

Higher Harmonic Generation Biopsy

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Traditional biopsy requires the removal, fixation, and staining of tissues from the human body. Its procedure is invasive and painful. Recently we have successfully demonstrated optical biopsy based on backward collected higher harmonic generation [1], which can perform *in vivo* examination and is noninvasive, highly penetrative, with no energy deposition and damage [2], without invasive pharmaceutical injection, and with three-dimensional imaging capability and sub-micron spatial resolution. Compared with previously demonstrated optical biopsy based on two-photon fluorescence, our demonstrated higher harmonic generation

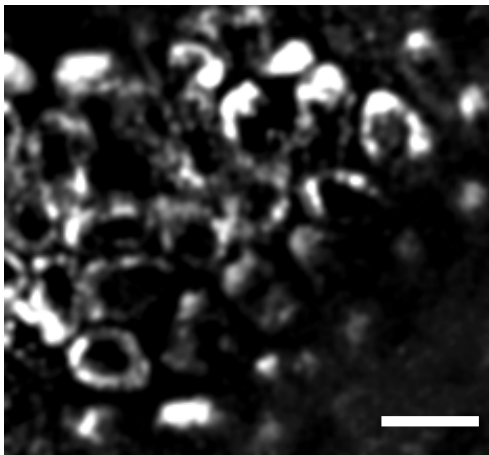


Figure 1: Horizontally sectioned backward-THG image taken beneath the human skin surface, showing the distribution of basal cells. Scale bar: 10 μm .

biopsy can avoid in-focus cell damages, multi-photon phototoxicity due to high optical intensity in the 800 nm wavelength region, and toxicity if exogenous fluorescence markers were required. From experimental results on human skin and animal sub-mucosa, our backward-collected higher harmonic generation biopsy can successfully reconstruct 3D cellular and subcellular images from skin surface through dermis. Besides, by utilizing backward propagating detection geometry, we will show that this technique is ideal for non-invasive clinical biopsy of human skin diseases and even useful for the early diagnosis of skin cancer symptom such as the angiogenesis.

and investigated. Third, potential of molecular imaging of cancer cells will be demonstrated and discussed. This work is sponsored by National Health Research Institute of Taiwan and NTU center for genomic medicine.

In this talk, several key issues will be addressed. First, optical damages in live specimens will be discussed. Second, physical origins of backward second harmonic generation and backward third harmonic generation (THG) will be formulated

[1] C.-K. Sun; C.-C. Chen, S.-W. Chu, T.-H. Tsai, Y.-C. Chen, and B.-L. Lin, "Multiharmonic generation biopsy of skin," *Optics Letters*, **28**, 2488-2490 (2003).

[2] C.-K. Sun; S.-W. Chu, S.-Y. Chen, T.-H. Tsai, T.-M. Liu, C.-Y. Lin, and H.-J. Tsai, "Higher harmonic generation microscopy for developmental biology," *Journal of Structural Biology*, **147**, 19-30 (2004).