Project Proposal: *The Application of OCT Lasers in Hair Follicle Imaging*

The function and resilience of hair plays a large role in our cultural identities and psychological well-being. Various forms of disorders associated with hair follicles comprise a significant portion of medical dermatology faced by skin specialists today. Some disorders of hair follicles involve hair loss, or alopecia, and a multitude of autoimmune disorders, such as hidradenitis suppurativa. Such diseases, while largely not life threatening, cause grave stress and psychological dysfunction in patients' lives. Researchers have even found that rates of depression and anxiety are higher in populations afflicted with visible skin diseases, those affecting hair in particular. Despite high levels of patient interest and sponsor resources made available to hair structure and disease research, progress developing efficacious treatments has been limited and unsatisfactory.

Some posit that advances in hair disorder treatments lag due to limitations with easily visualizing hair follicle morphology and evolution. Current methodologies resort to excision of scalp tissue, a painful, and often impractical convention, especially in children. Fortunately, the advent of imaging technology has begun to make less invasive hair follicle visualization a viable alternative. These include laser and in-vivo microscopic imaging. If successfully applied, these modalities would make monitoring hair follicle anatomy changes, disease processes, and efficacy of treatment more cost-effective and palatable by patients and research subjects.

Select imaging technologies have begun to show utility in diagnosis of various skin pathologies, such as melanoma and alopecia areata. I am interested in further studying multiple modalities of optical imaging to study hair follicles over time. To introduce this initiative using novel imaging technologies, we have initiated a project to study imaging modalities that will better characterize hair follicle biology. Ultimately our goal is to make hair disease pathology maximally accessible by researchers and clinicians. Information gathered during the initial phases of study will help us discern which techniques of hair follicle imaging are plausible and of most utility. If this first application of new technology is high yield, I would aim to further the imaging study by comparing hair follicles in healthy patients and those in patients with varying hair follicle disorders. All of these studies will continue to be designed in collaboration with the Beckman Laser Institute.

Study Design Summary:

Healthy patients will be recruited for imaging from research team personnel and their acquaintances. Potential control subjects will only be excluded if he or she has any signs of any type of hair follicle disease. To form the comparison cohort, patients with hair disorders will be recruited from UC Irvine Dermatology clinics. Patients will be welcome to participate despite varying durations of hair follicle disease diagnosis or types of treatment they are currently undergoing. The study will continue for two years. Control subjects will be imaged once for cross-sectional comparison data, while patients with diseases associated with hair follicles will be imaged in along different stages of their treatment.

These patients and control subjects will undergo hair follicle imaging with three different imaging technologies in order to maximize analysis potential. These modalities include multiphoton microscopy (MPM), optical coherence tomography (OCT), which has already begun development in hair follicle visualization, and spatial frequency domain imaging (SFDI), a technology currently being developed to visualize and diagnose melanomas. MPM is a form of in-vivo microscopy and has the potential to detect the intracellular anatomy of hair follicles. The amount of detail captured by MPM limits the imaging depth and area quality. OCT compliments MPM in that its images are less precise, but provide greater area and depth for analysis. OCT has recently been used to classify hair shaft diameter, cross-sectional surface area, and hair shape in alopecia area patients. Lastly SFDI combines two imaging techniques, polarization and hyperspectral, in order to examine the distribution of melanin and hemoglobin in skin. Although SFDI is of particular interest in diagnostic studies regarding melanoma, its utility in tracking blood sources has unexplored applications in hair follicle disorders. OCT, which has already been shown to effectively image hair follicles, will serve as the standard imaging technique by which to compare performance of MPM and SFDI in these varying new diagnoses.

This is a qualitative proof of concept pilot study. Data will be analyzed first for utility and then for patterns in potentially systematic quantification.

Data Collection Instruments:

Multiphoton microscopy (MPM/MPTflex) relies on nonlinear light-matter interactions to provide contrast and optical sectioning capability for high-resolution imaging. In biology, most of the systems have relied on two-photon excited fluorescence (TPEF) to produce images. With increasing applications of multiphoton microscopy to thick-tissue imaging, second-harmonic generation (SHG) from structural proteins has emerged as a potentially important new contrast mechanism.

In this study we will use a multiphoton tomograph (MPM/MPTflex), the same as the one previously used in IRB approved studies (HS#2008-6307, HS# 2011-8230). MPTflex is an MPM using a Spectra Physics MaiTai femtosecond laser tunable from 690nm to 1040nm as a source of two-photon excitation. We make use of an oil immersion Zeiss objective 40x with a numerical aperture 1.3. Average power at the sample keeps at 2 to 30 mW.

This system allows us to obtain simultaneously TPEF and SHG three dimensional images of the tissue. Images will be based on two-photon excitation of endogenous fluorophores and second-harmonic generation of intra-tissue collagen. In multiphoton microscopy (MPM), the major intracellular endogenous fluorophores are reduced nicotinamide adenine dinucleotide (NADH), flavin adenine dinucleotide (FAD), keratin and melanin. Also, an important endogenous fluorophore in MPM is the intra-tissue elastin.

Optical coherence tomography (OCT) is an imaging modality that uses reflected light from the sample. OCT uses the same principles of signal reflection as ultrasound imaging; however, in OCT the signal being reflected is infrared light. The initial light beam is split and measurements are made from the interference between the reference beam and the reflected beam. OCT has been previously used for scalp imaging in hair loss disease research.