

Epidemiology, Diagnostics and Treatment of Non-melanoma Skin Cancers

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Oscar Zaar, defended his doctoral thesis on March 22, 2018 at the Department of Dermatology and Venereology Institute of Clinical Sciences Sahlgrenska Academy, University of Gothenburg. Opponent was Gregor Jemec, Department of Dermatology, Roskilde Hospital, Health Science Faculty, University of Copenhagen, Roskilde, Denmark and Supervisor was John Paoli, Department of Dermatology and Venereology Institute of Clinical Sciences, Gothenburg, Sweden. The thesis is available at: <https://gupea.ub.gu.se/handle/2077/54538>.

Skin cancer, including malignant melanoma and non-melanoma skin cancer (NMSC), is a growing problem due to the increasing incidence in Sweden and in other Caucasian populations. NMSCs are diagnosed as often as all other cancers combined and include basal cell carcinoma (BCC), squamous cell carcinoma (SCC), precursors to SCC such as Bowen's disease (BD) and actinic keratosis (AK), as well as several rare skin cancers including Merkel cell carcinoma (MCC). The purpose of this thesis was to investigate novel aspects within the fields of epidemiology, diagnosis and treatment of NMSCs.

In study I, the incidence and clinical characteristics of Swedish patients with MCC was explored. During the study period from 1993 to 2012, the age standardised incidence of MCC almost doubled with an increase of 73–85% depending on the population used for age standardisation. The overall incidence for women and men per 100,000 persons, using the world population for age standardisation, rose from 0.11 to 0.19 between 1993 and 2012.

In study II, the effectiveness of photodynamic therapy (PDT) for the treatment of BD was evaluated retrospectively for 423 lesions in 335 patients. The study showed that PDT was a relatively effective treatment with a complete clearance rate of 63.4% after a median follow-up time of 11.2 months. BD lesions >20 mm in size and a single session of PDT were factors associated with statistically worse outcome.

In study III, a novel irradiation protocol in PDT for multiple AKs using a stepwise increase of light intensity, staying below 50 mW/cm² during the whole treatment session, was compared to the conventional irradiation protocol to assess pain levels during treatment and effectiveness. Both protocols had the same total light dose of 37 J/cm². The novel treatment protocol led to a small but statically significant decrease in pain (D 1.1 points on a visual analogue scale, $p < 0.01$). However, the clearance rate with the new protocol was slightly but significantly lower than that of the conventional protocol (91.2% vs. 93.7%, respectively) ($p = 0.04$).



Fig. 1. Gregor Jemec (Opponent), Oscar Zaar and John Paoli (Supervisor).

In study IV, the chemical composition of lipids in BCCs was mapped using Time-of-Flight-Secondary-Ion-Mass-Spectrometry (ToF-SIMS). ToF-SIMS was able to identify different lipids in healthy and cancerous tissue. Furthermore, sphingomyelin lipids were found in aggressive BCCs whereas phosphatidylcholine lipids were observed in less aggressive tumours.

In conclusion, the incidence of MCC has increased the last 20 years, PDT is a relatively effective treatment modality in BD, novel illumination protocols with lower light intensity can decrease pain in PDT and ToF-SIMS can be used to identify the lipid composition of BCCs.

LIST OF ORIGINAL PUBLICATIONS

1. Zaar O, Gillstedt M, Lindelöf B, Wennberg-Larkö AM, Paoli J. Merkel cell carcinoma incidence is increasing in Sweden. *J Eur Acad Dermatol Venereol* 2016; 30: 1708–1713.
2. Zaar O, Fougelberg J, Hermansson A, Gillstedt M, Wennberg A-M, Paoli J. Effectiveness of photodynamic therapy in Bowen's disease: a retrospective observational study in 423 lesions. *J Eur Acad Dermatol Venereol* 2017; 31: 1289–1294.
3. Zaar O, Sjöholm Hylén A, Gillstedt M, Paoli J. A prospective, randomised, within-subject study of ALA-PDT for actinic keratoses using different irradiation regimes. Submitted for peer review.
4. Munem M, Zaar O, Dimovska Nilsson K, Neittaanmäki N, Paoli J, Fletcher JS. Chemical imaging of aggressive basal cell carcinoma using time-of-flight secondary ion mass spectrometry. *Biointerphases*. 2018; 13: 03B402. E-publication ahead of print.