Metabolic Characterisation and Particle Tracking by Clinical Multiphoton Tomography

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Multiphoton microscopy has been beneficially utilised in biomedical research and first elementary clinical trials addressing the pathophysiology of skin diseases. By means of multiphoton excitation, endogenous biomolecules like NADH, collagen or elastin provide information about the subcellular morphology, epidermal architecture and physiological condition of the skin. To gain a deeper understanding of the linkage between cellular structure and pathophysiological processes, multiphoton-based intravital tomography (MPT) and fluorescence lifetime imaging (FLIM) were combined within the scopes of inflammatory skin[1], chronic wounds[2] and drug delivery in clinical application.

MPT-derived high resolution optical biopsies facilitated the non-invasive characterisation of human skin, envisioning a potential replacement of punch biopsy-related skin histology. Owing to its subcellular resolution, MPT provided evidence of a redistribution of mitochondria in keratinocytes, indicating an altered cellular metabolism. Advanced morphometric algorithms reliably revealed a perinuclear accumulation in lesional skin in contrast to an even distribution in healthy skin[3]. Moreover, the detection of the onset and progression of inflammatory processes and wound healing impairment could be achieved.

In a combined administration of sustained spectrometric perfusion/oxygenation measurements of the skin, MPT-FLIM based *in vivo* tracking of applied therapeutic agents further broadened our scope: We repetitively examined the permeation, the subsequent distribution and the metabolic effects of therapeutic agents, directly visualised in both the skin of healthy subjects and of patients in their course of disease[4].

Therefore, MPT-FLIM offers new insights into the pathophysiology and the individual therapeutic course of skin diseases. In conclusion, the verification of an altered cellular metabolism facilitates a better understanding of the processes of wound healing and inflammatory skin, envisioning future clinical areas of MPT-FLIM application.

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