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OPTICAL MARKERS THAT DISTINGUISH BENIGN MELANOCYTIC NEVI IN VIVO: A MULTIPHOTON MICROSCOPY STUDY

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Background: Multiphoton microscopy (MPM) is a laser-scanning microscopy technique that relies on non-linear light-matter interactions such as two-photon excited fluorescence (TPEF) and second harmonic generation (SHG) to achieve 3D images with sub-micron resolution. In MPM, the main sources of fluorescence are reduced nicotinamide adenine dinucleotide (NADH), flavin adenine dinucleotide (FAD), keratin, melanin, and elastin fibers while collagen is the main source of SHG signal. This presentation will focus on both qualitative and quantitative analysis of *in-vivo* microscopy images acquired from lesions diagnosed as common nevi, atypical nevi or melanoma.

Study: Imaging was performed with a clinical laser-scanning MPM-based tomograph (MPTflex, JenLab GmbH, Germany). We analyzed the MPM images corresponding to 15 lesions (5 in each group) both qualitatively and quantitatively. The qualitative analysis involved identifying morphological features of the lesions in the three groups and correlating MPM with histologic features. The quantitative analysis was based on TPEF and SHG derived from 3D MPM image analysis.

Results: Morphological changes imaged with MPM such as cytological atypia, lentiginous hyperplasia and appearance of nests of nevus cells on the sides of the rete ridges correlate well with histology. These morphological changes are also associated with variations in the TPEF and SHG signals. We defined a numerical "multiphoton melanoma index (MMI)" based on quantitative TPEF, SHG, and density of melanocytic dendrites in the upper epidermal layers. We show that the quantitative MMI scores corresponding to each group are significantly different from the scores in the other two groups.

Conclusion: These findings suggest that both qualitative and quantitative characteristics can be used to help guide further investigation of a larger number of patients in order to validate the proposed MMI scoring algorithm and evaluate the potential of MPM technology to distinguish dysplastic nevi from common nevi and melanoma.