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18TH ANNUAL CONGRESS
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SOCIETY
FOR
PHOTODYNAMIC
THERAPY**

BELGIUM

Brussels

FRIDAY 8 & SATURDAY 9 MARCH 2019





meeting organization

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Congress secretariat and hotel reservation

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Congress venue

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Dear Colleagues.

Welcome to the 18th Annual Congress of the European Society for Photodynamic Therapy in Dermatology, EURO-PDT. These series of Annual Congresses have developed into the largest and most important meetings on PDT in Dermatology in the World. While most participants come from Europe, increasingly participants come from other parts of the world. This year we are fortunate to be able to welcome Prof. Xiuli Wang from



the Dermatological University Clinic in Shanghai, which is the centre for PDT in Dermatology in China. The continuous development of PDT also for other indications than precancerous and cancerous skin lesions has broadened the use of PDT. Inflammatory acne and anogenital warts are two examples of diseases that benefit from PDT.

The speakers present their latest and most interesting data on PDT. We hope that this will generate interesting discussions and exchange of views between the participants, and that we all can take home with us valuable messages helping us in our research and/or management of patients.

Without the generous support from Galderma we would not have been able to organize this congress. A great thank you to Galderma from all of us.

Prof. Lasse R. Braathen
President EURO-PDT





training course



program **friday 8th march 2019**

- 08:30 Welcome and introduction of the agenda
[Lasse R. Braathen](#)
- 08:45 Interactive session: Introduction to practical PDT procedure – Patient selection – Lesion preparation – incubation
[Lasse R. Braathen](#), [Rolf-Markus Szeimies](#), [Colin A. Morton](#)
- 09:45 How to treat patients with AK (cPDT and DL-PDT) and NMSC (cPDT)
[Colin A. Morton](#)
- 10:15 The Basics of Conventional and Daylight-PDT, and the Field Cancerization Concept
[Lasse R. Braathen](#)
- 10:45 Break
- 11:00 PDT latest data (cPDT and DL-PDT)
[Rolf-Markus Szeimies](#)
- 11:30 Interactive session: Patient illumination with red light/daylight & simulated daylight (AK and NMSC)
[Lasse R. Braathen](#), [Rolf-Markus Szeimies](#), [Colin A. Morton](#)
- 12:00 Q&A and examination (multiple-choice)
- 12:30 Conclusion and Diploma Ceremony
[Lasse R. Braathen](#)



- 14:00 Welcome address - Euro-PDT President
Lasse R. Braathen, Bern, Switzerland
- 14:05 Welcome address - Local Congress President
Jan Gutermuth, Brussels, Belgium

SESSION 1: NMSC & PDT - BASIC ASPECTS

Chairs: Lasse Braathen, Jan Gutermuth

- 14:10 A review of the European Society for PDT (Euro-PDT) Annual Congress 2018
Lasse R. Braathen, Bern, Switzerland C01
- 14:30 PDT - What's new in guidelines and service standards
Colin Morton, Stirling, Scotland, UK C02
- 14:45 Skin cancer risk related to life UVR exposure and skin phototype
Peter Alshede Philipsen, Copenhagen, Denmark C03
- 15:00 Update of PDT in actinic cheilitis
Zoe Apalla, Thessaloniki, Greece C04
- 15:15 Non-invasive evaluation of therapeutic response of multiple AK of face and scalp treated with field cancerization treatments
Mariachiara Arisi, Brescia, Italy C05
- 15:30 Histological findings in AK resistant to PDT
Thomas Dirschka, Wuppertal, Germany C06
- 15:45 Histological subtype of treatment failures after noninvasive therapy for superficial BCC: an observational study
Lieke C.J. Van Delft, Maastricht, The Netherlands C07
- 16:00 An optimal ALA-PDT-DC vaccine for SCC
Xiuli Wang, Shanghai, China C08
- 16:30 Break



SESSION 2: PDT - LIGHT SOURCES

Chairs: Colin Morton, Thomas Dirschka

- 17:00 Low irradiance LED light compared to conventional PDT in the treatment of AK: a way to alleviate a painful treatment
Serge Mordon, Lille, France C09
- 17:15 PDT for AK: how low is the lower irradiance for an effective treatment?
Anne-Sophie Vignion-Dewalle, Lille, France C10
- 17:30 Low irradiance PDT in the treatment of AK
Patrick Gholam, Heidelberg, Germany C11
- 17:45 Light emitting fabrics PDT for the treatment of AK of the scalp/forehead: a randomized comparative clinical trial
Henry Abi Rached, Lille, France C12
- 18:00 Routine use of a flexible garment (Fluxmedicare®) for low-irradiance illumination in PDT of field cancerized areas
Rolf-Markus Szeimies, Regensburg, Germany C13
- 18:15 PDT with light emitting fabrics for vulvar extramammary Paget's disease
Laurine Ziane, Lille, France C14
- 18:30 Simulated daylight (SDL-PDT) treatment of AK with a new LED white light device: clinical results in a prospective observational pilot series in 30 patients
Serge Mordon, Lille, France C15
- 18:45 First clinical experiences on MAL-PDT with an artificial white light irradiation device (Dermaris®) in patients with multiple AK of the face and scalp: a split face study
Lutz Schmitz, Bochum, Germany C16
- 19:00 End of day
- 19:45 Meet in hotel lobby for congress dinner



SESSION 3: DAYLIGHT-PDT

Chairs: Yolanda Gilaberte, Serge Mordon

09:00 Daylight-Mediated PDT with MAL in AK treatment
Shantel Demay, Oakville, Canada C17

09:15 Increasing confidence in daylight PDT delivery in the UK
Ewan Eadie, Dundee, Scotland, UK C18

09:30 Daylight PDT without curettage: a clinical study
Hans Christian Wulf, Copenhagen, Denmark C19

09:45 Daylight-PDT with MAL applied at home for AK of the face or scalp: interventional study conducted in Germany
Sigrid Karrer, Regensburg, Germany C20

10:00 Efficacy of daylight PDT with MAL cream (Metvix®) to prevent AK and NMSC in organ transplant patients: a randomised pilot study
Isabel Bernad, Pamplona, Spain C21

10:15 Evaluation of the efficacy of daylight PDT for the treatment of AK in oculocutaneous albinism
Luiz Galvão, Fortaleza, Brazil C22

10:30 Break

SESSION 4: COMBINATION THERAPIES

Chairs: Hans Christian Wulf, Rolf-Markus Szeimies

11:00 Sequential treatment of daylight PDT and ingenol mebutate versus two sessions of daylight PDT for AK: an observational, prospective, comparison study
Yolanda Gilaberte, Zaragoza, Spain C23

11:15 PDT combined with other therapies to enhance patient outcomes
Christina Haak, Copenhagen, Denmark C24



11:30 A solution to the MOHS epidemic: PDT following curettage for BCC
Sheetal Sapra, Oakville, Canada C25

11:45 PDT combination therapies for AK: the more, the better?
Theresa Steeb, Munich, Germany C26

12:00 PDT: problems and solutions of laser-assisted PDT in a South German dermatologic practice after 15 years of experience
Martin Braun, Ueberlingen, Germany C27

12:15 Acral resistant warts successfully treated with curettage + microneedling + topical ALA-PDT
Stefano Caccavale, Naples, Italy C28

SESSION 5: NEW APPROACHES

Chairs: Claas Ulrich, Patrick Gholam

12:30 Optimization of sunscreen use
Hans Christian Wulf, Copenhagen, Denmark C29

12:45 Biodegradable polymeric nanoparticles enhanced the effectiveness of topical PDT for SCC
Lei Shi, Shanghai, China C30

13:00 Adjuvant concepts in field cancerization: PDT versus systemic therapies
Claas Ulrich, Berlin, Germany C31

13:15 Experience of intralesional PDT in hidradenitis suppurativa treatment
Maria Jesus Suarez Valladares, La Coruna, Spain C32

13:30 Granuloma annulare: report of 13 patients treated with PDT
Ana Julia García-Malinis, Huesca, Spain C33

13:45 Award ceremony and closing remarks
Lasse R. Braathen, Berne, Switzerland

14:00 End of meeting

glossary

AK	Actinic Keratosis
ALA	Aminolevulinic Acid
BCC	Basal Cell Carcinoma
nBCC	Nodular BCC
sBCC	Superficial BCC
CR	Complete response
Fx	Fractional
DL-PDT	Daylight PDT
LED	Light-Emitting Diode
MAL	Methyl Aminolevulinate
MOHS	Minister of Health and Sanitation
NMSC	Non-Melanoma Skin Cancer
PDT	Photodynamic Therapy
PpIX	Protoporphyrin IX
SCC	Squamous Cell Carcinoma
SD	Standard Deviation
VAS	Visual Analogic Scale

abstracts



Lasse R. Braathen
Bern, Switzerland

A review of the European Society for PDT (Euro-PDT) Annual Congress 2018

Colin Morton
Stirling, Scotland, UK

PDT - What's new in guidelines and service standards

Updated guidelines PDT have been produced by the British Association of Dermatologists, along with the publication of inaugural PDT Service Guidance and Standards. Both documents are accredited by the National Institute for Health and Care Excellence. They indicate high quality evidence to award a strong recommendation for the use of conventional PDT for patients with actinic keratoses (AK), Bowen's disease and superficial basal cell carcinomas (BCC), particularly for patients with multiple/large lesions and/or in poor healing sites. A 'consider' recommendation was given for PDT for thin (<2mm) nodular BCC and for daylight PDT for patients with confluent areas of AK on face/scalp. 'Consider' recommendations were awarded for field PDT as skin cancer prophylaxis as well as certain other early cancer as well as inflammatory/infectious dermatoses.

The Service Standards for PDT have been derived from an evidence-based review of the literature in order to develop guidance for the entire pathway of care of patients referred for PDT, to ensure appropriate staff training and safe delivery of treatment, with regular review of treatment response rates.

Wong TH, Morton CA, Collier N, et al . Guidelines for topical photodynamic therapy 2018, Br J Dermatol DOI10.1111/bjd.17309

<http://www.bad.org.uk/healthcare-professionals/clinical-services/service-guidance/pdt#>

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Peter Alshede Philipsen
Copenhagen, Denmark

Elisabeth Thieden, Ann-Sofie Sonne Holm-Schou,
Peter A. Philipsen, Jakob Heydenreich,
Hans Christian Wulf

Lifetime UVR exposure

Over a 14 years period (1999–2001, 2006 and 2012), 31 volunteers participated in sun behaviour studies with the same protocol wearing a personal UVR dosimeter and completed sun exposure diaries (15 946 measurements days, 126 days/person/year).

The participants individually maintained their UVR dose level and behaviour over the years. Eleven participants retired during the study period and received a non-significant 45% higher UV dose in 2012 ($p = 0.054$). Twenty participants still working, used sunscreen more often ($p = 0.019$) with higher SPF ($p < 0.001$) resulting in fewer unprotected days with risk behaviour ($p < 0.003$). Additionally, nine 30-year-old indoor workers (high school students in 1999) had fewer days sunbathing ($p = 0.008$) and fewer unprotected risk behaviour days ($p = 0.002$).

In conclusion working participants maintained their sun exposure while retirees had riskier behaviour with higher UVR dose, while the high school students changed to less risky behaviour.

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Zoe Apalla
Thessaloniki, Greece

Update of PDT in actinic cheilitis

Actinic cheilitis (AC) is a chronic neoplastic disorder of the lower lip vermilion. It is considered a precursor of squamous cell carcinoma (SCC), since it can progress from the in-situ into the invasive phase of SCC. Therefore, early and effective treatment is mandatory to reduce the risk of malignant transformation. Various therapeutic strategies, including local ablation, topical immunomodulation or chemotherapy, and surgical resection, have been proposed as therapeutic interventions for AC. Photodynamic therapy (PDT) with different treatment protocols and photosensitizers has been recently introduced as an alternative therapeutic option for AC. Daylight PDT (D-PDT) is a novel modality in which the activation of the topical photosensitizer is induced by the exposure to natural daylight without requiring preliminary occlusion. This simplified procedure is better tolerated by patients with AC as compared with conventional PDT.

5

Mariachiara Arisi
Brescia, Italy

C. Zane, M. Polonioli, C. Cozzi, S. Caravello,
C. Tomasi, P.G.Calzavara-Pinton

Non-invasive evaluation of therapeutic response of multiple AK of face and scalp treated with field cancerization treatments

Background: To date there are no study directed to the high frequency ultrasound study of AKs response to conventional treatments.

Objective: To assess and compare clinical, dermoscopic and high frequency ultrasound features in multiple AKs of face and scalp and skin field of cancerization after field-directed treatments.

Material and Methods: We randomized 90 patients with Olsen II AKs of the face and scalp to MAL-Photodynamic therapy (MAL-PDT), ingenol mebutate 0.015% gel (IngMeb) and diclofenac 3% gel (DHA). At baseline and 3 months after treatment, clinical, dermoscopic and high frequency ultrasound features were assessed.

Results: MAL-PDT induced a higher AKs area and modified-AKASI score reduction. It induced a higher reduction of the SLEB thickness and an improvement of dermic and SLEB echogenicity.

Conclusions: MAL-PDT was the most effective treatment and ultrasound confirmed its anti-elastotic effect on SLEB. Increased dermal echogenicity after MAL-PDT was confirmed dermoscopically by a reduction of lesional vascularization.

Statistical analysis:

Categorical variables were summarized using percentages, and continuous variables by calculating medians and range.

The medians of continuous variables were compared using the Wilcoxon test.

Any changes in clinical and ultrasound features with respect to treatment were defined using the non-parametric Kruskal-Wallis test for unpaired data. Based on the significant differences found, the comparison of each treatment was then defined by Mann Whitney test.

The Chi-square test was used to evaluate how dermoscopic data were influenced by treatment type.

Key Words:
AK, PDT, High frequency ultrasound, Ingenol mebutate, Diclofenac gel, Dermoscopy

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Thomas Dirschka
Wuppertal, Germany

Conrad von Dobbeler

Histological findings in AK resistant to PDT

Background: Actinic keratoses (AK) are common early in-situ carcinomas of the skin. Left untreated, AK may progress to cutaneous squamous cell carcinoma. Photodynamic therapy (PDT) is an established treatment option for AK. However, in field cancerization total lesion clearance is rarely achieved and some AK are resistant to treatment.

Objectives: To investigate treatment resistant AK histologically.

Methods: Histological investigation of treatment resistant AK after two consecutive cycles of conventional cMAL-PDT in 17 patients (13 male, 4 female, mean age 75 (7.9) years, Fitzpatrick type II: 82.3%. All AK were analyzed according to the AK I-III and Pro I-III classifications, acantholysis and follicular involvement.

Results: 13/17 AK (76.3%) of AK could be classified as basal proliferating AK grad III (Pro III), 9/17 (52.9%) exhibited acantholysis and 12/17 (70.6%) showed involvement of the follicular unit. 17/17 (100%) exhibited at least one of the aforementioned features.

Conclusions: Defined histological pattern as basal proliferation, acantholysis and involvement of the follicular unit are factors of poor treatment success.

Key Words:
AK, PDT, Histology, Field cancerization, Treatment resistance

Lieke C.J. Van Delft
Maastricht, The Netherlands

Patty J. Nelemans, Maud H.E. Jansen,
Aimee H.M.M. Arits, Marieke H. Roozeboom,
Myrurgia A. Hamid, Klara Mosterd,
Nicole W.J. Kelleners-Smeets

Histological subtype of treatment failures after noninvasive therapy for superficial BCC: an observational study

Background: Concerns were raised that recurrences after noninvasive therapy for basal-cell carcinoma (BCC) transform into non-superficial subtypes.

Objective: To evaluate the proportion of patients with a non-superficial treatment failure after noninvasive therapy for superficial BCC.

Methods: Data for 166 adults with histologically confirmed treatment failures was used from an RCT (March 2008-August 2010) with five year follow-up in patients with primary superficial BCC treated with methylaminolevulinic acid-photodynamic therapy (MAL-PDT), 5-fluorouracil, or imiquimod.

Results: A non-superficial subtype was found in 64 of 166 (38.6%) treatment failures: in 51.3% (38/74) for early and 28.3% (26/92) for later treatment failures ($p=0.003$, statistical significance tested with McNemar-analysis). The proportion of 'more aggressive' early failures was significantly lower following imiquimod (26.3%) compared to MAL-PDT (54.8%, $p=0.086$) and 5-fluorouracil (66.7%, $p=0.011$).

Conclusion: Non-superficial treatment failures after noninvasive therapy for superficial BCC occur mostly within 3 months post-treatment probably indicating underdiagnosis of the primary tumor rather than transformation.

Xiuli Wang
Shanghai, China

Jie Ji, Yunfeng Zhang, Haiyan Zhang,
Linglin Zhang, Lei Shi

An optimal ALA-PDT-DC vaccine for SCC

We developed an optimal dendritic cells (DC)-based cancer vaccine using ALA-PDT-induced apoptotic PECA cells (skin squamous cell carcinoma, SCC). The maturation of DCs induced by ALA-PDT-treated apoptotic PECA cells was studied using electron microscopy, FACS and ELISA. The anti-tumor immunity of the ALA-PDT DC vaccine was tested in mice. We observed the maturation of DCs could be potentiated by ALA-PDT treated SCC PECA cells. PDT induced apoptotic SCC cells are more capable in potentiating maturation of DCs than necrotic SCC cells, particularly using a light dose of 0.5J/cm² with a ALA concentration of 0.5mM. The mature DCs worked as SCC vaccines to prevent SCC growth. This optimal ALA-PDT-DC vaccine provided protection against SCC in mice, far stronger than that of DC vaccine obtained from freeze/thaw of SCC cells. Our results indicate that ALA-PDT is an effective method for the preparation of DC-based cancer vaccine for SCC.

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Serge Mordon
Lille, France

Anne Sophie Vignion-Dewalle, Elise Thecua,
Claire Vicentini, Cyril Maire, Pascal Deleporte,
Gregory Baer, Fabienne Lecomte, Laurent Mortier

Low irradiance LED light compared to conventional PDT in the treatment of AK: a way to alleviate a painful treatment

The conventional protocol (C-PDT) involving an irradiation with 37 J/cm² of red light after 3 hours of methyl 5-aminolevulinate incubation is effective for thin and non-pigmented AK. However, with an irradiance higher than 60 mW/cm², C-PDT is associated with high pain scores and many patients require pain management. This study aims to evaluate clinical studies comparing a PDT protocol involving irradiation with low-irradiance (lower than 20 mW/cm²) red light (Li-PDT) to C-PDT.

Li-PDT allows a significant and clinically relevant reduction in pain. Similar efficacy between Li-PDT and C-PDT at the same light dose is observed. A linear increase in pain with irradiance is obtained from pooling data reported in these studies: higher the irradiance, higher the pain (coefficient of determination: 0.726). The main advantages of Li-PDT compared to C-PDT are clearly an increased convenience and an improved tolerability for patients due to low pain.

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Anne-Sophie Vignion-Dewalle
Lille, France

Claire Vicentini, Gregory Baert, Elise Thecua,
Fabienne Lecomte, Laurent Mortier, Serge Mordon

PDT for AK: how low is the lower irradiance for an effective treatment?

Several clinical studies have recently reported that increasingly lower irradiances provide similar efficacy and better tolerability than standard high irradiances in red light photodynamic therapy of actinic keratosis (AK).

In order to determine how low is the lower irradiance for an effective treatment, we have compared irradiances measured during PDT using the Aktilite lamp (Galderma, Switzerland) with complete responses (CR) at 3 months. Measured in 114 AK of the forehead and scalp, irradiances were heterogeneous due to the imperfect match between the flat Aktilite lamp and the curvature of the treated area.

Of the 12 AK that received an irradiance lower than 8 mW/cm², 8 (66.7%) were in CR. Of the 7 AK that received an irradiance lower than 5 mW/cm², 4 (57.1%) were in CR. Due to a non-significant effect of irradiance on the complete response at 3 months, no lower irradiance limit for an effective treatment was found.

Low irradiance PDT in the treatment of AK

Background: PDT is effective in treating photodamaged areas with multiple actinic keratoses (AK). However, pain during therapy is still the most challenging obstacle. This intra-individual retrospective study compares pain and efficacy in patients using conventional PDT (c-PDT) vs. a low irradiance PDT protocol (li-PDT) with a reduced irradiance to 25% of c-PDT.

Methods: Thirty-one patients were treated with li-PDT and c-PDT on comparable fields of actinic damage on the forehead or the cheek. VAS pain scores were recorded and number and time to therapy interruptions were documented. AK numbers and grades were counted before and 4 weeks after PDT.

Results: Maintaining the total light dose of 37 J/cm², li-PDT resulted in significant less pain (VAS score 2.8 vs 7.6) and fewer therapy interruptions compared to c-PDT (P < 0.0005). No significant difference in treatment outcome was found (P = 0.068).

Conclusion: li-PDT reduces pain with at least comparable clinical outcome compared to c-PDT. Therefore, it is an effective and well-tolerated treatment for patients with multiple AK.

Light emitting fabrics PDT for the treatment of AK of the scalp/forehead: a randomized comparative clinical trial

Introduction: A major side effect of conventional Photodynamic therapy (C-PDT) is pain. We designed a light emitting fabrics (LEF) made of optical fibers connected to a light source that delivers homogenous light for PDT.

Objectives: Our primary objective was to compare LEF-PDT to C-PDT using topical 5-aminolevulinic acid efficacy for Actinic keratosis. Our secondary objective was to evaluate pain with a visual analogic scale (VAS).

Materials and Methods: We conducted a prospective bi-centric, randomized, open label, split-face comparative, and non-inferiority. Efficacy was evaluated by calculating the two-sided 95% confidence interval of the absolute difference in the rate of complete response at 3-months.

Results: 47 male patients with symmetrically distributed grade I/II AK were enrolled. The complete clinical response rate at 3 months with LEF-PDT was 79.3% vs 80.7% with C-PDT (p=0.34). The area treated with LEF-PDT had a lower average VAS of 0.32 compared to 7.43 with C-PDT (p<0.0001).

Conclusion: LEF-PDT was non-inferior to C-PDT, with significantly less painful sessions.

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Rolf-Markus Szeimies
Recklinghausen, Germany

Seyedeh Ghazal Hojati Taromsari, Cornelia Wiethoff,
Heike Haass

Routine use of a flexible garment (Fluxmedicare®) for low-irradiance illumination in PDT of field cancerized areas

Treatment of field cancerized areas on head and scalp with photodynamic therapy (PDT) is difficult since multiple illumination passes are required to achieve an optimal light dose deposit on curved surfaces. Daylight-PDT is a useful alternative, however its dependence on outdoor weather conditions and outside temperature only allows seasonal use. Based on an EC-founded project, the luminous medical device Fluxmedicare® was developed and is commercially available, consisting of three lasers as luminous source (638 nm; 12 J/cm²), connected to a fibre-optic based textile (18 x 20 cm) which delivers a controlled irradiance and homogeneity, whilst keeping the conformability/flexibility to illuminate curved surfaces.

So far 23 patients (mean age 74.4, 20 m, 3 f) were treated routinely for multiple AK (grade I and II) on field cancerized fields on scalp and décolleté. After lesion preparation, Metvix® was applied 30 min under a transparent plastic foil before exposure to continuous red light for 150 min. Due to the length of the light connectors, patients were able to move during the illumination process. VAS analysis revealed almost no pain during illumination (mean score 1.04, range 0-3), treatment was considered convenient by the patients. Side effects and cure rates were like DL-PDT.

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Laurine Ziane
Lille, France

E. Thecua, F. Lecomte, A-S. Vignion, C. Maire,
C. Vicentini, H. Abirached, D. Staumont, L. Mortier,
S. Mordon

PDT with light emitting fabrics for vulvar extramammary Paget's disease

Primary Extramammary Paget's disease (EMPD) mainly affects the genital regions, can progress into invasive tumor and widely affects patients' quality of life.

Surgery is the mainstay of treatment, but recurrences are common and multiple resections lead to severe functional alterations. Multiple clinical cases suggest that photodynamic therapy (PDT) could give relief on patients' symptoms, and control disease progression.

High pain levels experienced by patients during illumination sessions and complex shape of the genital area limit PDT benefits demonstration for EMPD. Light emitting fabrics technology could address these issues, and a lighting device dedicated to illumination of vulvar and perianal areas has been developed.

The PAGETEX® device is under investigation in an interventional clinical study (NCT03713203) which aims to determine if two PDT sessions performed two weeks apart with PAGETEX® allow a disease control at 3 months. Secondary objectives aim to assess treatment tolerance, quality of life evolution, residual PpIX fluorescence.

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Serge Mordon
Lille, France

Cyril Maire

Simulated daylight (SDL-PDT) treatment of AK with a new LED white light device: clinical results in a prospective observational pilot series of 30 patients

Natural DayLight-mediated PhotoDynamic Therapy (NDL-PDT) is an efficacious treatment option for thin actinic keratosis (AK) that offers advantages over conventional PDT in terms of tolerability, treatment duration, and cost. However rain and cold temperatures appear the main limitations of NDL-PDT. Indoor lightning (or simulated daylight: SDL-PDT) could offer an interesting alternative to NDL-PDT. A new light device (Dermaris, France) was evaluated for AK treatment. This system uses white LEDs with a broad waveband in the visible range with high amplitude at 630 nm. This system delivers 20 000 lux on a homogeneous 320cm² surface. 30 patients, with AK on the scalp, were treated. Immediately after MAL application, the light was switched on for 2h30 minutes (total dose: 26 /cm²). Pain, crust, pruritus and AK clearance were evaluated. No pain was observed during illumination. Crusts at Day 7 were observed in 14% and discomfort during 24 hours in 10% of patients. 30 % of patients required a 2nd session. In conclusion, this new device offers a very efficient alternative to conventional red light or DayLight PDT. The patient satisfaction is very high. This system is easy to install and could easily be used to treat other skin areas.

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Lutz Schmitz
Bochum, Germany

Eggert Stockfleth

First clinical experiences on MAL-PDT with an artificial white light irradiation device (Dermaris®) in patients with multiple AK of the face and scalp: a split face study

Background: Daylight photodynamic therapy (dl-PDT) is an effective treatment for patients with actinic keratoses (AKs). To overcome seasonal limitations, we aimed to determine the safety and efficacy of MAL-PDT with artificial white light (awl) emitting irradiation device.

Methods: Patients with AKs of the face and scalp received awl-PDT and dl-PDT with methyl aminolevulinate (MAL) one week apart in a split face-design. Awl-PDT was applied by a CE certified LED irradiation device (Dermaris®, main peaks at 448nm and 630nm; 20.000 Lux). The outcome should be assessed by AK area and severity index (AKASI) and lesion count (LC) prior to and 3 months after treatment. The pain was determined by use of a visual analogue scale (VAS). Safety was monitored by pulse and blood pressure measurements throughout treatment.

Results: First treated patients (n=4) showed comparable results regarding AKASI and LC reduction after two weeks of treatment. We observed no significant differences in blood pressure, pulse or pain throughout the treatment, yet.

Conclusion: Awl-PDT with MAL seems at this preliminary time point to be a comparable treatment alternative for patients with AKs on the head.

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Shantel D. J. Demay
Oakville, Canada

Shantel D. J. Demay, Sheetal Sapra, Kunal Sharma,
Rahul Sapra, and Priya Sapra

Daylight-Mediated PDT with MAL in AK Treatment

Background: Daylight-mediated photodynamic therapy is shown to be effective, tolerable, and convenient, with excellent patient satisfaction and cosmesis; however, it has not been studied in a Canadian population.

Objectives: To investigate the effectiveness, safety, and patient satisfaction of daylight-mediated methyl aminolevulinate (MAL)-PDT in the treatment of actinic keratosis (AK) in Canada.

Methods: A retrospective chart review of patients who received daylight-mediated MAL-PDT for AK at a single Canadian site from 2009-2016. Statistical methods include descriptive statistics.

Results: 112 patients were included. 177 sites were treated, mostly consisting of the face (n=92) and scalp (n=55). 13.4% of patients experienced side effects. Of the patients who expressed satisfaction, 83.3% reported being happy. 6.3% of patients were noted to be completely clear, 86.6% had a good response, 0.9% had a mild response, and 0% had no response.

Conclusions: Daylight-mediated MAL-PDT is a suitable treatment option for AK lesions in a Canadian population.

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Ewan Eadie
Dundee, Scotland, UK

Paul O'Mahoney, Luke McLellan, Sally Ibbotson

Increasing confidence in daylight PDT delivery in the UK

Daylight PDT (dPDT) is widely used as an effective, well-tolerated treatment in mainland Europe but uptake in the UK is limited. In 2013 we introduced a dPDT service in Scotland and have reported high levels of efficacy and satisfied patients. To build our confidence in this therapy, we established a programme of research focussed on investigation of the received light dose, to explore the optimal conditions for dPDT in the UK. Our results demonstrate that the dPDT season is longer than previously thought, particularly if low temperatures can be circumvented, and it can occur at periods of low UV exposure. The importance of sunscreen choice during treatment is also highlighted. Our research provides evidence to support increased use of dPDT in the UK and provides further confidence in this important therapy.

Daylight PDT without curettage. A clinical study

Performing daylight PDT has become routine to avoid pain and reduce inflammation. However, before application of MAL, curettage is still a prerequisite to increase MAL penetration into the skin. Curettage is inconvenient for the clinic and painful for the patient and may result in oozing and bleeding which might interfere with MAL absorption. Further, application of MAL after curettage causes stinging.

We investigated if curettage of the face and scalp, as part of d-PDT, could be avoided. To obtain sufficient PpIX concentration we changed the illumination time after MAL application to last between 60 minutes to 180 minutes (instead of 30 minutes to 150 minutes). The cure rate after 3 months was 85% and identical for both d-PDT with and without curettage. Avoiding curettage did not reduce the inflammation occurring after photodynamic therapy.

Daylight-PDT with MAL applied at home for AK of the face or scalp: interventional study conducted in Germany

The study objective was to evaluate patient reported outcomes, effectiveness and tolerability of patient self-applied daylight PDT with MAL for non-hyperkeratotic AK.

At baseline, the target anatomical area was delimited, skin preparation was discretionary. On day 1, the patient performed MAL DL-PDT at home, in accordance with instructions. Patient questionnaires were completed post-treatment. Effectiveness, pain and adverse events were assessed.

Patients (n=50) were mostly elderly (mean age: 73.4 years) men (86%). After treatment on day 1, 94% of patients were overall satisfied or very satisfied with the treatment and 98% found the instructions convenient. At 3 months, most patients were satisfied or very satisfied with treatment effectiveness (88%) and aspect of their skin (80%). At 3 months, 62% of overall lesions were completely clear. The main related AEs were mild and expected.

Patient self-application of MAL DL-PDT resulted in high levels of patient satisfaction, effectiveness and tolerability.

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Efficacy of daylight PDT with MAL cream (Metvix®) to prevent AK and NMSC in organ transplant patients: a randomised pilot study

Background: Daylight PDT is a treatment approved for the treatment of face and scalp actinic keratosis. The question is if daylight PDT with MAL could prevent the appearance of new actinic keratosis and non-melanoma skin cancer in organ transplant patients by repeated treatment of the cancerization field.

Methods: Design: Randomised, evaluator-blinded, intra-individual comparison trial. Interventions: 6 cycles of field treatment with DLPDT-MAL, 2 sessions 15 days apart at baseline, 3 and 9 months, or cryotherapy (double freeze-thaw) at baseline, 3 and 9 months. Follow-up at 15 and 21 months. Differences were analysed using paired t tests.

Results: 21 patients were evaluated. DLPDT-MAL showed fewer new lesions compared with cryotherapy at 3 months [mean, 4.26 [standard deviation (SD), 3.32] vs 6.83(SD,4.89); $p < 0.001$], 9 months [mean, 2.95(SD,3.25) vs 4.29(SD,3.44); $p = 0.037$], 15 months [mean, 3.0(SD,4.6) vs 4.62(SD,4.96); $p = 0.028$], and 21 months [mean, 3.71(SD,3.48) vs 4.90(SD,4.53); $p = 0.066$]. Patients tolerated DLPDT-MAL better than cryotherapy.

Conclusion: DLPDT-MAL appeared to be more effective to prevent new lesions than cryotherapy, and also showed better tolerance.

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Evaluation of the efficacy of daylight PDT for the treatment of AK in oculocutaneous albinism

Background: Oculocutaneous albinism (OCA) is a genetic condition observed commonly in northern Brazil. Daylight photodynamic therapy (DL-PDT) has been used to treat actinic keratosis (AK) in OCA with great tolerability and few local skin reactions.

Methods: Twenty-three patients with OCA and AK underwent two sessions of standard DL-PDT, a month interval between them. A skin biopsy was carried out one week before the first treatment and ninety days after the second one, to study histopathological and immunohistochemical variables.

Results: The Wilcoxon nonparametric test did not show a statistical difference between baseline and after treatment for the following variables: atypia grade ($p = 0.617$), dysplasia ($p = 0.705$), Ki-67 ($p = 0.458$), TP-53 ($p = 0.648$), survivin ($p = 0.213$).

Conclusion: DL-PDT in this study, in spite of being a safe therapeutic method and with a clinical response, was not an efficacious therapeutic option for skin field of cancerization in OCA.

Sequential treatment of daylight PDT and ingenol mebutate versus two sessions of daylight PDT for AK: an observational, prospective, comparison study

Daylight-PDT (DLPDT) and Ingenol mebutate (IM) are treatments for actinic keratosis (AK) and field cancerization.

The aim was to evaluate the effectiveness of sequential DL-PDT and IM compared to two sessions of DL-PDT for AK.

An observational, multicenter, prospective study included patients diagnosed with AK grades I-III on the head. Those patients who do not achieved a satisfactory clinical response after MAL-DL-PDT received either another session of DLPDT or IM.

Forty-three patients with an average number of AK of 9.58 (SD:1.16) were enrolled. 64.3% required a retreatment: 48.1% with DLPDT and 51.9% with IM. After one year of follow-up, higher clearance rates were observed with two sessions of DLPDT compared to DLPDT plus IM (75.2% vs. 54.6%, $p=0.0013$). Local skin reactions were more frequent in the group treated with IM ($p=0.0245$).

The combination of DLPDT and IM does not show a synergic effect for the treatment of field cancerization being not superior than DLPDT monotherapy.

PDT combined with other therapies to enhance patient outcomes

Background: Photodynamic therapy (PDT) is a well-established and effective treatment for actinic keratosis (AK) and field-cancerization. However, clearance rates are reduced in patients with severe photodamage. Within the last decade our research group has therefore focused on PDT combined with other therapies to enhance patient outcomes.

Objective: To summarize current knowledge and local experience on PDT combined with other therapies for intensified treatment of AK.

Methods: Studies on combination therapies have focused on two main strategies. First, physical pretreatment of skin with ablative fractional lasers, microneedles and microdermabrasion have been used to disrupt the skin barrier and increase uptake of topical photosensitizers. Second, topical antineoplastic agents combined with PDT have been used to exert a dual anti-cancerous treatment. Presentation of data will focus on applying theory into clinical practice.

Perspective: PDT combined with other therapies enables tailored treatment of AK and is promising for selected patients with severe photodamage.

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A solution to the MOHS epidemic: PDT following curettage for BCC

Background: Basal cell carcinoma (BCC) is the most common form of skin cancer in Canada. Photodynamic therapy with methyl aminolevulinate (MAL-PDT) provides high-level cosmesis difficult to accomplish with surgical techniques.

Objectives: To investigate the effectiveness, safety, patient satisfaction, and cosmetic outcome of MAL-PDT following curettage.

Methods: A retrospective chart review of patients who received MAL-PDT following curettage for BCC at a single Canadian site from 2009-2016. Statistical methods include descriptive statistics and multivariable generalized linear mixed effects models.

Results: 278 patients with 352 lesions were included. The cure rate was 90.3%. Nasal lesions were 2.82 (95% CI: 1.24–6.40, $p=0.01$) times more likely to recur. 18.3% of patients reported side effects. Of those who expressed satisfaction, 100% were happy. Of lesions with cosmetic data, 90.3% displayed a good response.

Conclusions: MAL-PDT following curettage is a viable treatment option and should be offered to patients as an alternative to surgical techniques.

Key Words:
BCC, MAL, Metvix®, PDT

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PDT combination therapies for AK: the more, the better?

Photodynamic therapy (PDT) is a highly effective treatment option for patients with actinic keratoses (AK) and is often combined with lesion-directed targeted pretreatment by ablative and non-ablative laser devices or field-directed topical interventions. However, whether PDT combined with either laser or topical interventions is more effective than PDT alone has been a subject of debate, and clear-cut evidence from randomised controlled trials (RCT) is lacking. To investigate the efficacy of combined interventions, we performed systematic literature searches and meta-analyses using a random-effects model. Overall, laser-assisted PDT showed significantly higher clearance rates compared to PDT monotherapy (RR 1.33, 95% CI 1.24- 1.42, $p<0.01$, 4 RCTs). Similarly, the lesion-specific clearance was higher for PDT plus topical intervention compared to monotherapy (RR 1.48; 95% CI 1.04-2.11; $p=0.03$, 3 RCTs). Taken together, the combination of PDT with a lesion-targeted approach or a field-directed treatment are efficient approaches and achieve higher AK clearance rates in comparison to PDT monotherapy.

Key Words:
AK, Carbon dioxide laser, Erbium YAG laser, Field cancerization,
Meta-analysis, PDT, Systematic review

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PDT: problems and solutions of laser-assisted PDT in a South German dermatologic practice after 15 years of experience

Our Clinic lies at Lake Constance, one of the sunniest regions in Germany.

In 2003, we started Classical PDT with MAL and red light very successfully in patients with AK, BCC and Bowen's disease. However, up to 80% of patients experienced pain during the illumination process.

From 2014, we performed laser-assisted PDT, with about 125 annual patients. MAL-Daylight-PDT was delivered since 2016 with high clearance rates and good tolerance. However, 16% of patients reported side effects like redness and swelling.

In 2018, we introduced an off-label protocol modification: Patients received first 1 course of fractionated CO₂-laser pre-treatment, followed by MAL incubation under occlusion for 2-3 hrs. Then, patients received a short light exposure with the Aktilite LED (approx. 3-6 J/cm²) and were consecutively sent out for 1h into daylight. So far, 15 patients have been treated with this modification and clearance rates of 87%, with few side effects and no need of analgesic drugs.

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Acral resistant warts successfully treated with curettage + microneedling + topical ALA-PDT

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Background: Topical ALA-PDT has been well documented to be successful in the treatment of viral warts. PDT has a limited role in the treatment of thicker lesions because the photosensitizer cannot penetrate keratotic lesions.

Methods: Our study was carried out between November 2017 and December 2018. Eligible participants had one or more plantar or palmar resistant warts. Twenty-six patients were recruited. They underwent a strong curettage, followed by the application of 5-ALA 10% cream on the viral wart, and by microneedling. Later, the pricked skin was covered for three hours by an occlusive polyurethane dressing, and finally irradiated with a red-light source.

Results: After 3 treatments of curettage+microneedling+ALA-PDT, 22 patients (84.6%) showed complete remission and two patients (7.7%) showed partial remission. The mean follow-up period after healing was 6.8 months.

Conclusion: We have demonstrated that the combination of curettage+microneedling+topical ALA-PDT may offer an effective and safe alternative for the treatment of acral resistant warts, even when PDT alone has already been insufficient.

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Optimization of sunscreen use

Sunscreen plays an important part in the protection against actinic keratosis and skin cancer. Sunscreen users are often inadequately protected and become sunburned. We investigated how much two consecutive sunscreen applications increased the quantity of sunscreen applied and decreased the skin areas left without sunscreen (missed area), compared to a single application. Thirty-one healthy volunteers in swimwear applied sunscreen two consecutive times. As sunscreens absorb black light, the darkness of the skin showing in black light photos was used to quantify the amount of sunscreen applied. After single application participants missed 20% and after double application 9% of their skin. The median participant had applied between 13% and 100% more sunscreen at the selected skin sites after double application than after single application. We recommend double application, especially before intense sun exposure.

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Biodegradable polymeric nanoparticles enhanced the effectiveness of topical PDT for SCC

Biodegradable polymeric nanoparticles (Bp-NPs) show low toxicity, good biocompatibility, therefore making it a good candidate for the delivery of photosensitizers to increase the bioavailability and improve therapeutic outcomes of PDT. Two types of Bp-NPs, Polylactic-co-glycolic acid (PLGA) nanoparticles and chitosan / methoxy polyethylene glycol - polylactic acid (CPP) nanoparticles were prepared to load the photosensitizer 5- aminolevulinic acid (ALA) and zinc phthalocyanine, respectively. The characteristics, safety and effectiveness were determined in vitro and vivo. Bp-Nps were spherical with smooth surfaces and high encapsulation efficiency. Bp-NPs increased the production of fluorescence and reactive oxygen species by photosensitizers and enhanced the effectiveness of PDT for SCC. No obvious toxicity was observed in vivo. Bp-NPs provide a promising photosensitizer delivery strategy for the topical photodynamic therapy of cutaneous SCC.

Adjuvant concepts in field cancerization: PDT versus systemic therapies

Unchanged intentional sun worshipping practices and work related UV exposure and steadily increasing life expectancies in many countries strongly contributes to the unchanged epidemiological trend of steadily increasing incidence rates in actinic keratoses (AK), cutaneous squamous cell carcinoma (cSCC) and basal cell carcinoma.

Primary as well as secondary prophylaxis (including modern field therapy measures such as DL- and cPDT for actinic keratoses) have shown a significantly therapeutic impact on the development of actinic keratoses while yet representing one of the only suitable therapies designed to manage large field of actinic field cancerization and possibly prevent AK from progressing into invasive cSCC. Systemic therapies lowering the progression rate of large areas of field cancerization included nicotinamide, oral retinoids and 5-FU prodrugs.

In the past months Checkpoint inhibitors such as anti PD1 antibodies were successfully evaluated for locally advanced and metastatic cSCC. Future concepts have to be evaluated exploring the use of PD1-inhibitors for actinic cancerization of large fields either alone or in combination with topically applied therapies such as PDT.

Experience of intralesional PDT in hidradenitis suppurativa treatment

Introduction: Hidradenitis suppurativa (HS) is a chronic, inflammatory, recurrent skin condition which nowadays has no cure. Photodynamic therapy (PDT) has been used since more than ten years ago with different results because of the depth of the disease. Intralesional PDT, could resolve this limitation.

Methods: Review of our experience of more than 60 patients with HS treated with intralesional PDT. This technique consists in the use of a photosensitizer gel (5-aminolevulinic acid 2%) introduced inside the fistulas or abscesses to treat to be incubated for two hours. Later an intralesional 630nm laser light irradiates the lesions through a fiber optic probe. Finally patients are reevaluated with different HS scales to identify the response of the technique.

Results: In case series of 38 patients 29 achieved complete response , and 18 of them needed only one session and 8 patients had persistence of lesions. Difference between basal and final Hidradenitis Severity Score showed a significant reduction of 24.5 points ($p < 0.001$). Dermatology Life Quality Index scores reached a reduction of 10 points ($p < 0.001$)

Conclusion: Intralesional-PDT could be an excellent local treatment for HS lesions. It has achieved high rate of remission in long time and without relevant complications.

Key Words:

Skin cancer, Immunooncology, Carcinogenesis, Local therapy, cSCC prevention, PD1, PDT

Granuloma annulare : report of 13 patients treated with PDT

Introduction: Numerous therapies have been used in the treatment of granuloma annulare (GA). We review the patients diagnosed with GA and treated with PDT.

Material and methods: A retrospective observational study was performed including all patients diagnosed with GA and treated with PDT between 2007 and 2018.

Continuous variables were described using means and standard deviations. Statistical analyses were carried out using SPSS software (version 20.0, Armonk, NY: IBM Corp).

Results: Thirteen patients were included in the study. Eleven patients (84.6%) were women and 2 men (15.4%), with an average of 53 years old. The most frequent locations was the back of the hands (54%). Seven patients (53.8%) responded to PDT treatment. The mean follow-up was 35 months. Ten patients (76,9%) experienced a recurrence of the lesions, with an average time of 25 months.

Discussion: The efficacy of PDT in the granuloma annulare is not very high but probably not worse than other treatments and without adverse effects.

posters



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Pemphigus chronicus benignus familiaris (Hailey-Hailey disease): Successful treatment using DL-PDT with methylaminolevulinate

We present the case of a 58-year-old female patient presenting with chronic recurrent, sharply circumscribed, erythematous, infiltrated, and partially oozing skin changes in the intertriginous of the submammary, right abdominal, and inguinal regions for 20 years. Also in the son dermatohistopathology revealed the diagnosis of Hailey-Hailey disease.

After frustrated conservative therapies, we performed a probative treatment using classical daylight-PDT with methylaminolevulinate (MAL), first in the area of the most disturbing lesions on the abdomen. The treatment was not painful, only a discrete phototoxic dermatitis occurred, which healed within 2 weeks. After 6 weeks and during follow-up (6 mo) there was a persistent decline in the symptoms, with fewer remaining asymptomatic skin lesions. The treatment of the remaining lesion is planned for this summer.

Hailey-Hailey's disease is a chronic relapsing genodermatosis. The treatment options range from topical application of steroids and antiseptics / antibiotics, the administration of botulinum toxin to extensive removal of diseased areas using dermabrasion or Er:YAG/CO2 lasers. Conventional PDT with red light has been used successfully, but the painfulness of the procedure is probably a limiting factor. With the addition of DL-PDT, another effective, painless and low-side-effect treatment option can enrich the therapeutic armamentarium.

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Daylight PDT: experience in the treatment of AK in two Portuguese Hospitals

Daylight-photodynamic therapy (DL-PDT) is an effective treatment of actinic keratoses (AK), nearly pain free and more convenient for both clinics and patients.

Our study included 30 patients from two Hospitals 200km apart (15 from Hospital de Braga and 15 from Centro de Saúde Militar de Coimbra) and was conducted in January and February of 2018. 16 males and 14 females, mean age 81, phototype I-III, with multiple AK I and II of the face and the scalp, treated with DL-PDT were prospectively studied. The median temperature and ultraviolet index during exposure were 10.5°C and 2 respectively. Patients were clinically evaluated after 3 and 6 months.

All the patients achieved clearance or at least a good response to treatment, reporting none or minimal discomfort.

This study confirms that DL-PDT is a good alternative to conventional PDT, being possible to perform in Portugal in every months of the year, including winter time.

Intralesional PDT in the treatment of BCC

Introduction: Basal cell carcinoma (BCC) is the most frequent skin cancer. It usually appears in pluripathological elderly people. Non-invasive treatments, such as photodynamic therapy (PDT), are a good alternative treatment in some cases, but its main limitation is tissue penetration. The injection of a photosensitizer plus an irradiation with a laser light should increase this penetration.

Material y methods: A retrospective study of 102 patients with all subtypes of BCC were studied. 51 patients were treated with surgery and 51 were treated with intralesional PDT (a 5- aminolevulinic acid 1% lyophilized dissolved into a saline solution injected into the lesion and a later irradiation with a laser beam of 630nm). Both groups were compared in terms of healing. Also, in I-PDT group the type of irradiation (intralesional or external) were compared.

Results:

80.4% vs 82.4% of patients were histologically confirmed as healed with surgery and I-PDT respectively (p 0.79). There were no difference in success rates between intralesional vs external irradiation in I-PDT group (p 0.46).

Conclusion: I-PDT achieved high clearance rates in the treatment of BCC similar to surgery. I-PDT might be an interesting and easygoing option of treatment where surgery is not possible.

Skin Cancer risk related to life UVR exposure and skin phototype

The association between objectively measured ultraviolet radiation (UVR) dose and skin cancer (SC) risk was investigated by their common relation to solar lentigines.

First the association between solar lentigines and SC risk were calculated using cross-sectional data with validated SC information, black light assessed solar lentigines, and objectively measured skin phototype. Secondly the association between personal lifetime UVR dose and solar lentigines were based on a longitudinal dataset (1999-2012). Those were finally combined to calculate SC risk related to UVR dose.

Solar lentigines ($p < 0.001$) and skin phototype ($p = 0.001$) were associated with SC. There was a borderline significant ($p = 0.06$) association between solar lentigines and lifetime UVR dose. Resulting in 1.23 times higher SC risk with double lifetime UVR. The SC risk was 35 times higher for very fair compared to dark Caucasian skin.

This indicates that skin phototype is of greater relative importance than lifetime UVR dose for skin cancer risk.

AK area and severity index: a tool to monitor treatment outcome in occupational dermatology

Background: In 2015 “squamous cell carcinoma or multiple actinic keratoses of the skin caused by natural UV irradiation” have been added to the list of occupational diseases in Germany. In this context, “multiple” signifies the occurrence of either more than five individual actinic keratoses or the presence of field cancerization $>4\text{cm}^2$.

Objectives: To objectively monitor treatment outcomes in patients suffering from occupational skin cancer (actinic keratosis) and receiving MAL-PDT.

Method: AKASI was determined in 10 patients, (8 male, 2 female; 61 to 83years, mean age: 73.1years) before and after two consecutive cycles of MAL-PDT.

Results: AKASI pre treatment was 2.4-13.6 (mean 7.92, SD 3.69); AKASI post treatment was 0.8-6.4 (mean 3.4, SD 2.09). 8/10 patients achieved AKASI 50 and 2/10 patients achieved AKASI 75. No patient reached AKASI improvement higher than 78.9.

Conclusions: AKASI proved to be a helpful tool to monitor MAL-PDT treatment outcome in occupational actinic keratoses. AKASI severity in our occupational patients was relatively high and treatment outcomes with regard to AKASI 75 response was lower than in non-occupational treatment settings.

notes

notes

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