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AN ADDED BENEFIT OF MASKS DURING THE PANDEMIC: UV PROTECTION

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Background: The rapid widespread use of masks during the COVID-19 pandemic presents a new potential avenue for protecting the lower half of the face from the harms of sun exposure. Universal masking policies could have a substantial impact on patients with photosensitivity disorders and in the prevention of skin cancer.

Objective: This project was undertaken to provide information on the ultraviolet (UV) shielding properties of masks. This synthesis of current research will help physicians counsel patients on optimal mask choices, from both dermatological and public health viewpoints.

Methods: A narrative literature review was conducted using articles from textile and dermatology journals published between 1994-2020. The variables impacting the UV protection of masks were reviewed, including fabric type, construction, porosity, and color. Other factors related to wear and use such as moisture, stretch, laundering, and sanitization are discussed in the context of the pandemic.

Findings: Black, tightly woven, triple-layered polyester cloth masks were determined to be optimal for protection against both UV radiation and SARS-CoV-2 in the community. Cotton masks should be washed before first use in fluorescent brightening agents. The UV protection of surgical masks and N95s is largely unknown.

Conclusion: The face masks for the public that are safest against pathogens such as SARS-CoV-2 are generally also the most protective against UV damage. Patients should be encouraged to invest in a high-quality mask to simultaneously help reduce the spread of SARS-CoV-2 and block sun exposure. Studies are needed on the UV protection of masks, especially N95s and surgical masks.

Category: Pilot/Exploratory experiments

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AUTOMATED DELINEATION OF THE DERMAL-EPIDERMAL JUNCTION ZONE IN VOLUMETRIC MULTIPHOTON MICROSCOPY IMAGING OF HUMAN SKIN *IN VIVO*

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Background and Objectives: Diagnostically important histologic features are often situated within the vicinity of the dermal-epidermal junction (DEJ) zone. Under conventional light microscopy, this region is visualized and assessed two-dimensionally from sections of biopsied skin. Here we propose a novel method to automatically delineate and quantify DEJ zone morphometrics in human skin on a three dimensional (3D) basis *in vivo*.

Method: 3D volumetric imaging under dual wavelength multiphoton excitation was carried out on the upper inner arms of 16 healthy volunteers. An automatic segmentation algorithm was developed to delineate the DEJ, thereby separating the epidermis and the superficial dermis. Quantitative characterization of the DEJ in terms of 3D interdigitation (I), arithmetic mean roughness (Sa), and root mean square roughness (Sq) were calculated. These DEJ features as a function of age were analyzed.

Results: The age range of the participants was between 24 to 65. The average and standard deviation value of the interdigitation index (I), arithmetic mean roughness (Sa) and root mean square roughness (Sq) were 1.22 ± 0.07 , 12.34 ± 4.89 , 16.77 ± 5.47 respectively. Linear regression shows that all three parameters are negatively correlated to age ($p < 0.05$, Spearman). These parameters suggest that the overall DEJ surface becomes flatter with chronological aging.

Conclusion: *In vivo* DEJ surfaces show age-dependent morphological differences. Three dimensional volumetric multiphoton microscopy imaging of the skin can be analyzed by automated segmentation algorithms to yield quantitative and objective assessments of DEJ morphology.

Category: Pilot/Exploratory experiments

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ASSESSING POST-MARKETING SURVEILLANCE DATA TO IDENTIFY SEVERE CUTANEOUS ADVERSE EVENTS OF IMMUNE CHECKPOINT INHIBITOR TREATMENTS

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The use of immune checkpoint inhibitors (ICIs) for treating cancer frequently entails skin adverse events (sAEs). While phase 3 studies reveal the most common sAEs, the frequency and range of rare sAEs and particularly of severe cutaneous adverse reactions (SCARs) remain unknown. The aim of this study is to identify the frequency of all sAEs and SCARs using post-marketing surveillance data. We performed a retrospective analysis of 19,376,458 adverse events reported to the FDA Adverse Event Reporting System. Reports included in the analyses ranged from mid-2014, to end-2019. Descriptive statistics and reporting odds ratios were used to assess the relative frequencies of sAEs and SCARs. The ICI cohort comprised of 42,059 patients reporting 95,386 AEs, of which 18.3% were sAEs. Across therapy regimen, the combination therapy had the highest proportion of sAEs, followed by anti-CTLA-4, and anti-PD-(L)1 monotherapy. While the frequency of SCARs in the ICI cohort was low, the most common were Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis, of which the latter showed a high mortality rate. Our data further reveals that the development of particular sAEs and SCARs is significantly associated with the used ICI drug and treated cancer type. In conclusion, the study demonstrates a broad heterogeneity of sAEs during ICI therapy and highlights that SCARs may be more frequent among them than assumed. It strongly suggests that medical centers offering ICIs for cancer treatment should ensure access to rapid dermatologic evaluation, for improvement of patient care.

Category: Pilot/Exploratory experiments

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LIGHT AND LASER-BASED TREATMENTS FOR GRANULOMA ANNULARE: A SYSTEMATIC REVIEW

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Background: Granuloma annulare (GA) is challenging to treat, especially when generalized. A systematic review to support the use of light and laser-based treatments for GA is lacking.

Methods: We performed a systematic review by searching Cochrane, MEDLINE and Embase. Title, abstract, full text screening and data abstraction were done in duplicate. Quality appraisal was performed using the Joanna Briggs Institute critical appraisal tool for case series.

Results: Thirty-one case series met the inclusion criteria, representing a total of 336 patients. Overall, the treatments with the most reported cases were psoralen plus ultraviolet A (PUVA), ultraviolet A1 phototherapy (UVA1) and ultraviolet (UVB) and/or narrowband UVB (nbUVB) which showed a complete response in 59% (n=77/131), 31% (n=27/86) and 39% (n=17/44) of treated patients respectively. The pooled complete response rates for other treatments were 68% (n=21/31) for laser/energy-based devices and 52% (n=13/25) for photodynamic therapy (PDT).

Conclusion: The body of evidence for light and laser-based treatment of GA is sparse. Our results suggest that PUVA has a high clearance rate for GA and the most reported cases, but in clinical practice its use may be limited by concerns of carcinogenesis. Laser devices and PDT have high clearance rates for patients with GA, but access to technology and impractical treatment delivery for generalized GA can be challenging. Although UVA1 and UVB/nbUVB appeared slightly less effective than other therapies, UVB/nbUVB can be considered an appropriate first-line treatment for patients with generalized GA in light of wider availability and a favorable long-term safety profile.

Category: Early experiments with well-defined objectives/hypotheses

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SPARING OF ATOPIC DERMATITIS IN THE DIAPER REGION: A SCOPING REVIEW

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Background: Atopic dermatitis (AD) is a chronic, inflammatory skin condition commonly affecting infants with notable sparing of the diaper region. Though sources anecdotally attribute this sparing to the physical barrier formed by the diaper and the subsequent retention of moisture, urine, sweat and feces, no studies have formally investigated the factors contributing to this sparing phenomenon.

Methods: We performed a scoping literature review to investigate the factors involved in sparing of AD in the diaper region, namely humidity, scratching, urine, sweat, feces, and microbiome composition.

Results: A total of 130 papers met the inclusion criteria, and extracted data was analyzed in an iterative manner. Increased local humidity facilitates protective changes at the cellular level and offsets transepidermal water loss. Exposure to urea from both sweat and urine may contribute to improved moisturization of the skin through its natural humectant properties and ability to modulate gene expression. Introduction of flora in feces contributes to the generation of protective immune responses and outcompete growth of pathogens such as *Staphylococcus aureus*. Finally, diapers physically prevent scratching, which directly interrupts the itch-scratch cycle classically implicated in AD.

Conclusion: Our study reviews factors that may contribute to the sparing of AD in the diaper region in infants. A limitation to our findings is that the studies reviewed here explore the impacts of these factors on AD broadly, and not explicitly in the diaper region. Additional studies investigating this may further our understanding of AD pathology and contribute to the development of effective therapeutics.

Category: Pilot/Exploratory experiments

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DIRECT AI-BASED PREDICTION OF CLINICAL MANAGEMENT BYPASSING DIAGNOSIS: APPLICATION TO SKIN LESIONS

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Existing machine learning approaches that suggest management decisions for skin lesions rely on predicting the underlying skin condition to infer a decision without considering the variability of decisions that may exist within a single condition. We present the first deep learning-based work to predict clinical management decisions directly from images without explicitly predicting the diagnosis. We use clinical and dermoscopic images of skin lesions and patient metadata from the Interactive Atlas of Dermoscopy dataset (1,011 cases; 20 disease labels; 3 management decisions) and demonstrate that predicting management labels directly is more accurate than predicting the diagnosis and then inferring the management decision ($13.73 \pm 3.93\%$ and $6.59 \pm 2.86\%$ improvement in overall accuracy and area under receiver operating characteristic curve [AUROC] respectively). Based on the retrospective analysis, directly predicting management decisions also considerably reduces the over-excision rate as compared to management decisions inferred from diagnosis predictions (24.56% fewer cases wrongly predicted to be excised). Furthermore, we show that training a model to also simultaneously predict the seven-point criteria and the skin lesion diagnosis yields an even higher accuracy ($4.68 \pm 1.89\%$ and $2.24 \pm 2.04\%$ improvement in overall accuracy and AUROC respectively) of management predictions. Finally, we demonstrate our model's generalizability by evaluating on the public MClass-D dataset (100 cases) and show that our model agrees with the clinical management recommendations of 157 dermatologists as much as they agree amongst each other. We believe that such a system has the potential to suggest management decisions to clinicians (as a second opinion) or directly to patients in under-served communities.

Category: Early experiments with well defined objectives/hypotheses

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CHOOSING WISELY CANADA RECOMMENDATIONS: RESOURCE STEWARDSHIP IN DERMATOLOGY

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Introduction: Resource stewardship not only allocates appropriate resources to those who would truly benefit, but it also protects patients from the impact of unnecessary tests, treatments, and procedures. The need for resource stewardship has been highlighted in recent years through organizations such as the Choosing Wisely campaigns, which aim to eliminate ineffective practises by developing lists of dedicated recommendations per specialty.

Methods: In collaboration with the Canadian Dermatology Association (CDA), a working group was formed to develop a preliminary list of recommendations through a review of the literature, inspiration from International *Choosing Wisely lists*, and in consultation with a diverse task force of Canadian dermatologists. The proposed final Top Five list was then submitted to the CDA Board of Directors where it passed by majority approval.

Results: All presented recommendations have been approved by the CDA. One such presented recommendation is: "Don't routinely use topical antibiotics on surgical wounds", motivated by relative cost, risk of sensitization leading to contact dermatitis, and lack of evidence for its use in preventing wound infection. Each recommendation is accompanied by a detailed explanation of the rationale and a comprehensive list of evidence-based sources.

Conclusion: These recommendations have been developed to reinforce resource stewardship in Canadian dermatology. Future directions include further research and development, distribution for increased accessibility, and the development of easy-to-read patient materials on tests, treatments, and procedures related to their diagnosis. We hope these recommendations will be of high clinical utility and trigger meaningful conversation amongst dermatologists and patients alike.

Category: Pilot/Exploratory experiments

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INCORPORATING CLINICAL KNOWLEDGE INTO A DEEP NETWORK FOR 7 POINT-CHECKLIST EVALUATION

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Background: The 7-point checklist is one of the most well-known and validated dermoscopic algorithms for melanoma detection. The algorithm consists of 7 criteria, three major criteria (atypical network, blue-white veil and atypical vascular pattern) and four minor criteria (irregular streaks, irregular dots, irregular blotches, and regression structures). Recently, several deep learning works have attempted to classify melanoma via the 7 content-based features simultaneously; however, these methods do not differentiate the major and minor criteria of the checklist.

Objectives: In this project, we implemented an improved deep network that fully utilized clinical domain knowledge to make use of the major and minor criteria of the checklist.

Methods: Paired dermoscopic images and clinical images were collected from 1011 lesions with their matched 7-points checklist annotations, from a publicly available dataset. Deep learning features were extracted using an auto-encoder based deep neural network and the features were classified into 7 criterion-classes independently. The major and minor criteria of the checklists were then observed and their orders were optimized in the final melanoma classification.

Results: The system achieved an average accuracy of 84% in detecting melanoma among non-melanoma lesions, outperforming state-of-the-art methods in the literature. In addition, the system can output the probability of melanoma from of each of the 7 criteria of a lesion individually. By implementing the clinical knowledge accumulated by experts and providing human-interpretable results, the proposed system would make the AI deep learning approach more interpretable and help improve diagnostic accuracy.

Category: Early experiments with well-defined objectives/hypotheses

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TOPICAL CHOLESTEROL AND LOVASTATIN FOR THE TREATMENT OF DISSEMINATED SUPERFICIAL ACTINIC POROKERATOSIS: A CASE SERIES

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Disseminated Superficial Actinic Keratosis (DSAP) is the most common variant of porokeratosis and presents as pink to brown plaques with a fine linear scaly border on chronically sun-exposed skin. There is increasing evidence linking missense mutations in the mevalonate kinase gene (MKV) with both sporadic and familial cases of DSAP¹. A recent case series highlighted the utility of topical cholesterol and lovastatin in the treatment of porokeratosis associated MKV mutations, including benefit in one case of DSAP².

We sought to determine the utility of topical cholesterol and lovastatin in an unselected population of patients with DSAP. Five patients with a clinical diagnosis of DSAP consented to treatment of a solitary affected limb and completed a one month course of twice daily therapy with 2% lovastatin and 2% cholesterol in white petrolatum. Patient global assessment of disease activity was assessed pre and post therapy. A single patient described significant improvement of the treated limb from "severe" to "almost clear". This patient had early onset of her DSAP in her third decade and two first degree relatives with DSAP indicating a strong genetic component. She was the only patient with early onset and a family history of DSAP. Two patients report improvement from "moderate" to "mild" disease and the final 2 patients had no change. There were no adverse effects reported from therapy.

Our case series provides support for the use of topical lovastatin and cholesterol in the treatment of selected cases of DSAP, with the greatest improvement noted when younger onset and strong family history was reported.

References

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Category: Early experiments with well defined objectives/hypotheses

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COMPUTERIZED LOCALIZATION AND TRACKING OF PIGMENTED SKIN LESIONS ON 3D WHOLE BODY TEXTURIZED SKIN MESHES

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While computerized approaches to classify skin conditions have shown the potential to reach a similar diagnostic performance as human experts using 2D color images, limited research considers using 3D whole-body skin images captured across time. 3D skin imaging provides context beyond a single localized photograph, such as the presence of multiple nevi (an important melanoma risk factor) and capturing the skin at multiple time points may allow for improved monitoring of lesion changes or the progression of treatments.

We propose a novel computational approach to detect and track lesions from 3D skin images. We map the 3D skin of human subjects to 2D texture images, train a deep region proposal artificial neural network to localize lesions within 2D texture images, and map the detected lesions to the 3D body. For subjects with multiple scans, we apply a matching algorithm to track lesions across time. We evaluated our method on three datasets. First, we scanned a mannequin with synthetic skin lesions under varying poses. Second, we augmented a dataset of 3D human meshes to produce 900 whole-body, skin-colored 3D meshes with different postures and lesions appearances. Finally, we also used a publicly available dataset of 3D scans that imaged the skin of real human subjects and manually annotated over 17,000 locations that appeared to the human eye to contain a pigmented skin lesion. We trained and tested our neural network using these manual annotations and achieved a recall of 0.84 and precision of 0.66 averaged per-scan.

Category: Early experiments with well defined objectives/hypotheses