Biomedical Engineering
FLORIDA INTERNATIONAL UNIVERSITY

Dr. Jessica Ramella-Roman

Project Title: Improving on two wavelengths retinal oximeter

Recently a new technique has been introduced [1], [2] [3] that relies uniquely on the acquisition of two images of the retina at two different wavelengths for the evaluation of retinal oximetry across the visual field. A CE marked device has been developed and has found great favor in the ophthalmic community [4]-[6]. (http://www.oxymap.com)

Briefly the technique works as follow: two images of the fundus are acquired with a fundus camera or equivalent tool, one in the green region of the spectrum (isosbestic wavelength) and one in the red region of the spectrum. Pixel intensity values on the vessel and near the vessel are used to calculate the local optical density (OD) at each wavelength. A calibration step is then applied, one artery and one vein within the visual field are selected their optical density is calculated as described above. Values of oxygen saturation taken from the literature (95% for arteries and 70% for veins) are imposed to the calibrating artery and vein and then used as known parameters to calculate oxygen saturation for all other wavelengths. The technique is gaining popularity because of its simplicity and consistent results on a single patient, yet the validity of the technique vis-à-vis large epidemiologic studies remains to be confirmed.

We have utilized a Monte Carlo model of light transport in the retina to determine the error associated with the two-wavelength technique and have shown that a new calibration methodology is necessary to make this technique viable for clinical use. The student will work both on instrumentation design and computational modeling to create a new calibration paradigm for retinal oximetry.

REFERENCES

[1] S. H. Hardarson, M. S. Gottfredsdottir, G. H. Halldorsson, R. A. Karlsson, J. A. Benediktsson, T. Eysteinsson, J. M. Beach, A. Harris, and E. Stefansson, “Glaucoma Filtration Surgery and Retinal Oxygen Saturation,” Investigative Ophthalmology & Visual Science, vol. 50, no. 11, pp. 5247–5250, Nov. 2009.

[2] S. H. Hardarson, S. Basit, T. E. Jonsdottir, T. Eysteinsson, G. H. Halldorsson, R. A. Karlsson, J. M. Beach, J. A. Benediktsson, and E. Stefansson, “Oxygen Saturation in Human Retinal Vessels Is Higher in Dark Than in Light,” Investigative Ophthalmology & Visual Science, vol. 50, no. 5, pp. 2308–2311, Apr. 2009.

[3] M. Hammer, W. Vilser, T. Riemer, and D. Schweitzer, “Retinal vessel oximetry-calibration, compensation for vessel diameter and fundus pigmentation, and reproducibility,” J. Biomed. Opt, vol. 13, no. 5, p. 054015, 2008.

[4] J. P. Paul, R. A. O'Connell, S. L. Hosking, A. J. Anderson, and B. V. Bui, “Retinal oxygen saturation: novel analysis method for the oxymap.,” Optom Vis Sci, vol. 90, no. 10, pp. 1104–1110, Oct. 2013.

[5] R. A. O'Connell, A. J. Anderson, S. L. Hosking, A. H. Batcha, and B. V. Bui, “Test-retest reliability of retinal oxygen saturation measurement.,” Optom Vis Sci, vol. 91, no. 6, pp. 608–614, Jun. 2014.

[6] J. V. Kristjansdottir, S. H. Hardarson, G. H. Halldorsson, R. A. Karlsson, T. S. Eliasdottir, and E. Stefansson, “Retinal oximetry with a scanning laser ophthalmoscope.,” Investigative Ophthalmology & Visual Science, vol. 55, no. 5, pp. 3120–3126, May 2014.

Project Title: Oral Mucosa Vessel Density

An inherited predisposition is one of the most important risk factors for colorectal cancer (CRC) and is implicated in 20 to 30% of all cases [1,2]. One of the most common inheritable colorectal cancer syndromes is familial adenomatous polyposis (FAP). FAP is caused by a germline mutation of the APC (Adenomatous Polyposis Coli) gene, conferring a multiplicity of adenomas at younger age and a near 100% risk of colorectal cancer by the sixth decade of life if a preventative colectomy is not performed. Presently, the recognition of the majority of individuals at increased risk for inherited forms of CRC occurs only after evaluation of family history revealing multiple generations with CRC and other tumours, which usually occurs at the time of diagnosis of CRC in the proband. Currently, there are no definitive phenotypic markers for many of the inherited forms of CRC to identify high-risk individual presymptomatically although several studies have shown that these individuals often develop benign soft tissue and bony tumors, desmoid tumors, extraintestinal cancers, and [3] hypertrophy of the retinal pigment epithelium [4].

Furthermore presymptomatic genetic testing is expensive and not entirely conclusive, as approximately 20% of individuals with apparent familial CRC have no detectable mutation [5], in this paper these individuals will be classified as No Mutation Found (NMF).

Light reflectance spectroscopy has been utilized to analyze vascular abnormalities and vessel structure in the oral mucosa of patients with another form of hereditary colorectal cancer, Hereditary nonpolyposis colorectal cancer (HNPCC) [6]. Utilizing this technique, investigators concluded that there was a measurable difference in the light reflectance patterns from the oral mucosal tissues of HNPCC patients compared to controls, with reflectance values in the 590-700 nm wavelength range significantly lower for individuals with HNPCC. However, Carrara et al. [7] performed a similar clinical test and showed that there was no considerable difference in oral mucosal reflectance between HNPCC carriers and controls. In a different study De Felice et al. [8] showed that increased oral vascular network complexity was related to gene mutation carrier status and appeared to be a consistent phenotypic marker for HNPCC.

The analysis of the geometrical characteristics of micro-vascular networks of the oral mucosa was successfully applied to other hereditary conditions such as Ehlers-Danlos syndrome, [9], Down syndrome [10], and achondroplasia [11, 12], to name a few.

The main goal of this study is to develop a system to measure vessels in the oral mucosa [13], oral mucosal vascular density (OMVD) in combination with a Kolmogorov complexity algorithm [14] can be used to assess the probability of an individual to be either FAP or HNCPP positive.

Deliverable

- A user friendly general user interface based on Matlab or other software that controls a camera and calculates the OMVD.
- Testing of the system on optical standards
- Testing of the system in human subject –Possible IRB
- Can the system be used to measure vascular flow?

References and links

W. M. Grady. “Genetic testing for high-risk colon cancer patients,” Gastroenterology 124(6), 1574-94 (2003).

W. M. Grady. “Genetic testing for high-risk colon cancer patients,” Gastroenterology 124(6), 1574-94 (2003).

J. Utsunomyia, and T. Nakamura, “Osteomatous changes and tooth abnormalities found in the jaws of patients with familial polyposis coli,” Br J Surg. 62,45-51 (1975).

E. L Traboulsi, A. J. Krush, E. J. Gardner, S. V. Booker, G. J. Offerhaus, J. H. Yardley, S. R. Hamilton, G. D. Luk, F. M. Giardiello, S. B. Welsh, P. Hughes and I. H. Maumenee, “Pigmented ocular fundus lesions: Prevalence and significance in Gardner syndrome,” N Engl J Med. 316,661-667 (1987).

P. Lichtenstein, N. V. Holm, P. K. Verkasalo, A. Iliadou, J. Kaprio, M. Koskenvuo, E. Pukkala, A. Skytthe , and K. Hemminki, “Environmental and heritable factors in the causation of cancer-analyses of cohorts of twins from Sweden, Denmark, and Finland,” N Engl J Med. 343(2), 78-85 (2000) .

C. De Felice, M. Gentile, A. Barducci, A. Bellosi, S. Parrini, G. Chitano, and G. Latini, “Abnormal oral mucosal light reflectance: a new clinical marker of high risk for colorectal cancer,” Gut. 55,1436-39 (2006).

M. Carrara, R. Marchesini, S. Tomatis, L. Bertario, and P. Sala, “Hereditary non-polyposis colorectal cancer carriers and abnormal light reflectance of oral mucosa,” Gut. 57.2. 279 (2008).

C. De Felice, G. Latini,G. Bianciardi, S. Parrini, G. M. Fadda, M. Marini, R. N. Laurini, and R. J. Kopotic, “Abnormal vascular network complexity: a new phenotypic marker in hereditary non-polyposis colorectal cancer syndrome,” Gut. 52(12), 1764-7 (2003).

C. De Felice , G .Bianciardi , L. Dileo , G. Latini and, S. , “Abnormal oral vascular network geometric complexity in Ehlers-Danlos syndrome,” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, Oral Endodontology 98, 429-34 (2004).

G. Latini, C. De Felice, S. Parrini, G. Chitano, and A. Verrotti, “Oral mucosa spectrophotometric changes in healthy parents of patients with Down syndrome,” Prenatal Diagnosis 24(9), 685-7 (2004).

M. Hammer, A. Roggan, and D. Schweitzer, “Quantitativd reflection spectroscopy at the human ocular fundus,” Phys Med Biol 47, 179-91 (2002).

C. De Felice , G. Latini, S. Parrini, G. Bianciardi, P. Toti, R. J. Kopotic, and D. M. Null, “Abnormal oral mucosal light reflectance in achondroplasia,” Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, Oral Endodontology 101(6), 748-52 (2006).

M. Sofka, and C. V. Stewart, “Retinal vessel centerline extraction using multiscale matched filters, confidence and edge measures,” IEEE Transactions on Medical Imaging 25(12), 1531-46 (2006).

R. N. Clark, “Reflectance Spectra,” AGU Handbook of Physical Constants, 178-88 (1995).

Project Title: An Imaging Pulse Oximeter Based on a Multi-Aperture Camera

Transmission and reflectance based pulse oximetry are commonly used in medicine [1]. Pulse oximeters are based on the light absorption of oxygenated hemoglobin (HbO2) and deoxyhemoglobin (Hb), for the assessment of oxygen saturation (SO2), which is the amount of oxygenated hemoglobin present in the blood. The detection of oxygen saturation is now going a step further utilizing images to facilitate insights that would otherwise be difficult to obtain [2,3]. Some applications of imaging pulse oximetry are monitoring of neoadjuvant chemotherapy, characterization of vascular skin lesions, and detection of tumors [4,5]. Image pulse oximetry could enable a physician to gain a better understanding of the area of interest while requiring less invasive testing.

Our imaging technique is based on synchronizing an imaging system to a photoplethysmographer. Photoplethysmography is the monitoring of time-varying changes in the volume of blood for a tissue. Light is directed onto an area of the skin and a photodetector is used to detect the light that is either reflected or transmitted through the skin, blood, and other tissue; the change in intensity is correlated to the change in blood volume. Within the plethysmogram signal, there is an AC signal and a DC signal. The AC component is a cardiac-synchronous signal caused by the arterial pulse and the DC component is a slow varying signal that is primarily caused by the total blood volume in the skin [6].
In a study done by Verkruvsse et al. [3] a consumer grade video camera was used to visualize the photoplethysmographic signal and determine a patient heart rate. With some additional filtering, they were able to distinguish arterial vasculature. Filtering was necessary because the DC component of the plethysmograph results in an offset that makes it difficult to know where the peak and trough are. By removing the DC offset arterial flow could be visualized. Their system used a broadband RGB filtering given by their specific imaging apparatus; consequently, quantitative data could not be ascertained.

A study done by Lee et al. [7], used noninvasive diffuse optical spectroscopy to monitor oxygen saturation during hypovolemic shock and fluid replacement. They too used a broadband source and were consequently unable to take into consideration the individual effects of oxyhemoglobin, deoxyhemoglobin, and melanin. Recently we have introduced a multi-aperture camera capable of taking 16 different images at known wavelengths in a single snapshot, we have used the system to determine oxygen saturation in the retina as well as skin wounds [8,9]. The system uses narrowband filters, which enable to quantitatively determine the concentration of oxyhemoglobin, deoxyhemoglobin, and melanin.

We propose a technique that uses a plethymographer to trigger the multi-aperture camera and take a snapshot at the peak and at the trough of the pulse waveform, the acquired images are finally used to calculate a value proportional to arterial oxygen saturation of the superficial skin vasculature

Deliverable

- Synchronization of a multiaperture camera with an off the shelf pulse oximeter
- Calibration of camera parameters

References and links

A. B. Hertzman and C. R. Spealman, “Observations on the finger volume pulse recorded photoelectrically,” Am. J. Physiol. 119, 334-335, (1937).
S. Hu, J. Zheng, V. Chouliaras, and R. Summers, ”Feasibility of imaging photoplethys- mography,” in Proceedings of the International Conference on BioMedical Engineering and Informatics, NewYork, pp. 72-75, (2008).

W. Verkruysse, L. O Svaasand, J S. Nelson, “Remote plethysmographic imaging using ambient light,” 16, (26) Optics Express (2008)
S. Wendelken, S. McGrath, G. Blike, and M. Akay, “The feasibility of using a forehead reflectance pulse oximeter for automated remote triage,” in Bioengineering Conference, 2004. Proceedings of the IEEE 30th Annual Northeast, (2004), pp. 180-181.
C. Zhou, R. Choe, N. Shah, T. Durduran, G. Yu, A. Durkin, D. Hsiang, R. Mehta, J. Butler, A. Cerussi, B. Tromber, A. Yodh, “Diffuse Optical Monitoring of Blood Flow and Oxygenation in Human Breast Cancer During Early Stages of Neoadjuvant Chemotherapy,” Journal of Biomedical Optics 12(5), September/October 2007.
J. A. Crowe and D. Damianou, “The Wavelength Dependence of the Photoplethysmogram and its implication to Pulse Oximetry,” in Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, (Institute of Electrical and Electronics Engineers, NewYork, 1992), pp. 2423-2424.
J. Lee, A. Cerussi, D. Saltzman, T. Waddington, B. Tromberg, M. Brenner, “Hemoglobin Measurement Patterns During Noninvasive Diffuse Optical Spectroscopy Monitoring of Hypovolemic Shock and Fluid Replacement,” Journal of Biomedical Optics 12(2) (March/April 2007).