

Raman Measurement of Carotenoids in Living Tissues

A validated method for determining meaningful aspects of human health

Over 50 full-length peer-review articles validate the use of Raman spectroscopy for the measurement of carotenoids in living tissues. Additional abstracts presented at scientific symposiums further confirm the validity of this method.

The Pharmanex BioPhotonic Scanner uses resonant Raman light to detect concentrations carotenoids in *intact* human skin as an indicator of nutritional intake and *in vivo* antioxidant status. Prior to being adapted for measurements in human skin, Raman resonance was validated for detection of carotenoid concentrations in *intact* human retinas (an indicator of macular health). Well over a dozen peer-reviewed articles have been published on the use of Raman spectroscopy to detect macular carotenoids *in vivo*. Raman spectroscopy has also been validated as an accurate measurement of skin carotenoid concentrations. Pharmanex has published three full-length studies in English, and an additional two full-length studies in Chinese (Chinese publications presented data that is entirely unique from data published in English journals; the Chinese papers are not simply translations of the English publications).

The Pharmanex BioPhotonic Scanner is highlighted in the highly respected textbook: *Krause's Food Nutrition and Diet Therapy* (12th Edition). It has also been given a complete chapter in the book *Carotenoids and Retinoids: Molecular Aspects and Health Issues*, which was edited by the distinguished Dr. Lester Packer (Father of the Antioxidants).

Pharmanex is not the only research group that has used and validated Raman spectroscopy for the measurement of skin carotenoid concentrations. Other research groups (all disinterested in Pharmanex, Nu Skin, or the sale of dietary supplements) have designed their own Raman spectrometers to measure skin carotenoids.

The following full-length studies are co-authored by at least one in-house Pharmanex scientist, and each of the following studies used the Pharmanex BioPhotonic Scanner:

1. Wood SM, Mastaloudis AF, Hester SN, Gray R, Kern D, Namkoong J, Draelos ZD. Protective effects of a novel nutritional and phytonutrient blend on ultraviolet radiation-induced skin damage and inflammatory response through aging defense mechanisms. *J Cosmet Dermatol*. 2017 Dec;16(4):491-499. Epub 2016 Nov 24. *Full-length article available at:* <http://onlinelibrary.wiley.com/doi/10.1111/jocd.12295/epdf>
2. Zidichouski JA, Mastaloudis A, Poole SJ, Reading JC, Smidt CR. Clinical validation of a noninvasive, Raman spectroscopic method to assess carotenoid nutritional status in humans. *J Am Coll Nutr*. 2009 Dec;28(6):687-93. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/20516269>
3. Bergeson SD, Peatross JB, Eyring NJ, Fralick JF, Stevenson DN, Ferguson SB. Resonance Raman measurements of carotenoids using light-emitting diodes. *J Biomed Opt*. 2008 Jul-Aug;13(4):044026. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/19021353>

4. Li CL, Bi SX, Zhu JS, Zhu ZG. New functions of carotenoids and clinical assessments. *Shanghai Journal of Preventive Medicine* 2006;6:261-264. [Article in Chinese] *No online abstract available.*
5. Li CL, Bi SX, Poole S, Smidt C, Zhu JS. Human Skin Carotenoids in 88,611 subjects measured by Biophotonic Scanner. *Chinese Journal of Clinical Pharmacy* 2006;15(2):124-125. [Article in Chinese] *No online abstract available.*

One review paper authored by Pharmanex scientists published as a full-length article:

6. Smidt, C.R., Burke, D.S. Nutritional Significance and Measurement of Carotenoids. *Current Topics in Nutraceutical Research*. 2004, Vol. 2, No. 2, pp. 79-91. Review.
Abstract at: <http://www.nchpjournals.com/journals/manuscript.php?msid=490#2>

The following publications are full-length studies conducted by third party research groups. Each of the studies used the Pharmanex BioPhotonic Scanner to measure skin carotenoids. Full-length versions can be purchased at the PubMed links provided below (abstracts available free of charge):

7. Li DG, LeCompte G, Golod L, Cecchi G, Irwin D, Harken A, Matecki A. Dermal carotenoid measurement is inversely related to anxiety in patients with breast cancer. *J Investig Med*. 2017 Sep 18. *Abstract at:* <https://www.ncbi.nlm.nih.gov/pubmed/28923881>
8. Wengreen HJ, Nix E, Madden GJ. The effect of social norms messaging regarding skin carotenoid concentrations among college students. *Appetite*. 2017 Sep 1;116:39-44. *Abstract at:* <https://www.ncbi.nlm.nih.gov/pubmed/28455259>
9. Spees CK, Hill EB, Grainger EM, Buell JL, White SE, Kleinhenz MD, Clinton SK. Feasibility, Preliminary Efficacy, and Lessons Learned From a Garden-Based Lifestyle Intervention for Cancer Survivors. *Cancer Control*. 2016 Jul;23(3):302-10. *Full-length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5097863/>
10. Janse VAN Rensburg A, Wenhold F. Validity and Reliability of Field Resonance Raman Spectroscopy for Assessing Carotenoid Status. *J Nutr Sci Vitaminol (Tokyo)*. 2016;62(5):317-321. *Abstract at:* <https://www.ncbi.nlm.nih.gov/pubmed/27928118/>
11. Perrone A, Pintaudi AM, Traina A, et al. Raman Spectroscopic Measurements of Dermal Carotenoids in Breast Cancer Operated Patients Provide Evidence for the Positive Impact of a Dietary Regimen Rich in Fruit and Vegetables on Body Oxidative Stress and BC Prognostic Anthropometric Parameters: A Five-Year Study. *Oxidative Medicine and Cellular Longevity*. 2016;2016:2727403. *Full-length article available free of charge at:* <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4861805/>

12. Aguilar SS, Wengreen HJ, Dew J. Skin Carotenoid Response to a High-Carotenoid Juice in Children: A Randomized Clinical Trial. *J Acad Nutr Diet*. 2015 Nov;115(11):1771-8. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/26254845>
13. Holt EW, Wei EK, Bennett N, Zhang LM. Low skin carotenoid concentration measured by resonance Raman spectroscopy is associated with metabolic syndrome in adults. *Nutr Res*. 2014 Sep 6. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/25249018>
14. Aguilar SS, Wengreen HJ, Lefevre M, Madden GJ, Gast J. Skin carotenoids: a biomarker of fruit and vegetable intake in children. *J Acad Nutr Diet*. 2014 Aug;114(8):1174-80. Epub 2014 Jun 18. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/24951435>
15. Ramírez-Vélez R, González-Ruiz K, García S, López-Alban CA, Escudero N, Agredo-Zúñiga RA. Non-invasive assessment of β -carotene levels in the skin of colombian adults. *Endocrinol Nutr*. 2012 Apr 13. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/22503818>
16. Rerksuppaphol S, Rerksuppaphol L. Carotenoid intake and asthma prevalence in Thai children. *Pediatr Rep*. 2012 Jan 2;4(1):e12. *Full-length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3357611/>
17. Richer SP, Stiles W, Graham-Hoffman K, Levin M, Ruskin D, Wrobel J, Park DW, Thomas C. Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration: The Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 973. *Optometry*. Nov 2011; 82(11) 667-680. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/22027699>
18. Lima XT, Kimball AB. Skin carotenoid levels in adult patients with psoriasis. *J Eur Acad Dermatol Venereol*. 2011 Aug;25(8):945-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21054574>
19. Harpenau LA, Cheema AT, Zingale JA, Chambers DW, Lundergan WP. Effects of nutritional supplementation on periodontal parameters, carotenoid antioxidant levels, and serum C-reactive protein. *J Calif Dent Assoc*. 2011 May;39(5):309-12, 314-8. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21721475>
20. Rerksuppaphol S, Rerksuppaphol L. Effect of fruit and vegetable intake on skin carotenoid detected by non-invasive Raman spectroscopy. *J Med Assoc Thai*. 2006 Aug;89(8):1206-12. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/17048431>

Book chapters or sections that discuss the Pharmanex BioPhotonic Scanner and related research:

21. *Carotenoids and Retinoids: Molecular Aspects and Health Issues*. Gellermann W, Zidichouski JA, Smidt CR, Bernstein PS. Raman Detection of Carotenoids in Human Tissue. In: Packer L, Obermueller-Jevic U, Kraemer K, and Sies H, eds. Champaign, IL: AOCS Press, 2005: Ch. 6, 86-114.
22. Mahan LK and Escott-Stump S. (Eds.). *Krause's Food, Nutrition and Diet Therapy*, 12th Ed. Philadelphia, PA: Saunders 2007; Ch. 15, 427-428.

Krause's Food & Nutrition Therapy has been considered one of the most authoritative nutrition texts for over 50 years worldwide. It provides a basic overview of nutrition as well as in-depth information on up-to-date nutrition therapies for medical conditions. Krause's is a text used by students in many allied health programs as well as other disciplines interested in the theoretical and clinical knowledge of the nutrition care process. It is commonly used as a reference for dietitians, nurses, doctors, dentists, life coaches, health educators and child development specialists.

Although Pharmanex (Nu Skin) owns exclusive rights for use of Raman spectroscopy in *for profit* settings, other research groups are permitted to develop their own Raman skin carotenoid devices for research purposes. The following studies use Raman spectroscopy to measure skin carotenoid concentrations. The Raman devices used in these studies were not the Pharmanex BioPhotonic Scanner. The fact that research groups other than Pharmanex (Nu Skin) have validated Raman measurement of skin carotenoids further confirms the legitimacy of this method. Full-length versions of the following studies can be purchased at the PubMed links provided below (abstracts available free of charge):

23. Conrady CD, Bell JP, Besch BM, Gorusupudi A, Farnsworth K, Ermakov I, Sharifzadeh M, Ermakova M, Gellermann W, Bernstein PS. Correlations Between Macular, Skin, and Serum Carotenoids. *Invest Ophthalmol Vis Sci*. 2017 Jul 1;58(9):3616-3627. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5520678/>
24. Beccarelli LM, Scherr RE, Dharmar M, Ermakov IV, Gellermann W, Jahns L, Linnell JD, Keen CL, Steinberg FM, Young HM, Zidenberg-Cherr S. Using Skin Carotenoids to Assess Dietary Changes in Students After 1 Academic Year of Participating in the Shaping Healthy Choices Program. *J Nutr Educ Behav*. 2017 Jan;49(1):73-78.e1. *Abstract at:* <https://www.ncbi.nlm.nih.gov/pubmed/28341018>
25. Nguyen LM, Scherr RE, Ermakov IV, Gellermann W, Jahns L, Keen CL, Miyamoto S, Steinberg FM, Young HM, Zidenberg-Cherr S. Evaluating the relationship between plasma and skin carotenoids and reported dietary intake in elementary school children to assess fruit and vegetable intake. *Arch Biochem Biophys*. 2015 Mar 9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/25765187>

26. Jahns L, Johnson LK, Mayne ST, Cartmel B, Picklo MJ Sr, Ermakov IV, Gellermann W, Whigham LD. Skin and plasma carotenoid response to a provided intervention diet high in vegetables and fruit: uptake and depletion kinetics. *Am J Clin Nutr.* 2014 Sep;100(3):930-7. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/25008856>
27. Darwin ME, Richter H, Ahlberg S, Haag SF, Meinke MC, Le Quintrec D, Doucet O, Lademann J. Influence of sun exposure on the cutaneous collagen/elastin fibers and carotenoids: negative effects can be reduced by application of sunscreen. *J Biophotonics.* 2014 Mar 18. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/24639418>
28. Ermakov IV, Ermakova MR, Rosenberg TD, Gellermann W. Optical detection of carotenoid antioxidants in human bone and surrounding tissue. *J Biomed Opt.* 2013 Nov 1;18(11):117006. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/24213478>
29. Ermakov IV, Ermakova MR, Bernstein PS, Chan GM, Gellermann W. Resonance Raman based skin carotenoid measurements in newborns and infants. *J Biophotonics.* 2013 Oct;6(10):793-802. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/23193015>
30. Mayne ST, Cartmel B, Scarmo S, Jahns L, Ermakov IV, Gellermann W. Resonance Raman spectroscopic evaluation of skin carotenoids as a biomarker of carotenoid status for human studies. *Arch Biochem Biophys.* 2013 Jun 30. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3818359/>
31. Chan GM, Chan MM, Gellermann W, Ermakov I, Ermakova M, Bhosale P, Bernstein P, Rau C. Resonance Raman spectroscopy and the preterm infant carotenoid status. *J Pediatr Gastroenterol Nutr.* 2013 May;56(5):556-9. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115129/>
32. Scarmo S, Cartmel B, Lin H, Leffell DJ, Ermakov IV, Gellermann W, Bernstein PS, Mayne ST. Single v. multiple measures of skin carotenoids by resonance Raman spectroscopy as a biomarker of usual carotenoid status. *Br J Nutr.* 2013 Sep;110(5):911-7. *Full length article available free of charge at:* <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3696054/>
33. Darwin ME, Sandhagen C, Koecher W, Sterry W, Lademann J, Meinke MC. Comparison of two methods for noninvasive determination of carotenoids in human and animal skin: Raman spectroscopy versus reflection spectroscopy. *J Biophotonics.* 2012 Jan 23. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/22271669>
34. Fluhr JW, Sassning S, Lademann O, Darwin ME, Schanzer S, Kramer A, Richter H, Sterry W, Lademann J. In vivo skin treatment with tissue-tolerable plasma influences skin physiology and antioxidant profile in human stratum corneum. *Exp Dermatol.* 2012 Feb;21(2):130-4. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/22142271>
35. Scarmo S, Henebery K, Peracchio H, Cartmel B, Lin H, Ermakov IV, Gellermann W, Bernstein PS, Duffy VB, Mayne ST. Skin carotenoid status measured by resonance Raman spectroscopy

as a biomarker of fruit and vegetable intake in preschool children. *Eur J Clin Nutr.* 2012 May;66(5):555-60. *Full length article available free of charge at:*
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3380427/>

36. Vierck HB, Darvin ME, Lademann J, Reißhauer A, Baack A, Sterry W, Patzelt A. The influence of endurance exercise on the antioxidative status of human skin. *Eur J Appl Physiol.* 2012 Jan 22. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/22270481>
37. Darvin ME, Fluhr JW, Meinke MC, Zastrow L, Sterry W, Lademann J. Topical beta-carotene protects against infra-red-light-induced free radicals. *Exp Dermatol.* 2011 Feb;20(2):125-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21255091>
38. Darvin ME, Fluhr JW, Schanzer S, Richter H, Patzelt A, Meinke MC, Zastrow L, Golz K, Doucet O, Sterry W, Lademann J. Dermal carotenoid level and kinetics after topical and systemic administration of antioxidants: enrichment strategies in a controlled in vivo study. *J Dermatol Sci.* 2011 Oct;64(1):53-8. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21763110>
39. Darvin ME, Haag SF, Meinke MC, Sterry W, Lademann J. Determination of the influence of IR radiation on the antioxidative network of the human skin. *J Biophotonics.* 2011 Jan;4(1-2):21-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/20151398>
40. Dayan SH, Arkins JP, Sharma V, Paterson E, Barnes D. A phase 2, double-blind, randomized, placebo-controlled trial of a novel nutritional supplement product to promote healthy skin. *J Drugs Dermatol.* 2011 Oct;10(10):1106-14. *Abstract at:*
<http://www.ncbi.nlm.nih.gov/pubmed/21968660>
41. Fluhr JW, Caspers P, van der Pol JA, Richter H, Sterry W, Lademann J, Darvin ME. Kinetics of carotenoid distribution in human skin in vivo after exogenous stress: disinfectant and wIRA-induced carotenoid depletion recovers from outside to inside. *J Biomed Opt.* 2011 Mar;16(3):035002. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21456863>
42. Haag SF, Taskoparan B, Darvin ME, Groth N, Lademann J, Sterry W, Meinke MC. Determination of the antioxidative capacity of the skin in vivo using resonance Raman and electron paramagnetic resonance spectroscopy. *Exp Dermatol.* 2011 Jun;20(6):483-7. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21366704>
43. Lademann J, Meinke MC, Sterry W, Darvin ME. Carotenoids in human skin. *Exp Dermatol.* 2011 May;20(5):377-82. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/21366698>
44. Lademann J, Schanzer S, Meinke M, Sterry W, Darvin ME. Interaction between carotenoids and free radicals in human skin. *Skin Pharmacol Physiol.* 2011;24(5):238-44. *Abstract at:*
<http://www.ncbi.nlm.nih.gov/pubmed/21447993>

45. Darvin ME, Haag S, Meinke M, Zastrow L, Sterry W, Lademann J. Radical production by infrared A irradiation in human tissue. *Skin Pharmacol Physiol*. 2010;23(1):40-6. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/20090407>
46. Ermakov IV, Gellermann W. Validation model for Raman based skin carotenoid detection. *Arch Biochem Biophys*. 2010 Dec 1;504(1):40-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/20678465>
47. Meinke MC, Darvin ME, Vollert H, Lademann J. Bioavailability of natural carotenoids in human skin compared to blood. *Eur J Pharm Biopharm*. 2010 Oct;76(2):269-74. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/20558286>
48. Scarmo S, Cartmel B, Lin H, Leffell DJ, Welch E, Bhosale P, Bernstein PS, Mayne ST. Significant correlations of dermal total carotenoids and dermal lycopene with their respective plasma levels in healthy adults. *Arch Biochem Biophys*. 2010 Dec 1;504(1):34-9. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957565/>
49. Mayne ST, Cartmel B, Scarmo S, Lin H, Leffell DJ, Welch E, Ermakov I, Bhosale P, Bernstein PS, Gellermann W. Noninvasive assessment of dermal carotenoids as a biomarker of fruit and vegetable intake. *Am J Clin Nutr*. 2010 Oct;92(4):794-800. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3133234/>
50. Blume-Peytavi U, Rolland A, Darvin ME, Constable A, Pineau I, Voit C, Zappel K, Schäfer-Hesterberg G, Meinke M, Clavez RL, Sterry W, Lademann J. Cutaneous lycopene and beta-carotene levels measured by resonance Raman spectroscopy: high reliability and sensitivity to oral lactycopene deprivation and supplementation. *Eur J Pharm Biopharm*. 2009 Sep;73(1):187-94. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/19442725>
51. Darvin ME, Fluhr JW, Caspers P, van der Pool A, Richter H, Patzelt A, Sterry W, Lademann J. In vivo distribution of carotenoids in different anatomical locations of human skin: comparative assessment with two different Raman spectroscopy methods. *Exp Dermatol*. 2009 Dec;18(12):1060-3. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/19650865>
52. Hesterberg K, Lademann J, Patzelt A, Sterry W, Darvin ME. Raman spectroscopic analysis of the increase of the carotenoid antioxidant concentration in human skin after a 1-week diet with ecological eggs. *J Biomed Opt*. 2009 Mar-Apr;14(2):024039. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/19405767>
53. Darvin M, Patzelt A, Gehse S, Schanzer S, Benderoth C, Sterry W, Lademann J. Cutaneous concentration of lycopene correlates significantly with the roughness of the skin. *Eur J Pharm Biopharm*. 2008 Aug;69(3):943-7. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/18411044>
54. Darvin ME, Patzelt A, Knorr F, Blume-Peytavi U, Sterry W, Lademann J. One-year study on the variation of carotenoid antioxidant substances in living human skin: influence of dietary

supplementation and stress factors. J Biomed Opt. 2008 Jul-Aug;13(4):044028. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/19021355>

55. Shao YH, He YH, Ma H, Nan N, Qian LS, Wang SX. [Carotenoid levels measured by resonance Raman in vivo]. Guang Pu Xue Yu Guang Pu Fen Xi. 2007 Nov;27(11):2258-61. Chinese. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/18260408>
56. Darwin M, Schanzer S, Teichmann A, Blume-Peytavi U, Sterry W, Lademann J. [Functional food and bioavailability in the target organ skin]. Hautarzt. 2006 Apr;57(4):286, 288-90. German. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/16485123>
57. Ermakov IV, Sharifzadeh M, Ermakova M, Gellermann W. Resonance Raman detection of carotenoid antioxidants in living human tissue. J Biomed Opt. 2005 Nov-Dec;10(6):064028. Review. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086339/>
58. Ermakov, I.V. Ermakova, M.R., Gellermann, W., Lademann, J. Noninvasive selective detection of lycopene and beta-carotene in human skin using Raman spectroscopy. J Biomed Opt. 2004 Mar;9(2):332-8. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/15065899>
59. Gellermann, W., Ermakov, I.V., Scholz, T.A. and Bernstein, P. S. Noninvasive laser Raman detection of carotenoid antioxidants in skin. Cosmetic Dermatology 2002;15(9):65-68. [*no online abstract available*]
60. Ermakov IV, Ermakova MR, McClane RW, Gellermann W. et al. Resonance Raman detection of carotenoid antioxidants in living human tissues. Optics Letters 2001;26:1179-1181. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/18049555>
61. Hata TR, Scholz TA, Ermakov IV, McClane RW, Khachik F, Gellermann W, Pershing LK. Non-invasive raman spectroscopic detection of carotenoids in human skin. J Invest Dermatol. 2000 Sep;115(3):441-8. *Abstract at:* <https://www.ncbi.nlm.nih.gov/pubmed/10951281>

Raman spectroscopy in the Eye

Prior to being adapted for measurements in human skin, Raman resonance was validated for detection of carotenoid concentrations in intact human retinas (an indicator of macular health). Well over a dozen full-length peer-reviewed articles have been published on the use of Raman spectroscopy to detect macular carotenoids. Many of the following full-length articles are available free of charge; all other links provide PubMed abstracts from which full-length articles may be purchased:

62. Bernstein PS, Ahmed F, Liu A, Allman S, Sheng X, Sharifzadeh M, Ermakov I, Gellermann W. Macular Pigment Imaging in AREDS2 Participants: An Ancillary Study of AREDS2 Subjects Enrolled at the Moran Eye Center. Invest Ophthalmol Vis Sci. 2012 Sep 14;53(10):6178-86. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3444209/>

63. Ward MS, Zhao da Y, Bernstein PS. Macular and serum carotenoid concentrations in patients with malabsorption syndromes. *J Ocul Biol Dis Infor.* 2008 Mar;1(1):12-8. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2600549/>
64. Sharifzadeh M, Zhao DY, Bernstein PS, Gellermann W. Resonance Raman imaging of macular pigment distributions in the human retina. *J Opt Soc Am A Opt Image Sci Vis.* 2008 Apr;25(4):947-57. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079576/>
65. Ermakov IV, Ermakova MR, Gellermann W. Simple Raman instrument for in vivo detection of macular pigments. *Appl Spectrosc.* 2005 Jul;59(7):861-7. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079574/>
66. Neelam, K.; O’Gorman, N.; Nolan, J.; O’Donovan, O.; Wong, H.B.; Au Eong, K.G. and Beatty, S. Measurement of Macular Pigment: Raman Spectroscopy versus Heterochromatic Flicker Photometry. *Invest Ophthalmol Vis Sci* 2005;46(3):1023-1032. *Full length article available free of charge at:* <http://www.iovs.org/cgi/reprint/46/3/1023>
67. Ermakov I, Ermakova M, Gellermann W, Bernstein PS. Macular pigment Raman detector for clinical applications. *J Biomed Opt* 2004; 9(1):139–48. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3086335/>
68. Bernstein PS, Zhao DY, Sharifzadeh M, Ermakov IV, Gellermann W. Resonance Raman measurement of macular carotenoids in the living human eye. *Arch Biochem Biophys* 2004;15;430(2):163-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/15369814>
69. Gellermann, W., Bernstein PS. Noninvasive detection of macular pigments in the human eye. *J Biomed Opt.* 2004 Jan-Feb;9(1):75-85. *Review. Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/14715058>
70. Zhao DY, Wintch SW, Ermakov IV, Gellermann W, Bernstein PS. Resonance Raman measurement of macular carotenoids in retinal, choroidal, and macular dystrophies. *Arch Ophthalmol* 2003;121(7):967-72. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/12860799>
71. Gellermann, W., Ermakov, I.V., McClane, R.W. Raman imaging of human macular pigments. *Optics Letters* 2002; 27(1):833–835. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/18007943>
72. Gellermann W, Ermakov IV, Ermakova MR, McClane RW, Zhao DY, Bernstein PS. *In vivo* resonant Raman measurement of macular carotenoid pigments in the young and the aging human retina. *J Opt Soc Am A Opt Image Sci Vis.* 2002;19(6):1172-86. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/12049355>
73. Bernstein PS, Zhao DY, Wintch SW, Ermakov IV, McClane RW, Gellermann W. Resonance Raman measurement of macular carotenoids in normal subjects and in age-related macular

degeneration patients. *Ophthalmology* 2002;109(10):1780-7. *Full length article available free of charge at:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3079575/>

74. Bernstein, P.S., Gellermann W. Measurement of carotenoids in the living primate eye using resonance Raman spectroscopy. *Methods Mol Biol.* 2002;196:321-9. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/12152212>
75. Bernstein, P.S. New insights into the role of the macular carotenoids in age-related macular degeneration. *Resonance Raman studies. Pure and Applied Chemistry* 2002;74(8):1419-1425. *Full length article available free of charge at:* <http://www.iupac.org/publications/pac/2002/pdf/7408x1419.pdf>
76. Ermakov IG, McClane RW, Gellermann W. Resonant Raman detection of macular pigments in the living human retina. *Optics Letters* 2001;26(4):202–204. *Abstract at:* <http://www.ncbi.nlm.nih.gov/pubmed/18033547>
77. Bernstein PS, Yoshida MD, Katz NB, McClane RW, Gellermann W. Raman detection of macular carotenoid pigments in intact human retina. *Invest Ophthalmol Vis Sci* 1998;39(11):2003-11. *Full length article available free of charge at:* <http://www.iovs.org/cgi/reprint/39/11/2003>

The following are available as abstracts only (with the exception of Wengreen 2010 which is available as a poster). **The tool used to measure skin carotenoids was the Pharmanex BioPhotonic Scanner:**

78. E.Hill, S.Clinton, E.Grainger, M.Belury, R.Kopec, M.Failla, G.Young, C.Spees. *Journal of the Academy of Nutrition and Dietetics.* Volume 117, Issue 9, Supplement, September 2017, Page A19 October, 2017. *Biobehavioral Intervention Improves Dietary Patterns and Biomarkers of Carotenoid and Fatty Acid Intakes in Overweight Cancer Survivors.* *Abstract at:* <https://doi.org/10.1016/j.jand.2017.06.350>
79. A.Braun, J.Portner, E.Grainger, E.Hill, G.Young, S.Clinton, C.Spees. *Journal of the Academy of Nutrition and Dietetics.* Volume 117, Issue 9, Supplement, September 2017, Page A23. *Electronic Motivational Interviewing Coaching for Overweight Cancer Survivors Improves Health Outcomes* *Abstract at:* <https://doi.org/10.1016/j.jand.2017.06.243>
80. E. Hill, S. Clinton, E. Grainger, A. Braun, N. Moran, E. Fitz, C. Chitchumroonchokchai, M. Failla, C. Spees. *Growing Hope: A Comprehensive Lifestyle Intervention Increases Fruit and Vegetable Intake and Carotenoid Status in Overweight Cancer Survivors.* *Journal of the Academy of Nutrition and Dietetics.* September 2016 Volume 116, Issue 9, Supplement, Page A82. *Abstract at:* <http://dx.doi.org/10.1016/j.jand.2016.06.290>
81. Hill EB, Clinton SK, Grainger EM, Braun AC, Moran NE, Fitz EA, Chitchumroonchokchai C, Failla ML, Spees CK. *Growing Hope: Comprehensive Lifestyle Intervention Increases Fruit and Vegetable Intake and Carotenoid Status in Overweight Cancer Survivors.* Presented at 13th

Annual Russell Klein Nutrition Research Symposium, Ohio State University March 3, 2016. *[no online abstract available]*

82. Schmitz AM, Grainger EM, Simpson C, Young G, Clinton SK. Validation of a Novel, Targeted Food Frequency Questionnaire to Estimate Dietary Carotenoid Intake. Presented at 13th Annual Russell Klein Nutrition Research Symposium, Ohio State University March 3, 2016. *[no online abstract available]*
83. Wengreen H, Aguilar S, Lefevre M. Skin Carotenoids as a Biomarker of Fruit and Vegetable Intake in Children. Presented at American Dietetic Association's Food & Nutrition Conference & Expo. Boston, Ma. November 6-9, 2010. *[no online abstract available]*
84. Duan L, Lu J, Li G, Zhu JS. Improvement of Skin Carotenoids Antioxidant Scores with G3 Drink and LifePak is affected by Endurance Training Intensity in Young Athletes. FASEB J. 2009 23:1007.3. *Abstract at:* http://www.fasebj.org/doi/10.1096/fasebj.23.1_supplement.1007.3
85. Wood SM, Mastaloudis A, Carlson J, Zidichouski JA, Holubkov R, Reading J, Stavens S, Askew EW, Morrow JD, Milne GL, Poole SL, Bartlett M. Consistency of correlations of serum and skin carotenoids as measured by high performance liquid chromatography and Raman spectroscopy. Presented at 15th International Symposium on Carotenoids, Okinawa Japan, June 2008. *[no online abstract available]*
86. Bi SX, Li CL, Guo HW, Poole SL, Zhu JS. The effects of lifestyles and LifePak on human skin carotenoids scores measured by resonance Raman spectroscopy BioPhotonic Scanner. FASEB Journal 2007;21(4):A709. *Abstract at:* <http://www.fasebj.org/doi/10.1096/fasebj.21.5.A709>
87. Carlson J, Stavens S, Holubkav R, Zidichouski J, Mastaloudis A, Smidt CR. and Askew, E. Associations of Antioxidant Status, Oxidative Stress, with Skin Carotenoids Assessed by Raman Spectroscopy (RS). Experimental Biology meeting abstracts. FASEB Journal 20: A824.3; 2006. *Abstract at:* <http://www.fasebj.org/doi/10.1096/fasebj.20.5.A1318-c>
88. Li CL, Guo HW, Bi SX, Zhu, ZG, Zhu JS. Skin Carotenoids Measured by Resonance Raman Spectroscopy BioPhotonic Scanner and the Effects of Life Styles and LifePak on Human Carotenoids Nutritional Status and Skin Scores. Asian Pacific Journal of Clinical Nutrition 2006;15(Suppl.):S79. *Abstract at:* http://apjcn.nhri.org.tw/server/APJCN/15/vol15apcns/IUNS-APCNS2006_HEC.pdf (see page 92 out of 207 of the linked PDF)
89. Stavens S, Carlson J, Holubkav R, Zidichouski J, Mastaloudis A, Smidt CR. and Askew, E. Associations of Fruit and Vegetable Intake with Serum Carotenoids and Skin Carotenoids Measured with Raman Spectroscopy (RS). FASEB Journal 20: A669.4;2006. *Abstract at:* <http://www.fasebj.org/doi/10.1096/fasebj.20.5.A1058-d>
90. Zukley LM, Nguyen V, Lowndes J, Smidt C, Angelopoulos TJ, Rippe JM, Effects of antioxidant supplementation on skin and serum carotenoids, FASEB Journal 2006;20:A145. *Abstract at:* <http://www.fasebj.org/doi/10.1096/fasebj.20.4.A145-a>

91. Zukley LM, Lowndes J, Greenstone CL, Melton R, Nguyen V, T J Angelopoulos, Rippe JM. Assessment of The Relationship Between Oxidative Stress, Antioxidant Status, Inflammation And Cardiorespiratory Fitness In The Obese. *Medicine & Science in Sports & Exercise*: May 2005. 37(5); pS385. http://journals.lww.com/acsm-msse/Fulltext/2005/05001/Assessment_Of_The_Relationship_Between_Oxidative.1991.aspx
92. Fiutem J, Zukley L, Geise T, Legowski P, Nguyen V, Dube T, Yount B, Smidt C, Angelopoulos T, Rippe J. Adiposity Negatively Influences Carotenoids and Antioxidant Status in Overweight Individuals. *Medicine and Science in Sports and Exercise*. 36 (5) Supplement S302, 2004. *[no online abstract available]*
93. Smidt, C.R., Gellermann, W., Zidichouski, J.A. Non-invasive Raman spectroscopy measurement of human carotenoid status. *Pharmanex Research Institute. FASEB* 18(4):A480, 2004. *[no online abstract available]*
94. Zidichouski, J.A., Poole, S.L., Gellermann, W. Smidt, C.R. (2004) Clinical validation of a novel Raman spectroscopic technology to non-invasively assess carotenoid status in humans. *Journal of Am. Coll. Nutr.* 23 (5): p.468. *[no online abstract available]*
95. Zukley L, Legowski P, Nguyen V, Geise T, Lowndes J, Melanson K, Angelopoulos T, Rippe J. The Effect of Weight Loss on Dietary Carotenoid and Skin Carotenoid Levels in Subjects Participating in a Weight Loss Study. *Obesity Research Suppl* 2004;12:A57. *[no online abstract available]*
96. Smidt C.R. and Shieh D. Non-invasive biophotonic assessment of skin carotenoids as a biomarker of human antioxidant status. *FASEB J* 2003, 17 (5): A1115. *[no online abstract available]*