8:40 a.m.

ADJUVANT USE OF A LONG-PULSED 1064 NANOMETER LASER FOR THE MANAGEMENT OF REFRACTORY LATE-ONSET NODULES RELATED TO POLYMETHYLMETHACRYLATE FILLERS

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Background: Soft-tissue fillers are injected to revolumize the face and restore a cosmetically pleasing appearance. One of the rare complications of soft-tissue fillers is the development of delayed onset nodules (granulomas). They occur months to years after the implantation of soft-tissue fillers and continue to be clinically challenging because much is unknown with regard to their pathogenesis and the optimal treatment options.
Objectives: Lasers can deliver photons that result in high peak temperatures at the target, and theoretically may disrupt the granuloma. We sought to determine if a long-pulsed 1064 nm Nd:YAG laser could be used to reduce delayed-onset nodules related to polymethylmethacrylate (PMMA) dermal fillers.
Methods: We conducted a retrospective review of 7 patients who presented to our clinic with delayed-onset nodules after PMMA dermal fillers who were then treated with a Nd:YAG laser. Six of these patients had demonstrated suboptimal responses to previous treatments such as intralesional triamcinolone, systemic antibiotics, and systemic corticosteroids. Patients were treated with two passes of a long-pulsed 1064 nm Nd:YAG laser utilizing a 10 mm spot size at a fluence of 60 J/cm^2, 35 ms pulse duration,1 Hz frequency and 2 passes.
Results: All 7 patients achieved subjective clinical improvement after Nd:YAG laser treatment, as rated by both the physician and patient.
Conclusion: Use of a long-pulsed 1064-nm Nd:YAG laser may serve as a useful adjunct for refractory delayed-onset nodules caused by PMMA dermal fillers, and represents a novel approach to management for these difficult to treat cases.

Category: Applied/functional experiments

8:50 a.m.

GRANZYME K CLEAVES PROTEASE-ACTIVATED RECEPTOR-2 AND INDUCES PRURITUS (ITCH)

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Pruritus (itch) is a significant and unpleasant symptom that accompanies many dermatological diseases. Current standard of care relies on antihistamines, which often fail to alleviate the symptom. Accumulating evidence suggests that itch is caused not only by histamine-dependent mechanisms but also by histamine-independent mechanisms such as protease-activated receptor-2 (PAR-2) activation of sensory neurons in the skin. PAR-2 is activated through proteolytic cleavage by a number of known serine proteases; however, itch-inducing proteases have not been fully explored in skin. Serine protease granzyme K (GzmK) is elevated in a number of skin inflammatory diseases that exhibit pruritus, including atopic dermatitis, chronic wound, and psoriasis. Therefore, we hypothesized that GzmK induces itch through PAR-2 cleavage in skin. Chinese Hamster Ovarian (CHO) cells transfected with the nluc-hPAR2-eYFP cleavage reporter were incubated with GzmK or trypsin (standard agonist against PAR-2) to evaluate PAR-2 cleavage. Relative to trypsin, a 15-minute incubation with 100 nM GzmK induced 20% cleavage of PAR-2, suggesting that GzmK activates PAR-2. To investigate the role of GzmK in pruritus in mouse skin, GzmK was intradermally injected into the cheeks of mice and scratch behavior was quantified. GzmK (1 ng (30.3 pmol) and 10 ng (303 pmol)) induced 33.5 and 57 scratch bouts in 20 minutes, respectively, compared to 21 scratch bouts with vehicle control over the same time period. In summary, GzmK may induce pruritus through a PAR-2-dependent mechanism.

Category: Applied/functional experiments

9:00 a.m.

CLINICAL RECOGNITION OF MERKEL CELL CARCINOMA BY DERMATOLOGISTS AND NON-DERMATOLOGISTS

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Merkel cell carcinoma (MCC) is a rare and aggressive cutaneous carcinoma. The rates of clinical accuracy in detection of MCC are currently unknown. This was a retrospective chart of the Sunset Database of pathologic records within VCH and PHSA. All reports with "Merkel" in the final pathologic diagnosis or addendum between June 1 2008 and June 1 2018 were analyzed. Reports of re-excision of previously diagnosed MCC or excisional biopsies of metastasized MCC were excluded. Clinical impression and differential diagnosis if provided was analyzed along with respective physician specialty. There were 65 cases of MCC identified with 26 cases biopsied by Dermatologists. MCC was correctly identified in the clinical impression or differential diagnosis in 8 cases. All 8 cases were biopsied by dermatologists with 0 of 39 cases from non-dermatologists identifying MCC in the clinical diagnosis. All dermatologists recognized cases of MCC as a neoplastic process and provided an impression or differential diagnosis encompassing neoplastic processes. Amongst non-dermatologists, 15 of 39 cases were recognized as a neoplastic process although no clinical impression or differential diagnosis was offered by 14 non-dermatologists on the submitted pathology requisitions. The clinical diagnostic sensitivity of MCC amongst dermatologists was 31% with an overall sensitivity of 12% amongst all practitioners. MCC was not considered as a diagnostic possibility amongst non-dermatologists. Given the poor clinical recognition of MCC and an increasing incidence of the disease, education and training on the clinical features of MCC is warranted for all physicians who deal with cutaneous lesions.

Category: Early experiments with a fine-hypotheses

9:10 a.m.

3D TOMOGRAPHIC IMAGING OF HUMAN SKIN *IN VIVO* AT SUBCELLULAR RESOLUTION WITH EXTENDED FIELD OF VIEW

Zhenguo Wu[1, 2], Yunxian Tian[1, 2], Jianhua Zhao[1, 2], Yimei Huang[1,2], Harvey Lui [1,2], Sunil Kalia[2,3,4], Haishan Zeng [1, 2]
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Three-dimensional *in vivo* imaging is an important method for comprehensively demonstrating biological systems in their natural states. It has been rapidly developed for brain and embryo imaging using fluorescent indicators. Imaging techniques, especially in 3D, for in vivo human skin are limited by the high optical scattering property of skin tissue, its heterogeneous and layered structure, dense tissue information, label-free requirement, involuntary motion, laser safety issues, and subject flexibility constraints. We developed a system for 3D tomographic imaging of human skin *in vivo* at subcellular resolution with a large field of view. This system features *XZ-Y* volumetric imaging with motion correction, thereby enabling continuous three-dimensional *in vivo* tissue exploration over an 8-millimetre range. Furthermore, the system integrated and co-registered reflectance confocal, two-photon fluorescence, and second harmonic modalities to provide three separate endogenous contrasts for examining a tissue volume of interest. *In vivo* data acquired from normal and cancerous skin has shown that the acquired tissue volume yields a wide field of view, high contrast, and multilayered tissue architecture when viewed in *XZ*-plane, and high-resolution cellular morphology when displayed in the *XY*-plane. This 3D imaging system is expected to enable a greater understanding of the spatial organization of skin cells in relation to their functions and also enhance our ability to noninvasively study the progress of skin diseases including the earlier diagnosis and monitoring of skin cancer.

Category: Early experiments with well-defined objectives

9:20 a.m.

INCIDENCE AND PROFILE OF SKIN CANCER IN PATIENTS TREATED WITH ULTRAVIOLET-B PHOTOTHERAPY

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The risk of skin cancer as a long-term side effect of Ultraviolet-B (UVB) phototherapy has not been adequately studied and quantified. To estimate the incidence and risk of skin cancers in patients treated with UVB phototherapy, a retrospective chart review was conducted on patients receiving UVB therapy from 1970 to 2018 at a university hospital dermatology center. Pathological ascertainment of basal cell carcinoma, squamous cell carcinoma, and melanoma for these patients was verified through linkage with an interhospital pathology database.
Follow up data were available for total of 3,540 patients (2,024 male and 1,516 female) representing 25,742.0 person-years. A total of 192 new skin cancers developed in 79 patients after receiving UVB phototherapy without systemic PUVA. There was a decreasing trend of skin cancer incidence with higher skin phototypes (272.7, 226.8, 150.5, 76.6, 35.6/100,000 person-years for skin types I to V, respectively). No statistically significant difference for skin cancer incidence was found between our cohort and the British Columbia general population ($p>0.05$, Z test for all types of skin cancer). Sub-analysis of multivariate logistic regression and survival analysis indicated no statistically significant correlations between cumulative dosage and the risk of skin cancer. The odds ratios of the upper *vs* lower tercile group for broad-band UVB and narrow-band UVB cumulative dosages were 0.87 ($p=0.85$) and 0.69 ($p=0.64$).
We observed a similar skin cancer profile between patients with UVB phototherapy and the general population. Our incidence and risk analysis suggest that UVB phototherapy is not correlated with skin cancer development.

Category: Applied/functional experiments

9:30 a.m.

AUTOMATED 3D DELINEATION OF THE DERMAL-EPIDERMAL JUNCTION ZONE USING IN VIVO MULTI-MODALITY MICROSCOPY OF HUMAN SKIN

Giselle (Yunxian) Tian[1,2,3], Zhenguo Wu[1,2,3], Harvey Lui[1,2,3], Jianhua Zhao[1,2,3], Sunil Kalia[1,2,4,6], Haishan Zeng[1,2,3]
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Background: Diagnostically important features can often appear within the region of the dermal-epidermal junction (DEJ) zone, which is usually assessed in two-dimensions (2D) using current microscopy approaches. We propose a new imaging method to non-invasively visualize DEJ zone morphology in three-dimensions (3D).
Method: 3D volumetric imaging was carried out on the upper inner arms of 8 healthy volunteers. An automatic segmentation method was developed to delineate the DEJ, thereby separating the epidermis and the superficial dermis. The algorithm includes three main steps: image preprocessing, surface and DEJ border segmentation, and 3D reconstruction.
Results: The skin cellular images were obtained using reflectance confocal microscopy (RCM) and multi-photon microscopy (MPM) in vivo non-invasively. The segmented DEJ boundary was displaced as a 3D surface. Quantitative measurements of epidermal thickness (ET) were performed. Our results suggest that 3D volumetric imaging and automatic segmentation algorithms enables a quantitative and objective approach for DEJ morphology assessment.

Category: Pilot/exploratory experiments

11:00 a.m.

TOPICAL TRETINOIN AS AN IMMUNOMODULATORY THERAPEUTIC FOR ALLERGIC AND AUTOIMMUNE DISEASE

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Topical retinoids are commonly prescribed for treatment of dermatological disorders, such as photodamage and inflammatory skin diseases. Recent investigations on endogenous retinoid signaling in the gut demonstrate the importance of retinoids in maintaining immune tolerance by inducing regulatory T cells. However, a potential role for topical retinoids to treat systemic inflammation has not been investigated. We hypothesize that topical application of the retinoid, tretinoin, can promote immune tolerance by reducing the generation of pathogenic T cells and increasing the number of regulatory T cells. We used contact hypersensitivity (CHS) and experimental autoimmune encephalomyelitis (EAE) models to explore whether skin pre-treated with tretinoin can promote tolerance in an antigen-specific manner. Mice were pre-treated with vehicle or tretinoin for three (CHS) or two (EAE) days once daily before sensitization to ovalbumin (OVA) or myelin oligodendrocytic glycoprotein respectively. In CHS, tretinoin pretreatment resulted in lower ear swelling and fewer OVA-specific CD8 T cells in the draining lymph nodes of treated animals, and interferon-gamma (IFNγ) production was lower within the CD4 and CD8 T cells. For EAE, tretinoin-treated animals had lower disease scores and less weight loss early in disease but the effect was not sustained to the experimental endpoint. Despite this, there was a trend to reduced IFNγ-producing CD4 and CD8 T cells in draining lymph nodes. The nature of topical immunomodulation as a non-invasive therapeutic intervention makes it an appealing treatment option. Further studies are warranted to verify the efficacy and mechanisms of topical retinoids on modulation of local and systemic immunity.

Category: Applied/functional experiments (animal models of disease and in vivo studies, etc)

11:10 a.m.

CAN DEEP LEARNING AUTOMATICALLY IDENTIFY SUSPICIOUS UGLY DUCKLING MOLES?

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In order to diagnose skin cancers such as malignant melanoma, careful visual inspection of all the patient's skin lesions must be undertaken. To this end, dermatologists have introduced several approaches which can be helpful in detecting melanomas. One commonly used approach identifies the existence of Ugly Duckling (UD) moles, which look different to the other moles on the same patient. Previous research has shown that the existence of an UD mole is strongly correlated to the existence of melanoma.
UD detection can be treated as a form of outlier detection problem which gets its data from the domain of clinical images. However there is a lack of expertly labelled data, so like many other outlier detection problems, this problem must be solved using unsupervised learning. Our proposed approach is to detect and extract each mole from the image. Then an embedding for each suspicious mole, based on the well-known ABCD criteria, will be calculated. These embeddings will then be used to calculate the similarity between each pair of moles.
We hypothesise that ugly duckling "outlier" and suspicious moles can be identified using this deep learning method, leading to improved identification of suspicious lesions which can then be chosen for excision. We propose to evaluate the method by automatically identifying UD and suspicious moles on full body back images of 80 patients (with mean about 25 moles per clinical image) with pathology-validated ground truth on excised lesions, and compare with dermatologists.

Category: Pilot/exploratory experiments (for study design, hypotheses creation, etc)

11:20 a.m.

ATOPIC DERMATITIS AND BONE HEALTH: A SYSTEMATIC REVIEW

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Background: Atopic dermatitis (AD) is associated with systemic inflammation and corticosteroid use, both of which can lead to poor bone health and fractures.
Objective: To investigate the relationship between AD and bone health, including bone mineral density, osteopenia, osteoporosis and fractures.
Methods: We conducted a systematic review of all published observational studies that examined the association between AD and the above bone health outcomes. MEDLINE and Embase databases were searched. Title, abstract and full text screening, data abstraction and quality appraisal were done independently in duplicate.
Results: We screened 3800 abstracts and included fifteen studies, including twelve cross-sectional and three cohort studies. In cross-sectional studies, AD was associated with decreased bone mineral density and increased odds of fracture. In cross-sectional studies and a cohort study, AD was associated with a higher prevalence of osteoporosis compared to controls. These findings were not consistent across all studies, with some studies finding no association between AD and bone mineral density, and osteopenia.
Limitations: Heterogeneity between studies precluded quantitative synthesis.
Conclusion: There is some evidence supporting an association between AD and poor bone health. Research is needed to clarify this association, underlying mechanisms and develop strategies to improve bone health of people with AD.

Category: Early experiments with well-defined objectives/hypotheses

11:30 a.m.

CAN A RAMAN SPECTRUM FROM NORMAL-APPEARING SKIN ADJACENT TO A SKIN LESION BE USED TO DETERMINE WHETHER THE LESION ITSELF IS CANCEROUS?

Jianhua Zhao[1,2], Haishan Zeng[1,2], Sunil Kalia[1,3,4], David McLean[1] and Harvey Lui[1,2]
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Background: Raman spectroscopy has been used for *in vivo* skin cancer detection with relatively high sensitivity and specificity, based on the spectra taken from *lesions*. The objective of this study is to explore whether the lesional "environment", i.e. normal-appearing skin adjacent to lesions, can discriminate whether the suspect lesion is cancerous or benign.
Methods: Raman spectra of lesions and the "normal" appearing skin adjacent within 5 cm to these lesions were acquired with an integrated real-time Raman spectroscopic system. In total 731 lesions were included in this study, and were divided into two categories: cancerous lesions (including malignant melanoma, basal cell carcinoma, squamous cell carcinoma and precancerous lesions, i.e. actinic keratosis, n = 340) and benign lesions (including melanocytic nevi and seborrheic keratosis, n = 391). Wavenumbers were selected from the spectra based on the "normal" spectra and patient demographics including patient age, gender, skin type and lesion location were also incorporated into the model. Multivariate statistical analysis, including principal component and general discriminant analysis (PC-GDA) and partial least squares for discriminant analysis (PLS-DA), were used for discrimination between cancer and benign cases based on leave-one-out cross-validation.
Results: The area under the receiver operating characteristic curve (ROC AUC) with 95% confidence interval (95%CI) based on the lesional spectra and patient demographics was 0.934 (0.917-0.952; PLS-DA). The ROC AUC based on the "normal" appearing skin adjacent to the lesions was 0.882 (0.858-0.906; PLS-DA). The contribution of analyzing the normal-appearing skin surrounding a suspect lesions towards the total discrimination of skin cancer and pre-cancer lesions was estimated to be as high as 94.4% (95%CI: 91.3-97.6%).
Conclusions: Spectral analysis of the skin surrounding suspect lesions can predict the clinical diagnosis of the lesions themselves in terms of cancerous behaviour.

Category: Applied/functional experiments (in vivo studies)

11:40 a.m.

INVESTIGATING THE ROLE OF IL-7 AND IL-15 ON TISSUE RESIDENT MEMORY T-CELLS IN THE RECURRENCE OF CONTACT HYPERSENSITIVITY

Touraj Khosravi-Hafshejani[1] and Jan P. Dutz[1]
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Allergic contact dermatitis and atopic dermatitis are chronic T-cell mediated skin diseases that recur upon environmental antigen/allergen exposure. Exacerbations develop on previously healed skin as a result of local memory to antigens/allergens mediated in-part by tissue resident memory T (Trm) cells. Trm cells are a subset of non-circulating memory T-cells characterized by their expression of CD69/CD103 that persist long-term in tissues. The background proliferation and homeostatic survival of both CD4 and CD8 Trm cells are primarily regulated by hair follicle-derived IL-7 and IL-15. Our aim is to use a mouse model of contact hypersensitivity (CHS) to the chemical allergen 2,4-dinitrofluorobenzene (DNFB) to study the role of IL-7/IL-15 on Trm cells during dermatitis exacerbations. C57/BL6 mice will be epicutaneously sensitized with DNFB. In our first experiment, a group of mice will be challenged 5 days later with DNFB inducing a CHS response, and the control group will receive an acetone/olive-oil vehicle. The skin of mice with DNFB allergy will be analyzed at different time points after the resolution of CHS (day 30 and months 3, 6, 12). The use of immunohistochemistry and flow-cytometry can detect for the presence of Trm cells and their IL-7/IL-15 receptors, as well as for the expression of IL-7/IL-15 cytokines. In our second set of experiments, mice with DNFB allergy will receive IL-7- and/or IL-15-receptor inhibitors and their CHS reaction will be monitored following subsequent DNFB re-challenge. The role of IL-7/IL-15-induced longevity of Trm cells may help better understand the drivers of chronic recurrent inflammatory skin diseases.

Category: Pilot exploratory experiments

11:50 a.m.

PREDNISONE PRESCRIBING HABITS IN THE ER FOR RASH.

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Background: Evidence-based guidelines direct treatment of specific severe acute skin disorders with systemic corticosteroid, such as oral prednisone. Observation during visiting dermatology clinics in Prince George, BC suggested significant referrals for non-descriptive skin "rash" that were prescribed prednisone in the ER. In some cases, this was felt inappropriate and/or there was inadequate follow up. The primary purpose of this study was to determine the prevalence of prednisone prescription for nonspecific dermatology diagnoses in patients presenting to the Emergency Room (ER) at University Hospital of Northern British Columbia (UHNBC) in Prince George, BC, as well as the proportion of patients referred for follow-up.
Methods/Results: A quantitative retrospective chart review was performed of UHNBC ER visits with ICD-10 diagnostic code R21 ("rash and other nonspecific skin eruption") between January 1, 2016 and December 31, 2018 (N= 463). 10.4% of ER patients with "rash and other nonspecific skin eruption" were prescribed prednisone. Most were given a nonspecific diagnosis (45.8%) or were uncertain (25.0%), and few specific diagnoses were included (29.2%). Most patients were referred to a general practitioner (GP) (56.3%); or not referred (35.4%), sent to other providers (4.2%), GP dermatology (2.1%), or a dermatologist (2.1%).
Conclusion: Based on ER prescribing trends, we suspect prednisone is used empirically to treat unclear skin diagnoses. It is possible this issue is related to the lack of a full-time dermatologist in Prince George and perceived lack of support for making specific diagnoses. This suggests a need for further education in utilizing current guidelines when considering prednisone.

Category: Pilot/exploratory experiments (for study design, hypotheses creation, etc)

1:00 p.m.

GRANZYME K: A NOVEL PLAYER IN PSORIASIS DEVELOPMENT

Katlyn Richardson[1,2], Christopher Turner[1,2], Sho Hiroyasu[1,2], Richard Crawford[2,3], Angela Burleigh[2,3], David Granville[1,2,4].
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Background. Psoriasis is characterized by skin inflammation and epidermal proliferation forming thick scaly plaques. Current therapies are not ideal and often present with side effects. As such, a deeper understanding of the pathological mechanisms of psoriasis are necessary. Granzyme K (GzmK) is a serine protease recently elucidated as a mediator of cutaneous inflammation. Elevated GzmK is observed in human psoriatic skin lesions. However, its role in psoriasis is unknown.
Hypothesis. *GzmK contributes to the onset and progression of psoriasis through the augmentation of inflammation and/or epidermal proliferation.*
Methods. GzmK expression was evaluated histologically in skin from people with and without psoriasis. The role of GzmK was investigated in a murine model of psoriasis, comparing GzmK-/- to wild-type (WT) mice. Psoriasis severity was assessed macroscopically for onset and severity of erythema and plaque formation. Psoriasis tissue was examined histologically for epidermal thickness and inflammatory cell infiltrate. To elucidate a mechanistic role, we are currently culturing keratinocytes with GzmK for assessment of epidermal proliferation, cytokine expression and to define the GzmK degradome as it pertains to the epidermis.
Results. GzmK positive cells were elevated in lesional psoriasis skin compared to healthy skin. Lymphocytes and dendritic cells were identified as the predominant cell sources of GzmK. Psoriatic GzmK-/- mice exhibited reduced erythema and plaque formation compared to WT mice. In vitro, GzmK induced keratinocyte proliferation.
Conclusion. GzmK is elevated in human psoriasis tissue and may contribute to psoriasis development. This study will provide rationale for pursuing GzmK-targeted inhibitors for the treatment of psoriasis.

Category: Applied/functional experiments (animal models of disease and in vivo studies, etc.)

1:10 p.m.

MELANOMA GUIDELINE ADHERENCE WITHIN THE NORTHERN HEALTH AUTHORITY

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Background: In the treatment of melanoma the initial biopsy heavily impacts the subsequent management based on Breslow thickness. Current UK, USA, and Australian guidelines recommend complete excisional biopsies except for cases with special considerations – such as acral or cosmetically sensitive areas. There is currently no available data on whether melanoma excisional guidelines are being followed within the Northern Health Authority (NHA). Anecdotally we believe that guideline adherence is suboptimal within the NHA.
Objective: To determine the guideline adherence rate for margin recommendations of confirmed melanomas within the NHA and to compare the initial incisional/excisional margins to final surgical excisional margin.
Hypothesis: We hypothesize that the current adherence rate to current melanoma guidelines is suboptimal within the NHA.
Proposed Methods: The project will employ a retrospective chart review of pathology reports for all confirmed melanoma cases within the NHA. The initial margins of the incisional/excisional biopsy will be compared to current melanoma guideline recommendations from the UK, USA, and Australia. We will also compare the surgical margins to the current guideline recommendations for surgical excisions. Finally, the study will compare the initial incisional/excisional margins to the final surgical excisional margins.
Impact: This will provide the only known audit of the adherence rate of current melanoma guidelines within the NHA. Consequently, this study will shed light on the current state of melanoma treatment within the NHA.

Category: Early experiments with well-defined objectives/hypotheses.

1:20 p.m.

PROBING CUTANEOUS MOLECULAR FEATURES OF PSORIASIS AND ECZEMA BY NON-INVASIVE RAMAN SPECTROSCOPY

Yi Hui Wei[1] , Harvey Lui[2,3] , Jianhua Zhao[2,5] , Haishan Zeng[2,5] , Sunil Kalia[2,3,4]
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Psoriasis and eczema are common chronic inflammatory skin diseases. The pathophysiology of psoriasis and eczema has mostly been studied by cytokine analysis and histology, for which invasive procedure is needed. Raman spectroscopy is a non-invasive optical tool that probes vibrational signal of chemical bonds. The objective of this study is to identify molecular features and patterns characteristic of psoriasis and eczema. Patients with psoriasis or eczema were recruited. Raman spectra were measured on lesional sites using a real-time Raman spectrometer system under double-excitation of 690 nm and 785 nm. For each lesional site paired measurements from adjacent normal-appearing skin were taken. 36 psoriasis patients and 26 eczema patients were measured. Elevated water to protein ratio was found to be a potential marker of eczema activity ($p<0.05$) but not a marker for psoriasis ($p=0.37$). Eczema showed decreased lipid to protein ratio (87% of non-lesional, $p<0,05$) and ceramide deficiency on Raman spectra ($p<0.05$). Psoriasis showed a decreased lipid to protein ratio similar to that of eczema (88% of non-lesional, $p<0.05$). Ceramide deficiency was also noted on psoriasis spectra ($p<0.05$). The peak at about 2458 cm^{-1}, which has not been assigned at the moment, distinguished between psoriasis and eczema lesions ($p<0.05$). In summary, our study shows that molecular profiles can be used as biomarker for pathological changes in psoriasis and eczema and it is possible to obtain those non-invasively. Thus, there is potential use of optical tools for assessing molecular response from different types of treatment.

Category: Early experiments with well-defined objectives/hypotheses

1:30 p.m.

VOLUMETRIC SKIN PROPERTY ASSESSMENT ACHIEVED BY POLARIZATION SENSITIVE OPTICAL COHERENCE TOMOGRAPHY

Xin Zhou[1], Daniel C. Louie[2,3,4], Sina Maloufia[1], Lioudmila Tchvialevac[3,4], Shuo Tang[1], and Tim K. Lee[2,3,4]

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Background: Melanoma is a deadly cancer which is difficult for early detection due to its natural similarity with benign nevi. Recent investigations on surface roughness have shown the value of light polarization based techniques in melanoma detection.

Objective: To propose and test the volumetric assessment with polarization sensitive optical coherence tomography (PS-OCT) for skin properties.

Methods: PS-OCT has two signal channels. The intensity channel visualizes the layered structure and surface roughness profile of skin in 3D. The degree of polarization uniformity (DOPU) can assess the polarization properties such as micro-roughness. Skin phantoms of different surface roughness ranging from 1 to 68 μm were studied. PS-OCT was also applied to in vivo imaging of human skin.

Results: For rougher surfaces, the roughness can be quantified from the surface profile visible in the intensity channel. In smoother surfaces for which the profile is not sensitive, the DOPU decreases with roughness in a quantifiable correlation. The contrast in the DOPU channel is sensitive to polarization and phase fluctuations. Smoother surfaces tend to maintain the polarization state, whereas the height differences in a rougher surface contribute to larger phase shifts between light waves within the coherence volume, leading to greater depolarization. The skin at a palm edge shows lower DOPU compared to the skin on a dorsal hand, an indication of greater polarization state modification caused by skin roughness.

Conclusion: DOPU is a very promising feature which is associated with skin micro-roughness. Volumetric assessment with PS-OCT could provide a comprehensive evaluation for clinic investigations.

Category: Early experiments with well-defined objectives/hypotheses

1:40 p.m.

IMPROVING ACCURACY AND INTERPRATION OF DEEP MELANOMA CLASSIFICATION USING 7-POINT CHECKLIST

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Background and Objectives: The 7-point checklist is one of the 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). These criteria can be considered as content-based features of a lesion and they could be combined to predict malignancy. Meanwhile, many deep learning frameworks have been proposed for melanoma detection. However, one of the limitations of these frameworks is that the final learning model is a black box and no explanation could be given to the classification results. Recently, a published deep learning work suggested classifying melanoma via the 7 content-based features simultaneously. In this project, we propose to further improve the published network by evaluating the relationship between the major and minor criteria as in 7-point checklist. **Hypothesis:** we hypothesize that the performance and the interpretation of the deep learning networks could be improved by optimizing the order of 7 criteria in ensemble classifier chain algorithm and thus introducing the information from major criteria for minor ones.
Proposed Methods: Paired dermoscopic images and clinical images are collected from 1011 lesions with their matched 7-points checklist information, the presence and absence of the criteria, from a publicly available dataset. Deep learning features are extracted using an auto-encoder based deep neural network and the features are then combined by feature deduction and classified into 7 criteria classes in the constrained ensemble classifier chain.

Category: Early experiments with well-defined objectives/hypotheses

1:50 p.m.

SKIN EXPOSURE TO NARROW BAND UVB LIGHT MODULATES THE HUMAN INTESTINAL MICROBIOME

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Background: The recent worldwide rise in chronic inflammatory diseases such as inflammatory bowel diseases has been linked to Western lifestyle and environment. These include decreased exposure to sunlight, as well as dysbiotic composition of the gut microbiome. It remains unclear if there are any direct links between UVB light and the gut microbiome.
Aim: In this study we investigated whether exposing the skin to Narrow Band Ultraviolet B (NB-UVB) would modulate the composition of the human intestinal microbiota.
Methods: The effects of NB-UVB light were studied in a clinical pilot study using a healthy female cohort (n=21). Participants were divided into those that took vitamin D supplements throughout the winter prior to the start of the study (VDS+) and those who did not (VDS-).
Results: After three NB-UVB light exposures within the same week, the serum 25(OH)D levels of participants increased on average 7.3 nmol/L. Fecal microbiota composition analysis using 16S rRNA sequencing showed that exposure to NB-UVB significantly increased alpha and beta diversity in the VDS- group whereas there were no changes in the VDS+ group. Bacteria from several families were enriched in the VDS- group after the UVB exposures. The serum 25(OH)D concentrations showed a positive correlation with the relative abundance of the *Lachnospiraceae.*
Conclusions: This is the first study to show that humans with low 25(OH)D serum levels display changes in their intestinal microbiome in response to NB-UVB skin exposure, suggesting a novel skin-gut axis that could be used to promote intestinal homeostasis and health.

Category: Pilot/exploratory experiments

2:00 p.m.

COMPREHENSIVE RNA-SEQUENCING ANALYSIS IN VITILIGO LESIONS

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Vitiligo is an acquired depigmentation disease with no satisfactory therapy. To understand the host gene expression changes involved in vitiligo process and identify the potential signatures for clinical diagnosis, we performed a whole genome-wide transcriptome profile of skin tissues from patients with vitiligo and healthy controls.37 samples of paired lesional and non-lesional skin (LS and NLS) biopsies from the same vitiligo patients. Biopsies of 9 healthy volunteers were taken as healthy normal skin(HNS) control. The differentially expressed genes (DEGs) between groups were assessed by t-Test with a criteria of $P<0.05$, fold-change(FC)=2 for comparisons of LS versus NLS, LS versus HNS, segmental versus non-segmental vitiligo, and $P<0.2$, FC=1.5 for comparisons of patients whose good response to NBUVB/Tacrolimus treatment were good versus bad, or patients whose onset >12 months versus <12 months. The R-package was used to generate heatmap plotting. The gene-list analysis web portal Metascape was used to do functional pathway analysis. 533 genes are overexpressed in LS compared to NLS, highlighting 20 pathways mainly involved with adaptive immune response and fat metabolism. 78 are downregulated, highlighting 9 pathways mainly involved in melanin biosynthesis. 92 genes are overexpressed in non-seg vitiligo with 7 specific pathways. 213 genes are overexpressed in patients with good treatment response with 16 specific pathways, while 217 overexpressed genes and 14 pathways specific to patients with bad response. 256 overexpressed genes and 20 pathways are specific to patients with onset less than 12 months, while 145 overexpressed genes and 7 pathways specific to those more than 12 months.

Category: Pilot/exploratory experiments