In vivo and in situ Tomographic Micro-Diagnosis using Functional OCT

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1. Introduction
In atherosclerosis, malignant neoplasm and osteoarthritis and so on, since the disease condition should reach progressive stages with the microscopic tissue degeneration of biomechanical and biochemical tissue characteristics, the development of the non-invasive micro-diagnostic system has been required to carry out clinically tomographic visualization at the micro scale. Recently, Optical Coherence Tomography (OCT), based on the low coherence interferometry, has been being improved as a 3-dimensionally and tomographically subsurface imaging of micro structural biological tissue with high resolution of 1 to 10μm. However, biomechanical properties; vulnerability and visco-elasticity, and biochemical characteristics; drug infiltration and water content, have never estimated exhaustively, because OCT can provide only morphological tissue distribution as scattering intensity profile generated from spatial variation of refractive index. In this study, a tomographically diagnostic method "Multi-Functional OCT", is proposed and in/ex vivo performed as a 3-dimensional non-invasive detection with micro scale, which can offer the biomechanical properties "strain" by "OCSA", and the biochemical characteristics "delivered drug" and "water content" by "OCD" and "OCM", the biological tissue characterization of fibrous/lipid by "ARV", respectively.

2. Multi-Functional OCT
2.1 3-Dimensional Optical Coherence Straingraphy
Optical Coherence Straingraphy, "OCSA", has been developed as a 3-dimensionally tomographic and non-invasive visualizing technique of strain distribution. This can provide the accurate 3-dimensional displacement vector distribution from synthetic OCT images before and after deformation, by recursively applying the speckle cross-correlation technique based on 3D-FFT as well as the high-accurate subpixel analysis, i.e. upwind gradient method and volume deformation method. So this technique can resolve approximately 0.02 pixel of tissue displacement, resulting in the spatial distribution of 3-dimensional strain tensor extracted by the weighted moving least square method.

2.2 Optical Coherence Dosigraphy
Optical Coherence Dosigraphy, "OCD", is based on 2-Color OCT system, which is composed of two-band light sources having different optical absorption properties of delivered drug. OCD can employ as a tomographic scanner of delivered drug infiltration with micro scale, thus can be an effective modality as a micro-visualizing assay of DDS. Similarly, Optical Coherence Moisturegraphy, "OCM", is also constructed under 2-Color OCT system, where optical absorbance of water inside tissue is quite different. This is capable of tomographically in vivo diagnosing the water concentration map with approximately 4% resolution at the micro scale.

2.3 Attenuation, Reflection and Variance OCT
Attenuation, Reflection and Variance OCT, "ARV", is proposed as a tomographically visualizing technique of fibrous/lipid tissue characterization. This classification can be offered by harnessing optical information interacted with complicated biological tissue confused in OCT interference signals, i.e. attenuation, reflection, variance. Three parameters were extracted with almost the same high resolution as OCT, by means of weighted moving least square method. Actually, ex vivo applying ARV to atherosclerotic plaques of WHHL rabbits, extracted signals can be validated to be separately correlated with fibrous and lipid tissue comparing with histological images.

3. Application study of OCSA to Skin
OCSA were in vivo applied to human's skin so as to evaluate the applicability to skin care and cosmetic research. Figure 1 shows OCT image of fingertip, the horizontal high-intensity line on the top of image shows the skin surface, as OCT beam was scanning from the upper side. The high intensity wavy structure, where is under about 300μm from surface, can appear the boundary of stratum corneum and epidermis. This wounding structure could form the fingerprint structure, which could generate 3-dimensional anisotropic strain distribution by loading and deforming. As shown by Fig.1, OCSA can discover 3-dimensional shear strain distribution inside skin, which occurs alternately like a striped shape, corresponding to wavy concave location at the boundary.

Fig. 1 3D-OCT image (a) and 3D-OCSA εxy (b) image of finger pad skin tissue

4. Conclusion
The author proposed "Multi-Functional OCT", i.e. OCSA, OCM, OCD and ARV, as a novel in vivo tomographic visualizing technique, which can provide clinically, microscopically and non-invasively biomechanical strain, water content, delivered drug and fibrous/lipid tissue characterization, respectively.