Raman Spectroscopy in Medicine

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Projects

Raman Detection of Carotenoid Pigments

Coherence Domain Optical Imaging

Photodynamic Therapy

Solid State Laser Development

Funding:

National Institute of Health

National Eye Institute

Research to Prevent Blindness, Inc.

Spectrotek, L.C.

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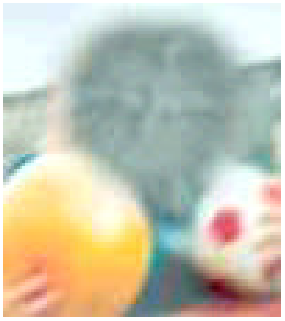
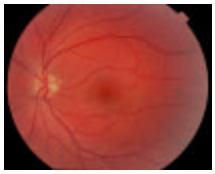
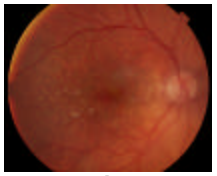
Age-related Macular Degeneration (AMD)





Healthy retina



Dry AMD

Wet AMD

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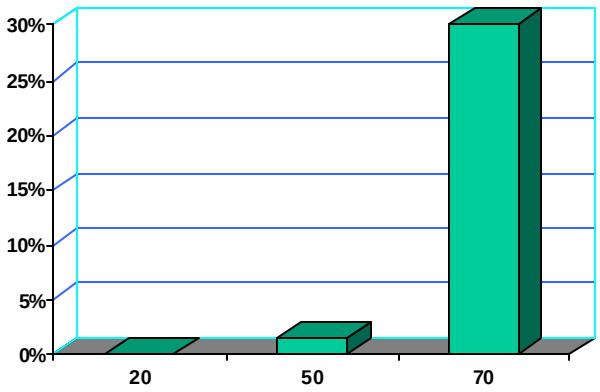
AMD Risk versus Age



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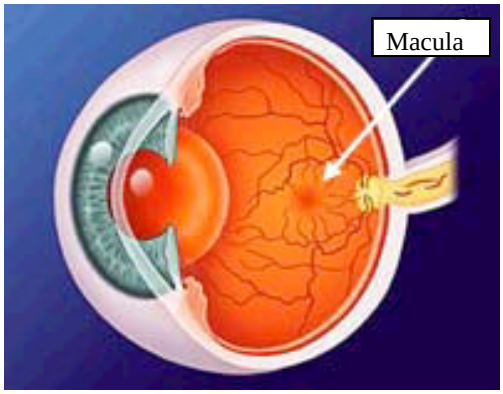
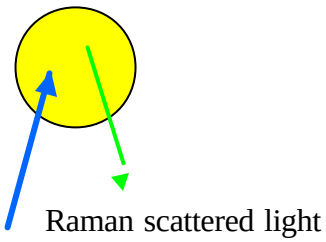
Carotenoids in Human Retina

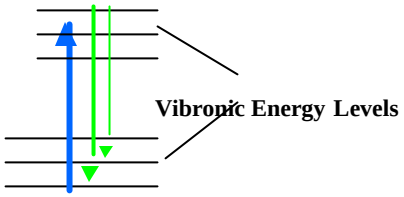
- **Macula: retinal area of highest visual acuity**
- **High concentrations of xanthophyll carotenoids lutein and zeaxanthin (yellow coloration)**
- **Role of carotenoids: optical filtering; antioxidants (protection of macula from light-induced damage)**
- **Individuals with high dietary intakes and blood levels of lutein and zeaxanthin have a lower rate of visual loss from age -related macular degeneration (AMD), the leading cause of blindness in the elderly.**



Raman Scattering

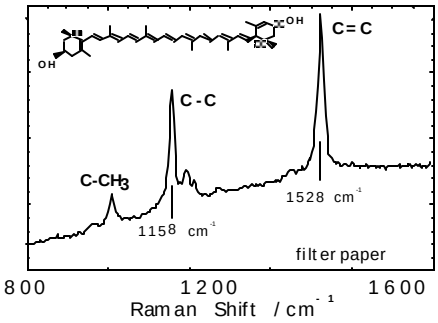
Sir Chandrasekhar Raman, Nobel Prize in Physics 1930





Carotenoid molecules shift blue laser light color to green

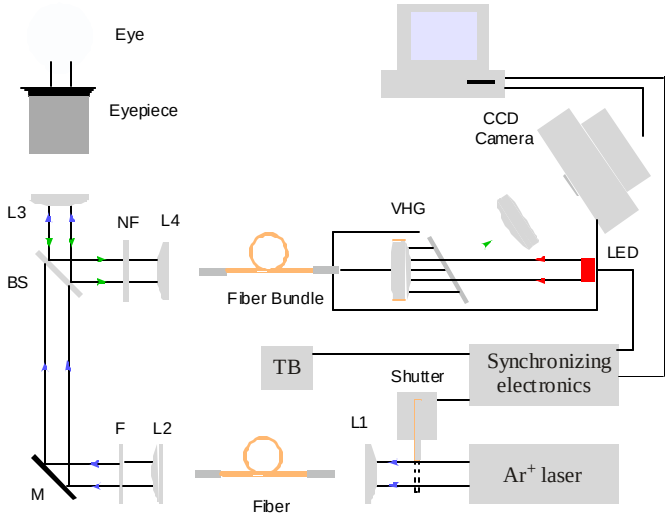
Raman Spectroscopy of Carotenoids



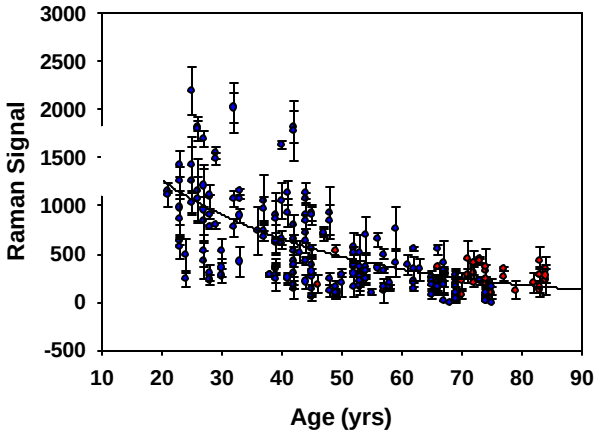
Carotenoids have a characteristic Raman spectral “fingerprint” generated from vibrations of their long carbon backbone.

Any other molecule would produce a different fingerprint (peaks with different locations and intensities)

Portable Clinical Raman Instrument



Loss of Macular Pigment with Increasing Age



Comparison of Health Screening Tests

Cholesterol Test	Heart Disease
PSA Test	Prostate Cancer
PAP Smear	Cervical Cancer
Mammography	Breast Cancer
Bone Density Test	Osteoporosis

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Carotenoids in other Tissues

Largest Organ of the Human Body ?

! Skin !

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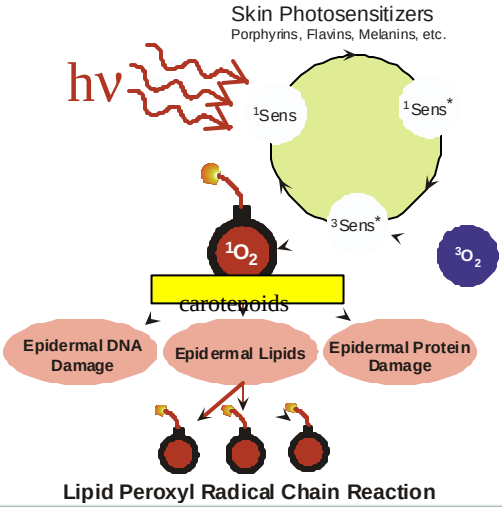
Sunlight - induced
Singlet Oxygen / Reactive Oxygen Species



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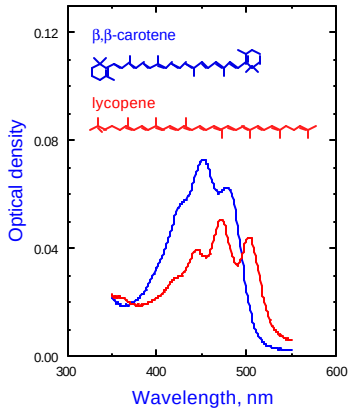
Lycopene and b -Carotene

- **Most potent singlet oxygen quenchers found in the human body**
- **Predominant carotenoids found in skin**
- **Lipophilic molecules making them especially well suited to act as chain-breaking antioxidants in the lipid-rich epidermis**
- **Resonant Raman spectroscopy for non-invasive detection ?**

Absorption



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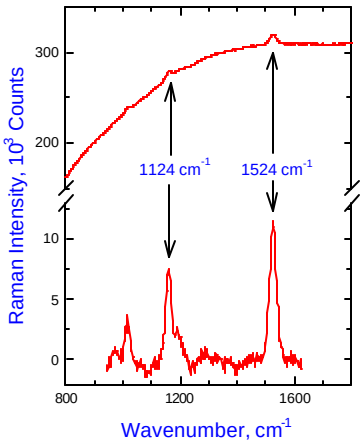
Raman Spectra of Human Skin Measured in Vivo



Typical Raman spectra for human ventral forearm skin, measured in vivo. Illumination conditions: 488 nm laser wavelength, 10 mW laser power, 20 sec exposure time, 2 mm spot size. Spectrum shown at top is spectrum obtained directly after exposure, and reveals broad, featureless, and strong fluorescence background of skin with superimposed sharp Raman peaks characteristic for carotenoid molecules. Spectrum at bottom is difference spectrum obtained after fitting fluorescence background with fifth-order polynomial and subtracting it from top spectrum. The main characteristic carotenoid peaks are clearly resolved with good signal-to-noise ratio, at 1159 and 1524 cm^{-1}.

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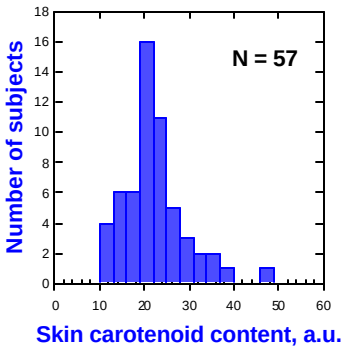
Non-Invasive Laser Raman Detection of Carotenoids in Human Skin

- **Feasible to assess carotenoid content in large numbers of subjects**
- **Permits study of correlation between disease and tissue antioxidant levels**
- **Also: Nutrition (bioavailability studies, uptakes, correlation with blood levels, etc.)**

Skin measurements GRC Ventura 2001



Summary

- **Measured carotenoid antioxidants in living human tissues in vivo using novel non-invasive optical method**
- **Sensitive, specific and precise optical technique**
- **Future use: Improve the health of the world with simple high-tech screening test**

Patents

US005873831A

United States Patent [19]
Bernstein et al.

[11] **Patent Number: 5,873,831**
[45] **Date of Patent: Feb. 23, 1999**

[54] **METHOD AND SYSTEM FOR MEASUREMENT OF MACULAR CAROTENOID LEVELS**

[75] Inventors: **Paul S. Bernstein**; **Werner Gellermann**; **Robert W. McClane**, all of Salt Lake City, Utah

[73] Assignee: **The University of Utah Technology Transfer Office**, Salt Lake City, Utah

[21] Appl. No.: **815,936**

[22] Filed: **Mar. 13, 1997**

[51] **Int. Cl.**[6] **A61B 6/00**
[52] **U.S. Cl.** **600/473**; 600/475; 600/476; 600/477; 600/310
[58] **Field of Search** 600/473, 476, 600/475, 477, 310, 318; 356/301, 303; 606/2–4, 10

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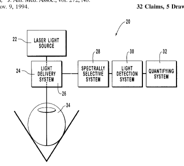
Primary Examiner—Brian Casler
Attorney, Agent, or Firm—Workman, Nydegger & Seeley

[57] **ABSTRACT**

The present invention is directed to a new and useful method and apparatus for use in determining the levels of macular pigments in the tissue of live subjects. Specifically, the method and apparatus of the present invention provide a non-invasive, rapid, and objective determination of the macular carotenoid levels, and in turn, offer valuable diagnostic information applicable to large populations. The present invention measures the levels of macular carotenoid pigments, as well as other retinal materials. Monochromatic laser light is projected onto a retina, preferably in the macular area. A very sensitive detection system then detects light scattered from the retina. The majority of the light is scattered elastically at the same wavelength of the laser in a manner known as Rayleigh scattering. A very small fraction of laser light is scattered inelastically at a wavelength different from that of the laser in a manner known as Raman scattering. The Raman scattered light is selected and then routed to a detection system, wherein the results are calibrated against actual standards for the particular retinal material being tested.

32 Claims, 5 Drawing Sheets



US006205354B1

(12) **United States Patent**
Gellermann et al.

(10) **Patent No.: US 6,205,354 B1**
(45) **Date of Patent: Mar. 20, 2001**

(54) **METHOD AND APPARATUS FOR NONINVASIVE MEASUREMENT OF CAROTENOIDS AND RELATED CHEMICAL SUBSTANCES IN BIOLOGICAL TISSUE**

(75) Inventors: **Werner Gellermann**; **Robert W. McClane**; **Nikita B. Katz**; **Paul S. Bernstein**, all of Salt Lake City, UT (US)

(73) Assignee: **University of Utah**, Salt Lake City, UT (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/335,932**

(22) Filed: **Jun. 18, 1999**

(51) **Int. Cl.**[7] **A61B 6/00**

(52) **U.S. Cl.** **600/477**; 356/301
(58) **Field of Search** 600/473, 476, 600/475, 477, 310, 318; 356/301, 303; 606/2–4, 10

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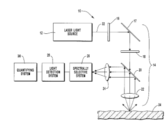
Primary Examiner—Brian L. Casler
(74) *Attorney, Agent, or Firm*—Workman, Nydegger & Seeley

(57) **ABSTRACT**

A method and apparatus are provided for the determination of levels of carotenoids and similar chemical compounds in biological tissue such as living skin. The method and apparatus provide a noninvasive, rapid, accurate, and safe determination of carotenoid levels which in turn can provide diagnostic information regarding cancer risk, or can be a marker for conditions where carotenoids or other antioxidant compounds may provide diagnostic information. Such early diagnostic information allows for the possibility of preventative intervention. The method and apparatus utilize the technique of resonance Raman spectroscopy to measure the levels of carotenoids and similar substances in tissue. In this technique, laser light is directed upon the area of tissue which is of interest. A small fraction of the scattered light is scattered inelastically, producing the carotenoid Raman signal which is at a different frequency than the incident laser light, and the Raman signal is collected, filtered, and measured. The resulting Raman signal can be analyzed such that the background fluorescence signal is subtracted and the results displayed and compared with known calibration standards.

32 Claims, 7 Drawing Sheets



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