disease prior to clinical observations of diabetic retinopathy. DLS can also be used to identify cholesterol deposits in the anterior chamber; an important parameter in assessing the cardiovascular health. When there is ocular involvement, these diseases can be detected by DLS and treated before the onset of irreversible damage.

Raman Spectroscopy:

In DLS or Rayleigh scattering described above elastic collisions take place between an incident photon and the scattering molecule. Thus the relative frequency shift (or energy exchange) in the scattered photons is very small. The Raman scattering is the result of inelastic collisions in which the scattered photons exchange energy with the vibrational energy modes of an atom. This frequency shift (or the difference in frequency of an incident photon and the scattered photon) points to a specific structural information about a constituent molecule analogous to a certain specific fingerprint which can identify any species present in the system being investigated. However, the Raman signal is very weak. Out of 10^6–10^{10} incident photons only 1 scattered photon exhibits a Raman shift. Because of this, the Raman method has remained limited to chemistry research laboratories, since its discovery in 1928. In the past 5 to 10 years, this scenario has started to change. Thanks to innovations in opto-electronics, Raman methods are being applied in real-world (industrial) settings[12] (see McCreery). Ophthalmic tissues should find Raman to be an attractive diagnostic probe because water is a poor Raman scatterer. Sebag et al.[13] used Raman spectroscopy to study human vitreous in proliferative diabetic retinopathy (PDR). They found Raman peaks corresponding to C=C and C-H bonds indicating non-enzymatic glycation in the diabetic vitreous. This important finding hinted that Raman can be applied to elucidate the molecular events underlying these abnormalities. Recently Bernstein[14] reported Raman measurements of macular caretonoid pigments in the human retina as an index to non-invasively diagnose age-related macular degeneration (AMD). He plans to begin clinical trials using Raman to monitor patient response to lutein and zeaxanthin supplementation to treat AMD. These natural substances are commonly found in green leafy vegetables (spinach, collard green, broccoli) and in yellow and orange colored fruits and vegetables (peaches, nectarines, persimmons, and corn). Recently Borchert et. al.[15], applied Raman to measure glucose levels in-vitro of both steady-state and rising rabbit aqueous humor levels . The Raman spectra of animal and human lenses has been discussed by Ozaki in her review article[16]. However, a substantial amount of work remains to be done for this method to be clinically viable. First, comprehensive spectral data libraries must be generated and established. It then can be used as searchable fingerprints (indices) for ocular and other diseases. This goal may be achievable in the not too distant future. In terms of engineering design, we can easily perform Raman measurements in our device using the DLS fiber optic probe (figure 1), by adding filters at the detector end, and replacing the digital autocorrelator with a multi-channel spectrum analyzer.

Laser Doppler Velocimetry (LDV):

As we indicated above the microgravity environment of space changes normal blood distribution in the body of a space traveler. If unchecked during long-duration space flights, this may cause severe abnormalities in blood flow to brain and eye and therefore may cause cerebral and ocular dysfunction. The human retina contains photoreceptors (cells in the form of rods and cones) that contain molecules of rhodopsin which detect light. About 6 million cones determine our ability to perceive detail (color, sharpness, etc.). The retina gets nutrients and removal of waste products via blood flowing through a vascular tissue (chorid) situated behind the retina. A slight decrease in the amount of blood flowing through the choroid, especially unchecked for longer periods of time, may impede the normal function of the retina and result in vision abnormalities. Recently Grunwald[17] has shown that in older patients AMD results in an accumulation of abnormal substances between the retina and the choroid. Grunwald et al.[18], using laser Doppler flowmetry, have shown decrease in choroidal blood flow due to aging. These important findings may indeed lead to treatment of AMD. No treatment (medical or surgical) for AMD is available in clinical practice at this point in time. New developments in opto-electronics have made innovative LDV systems useful in clinical ophthalmological settings. These have been reported by Geiser, et. al.[19], Yoshida, et al.[20], and Feke, et. al.[21]. Essentially LDV is an extension of the DLS technique. In a DLS experiment the diffusion due to the Brownian motion of the suspended particles in a fluid is monitored.

In LDV the particles are monitored as they flow through a laser beam allowing non-invasive, quantitative measurements of their velocity (or flow). At the center of the major retinal vessels (diameter 50 to 160 μm) the blood flow is typically in the range 0.01 to 10 mm/sec. This corresponds to a Doppler shift frequency in the range 20 Hz to 20 KHz. In our helmet/goggles configuration LDV measurements can be made by a fiber optic probe (figures 3 and 4), just like a DLS measurement, with the exception that a heterodyne scheme of detection is employed in which a portion of incident light beam (or a local oscillator) is mixed (or beat) with the scattered light at the photodetector. The local oscillator can simply be the reflection from the vessel wall. The analyzed data yields an average velocity or a distribution of red blood cell velocities.

Corneal Autofluorescence:

The human eye consists of different tissues exhibiting natural fluorescence. This phenomenon in the ocular tissue, known as autofluorescence (AF), has been found to increase with age in healthy individuals[22]. Accumulation of fluorescent proteins in ocular tissue can result from chronic exposure to the UV or UVA radiation in sunlight. This accumulation of fluorophores may also be responsible for lens opacification and can be considered a risk factor for cataract formation. Mars-bound astronauts will travel through space at least for three years (round-trip). During this long journey they may be exposed to high doses of UV/UVA radiation, and therefore, the AF level of their ocular tissue should be monitored. Studies of the AF properties of the ocular media have shown that ocular AF can be related to metabolic disorders[23,24]. Thus pre-pathological states can easily be studied by measuring AF intensity from the corneal tissue since it is readily accessible (no dilation drops needed) and its intensity is not age dependent. Corneal AF is mainly due to the pyridine nucleotides and flavoproteins found in the corneal epithelium and the endothelium. The accumulation of these fluorophores can be related to the severity or duration of some pathologies, and therefore the corneal AF can be exploited as a diagnostic index of this class of disorders. In particular, an increase in the corneal AF has been observed in the presence of early stage diabetic retinopathy (DR)[25] by using a novel instrument[26]. A picture of the prototype of this instrument is shown in figure 5a. The excitation light from two Blue LEDs passes through a suitable set of barrier filters and impinges tangentially on the patient cornea. The excitation light so obtained has a spectrum included between 460 and 480 nm. The fluorescence light from the cornea is collected axially using a camera objective. A suitable set of emission filters select the wavelengths of interest (500 to 540 nm). The fluorescence light signal is then converted to an electric signal using a photomultiplier tube. The AF data are recorded in sixteen measurement cycles during a period of 10 seconds and the average is calculated. Figure 5b shows the results of preliminary clinical test performed on about 90 diabetic subjects. An average increase of about 70 percent of the corneal AF between patients with negligible DR (grade 1) and with background DR (grade 2) was observed. Whereas, corneal AF mean value of patients with (pre-) proliferative DR (grade 3)shows a decrease of about 26 percent with respect to background DR (grade 2). These preliminary clinical data demonstrate that the method can be exploited to diagnose early stages of DR.

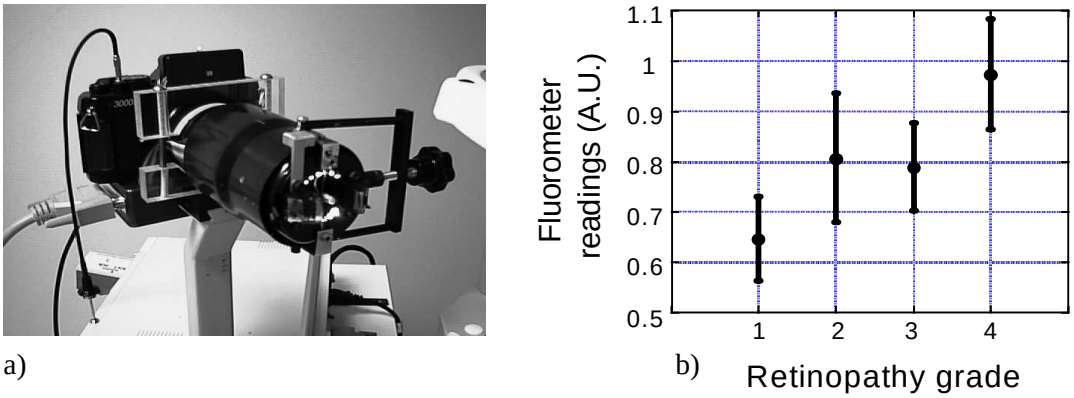


Figure 5.—a) Simple corneal fluorometer developed during a collaboration between the Biomedical optics group (University of Brescia, Italy) and the Ophthalmic clinic of Leiden (Leiden, Holland). b) results of a preliminary clinical test performed on about 90 diabetic subjects (the bars represent the standard error in the measurements).

Optical Activity Measurements for Blood Glucose Monitoring:

Certain objects possess chiral properties. For example, left and right hands are nonsuperimposable mirror images and thus are chiral objects. Glucose molecules being chiral are optically active. They rotate the plane of polarized light to right (clockwise)[27]. The rate of rotation is directly proportional to the amount of glucose present in a solution. The specific rotation $[\alpha]$ is given by $[\alpha] = \alpha/C.L$, where α is the actual rotation measured by an instrument called a polarimeter, C is the concentration (gm/mL), and L is the sample length (optical path length) in decimeters. The aqueous humor of the eye exhibits low scattering properties and its glucose concentration closely matches blood glucose levels[28]. Thus the polarimetric optical approach is attractive since the visible spectrum and significant path lengths in the anterior chamber of the eye can be used. Recently Cameron et al.[29], developed a polarimeter and measured glucose levels in vitro even in the presence of another optically active compound, albumin, which is also found in the aqueous. However, motion artifacts prevented in vivo glucose measurements from being made (see Klonoff)[30].

The working principle of a simple polarimeter suitable for making measurements in the aqueous humor is shown in figure 6. The light emitted by the unpolarized monochromatic optical source S is linearly polarized by the rotating polarizer Pr. Beam splitter BS deflects part of the excitation beam towards the reference analyzer which includes the polarizer P1 and the photodetector PD1. The remaining excitation beam is forwarded through the sample under test and is detected by the measurement analyzer, which includes the polarizer P2, and the photodetector PD2. If the angular speed of the polarizer Pr is constant, the intensity of light impinging onto the detectors PD1 and PD2 exhibits a sinusoidal trend. The relative phase between these sinus signals is proportional to the angle by which the light was rotated in the sample. This system is still being developed in collaboration (NASA/NCMR, Univ. of Brescia) and is in its infant stage of development[31]. We, however, do not anticipate using optical components such as mirrors and prisms or see any need for index matching in which the cornea has to touch the instrument surface, as experienced in previous investigation using conventional methods.

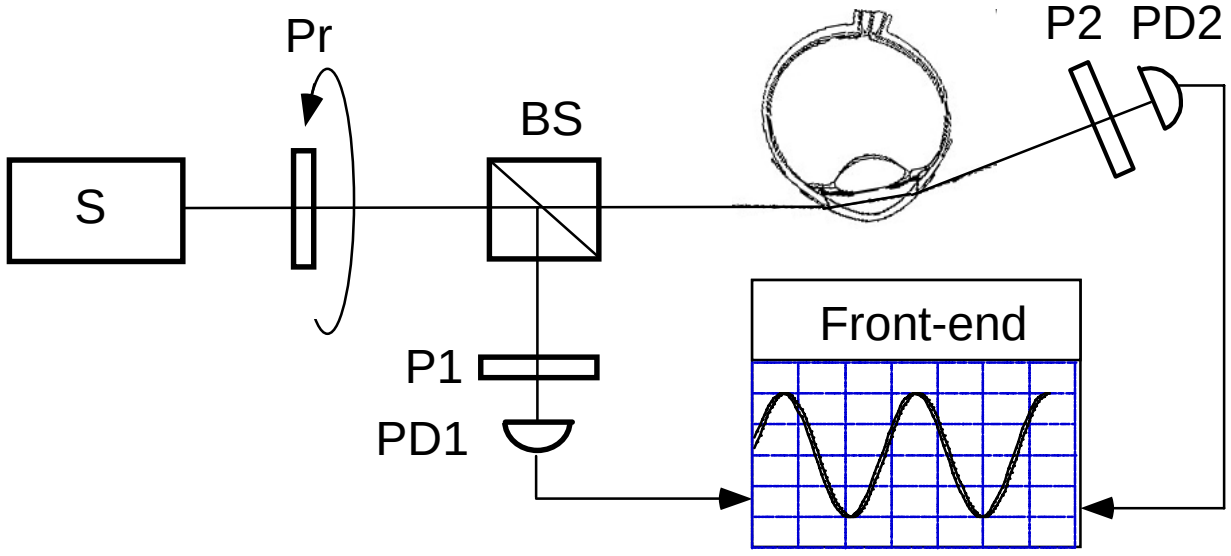


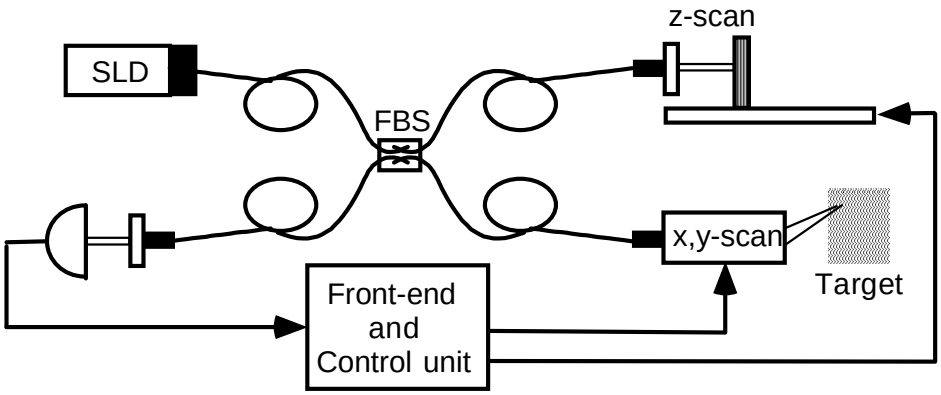
Figure 6.—Schematics of a blood glucose monitoring system.

Optical Coherence Tomography (OCT):

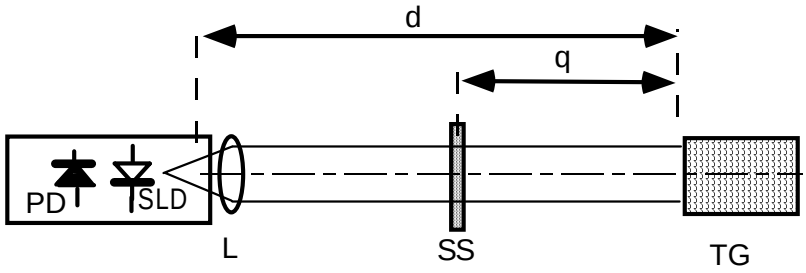
OCT is a near infrared optical ranging imaging technique. The images obtained by OCT are of much higher resolution (~1 μm) compared with images obtained by low frequency ultrasound, pulse-echo imaging. (~100 μm) . The two-dimensional image of optically reflecting and back scattering from tissue microstructure in OCT is constructed using low-coherence interferometry. Photons which have scattered multiple times (multiple scattering) are rejected by coherent detection because it takes advantage of short temporal coherence of broadband light source e.g. light emitting diodes (LED's). The interferometric system selects photons that have traveled a specific distance in the tissue. The beam scans turn the one dimensional depth profile into a two-dimensional image, to obtain retinal images. Huang, et al.[32], and Fercher, et al.[33], have shown that high resolution OCT images provide detection of subsurface retinal changes that are not seen by ophthalmologists in conventional settings. This is important in monitoring injury to the optic nerve from glaucoma. Most biological tissues highly scatter in the visible and near IR range.

In ophthalmology, OCT represents a novel, noninvasive, noncontact, transpupillary tool, which can image the fine anatomic structures within the eye, structures too fine to adequately assess by conventional techniques. Tomographic images of ocular tissues ranging from the cornea to retina have been obtained with a resolution in the order of few micrometers[34]. The appearance of a variety of anterior/posterior segment pathologies can be diagnosed using OCT including, cataract, glaucoma, diabetic retinopathy, macular holes, epiretinal membranes, cystoid macular edema, central serous choroidopathy and optic disc pits.

Our approach is to construct a low-cost OCT with fiber optic components. Using micromachining technique, even this system could be integrated in a goggles-like device, thus allowing fast, near real-time acquisition of tomographic images of the astronauts' ocular tissues. The simplest optical setup for OCT is shown in figure 7a. It comprises a Michelson interferometer with a variable optical path difference (OPD). The light emitted by the short coherent light source SLD is coupled into the optical 50/50-fiber coupler FBS. The reference arm length is modulated by the z-scanner that changes very quickly the OPD whereas, the object beam is scanned by two galvano scanners (x, y). Both, the reference beam and the light reflected back by the target, are mixed inside the coupler and are detected by the photodetector PD. By moving x, y, z - scanners, different planes of target satisfy equation OPD=0 and contribute to interference phenomena onto photodetector PD. Therefore, the target reflectance map can be reconstructed as a function of the scanning coordinates. An interesting OCT configuration, named self-mixing super-luminescent diode (SM-SLD), has been recently proposed[35]. Super-luminescent diodes (SLD) have a monitor photodiode placed in the same case of the optical source. This photodetector is generally used to monitor the optical power at the emitting junction back-face, in order to stabilize the emitted optical power. A different use of the monitor photodiode has been proposed: any light which is reflected back to the emitting junction causes a certain variation of the emitted optical power, and this variation can be detected using the monitor photodiode (SM-SLD). The basic setup of an interferometer based on SM-SLD is shown in figure 7b. In this interferometric scheme the light from the SLD is collimated by lens L. Part of the excitation light is back-reflected by a semireflecting slab SS. This light, such as the light reflected by TG, retraces the main beam back to the emitting junction causing a level variation of the emitted power. The beams reflected by TG and by SS do not interfere since their optical path difference (OPD) is much higher than the coherence length of the optical source.



a)



b)

Figure 7.—a) Standard fiber optic setup for OCT. b) Working principle of a OCT system based on a self-mixing superluminescent diode.

However, the emitting junction interface (semiconductor-air) provides a second reflection of the incoming beams which retrace again the main beam back to SS and TG. Interference phenomena in the emitting junction can be observed if d=2q [scattering wave vector $q = (4\pi n/\lambda)\sin(\theta/2)$]. The major advantages of the SM-SLD technique are that (i) the interference signal is optically amplified by the high-gain active medium, making its detection more simple and enhancing SNR, and (ii) a single device is used as emitter and detector making the system compact, stable and inexpensive. Preliminary test on biological tissue has been performed on a fly wing. Figure 8 shows the recovered map of reflectivity. X and Y are the two coordinates in the plane of the sample, whereas Z is the coordinate along the optical axis of the interferometer. Photograph of the wing was obtained by using a fiber optic microscope and the rectangle bounds (see inset) the inspection area in the (x, y) plane. The line in the rectangle defines the inspection area in the plane (x, z). Good agreement between the sample morphology and reflectivity map can be observed.

Figure 9 shows an OCT image of the anterior chamber of a bovine eye. Note that superb signal to noise ratio has been obtained using an optical power as low as 120μW.

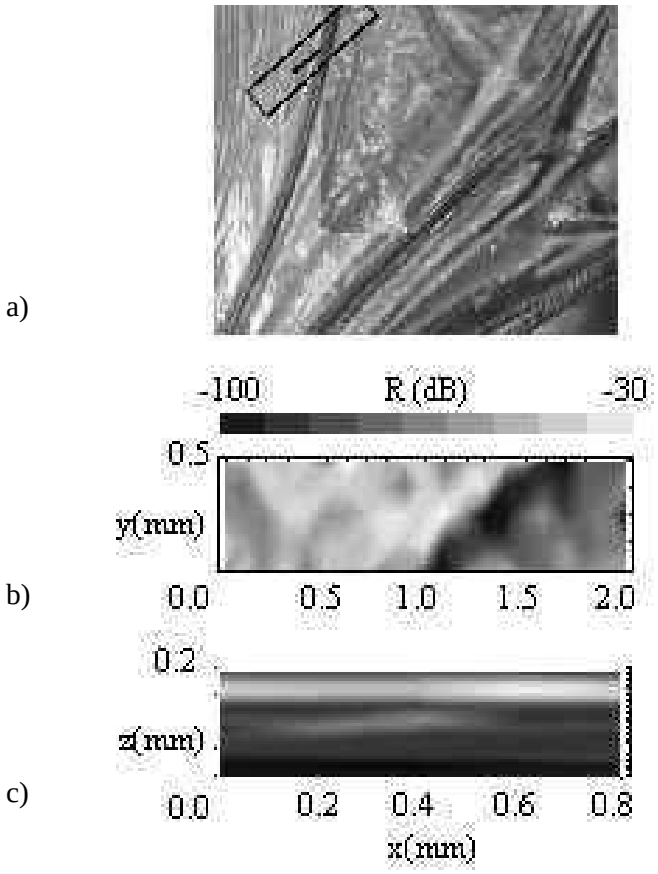


Figure 8.—Reflectivity maps: a) Fly wing. (b) and (c) are the reflective maps of the inset area of (a) in the x-y and x-z plane respectively. Image resolution is about 20 microns.

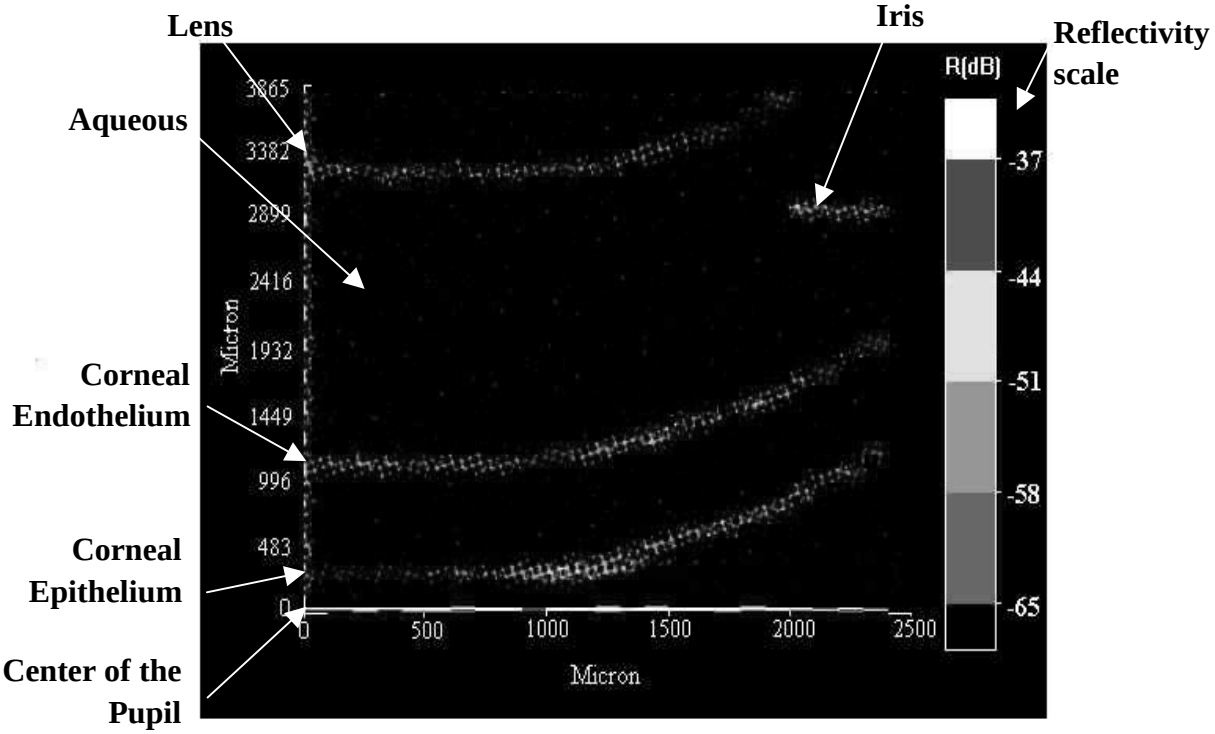


Figure 9.—OCT Image of a Bovine eye.

Scanning Laser Ophthalmoscope (SLO):

SLO is capable of imaging all ocular structures digitally. Visual function testing can be performed as a means of assessing not only ocular physiology, but central nervous system function as well. SLO's are available commercially. This device is being looked at for future inclusion and integration.

Reflectometry/Oximetry (OXM):

A non-invasive optoelectronic device based upon the effects of oxygen on light reflected from the fundus (inside of the back of the eye) has been developed by Delori[36,37,38]. Studies have shown that this approach can accurately quantify the degree of oxygenation in retinal arteriole of venial as well as the capillary plexus of the anterior optic nerve. such an approach would be useful as a method for evaluating the effects of prolonged from weightlessness on central nervous system circulatory physiology.

CONCLUSION

The eye is a window to the world for those of us who have the gift of sight. This paper shows that the eye is also the window to the body. Fully utilizing the opportunities provided by this fact promise great returns insofar as easily and accurately assessing health, and diagnosing departures for health early in the natural history of disease and thus to cure a number of potentially debilitating diseases. We have presented the concept of an advanced instrument which integrates a variety of non-invasive optical techniques that have been successfully demonstrated in clinical and/or laboratory tests. These techniques are readily interfaced with computer technology that by transmitting information from remote sites make tele-healthcare a reality. As our daring crew members explore the cosmos, this device will be available to monitor and help preserve their health.

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (*Leave blank*)	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	April 2000	Technical Memorandum

4. TITLE AND SUBTITLE

Monitoring Astronaut Health at the Nanoscale Cellular Level Through the Eye

5. FUNDING NUMBERS

WU–101–51–00–00

6. AUTHOR(S)

Rafat R. Ansari, Bhim S. Singh, Luigi Rovati, Franco Docchio, and Jerry Sebag

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

National Aeronautics and Space Administration
John H. Glenn Research Center at Lewis Field
Cleveland, Ohio 44135–3191

8. PERFORMING ORGANIZATION REPORT NUMBER

E–12243

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)

National Aeronautics and Space Administration
Washington, DC 20546–0001

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

NASA TM—2000-210041

11. SUPPLEMENTARY NOTES

Prepared for the Third Annual International Conference on Integrated Nano/Microtechnology for Space Applications sponsored by the Institute for Advanced Interdisciplinary Research, Houston, Texas, January 23–28, 2000. Rafat R. Ansari, National Center for Microgravity Research, 21000 Brookpark Road, Cleveland, Ohio 44135; Bhim S. Singh, NASA Glenn Research Center; Luigi Rovati and Franco Docchio, University of Brescia, Brescia, Italy; Jerry Sebag, Doheny Eye Institute, University of Southern California Medical School, 1975 Zonal Avenue, Los Angeles, California 90033–1039. Responsible person, Bhim S. Singh, organization code 6712, (216) 433–5008.

12a. DISTRIBUTION/AVAILABILITY STATEMENT

Unclassified - Unlimited
Subject Category: 12 Distribution: Nonstandard

This publication is available from the NASA Center for AeroSpace Information, (301) 621–0390.

12b. DISTRIBUTION CODE

13. ABSTRACT ***(Maximum 200 words)***

A user friendly goggles-like head-mounted device equipped with a suite of instruments for several non-invasive and quantitative medical evaluation of the eye, skin, and brain is desired for monitoring the health of astronauts during space travel and exploration of neighboring and distant planets. Real-time non-invasive evaluation of the different structures within the above organs can provide indices of the health of not just these organs, but the entire body. The techniques such as dynamic light scattering (for the early detection of uveitis, cholesterol levels, cataract, changes in the vitreous and possibly Alzheimer's disease), corneal autofluorescence (to assess extracellular matrix biology e.g., in diabetes), optical activity measurements (of anterior ocular fluid to evaluate blood-glucose levels), laser Doppler velocimetry (to assess retinal, optic nerve, and choroidal blood flow), reflectometry/oximetry (for assessing ocular and central nervous system oxygen metabolism), optical coherence tomography (to determine retinal tissue microstructure) and possibly scanning laser technology (for intraocular tissue imaging and scanning) will be integrated into this compact device. Skin sensors will also be mounted on the portion of the device in contact with the periocular region. This will enable monitoring of body temperature, EEG, and electrolyte status. This device will monitor astronaut health during long-duration space travel by detecting aberrations from pre-established "norms", enabling prompt diagnosis and possibly the initiation of early preventative/curative therapy. The non-invasive nature of the device technologies permits frequent repetition of tests, enabling real-time complete crew health monitoring. This device may ultimately be useful in tele-medicine to bring modern healthcare to under-served areas on Earth as well as in so-called "advanced" care settings (e.g. diabetes in the USA).

14. SUBJECT TERMS

Bio-astronautics; Space exploration; Optical diagnostics; Health

15. NUMBER OF PAGES

21

16. PRICE CODE

A03

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	