Press Release

JenLab built CARS tomographs and pioneered clinical CARS imaging in patients with psoriasis

Jenlab accomplished the translation from lab microscopes to a clinical diagnostic tool for high-resolution optical *in vivo* biopsies with chemical vibrational fingerprints. The first patients and volunteers have been investigated with this novel clinical multimodal tomograph in Europe Union's largest hospital, the ***Charite*** in Berlin. Label-free 3D optical biopsies from the skin provided information on morphology at a subcellular level and also lipid and water content. Optical biosies were obtained completely non-invasively, that is without any mechanical or chemical treatments.

So far, label-free optical sectioning of human *in vivo* tissue had been performed with JenLab's clinical multiphoton tomographs **DermaInspect™** and the Prism Award winning **MPTflex™.** These optical biopsies were based on 3D images of fluorescent endogenous biomolecules such as NAD(P)H, flavins, melanin, keratin, and elastin. In addition, collagen was imaged using a nonlinear process called second harmonic generation (SHG). The tomographs employ a single near infrared (NIR) tunable femtosecond laser beam. A limitation of these fluorescence/SHG tomographs so far was the missing information from non-fluorescent and non-SHG active intratissue components such as the major important tissue molecules water and lipids.

Water and lipids can be imaged with Coherent Anti-Stokes Raman Scattering (CARS). However, no clinical CARS was performed up to now. The only available tools for CARS imaging were microscopes for the investigation of cells and ex-vivo tissue. CARS tomography alone without the information on the distribution of autofluorescent molecules and collagen would not be sufficient for pathologists to decide whether or not tissue is abnormal. However, a combination of multiphoton fluorescence/SHG tomography (MPT) and CARS imaging would provide excellent information combined with subcellular resolution.

JenLab together with **Charite**'s dermatologists and engineers from the company **APE GmbH** accomplished the first clinical CARS imaging in patients with dermatological disorders as reported online in *SPIE.TV*, *SPIE Proceedings*, and the journal *Laser Phys. Letters* (1-5).

The novel certified clinical hybrid tomograph **MPT-CARS** is a combination of the clinical multiphoton tomograph **DermaInspect™** and the *add-on* CARS module based on **APE**'s optical parametric oscillator (OPO). The OPO provides the required second laser beam for CARS imaging. The CARS signal relies on the wavelength difference between **DermaInspect's** tunable femtosecond "pump" laser beam (710-920nm) and the OPO's "Stokes" laser beam (1000-1300 nm) that has to be tuned to match vibrational modes of the molecule of interest.

In order to image the intratissue lipid distribution in patients suffering from *psoriasis*, *cancer*, and other skin diseases, the tomograph **MPT-CARS** wavelengths were tuned to 811 nm and

1053 nm, respectively. The CARS signal from lipids arises in the red spectral range (660 nm) from the symmetric CH_2 stretch vibration band near 2845 cm^{-1} and could be detected with a red-sensitive photomultiplier. Collagen was detected in the blue spectral region due to SHG and the biomolecules NAD(P)H, flavins, keratin, elastin, and melanin in the green/yellow. The combined mean power of both beams did not exceed 50 mW as required by the *European Notified Body* for the approval of medical products ("Zulassungsstelle"). The standard acquisition time for an optical section (0.4x04 mm^2) was 7 seconds. Up to 20 sections at different tissue depths were obtained per region of interest with a piezodriven high NA objective.

The distribution of topically applied lipid-water-emulsions was investigated in time-lapse studies that are of high interest for cosmetics and pharmaceutical companies.

Further clinical studies are currently performed within the German *BMBF* project *ChemoPraevent* to further evaluate the potential of this multimodal hybrid multiphoton tomograph **MPT-CARS** for early diagnosis of skin diseases, optimization of treatment procedures, the evaluation of the efficacy of cosmetics, and the investigation of side effects of pharmaceutical drugs such as chemotherapy agents.

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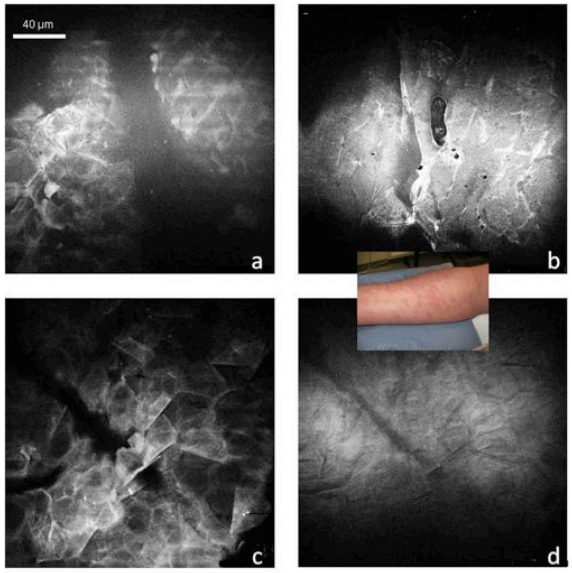

Fig 1. Clinical CARS images. Top raw: healthy skin, bottom raw: patients suffering from psoriasis, left: autofluorescence, right: CARS from *Laser Phys. Lett. 2011*

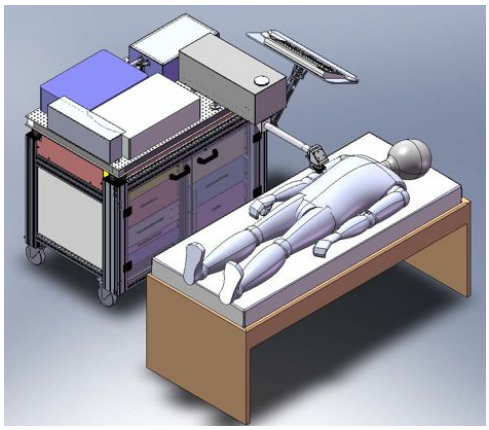

Fig. 2. Certified clinical CARS tomograph at the Charite hospital.

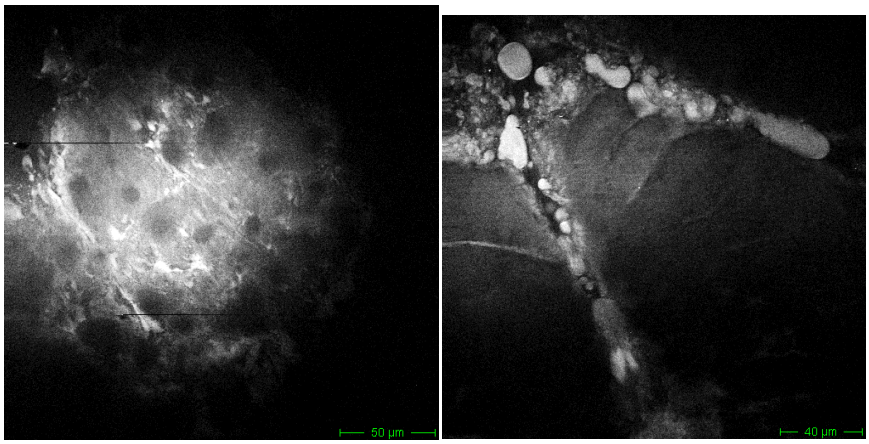

Fig. 3 CARS images at the skin surface. Left: Optical *in vivo* CARS section of the *stratum corneum* of psoriasis affected skin. Right: CARS image after topical application of an omega3-oil containing cosmetic emulsion.