This paper appears in: *Lasers and Electro-Optics*, CLEO/Pacific Rim 2001. The 4th Pacific Rim Conference, Chiba, Japan, 15-19 July 2001
Volume1, pages: I-234 - I-235, 2001
ISBN: 0-78036738-3

MJ1-5

Confocal probing of skin during it clearing

I.V. Meglinski[◇], S.J. Matcher[†], A.N. Bashkatov[*], E.A. Genina[*] and V.V. Tuchin[*]
[◇] - School of Mechanical Engineering, Cranfield University, Cranfield, Bedfordshire MK43 0AL, UK
[†] - School of Physics, University of Exeter, Exeter, EX4 4QL, Devon, UK
[*] - Department of Physics, Saratov State University, Saratov, 410026, Russia

Abstract - The effect of temporal skin tissues clearing produced by diffusion of the osmotically active chemical agents into the skin are studied with a confocal probing. Skin tissues optical properties and their changes are presented.

Diffusive injection of the osmotically active chemical agents in living tissues produces temporal effect of the light scattering reducing [1, 2]. The preliminary experiments on the rat skin where various solutions of *glucose*, *glycerol*, *trazograph*, *polyethylen glycol*, cosmetic lotions and gels taken in the capacity of innocuous chemical agents show that diffusion of the chemicals into skin temporary pushes water out of the upper skin tissues [2, 3]. The matching of the refractive indices of the structural elements of skin is caused. This temporary increases the transparency of upper skin layers, that, respectively, allows the unrestricted light to permeate deeper into tissues. The augment of the skin layers transparency typically increases for 10-40 minutes, depending on the chemical agent. Then due to the physiological response of the organism water content of skin tends back to initial level and the transparent skin returns to normal.

Presumably the increasing of the upper skin layers transparency can improve the penetration depth, image contrast and spatial resolution in confocal microscopy, optical coherence tomography (OCT) and other medical diagnostic techniques and could be useful in laser surgery as well.

The purpose of the present work is a theoretical examination of how the changes of the optical properties of the upper skin layers affect the confocal probing and what depth of the effective detection we can rich.

Taking into account possible variations in thickness of skin layers and following computational model of the skin developed recently [4], we calculate the detection depth sensitivity (DDS) for a confocal probing.

The details of how we do our simulation are justified shortly. Following the ray-tracing coupled with Monte Carlo technique [5] we simulate photon packets confocal injection and detection for multi-layered highly scattering medium, modelling human skin. Monte Carlo method has been widely described and involves modelling stochastic processes such as light absorption and scattering using computer generating random number to generate random scattering lengths and angles, *etc.* Our simulation of DDS [6-7] for skin is based on the recently developed Monte Carlo technique [4].

We correspond skin tissues optical properties to *Caucasian* type of skin with respect to visible/NIR range of spectra [8]. Changes in the optical properties of skin tissues due to their chemical acting are estimated regarding the variations of the osmotically active chemical agents diffusion at different depths in skin and its structure.

The discussion of skin tissues optical properties and their changes with the *glycerol* and *40%-glucose* solution injection into skin is given. We correspond the average reflectance indices of the skin layers during their clearing to the refractive indices of *glycerol* and 40% *glucose* solutions, i.e. 1.454 and 1.39, respectively.

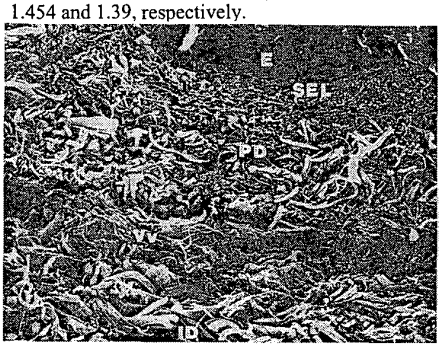

FIG.1. Scanning electron micrographs of the skin [9]. **E** represents *Living epidermis*; **SEL** shows fine connective tissue of the subepidermal layers; **PD** presents the *Papillary dermis*; **Vv** is the layer with horizontal blood vessels *Upper blood net plexus*; **ID** shows the collagen fibre bundles of the *Reticular dermis*.

The different size and packing of the collagen fibre bundles (see FIG.1) produce the spatial-time variations in the diffusions of *glucose* and *glycerol* solutions into the skin. For example, the *Stratum corneum* greatly clears in the first minute of the

process. It is connected mainly with immersion of upper layer of dead cells just after administering of the agent. Therefore main decreases of the scattering coefficient μ_s of *Stratum corneum* is observed both with *glycerol* and *glucose* solutions diffusion. Then the slower diffusion process takes place. Intradermal diffusion of chemical agents is characterised by retarding in the *Upper blood net plexus*, that seems to be explained by blood vessels orientation (see FIG.1). In deep skin layers the character of the chemical agents diffusion is roughly homogeneous.

We emphasise that the optical properties of *Upper blood net plexus* and *Deep blood net plexus* are changed a little, due to the high (1-2%) volume fraction of blood in the layer. The optical properties of the *Deep blood net plexus* and *Subcutaneous fat* layers are changed a little as the chemical agents diffusion have not rich this depth during 20 minutes of acting.

We determine the average diffusion coefficient of 40% *glucose* solution in *Reticular dermis* as 2.56×10^{-4} mm^2/sec at the $37°C$ of skin, and the variations of the diffusion coefficient in the layers are $0.1\text{-}0.3\times10^{-4}$ mm^2/sec.

Regarding dynamic of the *glucose* diffusion into the skin we choose the characteristic time intervals 5, 10 and 20 minutes. Whereas different molecular nature of the *glycerol* produces the complex oscillations in the diffusion into the skin.

As an example FIG.2 presents the results of simulation of DDS for the confocal probing of skin during it clearing with the 40% *glucose* solution.

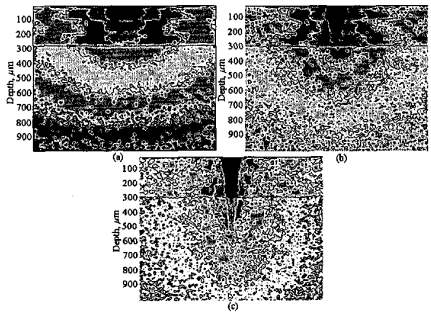

Fig.2. DDS for a confocal skin probing during the 40% *glucose* solution diffusion. (a) - 5 minutes, (b) - 10 minutes, and (c) - 20 minutes chemical diffusion. The confocal probe parameters are: lens diameter - 5 *mm*, focal length - 10 *mm*, the pinhole diameter - 10 *μm*, and height of lens above the surface - 9.7 *mm*.

The results of simulation show that signal spatial localisation offered by a confocal probe in the skin tissues during their clearing is potentially useable for the *Reticular dermis* monitoring. The pathlength in a forward direction for the incident radiation increases as the unrestriction of incident light on the refractive index mismatching decreases. So, after 20 minutes of the 40% *glucose* solution diffusion into the skin, we can detect signal from the tissues located twice as deep in skin, i.e at the depth 700-800 *μm*.

We emphasise that hypodermal injection of osmotic active agents increases the speed of the tissue clearing as the agents diffuse straight into the dermal layers with the exception of the *Stratum corneum* barrier. Whereas, at the superficial administering of the clearing agent on the skin the diffusion speed decreases and the time of the clearing increases. The obtained results may be useful to evaluate the capabilities of skin imaging systems based on the confocal probing.

IVM and SJM acknowledge financial support of EPSRC grant GR/L89433, and ANB, EAG and VVT acknowledge financial support of grant "Leading Scientific Schools" No.00-15-96667 of the Russian Basic Research Foundation and by Award No. REC-006 of the U.S. Civilian Research & Development Foundation for the Independent States of the Former Soviet Union (CRDF).

[1] V.V.Tuchin *et al.*, *J.Biomed.Opt.*, **2**, 401-417, 1997.
[2] G.Vargas, *et al.*, *Laser in Surgery and Medicine*, **24**, 133-141, 1999.
[3] V.V. Tuchin, *et al.*, *Proc. SPIE*, **3863**, 10-21, 2000.
[4] I.V. Meglinsky, S.J. Matcher, *Med. & Biol. Eng. & Comput.*, **39**, 2001.
[5] J.M. Schmitt and K. Ben-Letaief, *JOSA A*, **13**, 952-961, 1996.
[6] M. Hiraoka, *et al.*, *Phys. Med. Biol.*, **38**, 1859-1876, 1993.
[7] E.Okada, *et al.*, *Phys. Med. Biol.*, **40**, 2093-2108, 1995.
[8] V.V. Tuchin, *Tissue Optics: Light Scattering Methods and Instruments for Medical Diagnosis*, SPIE Press **TT38**, 2000.
[9] K.A. Holbrook and P.H. Byers, *American Journal of Medical Genetics*, **34**, 105-121, 1989.