Tudományos közlemények a biofoton szkenner szerepéről

Összefoglalás
A Raman féle spektroszkópia elvén a bőr karotin típusú vitaminjainak koncentrációja nagy biztonsággal megmérhető.
A bőr karotin koncentrációja párhuzamosan korrelál a szervezet totális antioxidáns kapacitásával.
A bőr karotenoid koncentráció párhuzamosan korrelál a táplálkozás minőségével (zöldség és gyümölcsfogyasztás)
Következésképp: a szkenner olcsó, pontos, kíméletes, gyors módszer a táplálkozás minőségének és a szervezet antioxidáns kapacitásának szűrésére, az oxidatív stressz kimutatására, az életmódi változtatások, az antioxidáns táplálék-kiegészítők hatásának nyomonkövetésére.

1. Associations of Antioxidant Status, Oxidative Stress, with Skin Carotenoids Assessed by Raman Spectroscopy (RS)

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We evaluated the associations of: 1) human skin carotenoids measured by RS with conventionally measured serum carotenoids, 2) RS with serum levels of vitamins C and E, and markers of antioxidant capacity (ORAC) and oxidative stress (TBARs, urinary isoprostanes). Following approval by the University of Utah IRB, consent was obtained from 320 apparently healthy male and female corporate employees participating in their annual health risk assessment. Skin carotenoids were measured with RS 473nm excitation at a standardized location in the palm of the hand. Blood and urine samples were collected to assess serum antioxidants, ORAC and oxidative stress markers. Co-variates included BMI, dietary and lifestyle behaviors. Pearson correlations and regression analyses (n = 295) indicated a significant correlation with skin levels and a composite serum carotenoid score ($r = .80$; $p < 0.001$). RS skin measures were also associated with serum levels of vitamins C ($r = .33$; $p < 0.001$) and E (alpha tocopherol; $r = .30$; $p< 0.001$) and inversely associated with urinary isoprostanes ($r = .23$; $p < 0.001$), but not TBARS. There was no significant difference by gender, however, older and heavier subjects had lower serum carotenoid and RS carotenoid levels than their leaner counterparts. The data suggest RS offers a safe, non-invasive alternative to drawing blood for assessing carotenoid status, and also modestly correlates with other antioxidant nutrients (vitamins C and E).

(A Raman spektroszkópia a vérvételen alapuló karotin státus mérések kitűnő és nem invazív alternatívája; a mérési eredmények bizonyos mértékig más antioxidánsok (C- és E-vitamin szintjével is korrelálnak)

2. J Biomed Opt. 2004 Mar-Apr;9(2):332-8.
Noninvasive selective detection of lycopene and beta-carotene in human skin using Raman spectroscopy.

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The predominant long-chain carotenoids found in human skin are lycopene and beta-carotene. They are powerful antioxidants and thought to act as scavengers for free radicals and singlet oxygen formed by normal metabolism as well as excessive exposure of skin to sunlight. The specific importance of the particular representatives of the carotenoid antioxidants regarding skin defense mechanisms is of strong current interest. We demonstrate fast and noninvasive detection of beta-carotene and lycopene concentrations in living human skin using Raman detection of the molecules' carbon-carbon double bond stretch vibrations. Employing excitation with suitable blue and green laser lines, and taking advantage of differing Raman cross sectional profiles for beta-carotene and lycopene, we determine the relative concentration of each carotenoid species. This novel technique permits the quantitative assessment of individual long-chain carotenoid species rather than their composite level in human

skin. The obtained results reveal significant differences in the carotenoid composition of the subjects' skin and show that the ratio between beta-carotene and lycopene concentration can vary from 0.5 to 1.6. The technique holds promise as a method for rapid screening of carotenoid compositions in human skin in large populations and should be suitable for clinical studies correlating carotenoid status with risk for cutaneous diseases. (c) 2004 Society of Photo-Optical Instrumentation Engineers.

Publication Types:
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3: J Biomed Opt. 2005 Nov-Dec;10(6):064028.
Resonance Raman detection of carotenoid antioxidants in living human tissue.

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Increasing evidence points to the beneficial effects of carotenoid antioxidants in the human body. Several studies, for example, support the protective role of lutein and zeaxanthin in the prevention of age-related eye diseases. If present in high concentrations in the macular region of the retina, lutein and zeaxanthin provide pigmentation in this most light sensitive retinal spot, and as a result of light filtering and/or antioxidant action, delay the onset of macular degeneration with increasing age. Other carotenoids, such as lycopene and beta-carotene, play an important role as well in the protection of skin from UV and short-wavelength visible radiation. Lutein and lycopene may also have protective function for cardiovascular health, and lycopene may play a role in the prevention of prostate cancer. Motivated by the growing importance of carotenoids in health and disease, and recognizing the lack of any accepted noninvasive technology for the detection of carotenoids in living human tissue, we explore resonance Raman spectroscopy as a novel approach for noninvasive, laser optical carotenoid detection. We review the main results achieved recently with the Raman detection approach. Initially we applied the method to the detection of macular carotenoid pigments, and more recently to the detection of carotenoids in human skin and mucosal tissues. Using skin carotenoid Raman instruments, we measure the carotenoid response from the stratum corneum layer of the palm of the hand for a population of 1375 subjects and develop a portable skin Raman scanner for field studies. These experiments reveal that carotenoids are a good indicator of antioxidant status. They show that people with high oxidative stress, like smokers, and subjects with high sunlight exposure, in general, have reduced skin carotenoid levels, independent of their dietary carotenoid consumption. We find the Raman technique to be precise, specific, sensitive, and well suitable for clinical as well as field studies. The noninvasive laser technique may become a useful method for the correlation between tissue carotenoid levels and risk for malignancies or other degenerative diseases associated with oxidative stress.

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(Az egészség-betegség kérdésében egyre nagyobb szerepet tulajdonítanak a karotin típusú antioxidáns vitaminoknak. Ugyanakkor eddig nem volt olcsó, gyors, nem invazív vizsgáló módszer. A Raman spektroszkópián alapuló műszerrel a kézbőr *stratum corneum* karotin-válaszát detektáltuk. Véleményünk szerint a berendezés az antioxidáns status jó indikátora)

4: J Invest Dermatol. 2000 Sep;115(3):441-8.
Comment in:
J Invest Dermatol. 2004 Feb;122(2):544-6; author reply 546-8.
Non-invasive raman spectroscopic detection of carotenoids in human skin.

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Carotenoids are thought to play a significant part in the skin's anti-oxidant defense system, and may help prevent malignancy. Inability to measure skin carotenoid content readily has, however, made it difficult to establish the relationship between carotenoid concentration and the occurrence of cutaneous malignancy. We have measured in vivo carotenoid concentration using a noninvasive optical method, Raman spectroscopy. To validate our instrumentation, abdominoplasty skin was evaluated by both Raman spectroscopy and high-performance liquid chromatography determination for carotenoid content. Evaluation of the Raman signal in specific carotenoid solutions was also performed. Precision of Raman measurements within skin sites, within subjects, and between subjects was measured. Sensitivity of the method was evaluated as a function of anatomical region and the distribution of carotenoids within the stratum corneum. Lastly, we evaluated the Raman signal in actinic keratosis and basal cell carcinoma lesions and perilesional skin and compared this with region-matched sites in healthy subjects. Our results indicate that the Raman scattering method reflects the presence of carotenoids in human skin and is highly reproducible. Evaluation of five anatomical regions demonstrated significant differences in carotenoid concentration by body region with the highest carotenoid concentration noted in the palm. Comparison of carotenoid concentrations in basal cell carcinomas, actinic keratosis, and their perilesional skin demonstrate a significantly lower carotenoid concentration than in region-matched skin of healthy subjects. These results represent the first evidence that carotenoid concentration in the skin correlate with the presence or absence of skin cancer and precancerous lesions.

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(A Raman spektroszkópia során nyert értékeket a hagyományos HPLC technika -high performance liquid chromatography- mérési eredményeivel hasonlítottuk össze. Eredményeink szerint a Raman módszer a bőr karotin tartalmát jól jelzi.)

5: Non-invasive Raman spectroscopy measurement of human carotenoid status

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Carotenoids are an important group of dietary antioxidants with many health benefits. Serum or plasma carotenoid measurements are commonly used to assess human carotenoid status and to monitor reported intake of fruits, vegetables and dietary supplements. Recently, a Raman spectroscopy (RS) method was developed to safely assess skin carotenoids non-invasively (Biophotonic Scanner, Pharmanex). To help validate this method, 104 healthy adults (64 men, 40 women) were recruited for this study. After an overnight fast, each subject provided a blood sample, and skin carotenoids were assessed at the palm of the hand using RS (473 nm excitation). Blood serum was analyzed for carotenoids by HPLC. Results show a highly significant correlation between serum total carotenoids and skin carotenoids as assessed with RS ($r = 0.78$, $p < 0.001$). Mean serum total carotenoid concentration was 1.44 mcg/ml (range: 0.37 – 3.36) and the mean Raman response for skin measurements was 28,808 counts (range: 14,524 – 56,298). Among individual carotenoids, correlations were strongest for beta-carotene, followed by alpha-carotene, lutein/zeaxanthin, lycopene and beta-cryptoxanthin. Based on these results, RS is able to estimate serum total carotenoids with a variability of +/- 10 % and 95 % confidence. This high correlation between serum and skin carotenoid measurements helps validate RS as a novel, non-invasive, rapid, and field-usable tool to assess human carotenoid status. Supported by Pharmanex, LLC.

(A bőr karotin score és a vér HPLC értékek szoros korrelációja igazolja a Biofoton Szkenner használhatóságát a karotin státus gyors, nem invazív vizsgálatára.)

6: Published in: Journal of the American College of Nutrition, Vol, 23, No. 5, October 2004, p.468
Clinical Validation of a Novel Raman Spectroscopic Technology to Non-Invasively Assess Carotenoid Status in Humans.

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Carotenoids are an important group of dietary nutrients demonstrated by research and epidemiological studies to provide human health benefits. HPLC quantification of carotenoids from blood serum (invasive) is the current accepted means of assessment. Recently, a Raman-spectroscopic (RS) method was introduced as a non-invasive alternative to assess carotenoid status in humans (Smidt et al, 2004). To further validate the RS method, 372 healthy adults participated in a clinical trial (IRB approval #1053052). Within an 8-day period, each subject provided 3 fasted blood samples and 3 same-day RS determinations of skin carotenoids. The primary clinical endpoint was to mea - sure the intra-individual variability (IIV) for each testing method. The IIV for RS method was significantly ($p=0.031$) less (9.48%) than that observed using the serum/HPLC method (10.44%). Three separate correlation plots were produced and all showed highly significant correlations (range .78 – .82, $p<.0001$) between total serum carotenoid level and RS-derived skin carotenoid scores. For one such plot, the mean serum total carotenoid concentration was 1.08 ± .51µg/ml (range: 0.21 – 3.74) and the mean Raman response for skin measurements was 19,640 ± 7754 counts (range: 5,933 – 56,606). Among individual carotenoids, correlations were strongest for beta-carotene, followed by alpha-carotene, beta-cryptoxanthin, lutein/zeaxanthin, and lycopene and all were significant. Based on these results, RS appears to estimate the level of skin carotenoids with a variability that was significantly less than carotenoid determination using serum. These data provide further validation the RS technology as a viable non-invasive and alternative method to rapidly assess carotenoid status in humans.

7: Current Topics in Nutraceutical Research, Volume 2, Number 2, pp. 79-91 (2004)
Nutritional Significance and Measurement of Carotenoids

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ABSTRACT: Carotenoids are found in many foods fruits and are partly responsible for the well-documented health benefits of diets rich in fruits and vegetables. For example, lutein and zeaxanthin prevent cataracts and macular degeneration; b-carotene and lycopene protect the skin from ultraviolet radiation damage; lutein and lycopene may benefit cardiovascular health, and lycopene may help prevent prostate cancer. Because of these and other marked health benefits, an accurate assessment of human carotenoid status is important. Carotenoid status can serve as a tool to monitor compliance to healthy diets rich in fruits and vegetables or dietary supplements. Currently, carotenoid levels are assessed with blood serum or plasma HPLC measurements. However, such methods are invasive, expensive and impractical for general use in large populations. Skin carotenoid levels correlate well with blood levels and may more accurately indicate carotenoid status, because unlike bloodskin carotenoids are not influenced by postprandial fluctuations. Recently, a convenient, rapid and non-invasive measurement of skin carotenoid status using Raman spectroscopy has been developed. This method can become a strong motivator for people to consume the recommended five to nine fruits and vegetables daily and well-balanced dietary supplements.

8: Associations of Fruit & Vegetable Intake with Serum Carotenoids, & Skin Carotenoids Measured with Raman Spectroscopy (RS)
Published in: FASEB Journal, volume 20, abstract # 669.4, 2006.
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Journal Reference:
Stavens, S., Carlson, J., Holubkav, R., Zidichouski, J., Mastaloudis, A., Smidt, C.R. 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.

We evaluated the associations of fruit and vegetable intake with both conventionally measured serum carotenoids and skin carotenoids measured by RS. Following approval by the University of Utah IRB, consent was obtained from 320 apparently healthy male and female corporate employees participating in their annual health risk assessment. Skin carotenoids were measured with RS 473nm excitation in standardized location in the palm of the hand. Blood samples were taken to assess serum nutrients including carotenoids. Fruit and vegetable intake was assessed with a modified Block fruit and vegetable food frequency questionnaire (FVFFQ). Co-variates included BMI, lifestyle behaviors and dietary supplement intake. Pearson correlations and regression analyses revealed similar modest significant correlations with both the FVFFQ composite serving score and a composite serum carotenoid score (r=.21; p=0.0003; n=285) and with the RS skin carotenoid score (r=.28; p<0.0001; n=296). These relationships were independent of supplement intake which had a stronger significant relationship with serum carotenoid levels (r=.52; p<0.0001; n=285) and RS carotenoid levels (r=.48; p<0.0001; n=296). These results indicate RS scanner has potential utility as a rapid screening method that reflects fruit and vegetable intake similar to a FVFFQ as well as serum blood measures, without the risk of time associated with collecting and analyzing blood samples.

9: J Med Assoc Thai. 2006 Aug;89(8):1206-12.
Effect of fruit and vegetable intake on skin carotenoid detected by non-invasive Raman spectroscopy.

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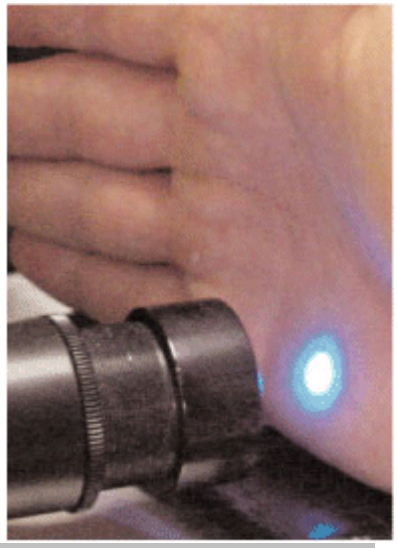

BACKGROUND: Epidemiologic studies found the inverse correlation between fruit and vegetable intake and the risk of cardiovascular disease, various cancers, insulin resistance, and other chronic conditions. Skin carotenoid levels are highly correlated with serum levels; however, the direct measurement of skin carotenoids is difficult to perform. Raman spectroscopy has been described as a highly sensitive, specific and accurate method of skin carotenoid detection. OBJECTIVE: The authors assessed the relation between fruit and vegetable intake and skin carotenoid levels measured by Raman spectroscopy. MATERIAL AND METHOD: Twenty-nine healthy volunteers were enrolled in the present study. Demographic data and fruit and vegetable intake were recorded. Skin carotenoid levels were measured by Raman spectroscopy and were reported as Skin Carotenoid Score (SCS). The data were compared and were reported as 3 groups based on the amounts of fruit and vegetable intake. RESULTS: There were no significant differences of age, body weight, height and body mass index among the groups. Mean skin carotenoid score of low fruit and vegetable intake (25,733 +/- 2,956) was significantly lower than SCS of moderate intake (31,333 +/- 4,792, p = 0.03) and high fruit and vegetable intake (35,125 +/- 6,081, p < 0.01). Mean SCS of underweight participants (29,250 +/- 4,621) was not significantly different from normal (33,384 +/- 6,614) and overweight participants (27,575 +/- 3,811), p =0.06. CONCLUSION: Using Raman spectroscopy, the authors found that skin carotenoid levels were directly correlated with the degree of fruit and vegetable intakes. We suggest that Raman spectroscopy should be possible to replace the invasive chemical technique for the dermatologic carotenoid measurement.

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(A bőr karotin szint erősen korrelál a szérum karotin szitjével. A Raman spetroszkópián alapuló szkenner technikát alkalmazva a szerzők megállapítják: a bőr karotin szintje közvetlen függvénye a vizsgált személyek gyümölcs és zöldség fogyasztásának. Rossz minőségű étrend esetén a *skin carotenoid score* értéke 25.733, közepes zöldség és gyümölcsfogyasztás mellett 31.333, míg magas zöldség és gyümölcsfogyasztás mellett 35.125 volt. A berendezés tehát alkalmas táplálkozás minőségének gyors felmérésére és az oxidatív stressz betegségek rizikójának szűrésére!)