Structural imaging of collagen in biological tissues using Second Harmonic Generation microscopy

Margaux Schmeltz[1], Clothilde Raoux[1], Gaël Latour[1,2], Marie-Claire Schanne-Klein[1]

[1] *Laboratoire d'Optique et Biosciences, CNRS, Inserm, Ecole Polytechnique-IP Paris, Palaiseau*
[2] *Université Paris-Saclay, Gif-Sur-Yvette, France*
Email: marie-claire.schanne-klein@polytechnique.edu

Second harmonic generation (SHG) microscopy is the gold standard technique for collagen imaging without any labeling and with an unmatched sensitivity and specificity in intact tissues [1]. Collagen is a major component of connective tissues such as arteries, skin, bones and cornea. It is characterized by a 3D multiscale structure that is a key distinctive feature of every tissue and governs its functional behavior. A defective collagen 3D structure leads to tissue malfunctions, which is the case in many diseases featuring tissue remodeling. 3D imaging of collagen is therefore a major biomedical concern to decipher the relationship between structure and function in tissues and to implement sensitive and reliable diagnosis of diseases affecting collagen structure.

Analysis of collagen SHG images is however a complicated issue because SHG is a coherent optical signal and because biological tissues exhibit complex and often heterogeneous structures. In this context, we have implemented polarization-resolved SHG imaging, which provides the mean orientation of collagen fibrils in the imaging plane as well as their degree of orientational disorder [2, 3]. The normalized difference of SHG signals excited with left and right circular polarizations (that is SHG circular dichroism), on the other hand, specifically visualizes collagen fibrils oriented out of the imaging plane and probes their degree of polarity [3]. These advanced SHG modalities are efficient tools for quantitative structural imaging of collagen-rich tissues.

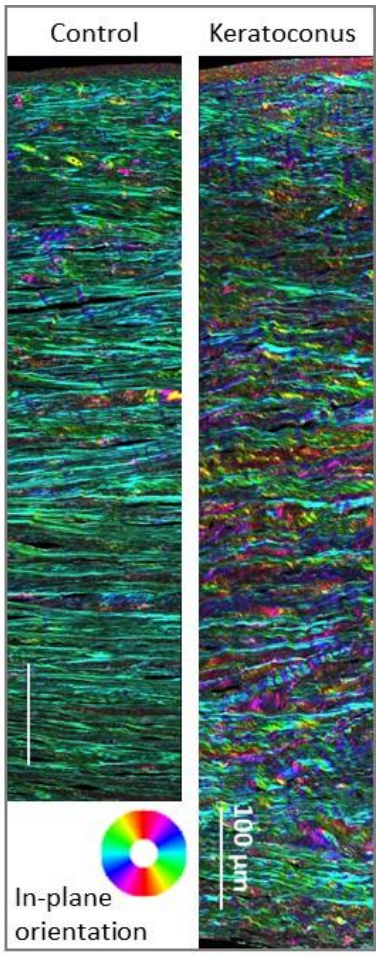

***Figure 1** : polarization-resolved SHG imaging of histological sections of healthy and pathological Human corneas (from [2]).*

[1] S. Bancelin et al, *Nat. Commun.,* **2014**, *5,* 4920.
[2] C. Raoux et al, *Biomed. Opt. Express,* **2021**, *12(7),* 4163-4178.
[3] M. Schmeltz et al, *Sci. Adv.,* **2021**, *7(29),* eabg1090.
[4] M. Schmeltz et al, *Optica* **2020**, *7(11),* 1469-1476.