

FINAL REPORT

Center of Excellence for Laser Applications in Medicine Microscope ER61229

DOE Patent Clearance Granted
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The Center of Excellence for Laser Applications in Medicine Schepens Eye Research Institute (SERI) is a Center for:

A core group of researchers who support each other and their various projects for real-time medical imaging and diagnostics in contiguous space at SERI.

Clinical collaborators who participate in the core research at SERI, MEEI and local ophthalmology practices, and at associated sites around the world.

Industrial partners who transfer our technology to commercial products that will reach clinical usage everywhere.

Students, post-doctoral associates and medical fellows who work with us and learn how to develop and how to practice real-time medical imaging and diagnostics.

Research projects within the Center are primarily independently funded, but the innovative new technologies that make us unique depend on critical support from the Center of Excellence for Laser Applications in Medicine. As we close out the Center of Excellence funding, most of the projects have become mature enough to be started on the route to commercial development that will guarantee their eventual use in clinical medicine or to availability to researchers beyond the Center. Others, more long-term and less applied as yet, are now sufficiently well covered by their other funding, though the flexibility of the Center of Excellence funding will be missed.

Projects

Microlaser microscope: This central project of the original Center of Excellence Grant has matured and given way to industrial efforts and collaborations outside the Center. Further development at SERI is currently restricted to support functions

The idea here is that of an array of vertical cavity surface emitting lasers imaged on an object, which is in turn re-imaged on an array of detectors, forming a tandem scanning confocal microscope that is micro-miniaturized. This was demonstrated in a number of forms, and still waits the advent of large, matrix addressable arrays.

Tandem Scanning Ophthalmoscope: A first bread-board version has demonstrated optical sectioning using SLMs that are digital micro-mirrors (MEMS technology). A group of researchers around the world is getting around the manufacturer's unwillingness to help in any but consumer product development, and we are profiting by this shared expertise. This is a project that has been delayed by procurement problems, and has now outlasted its (minimal) funding. Because there seemed to be no fundamental problems with the basic idea, we carried it on without funding to a demonstration of the basic ophthalmoscope function in a real eye.

A tandem scanning microscope is a type of confocal microscope that uses a mask at an image plane to illuminate the object, and an identical mask at another optical conjugate of those planes to allow confocal detection. The mask is then moved until the whole object field is tiled. In our implementation the masks are generated by spatial light modulators (SLMs). We have found that the SLMs that we originally proposed is, indeed, the appropriate one. That makes for considerable difficulty, since the manufacturer, Texas Instruments, does not support the device for any but large consumer uses like video projectors. We, and a group of researchers world-wide are solving that problem by reverse engineering, which is working. We expect the eventual commercial TSO to be independent of this supplier, since the patent is running out and others are entering the field.

Video-rate Confocal Scanning Laser Microscope for in Vivo Imaging: This is a project of Dr. Webb's, started at the Center of Excellence and long since launched into commercial phase with Lucid Technologies of Rochester, NY. The product is a confocal microscope of the laser scanning variety that works at high enough frame rates to image cells in living human tissue. FDA has approved it's sale as a microscope.

This *in vivo* confocal microscope runs at video rates and images to about 500 μm deep in tissue. It is finding many more clinical uses than the ones originally expected of it, and is generating about 10 serious peer-reviewed papers a year, though not under Center of Excellence support any longer.

Stabilized Imaging for the Scanning Laser Ophthalmoscope: An SBIR with Physical Sciences, Inc. of Andover, MA, is in phase II, and there is excited acceptance in the ophthalmic research community, as well as interest in other areas of medical imaging. New work on the improved version is just beginning. No further Center of Excellence support will be needed, but this is one of the strong successes of the program.

The idea here is to illuminate a spot on the retina with 950 nm light, dither than spot in a known pattern, and detect changes in the reflected light to derive a feedback signal that drives the SLO raster display so that the image is stable. We have been able to add 100 video frames coherently, improving signal-to-noise ratio by a factor of 10, or reducing light dosage by a factor of 100. Features that would otherwise be unrecordable in the moving eye are now visible.

Photoreceptor optics and retinal imaging: This project of Dr. Burns uses the instrument of the Spatially Resolved Refractometer project, to understand how retinal and refractive errors interact in the eye. The existing prototype continues to give useful results, but we have converted to the new commercial model, and are finding it already useful in this work. Dr. Burns has included this in his competing renewal of his NIH grant proposal, which has been funded.

The photoreceptors of the retina have a directionality that is measured in Dr. Burns' photoreceptor alignment reflectometer (PAR), reducing hour-long sessions to measure this Stiles-Crawford effect to a few minutes. These measurements, coupled with the Spatially Resolved Refractometer (SRR) have shown that the central point (in the eye's pupil) at which the photoreceptors aim coincides with the part of the pupil that has least aberrations – but only in about 70% of subjects.

Multiply Scattered Light Tomography: This is one of the vertical cavity surface emitting laser (VCSEL) based imaging variants derived from the original microlaser microscope project. Drs. Elsner

and Webb an enthusiastic industrial partner, Laser Diagnostic Technologies of San Diego, CA, have a Phase II SBIR, and LDT is proceeding with a commercial instrument.

Drs. Elsner has shown that layers deep in the retina (where age-related macular degeneration starts) may be imaged in the multiply scattered light that is rejected by the confocal pinhole of the scanning laser ophthalmoscope. Then, by using VCSELs as source for both confocal and confocally rejected light, a single detector can image both views, time-domain multiplexing them at video rate. The resultant image has the virtue of being able to orient the subtle deep features by the more distinct and familiar superficial features.

Polarization imaging: A new project of Drs. Elsner and Burns, with partners in San Diego, CA at Laser Diagnostic Technologies, has been to develop a new technique with polarimetry to visualize different structures in the eye. A proposal to NIH is not sure of funding, but we are confident that it will eventually find support.

There have been a number of ellipsometric measures of the retina, and this is one that seems less complex than currently available ones. Based on scanning laser ophthalmoscope imaging, and using our experience with time-domain multiplexing them at video rate, we think we can map the full Mueller matrix of the retina to form a diagnostically useful image.

Augmented Vision for Low Vision Rehabilitation: This is a novel concept of augmented vision, based on a new method of image enhancement applied to see-through display devices. It can be used for both enhancement for central scotoma and field expansion for peripheral loss. This has very exciting early results with visually impaired patients. Drs Peli and Webb have been awarded a new BRG grant that is already taking the work forward.

Dr. Peli, an expert on head-up and virtual display devices and on low-vision rehabilitation, has developed algorithms to enhance the visual scene for visually impaired patients. He couples this with new devices to change the visual field accessible to patients by means of field-shifting (Fresnel) prisms and other optical manipulators that can be built into eyeglasses. Dr. Webb's role is to design the ultimate optics for the devices, once the image enhancement is mature.

Noninvasive Measurement of RPE Lipofuscin: Lipofuscin accumulates with age in the retinal pigment epithelium, and appears to be correlated with onset of age-related macular degeneration. This project of Dr. Delori's is building up substantial data for understanding that correlation. Dr. Delori's work is pivotal for a Phase II SBIR with OcuMetrics, Inc. of Mt View, CA. Currently awaiting review of his grant proposal, Dr. Delori's work to detect the A2E fluorescence in the retina is at some risk for being interrupted unless we can support him for a few months.

Dr. Delori is currently investigating the fluorescence of A2E (a fluorophore of the aging retina) and is performing experiments to define how much of the fluorescence of A2E can be detected in-vivo. A2E has been identified by biochemist and cell biologists as a potential contributor to age-related decline in retinal pigment epithelium (RPE) cell function. Detection of this fluorophore in-vivo could provide much needed information about the viability of RPE cells, and provide a tool to monitor cell health in aging and age-related macular degeneration.

The enabling technology for Dr. Delori's work is a retinal fluorometer that can distinguish all of the contributing light from the retina and the rest of the eye, allowing measurement of the critical endogenous fluorescence from lipofuscin. Dr. Delori's work is to correlate this measurement with other markers of age-related macular degeneration over time in an aging population. Others have taken his results and use lipofuscin fluorescence as a diagnostic in the clinic. Dr. Delori continues to work on the basic mechanism and his enabling technology for evaluating it.

Spatially Resolved Refractometer: The spatially resolved refractometer (SRR) is in use by the Emory Vision Correction Center in Atlanta, GA, and as well as by the group at SERI. A simpler and more efficient (in patient time) instrument designed by Drs. Webb and Burns has been working in prototype form, and three new instruments are now in use, two in the Emory Clinic and one for Dr. Burns and his collaborators at SERI. This is now fully supported by the Emory group.

The idea here is to measure the aberrations of the eye, using a null method with the patient as measurer. A spot falls on the retina, passing through selected parts of the pupil, and the patient moves the spot to a central retinal location defined by another target that he or she sees. It's like a simple video game, and takes about 3 minutes to measure the whole eye. We use this to explore the effect of aberrations on vision and the development of vision in children. Our Emory collaborators use the SRR to guide LASIK surgery of the cornea, for better outcomes in surgical correction of vision.

Interferometric studies of the tear film: Dr. Doane's optical evaluation of the health of the tear film in both dry-eye patients and contact lens wearers is finishing a Phase II SBIR with OptoVision in Boston, with a commercial instrument planned. Dr. Doane is retiring this year.

This project has been important in a clinical setting for some time. The health of the tear film is evaluated by measuring its change in thickness after blinks. A fully functioning tear film wets the cornea and flows off it smoothly, without islands of accelerated dryness or increased viscosity that leads to incomplete coverage. A dry cornea is both painful and unable to pass light properly. This interferometric measure has been very successful, and Dr. Doane (in retirement) continues to monitor the use of his instrument and copies of it in local clinics.

Flow Cytometry: This is a continuing collaboration with Shapiro Laboratory for innovations in flow cytometry. A commercial device using these designs is under development, but an early version is already incorporating some of the concepts. (Luminex, Austin Texas). Further innovative designs with other small companies are in the works, but funding is not necessary at present.

Dr. Webb is one of the originators of flow cytometry, and his optical designs are in use extensively. However, with the need to assess CD4 occurrence in HIV diagnosis, and with a push to record ever smaller entities (bacteria, viruses, and even DNA molecules), new technology is continually proposed. Dr. Shapiro, possibly the world's expert on flow cytometry, uses Dr. Webb for optical design in a number of new variants on the basic flow cytometer. The task is always to deliver light to the flow chamber and assess the remitted light, discriminating against light scattered from the chamber walls or other surfaces in the light path. We have recently formulated some general principles, based on our experience in confocal microscopy.

Seeing Machine: In collaboration with Elizabeth Goldring at MIT, Dr. Webb has made the scanning laser ophthalmoscope (SLO) available as a seeing machine for the visually impaired. Because that is not the SLO's primary function, it is an inappropriate instrument for such a use. We have now designed an inexpensive alternative based on video projector technology, and feel that will be a useful device both as a low-vision aid and as a display device in vision research. This effort is entirely unfunded, so it has been dependent on Dr. Webb's support through the Center of Excellence program. Funding has been requested (of NEI) for follow-on work.

The SLO works so well in part because it is a high brightness display, it uses a saturated color (the laser), and because its display is in Maxwellian view. That means that the beam entering the eye uses only a small part of the pupil, the sub-beams being substantially collimated at the pupil. With the resources of the video projector, we feel we can achieve Maxwellian view, and because there is much more light than we need, we can reach the brightness and saturation required.

Training: Students, post-doctoral and clinical fellows are an important focus of our efforts. The Center attracts an interesting mix of physicians seeking additional training in basic research that has clinical potential and basic scientists with an interest in real-time medical imaging and involving technology that may be unique in medical training. This is a function that depends on the ongoing projects, so it will essentially vanish when the program ends.

Refereed papers: The Center has produced 23 refereed papers and patents published or in press, since August 2000.

1. Burns, S. A. and S. Marcos (2000). Evaluating the role of cone directionality in image formation. OSA Trends in Optics and Photonics. V. Lakshminarayanan. Washington, D.C., Optical Society of America. Vol 35, Vision Science and It's Applications: 22-25.
2. Burns, S.A. "The Spatially Resolved Refractometer", Journal of Refractive Surgery 16(5): S566-S569.
3. Burns, SA, and Marcos, S " Measurement of the Image Quality of the eye with the Spatially Resolved Refractometer", in Customized Corneal Ablations MacRae, Krueger, and Applegate (eds), Slack Publishing, (in press, 2000).
4. Delori FC, Goger DG, and Dorey CK. "Accumulation of lipofuscin in the retinal pigmented epithelium; Age relationship and spatial distribution in normal subjects," Invest Ophthalmol Vis Sci. In review
5. Delori FC, Goger DG, Hammond BR, Snodderly DM, and Burns SA. "Macular Pigment Density Measured by Autofluorescence Spectrometry" J.Opt.Soc.Am. A.. In Press
6. Delori, FC, Hammond B, Snodderly DM, and Burns SA "A novel technique for measuring macular pigment" Journal of the Optical Society, A, (in press).
7. Elsner, AE, Dreher, A, and Webb RH, Apparatus for near simultaneous observation of directly scattered image field and multiply scattered image field. (pending).

8. García-Pérez MA, Peli E. (2001) Artifacts of cathode-ray tube displays for vision research. *Spatial Vision*, In press.
9. Hang, Z, Lazarev, V, and Webb, RH Optical confocal device having a common light directing means. 6,121,603 (2000).
10. Li L, Nugent A, and Peli E. Are jagged (pixelated) letters easier to recognize than smooth (anti aliases) letters in the periphery? *Visual Impairment Res* 2001, in press.
11. Marcos, S, Burns, S.A. "On the symmetry between eyes of wavefront aberration and cone directionality", *Vision Research* 40, 2437- 2447, 2000.
12. McLellan JS, Marcos S, and Burns SA "Aging and Wavefront Aberrations" *Investigative Ophthalmology and Visual Science* (in press).
13. Moreno-Barriuso E, Marcos, S, Navarro, R, Burns SA "Comparing Laser Ray Tracing, Spatially Resolved Refractometer And Hartmann-Shack Sensor To Measure The Ocular Wave Aberration" *Optometry and Visual Science* (in press).
14. Peli E, Hedges R, Tang J and Landmann D. A binocular stereoscopic display system with coupled convergence and accommodative demands. *SID 2001, Digest of Technical Papers, 2001.*, San Jose, CA. Society for Information Display. In press.
15. Peli E. Contrast sensitivity function and image discrimination. *J Opt Soc Am A* 2001, in press.
16. Peli E. (2001) Vision multiplexing - an engineering approach to vision rehabilitation device development. *Optometry and Vision Science*, in press.
17. Peli E. and Lang A. The appearance of images through a multifocal intra ocular lens. *J Opt Soc Am A* 2001, in press.
18. Peli E. and Geri G. A. Discrimination of wide-field images as a test of a peripheral-vision model. *J Opt Soc Am A* 2001 in press.
19. Peli E. Field expansion for homonymous hemianopia by optically induced peripheral exotropia. *Optom Vision Sci* 2000;77:453-464.
20. Remky, A, Elsner, A E, Morandi, A, Beausencourt, E, and Trempe, C L, Blue-on-Yellow Perimetry with a SLO: Small Alterations in the Central Macula with Aging. *J Optical Society of America A* (In press).
21. Remky, A., Lichtenberg, K, Elsner, A E, and Arend, O. Short-wavelength automated perimetry in Age-related maculopathy. *B. Journal Ophthalmology* (In press).
22. Vargas-Martin, F. and Peli, E. Augmented view for tunnel vision: device testing by patients in real environments. *SID 2001, Digest of Technical Papers, 2001.* San Jose, CA. Society for Information Display. In press.

23. Webb RH, Burns SA and Penney, CM, Coaxial spatially resolved refractometer 6,000,800 (1999).
Also 6,099,125 (2000).

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A.4. Journal Article(s)

Arend O, Remky A, Elsner AE, Bertram B, Reim M, and Wolf S. Quantification of cystoid changes in diabetic maculopathy. *Invest. Ophthalmol. Vis. Sci.* 36, 608-613, 1995.

Arend O, Remky A, Elsner AE, Wolf S, Reim M. Indocyanine green angiography in traumatic choroidal rupture: clinico-angiography case reports. *German J of Ophthalmology* 4:257 - 263, 1995.

Arend O, Weiter JJ., Goger DG, and Delori FC. Fundus fluorescence measurements in patients with age-related macular degeneration (In German). *Ophthalmologie*. 1995; 92: 647-653.

Beausencourt E, Elsner AE, Hartnett ME, Trempe CL. Quantitative analysis of macular holes with scanning laser tomography. *Ophthalmology* 104, 2018-2029, 1997.

Bradley A, Zhang H, Applegate RA, Thibos LN, and Elsner AE. Entoptic image quality of the retinal vasculature. *Vision Res.* 38, 2685-2696, 1998.

Burns S.A., Wu S., Delori F., and Elsner AE Direct Measurement of human cone photoreceptor alignment. *J. of the Optical Society A* 12, 2329-2338, 1995.

Burns SA, and Elsner AE, "Color-matching at high illuminances: photopigment optical density and pupil entry" *J. Opt. Soc. Amer.* 10, 221-230, 1993.

Burns SA, Kreitz M, and Elsner AE "Apparatus Note: A computer controlled, two color, laser-based optical stimulator for vision research". *Applied Optics* 30: 2063-2065, 1991.

Burns, S. A. and S. Marcos (2000). Evaluating the role of cone directionality in image formation. *OSA Trends in Optics and Photonics. V. Lakshminarayanan*. Washington, D.C., Optical Society of America. Vol 35, Vision Science and It's Applications: 22-25.

Burns, S.A "The Spatially Resolved Refractometer", *Journal of Refractive Surgery* 16(5): S566-S569.

Burns, SA, and Marcos, S " Measurement of the Image Quality of the eye with the Spatially Resolved Refractometer", in *Customized Corneal Ablations* MacRae, Krueger, and Applegate (eds), Slack Publishing, (2000).

Burns, SA, Wu, S, He, J, and Elsner, AE, Variations in photoreceptor directionality across the central retina, *J. Optical Society Amer, A* 14, 2033-2040, 1997.

Chen, JF, Elsner, AE, Burns, SA, Hansen, RM, Lou, PL, Kwong, KK, Fulton, AB "The Effect of Eye Shape on Retinal Responses". *Clin. Vis. Sci.*, 7, 521-530, 1992.

Delori FC and Burns SA "Fundus reflectance and the measurement of crystalline lens density," J. Opt. Soc. Am. A. 1995a; 13:215-226.

Delori FC, Dorey CK, Staurenghi G, Arend O, Goger DG, and Weiter JJ. "In-vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics" Invest Ophthalmol Vis Sci. 1995b; 36: 718-729.

Delori FC, Goger DG, and Dorey CK. "Accumulation of lipofuscin in the retinal pigmented epithelium; Age relationship and spatial distribution in normal subjects," Invest Ophthalmol Vis Sci.

Delori FC, Goger DG, Hammond BR, Snodderly DM, and Burns SA. "Macular Pigment Density Measured by Autofluorescence Spectrometry" J.Opt.Soc.Am. A.. In Press

Delori FC, Staurenghi G, Arend O, Dorey CK, Goger DG, and Weiter JJ. "In-vivo measurements of lipofuscin in patients with Stargardt's disease," Invest Ophthalmol Vis Sci. 1995c; 36: 2337-2331.

Delori FC. Spectrophotometer for noninvasive measurement of intrinsic fluorescence and reflectance of the ocular fundus. Applied Optics. 1994. 33: 7439-7452

Delori, FC, and Burns SA. "Estimates of Lens Density from Fundus Reflectometry" J. Opt. Soc. Amer. A. 13,215-226, 1996.

Delori, FC, Hammond B, Snodderly DM, and Burns SA "A novel technique for measuring macular pigment" Journal of the Optical Society, A, (in press).

Doane MG, Lee ME: The use of tear film interferometry as a diagnostic tool for the evaluation of the normal and dry-eye tear film. Adv. Exp. Med. Biol. 1997.

Doane MG: Abnormalities in the structure of the superficial lipid layer on the in-vivo dry-eye tear film. Adv. Exp. Med. Biol. 1994; 350:489-493.

Doane MG: Tear film interferometry as a diagnostic tool for the evaluation of the normal and dry-eye tear film. Adv Exp Med Biol. 438:297-303, 1998.

Elsner AE, Burns SA, and Webb RH, Mapping cone photopigment optical density, J. Opt. Soc. Amer., A. 10:1-7, 1993.

Elsner AE, Burns SA, and Weiter JJ. Retinal densitometry in retinal tears and detachments. Clinical Vision Sciences 7, 489-500, 1992.

Elsner AE, Burns SA, Beausencourt E, Weiter JJ. Foveal cone photopigment distribution: small alterations associated with macular pigment distribution. Investigative Ophthalmol Vis Sci., 39, 2394-2404, 1998.

Elsner AE, Burns SA, Weiter JJ, and Delori FC., "Infrared imaging of subretinal structures in the human ocular fundus," Vision Res. 1996; 36:191-205.

Elsner AE, Burns SA, Zhòu Q, Dreher AW. Detection and localization of subretinal structures in three dimensions using a new technique: multiple scattered light tomography. Invest. Ophthalmol and Vis. Sci, 4244, S922, 1998.

Elsner AE, Burns SA, Zhou Q, Dreher AW. Polarization modulation from in vivo human ocular fundus images. Optics and Photonics News, 8 (9), 72, 1998.

Elsner AE, Dreher AW, Zhou Q, Beausencourt E, Burns SA, Webb RH. "Multiply scattered light tomography: vertical cavity surface emitting laser array used for imaging subretinal structures". Lasers and Light in Ophthalmology, 8, 193-202, 1998.

Fine E M, Peli E. Enhancement of text for the visually impaired. J Optical Soc Am A 1995, 12: 1439-1447.

Fine EM, Peli E and Reeves A, Simulated Cataract Does Not Reduce the Benefit of RSVP. Vision Research, 1997, 37: 2639-2647.

Fine EM, Peli E. Scrolled and RSVP text are read at the same rate by the visually impaired. J Optical Soc Am A 1995, 12: 2286-2292.

Fine, EM and Peli, E, The benefits of RSVP over scrolled text vary with letter size. Optometry and Vision Science, 1998, 75: 191-196.

García-Pérez MA and Peli E. The transition from DeVries-Rose to Weber's laws: Comments on Rovamo, Mustenson and Näsänen (1995). Vision Research 1997, 37: 2573-2576.

García-Pérez MA, Peli E. (2001) Artifacts of cathode-ray tube displays for vision research. Spatial Vision,

García-Pérez MA. and Peli E. "Lack of covariation of the effects of luminance and eccentricity on contrast sensitivity." Optometry and Vision Science, 1999, 76: 63-67

García-Pérez MA. and Peli E. "Imputation of direction of motion in one dimension." J Optical Soc Am A, 1999, 16: 1531-1540.

Gorrand JM and Delori FC "Reflectance and curvature of the inner limiting membrane at the foveola". J Opt Soc Am A (1999).

Gorrand J-M and Delori FC, "A model for assessment of cone directionality," J. Modern Optics. 1997; 44:473-491

Gorrand J-M and Delori FC, "A reflectometric technique for assessing photoreceptor alignment," Vision Res. 1995; 35: 999-1010.

Hartnett ME and Elsner AE. Characteristics of exudative age-related macular degeneration determined in vivo with confocal direct and indirect infrared imaging. *Ophthalmology*, 103:58-71, 1996.

Hartnett, ME, Weiter, J.J., Staurengi, G., Elsner, AE Deep retinal vascular anomalous complexes in advanced age-related macular degeneration, *Ophthalmology*, 103:2042-2053, 1996.

He, J., Marcos, S, Webb, RH and Burns, SA "Measurement of the wave-front aberration of the eye using a fast psychophysical procedure." *JOSA A* 1998;15 2449 - 2456.

He, JC, Burns, S.A., and Marcos, S. "Comparison of cone directionality determined by psychophysical and reflectometric techniques" *J. Opt. Soc. Amer.* (in Press).

He, JC, Burns, S.A., and Marcos, S. "Monochromatic Aberrations in the Accommodated Human Eye" *Vision Research* (in Press).

Kelley LM, Walker JP, Wing GL, Raskauskas PA, Elsner AE. Scanning laser ophthalmoscope imaging of age related macular degeneration and neoplasms. *Journal of Ophthalmic Photography* 3, 89-94, 1997.

Kunze C, Moraes L, Elsner AE, Hartnett ME. Alterations in the foveas of aging subjects and patients with ARM, and AMD. Retinal sensitivity in pigment epithelial detachments correlates to three-dimensional extent, to be presented at the American Academy of Ophthalmology, 1998.

Kunze, C, Elsner, AE, Beausancourt, E, Moraes, L, Hartnett, ME, and Trempe, CL "Spatial extent of pigment epithelial detachments in age-related macular degeneration" *Ophthalmology* 106 (in press 1999).

Li L, Nugent A, and Peli E. Are jagged (pixelated) letters easier to recognize than smooth (anti aliases) letters in the periphery? *Visual Impairment Res* 2001

Lichtenberg K, A. Remky, Elsner AE. Blau/Gelb-Perimetrie bei nicht-exsudativer altersbedingter Maculadegeneration *Der Ophthalmologe* 95 (Suppl.1): S.51-52, 1998.

Marcos S, Burns SA and He J, "A Model for cone directionality reflectometric measurements based on scattering." *Journal of the Optical Society of America A* 15, 2012-2022, 1998.

Marcos S, Tornow R-P, Elsner AE, and Navarro R. Foveal cone spacing and cone photopigment density difference: Objective measurements in the same subjects. *Vision Research* 1997 37, 1909-1915.

Marcos S., Tornow R-P., Elsner AE, and Navarro R. Foveal cone spacing and cone photopigment density difference: Objective measurements in the same subjects. *Vision Research*.

Marcos, S, and Burns, S.A. "Cone spacing and waveguide properties from cone directionality measurements" J. Opt. Soc. Amer. A 16, 995-1004, 1999.

Marcos, S, Burns, S.A. "On the symmetry between eyes of wavefront aberration and cone directionality", Vision Research 40, 2437- 2447, 2000.

Marcos, S, Burns, S.A., Moreno-Barriuso, E, and Navarro, R "A new approach to the study of ocular chromatic aberrations" Vision Research (in Press).

Marcos, S, Burns, SA, and He, J "A Model for cone directionality reflectometric measurements based on scattering." Journal of the Optical Society of America A 15, 2012-2022, 1998.

McLellan JS, Marcos S, and Burns SA "Aging and Wavefront Aberrations" Investigative Ophthalmology and Visual Science.

Moraes L, Elsner AE, Kunze CL, Trempe CL, Hartnett ME. Correlation in patients with age-related maculopathy between retinal sensitivity and anatomic abnormalities using a scanning laser ophthalmoscope. Invest. Ophthalmol and Vis. Sci, 2745, B602, 1998.

Moreno-Barriuso E, Marcos, S, Navarro, R, Burns SA "Comparing Laser Ray Tracing, Spatially Resolved Refractometer And Hartmann-Shack Sensor To Measure The Ocular Wave Aberration" Optometry and Visual Science.

Ormerod LD, Fariza E and Webb RH, Dynamics of external ocular blood flow studied by scanning angiographic microscopy. Eye, 9 605-614 (1995).

Peli E Limitations of image enhancement for the visually impaired. Optometry and Vision Science 1991;6: 15-24.

Peli E. Perception and interpretation of high-pass filtered images. Optical Engineering 1992;31:74-81.

Peli E and García-Pérez MA. Contrast sensitivity in dyslexia: Deficit or artifact? Optometry and Vision Science, 1997, 74: 986-988.

Peli E, (1998) Emmetropia or Ametropia? an invited answer for the Consultation Section. Ann. Ophthalmol. 30:7-9.

Peli E, Arend L, and Labianca AT Contrast perception across changes in luminance and spatial frequency. J Optical Soc Am A 1996, 13: 1953-1959.

Peli E, Hedges R, Tang J and Landmann D. A binocular stereoscopic display system with coupled convergence and accommodative demands. SID 2001, Digest of Technical Papers, 2001., San Jose, CA. Society for Information Display.

Peli E, In search of a contrast metric: matching the perceived contrast of Gabor patches at different phases and bandwidths. Vision Research, 1997, 37: 3217-3224.

Peli E, The visual effects of head-mounted-display (HMD) are not distinguishable from those of desk-top computer display. Vision Research, 1998, 38: 2053-2066.

Peli E. Suprathreshold contrast perception across differences in mean luminance: effects of stimulus size, dichoptic presentation, and length of adaptation. J Optical Soc Am A 1995, 12:817-823.

Peli E. "Simple 1-D image enhancement for head-mounted low vision aid". Vision Rehabilitation Research, 1999, 1: 3-10.

Peli E. "The visual effects of head-mounted-display (HMD) are not distinguishable from those of desk-top computer display". Vision Research, 1998, 38: 2053-2066.

Peli E. Contrast sensitivity function and image discrimination. J Opt Soc Am A 2001,

Peli E. Display nonlinearity in digital image processing for visual communication. Optical Engineering 1992;3: 2374-2382.

Peli E. Test of a model of foveal vision by using simulations. J Optical Soc Am A 1996, 13: 1131-1138.

Peli E. (2001) Vision multiplexing - an engineering approach to vision rehabilitation device development. Optometry and Vision Science,

Peli E. and Lang A. The appearance of images through a multifocal intra ocular lens. J Opt Soc Am A 2001

Peli E. and Geri G. A. Discrimination of wide-field images as a test of a peripheral-vision model. J Opt Soc Am A 2001

Peli E. Field expansion for homonymous hemianopia by optically induced peripheral exotropia. Optom Vision Sci 2000;77:453-464.

Peli E. In search of a contrast metric: matching the perceived contrast of Gabor patches at different phases and bandwidths. Vision Research 1997.

Rajadhyaksha M and Webb RH, Plate Beam-Splitter to Produce Multiple Equal-Intensity Beams, Applied Optics 34 8066-8067 (1995).

Rajadhyaksha M, Anderson, RR and Webb, RH, "Video-rate confocal scanning laser microscope for imaging human skin and oral mucosa in vivo." Applied Optics 1999; 38, 2105-2115.

Rajadhyaksha M, Gonzalez S, Zavislan JM, Anderson RR and Webb RH, "Near-infrared confocal microscope improves imaging of human skin in vivo". *Journal of Investigative Dermatology*.

Rajadhyaksha M, Grossman M, Esterowitz D, Webb RH, and Anderson RR, In vivo confocal scanning laser microscopy of human skin: melanin provides strong contrast, *Journal of Investigative Dermatology* 6 946-952 (1995).

Raskauskas P, Walker JP, Wing GL, Fletcher DC, Elsner AE: "Small Incision Cataract Surgery and Placement of Posterior Chamber Intraocular Lens in Patients with Diabetic Retinopathy", *Ophthalmic Surg Lasers*, 30:6-11, 1999.

Remky A, Arend O, Elsner AE, Toonen F, Reim M, and Wolf S. Digital imaging of central serous retinopathy using infrared illumination. *German J Ophthalmology* 4, 203-206, 1995.

Remky A, Beausencourt E, and Elsner AE. Angioscotometry with the SLO: comparison of the effect of different wavelengths. *Invest. Ophthalmol. Vis. Sci*.

Remky A, Beausencourt E, Hartnett ME, Termpe CL, Arend O, Elsner AE. "Infrared imaging of cystoid macular edema." *Graefe's* .

Remky A., Arend O., Beausencourt E., Elsner AE, and Bertram B. Retinale Gefasse vor und nach Photokoagulation bei deibetischer Retinopathie. *Klin Monatsbl Augenheilkunde*, 209, 79-83, 1996.

Remky A., Elsner AE, Pauen S., Arend O, Kelley L, Walker JP, Raskauskas PA, Wing GL. Aging effects of retinal vessel diameter in normals and patients with age-related maculopathy. *Invest. Ophthalmol and Vis. Sci*, 1791, S384, 1998.

Remky, A, Elsner, A E, Morandi, A, Beausencourt, E, and Trempe, C L, Blue-on-Yellow Perimetry with a SLO: Small Alterations in the Central Macula with Aging. *J Optical Society of America A*.

Remky, A., Lichtenberg, K, Elsner, A E, and Arend, O. Short-wavelength automated perimetry in Age-related maculopathy. *B. Journal Ophthalmology*.

Tearney GJ, Webb RH, Bouma BE, Spectrally encoded confocal microscopy. *Optics Letters* 1998; 23 152-154.

Vargas-Martin, F. and Peli, E. Augmented view for tunnel vision: device testing by patients in real environments. *SID 2001, Digest of Technical Papers*, 2001. San Jose, CA. Society for Information Display.

Wan D-S, Rajadhyaksha M and Webb RH, "Analysis of spherical aberration of a water immersion objective: applications to specimens with refractive indices 1.33-1.40". *J Microscopy*.

Webb RH and Rogomentich F, Microlaser microscope using self detection for confocality, Optics Letters, 20,533-535,(1995).

Webb RH Confocal Optical Microscopy Reports on Progress in Physics 59 427-471 (1996).

Webb RH, and Dorey CK, The Pixelated image. In Handbook of Biological Confocal Microscopy, 3rd edition James Pawley ed. 55-67 (1995) Plenum.

Webb RH, Concentrator for laser light. Applied Optics, 31:5917-5918, 1992.

Webb RH, Hughes GW, Detectors for video rate scanning images, Applied Optics, 32: 6227-6235(1993).

Webb RH. Bibliography on Confocal Scanning Microscopes. In Handbook of Biological Confocal Microscopy, 3rd edition James Pawley ed. 571-577 (1995) Plenum.

Webb, RH and F Rogomentich, A confocal microscope with large field and working distance, Applied Optics 38 4870-4875 (1999).

Webb, RH, Theoretical Basis of Confocal Microscopy, Methods in Enzymology.

Weinhaus RS, Burke JM, Delori FC, and Snodderly DM, "Comparison of fluorescein angiography with microvascular anatomy of Macaque retinas," Exp. Eye Res. 1995. 61, 1-16.

Weiter JJ, Hochman M, Elsner AE, Burns SA. Foveal photopigment variation in AMD and relation to prognosis for visual acuity. Invest. Ophthalmol and Vis. Sci, B671, S384, 1998.

Wolf S, Remky A, Elsner AE, Arend O, and Reim M. Indocyanine green video angiography in patients with retinal pigment epithelial detachments. German J. of Ophthalmology 3, 224-227, 1994.

Wolf S, Wald K, Elsner AE, and Staurengi G. Indocyanine green choroidal videoangiography: A comparison of imaging analysis with the scanning laser ophthalmoscope and the fundus camera. Retina 13, 266-269, 1993.

Wu, S, Burns, SA, Elsner, AE, Eskew, RT, and He, J. Rapid sensitivity changes on flickering backgrounds: tests of models of light adaptation, J. Optical Soc. Amer 14, 2367-2378, 1997.