Abstract
Reflectance confocal microscopy is a powerful in-vivo modality for imaging superficial layers of biological tissue, especially for human skin. Three dimensional imaging capability enables confocal microscopy to resolve structures of upper skin layer cells. However, sub-cellular structure and corresponding functional organelles play more important parts in skin diseases diagnosis and monitoring. We present a new multi-spectral reflectance confocal microscopy to achieve sub-cellular functional imaging in skin by utilizing our unique Keck multi-modality microscope. Spectral information and a modified Mie scattering model are incorporated to identify distribution of melanin and mitochondria in cells. Ex-vivo and phantom experimental results are presented. Further development of this new modality may lead to future clinical applications.

State of the Art
• Spectrally encoded confocal microscopy is developed to increase resolving ability, but spectral information is not utilized. [1]
• Spectral analysis with confocal microscopy is mainly focused on fluorescence imaging, but no work on reflectance spectral confocal microscopy has been reported in the literature yet.

Significance and Challenges
• Multi-spectral confocal microscopy incorporates 4-D information to achieve sub-cellular functional imaging.
• Direct spectral analysis of conventional reflectance confocal images may avoid invasive stain procedure of fluorescent dyes.
• A proper spectral un-mixing algorithm may be needed to separate the measured mixture spectra into independent physically meaningful spectra for further identifying small organelle within cells.
• A scattering model for spherical scatter with laser beam is needed to develop a physical-based classification procedure.

Technical Approaches
• Utilize ability of tunable wavelength of our Keck multi-modality microscope to obtain spectral confocal images.
• Apply a non-negative un-mixing algorithm of alternating least square and multivariate curve resolution (ALS-MCR) procedure for spectra separation. [2]
• Adopt a localization approximation (LA) to model light scattering of spherical particles with incident gaussian laser beam. [3,4]

References
5. Blair Simon, RICC and NSF Poster, 2006

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