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Diagnostic aspects of lichen sclerosus and skin cancer studied with laser scanning microscopy

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Arvid Carlsson föreläsningssal,

Medicinaregatan 3A, den 18:e september 2020, klockan 9:00

av Despoina Kantere

Fakultetsopponent:

Professor Merete Haedersdal

University of Copenhagen, Denmark

Avhandlingen baseras på följande delarbeten

I. The clinical spectrum of lichen sclerosus in male patients—a retrospective study. Despina Kantere, Gun-Britt Löwhagen, Gunilla Alvengren, Anna Månesköld, Martin Gillstedt and Petra Tunbäck. Acta Derm Venereol 2014; 94: 542-546

II. Exploring laser scanning microscopy as a non-invasive diagnostic tool for genital lichen sclerosus. Despoina Kantere, Noora Neittaanmäki, Kristina Maltese, Ann-Marie Wennberg Larkö, Marica B. Ericson, Petra Tunbäck. In manuscript

III. Anti-Stokes fluorescence from endogenously formed protoporphyrin IX – Implications for clinical multiphoton diagnostics. Despina Kantere, Stina Guldbrand, John Paoli, Mattias Goksör, Dag Hanstorp, Ann-Marie Wennberg Larkö, Maria Smedg and Marica B. Ericson J Biophotonics. 2013;6(5):409–415. doi:10.1002/jbio.201200119

IV. Label-free laser scanning microscopy targeting sentinel lymph node diagnostics – A feasibility study *ex vivo*. Despoina Kantere, Jan Siarov, Shahin De Lara, Samad Parhizkar, Roger Olofsson Bagge, Ann-Marie Wennberg Larkö, and Marica B. Ericson. Translational Biophotonics. 2020; https://doi.org/10.1002/tbio.202000002

V. Report on fluorescence lifetime imaging using multiphoton laser scanning microscopy targeting sentinel lymph node diagnostics. Jeemol James, Despoina Kantere, Jonas Enger, Jan Siarov, Ann-Marie Wennberg Larkö and Marica B. Ericson. J Biomed Opt. 2020;25(7):1–8. doi: 10.1117/1.JBO.25.7.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

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Diagnostic aspects of lichen sclerosus and skin cancer studied with laser scanning microscopy

Despoina Kantere

Department of Dermatology and Venereology, Sahlgrenska University Hospital, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Abstract

Histopathologic examination of tissue biopsies is the current gold standard for the diagnosis of dermatological problems. Similarly, in oncology, sentinel lymph node (SLN) biopsy is the state-of-the-art diagnostic method for metastasis screening. Although these methods are safe, they are associated with some limitations, particularly because they are invasive, labor-intensive, and time-consuming. Moreover, histopathological analysis does not always lead to conclusive results. Therefore, there is a need for the development of fast, accurate, and non-invasive diagnostic procedures, complementary to these standard techniques. It seems that laser scanning optical microscopy modalities have the potential to meet this need. Regarding this, the present study was conducted to explore the efficiency of two of these methods, namely reflectance confocal microscopy (RCM) and multiphoton microscopy (MPM), in dermatological and oncological applications. Particular focus was given to lichen sclerosus (LS), basal cell carcinoma (BCC), and malignant melanoma (MM) metastases, all of which are important disorders requiring improved diagnostic methods. This thesis builds upon the work reported in five papers. The first two papers involved the investigation of LS. In the first paper, we reported the clinical signs of LS, namely hypopigmentation, petechiae, and preputial constriction, based on which the diagnosis of LS was established. In the second paper, it was found that RCM could visualize the thick fiber structures corresponding to sclerosis in the dermis, thereby facilitating the differentiation of LS from normal penile skin. In the third paper, it was observed that the application of methyl-aminolaevulinic acid (MAL) on BCCs could not increase the contrast when imaged with *ex vivo* MPM. Furthermore, it was found that MAL-induced fluorescence cannot be excited by the expected two-photon excitation route when studied with MPM; rather, a one-photon process (i.e., anti-Stokes fluorescence) takes place. This finding is important not only for diagnostic aspects but also for future work in which photodynamic effects might be required. The fourth and fifth papers involved the investigation of MM metastases in lymph node tissues. It was found that particularly *ex vivo* MPM can enable the visualization of the characteristic morphologic features in this type of tissue. Furthermore, by extending the spectroscopic information to include also fluorescence life-time, the latter has the potential to increase the diagnostic ability. Taken together, the obtained results were indicative of the potential of laser scanning microscopy techniques as diagnostic tools for the detection of LS, BCCs, and MM metastases to lymph nodes. Future studies are encouraged to fully explore the potential of these techniques to be used for dermatological and oncological investigations in a non-invasive/intravital manner.

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