8:40 a.m.

ANNULAR AND POLYCYCLIC CUTANEOUS ERUPTIONS WITH HYPER-FERRITINEMA AND FEVER RESPONDING TO TOCILIZUMAB – ATYPICAL ADULT ONSET STILL'S DISEASE?

<u>Misha Zarbafian</u>[1], Jan P Dutz[1,2]

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We report on the clinical courses of 5 patients with prolonged histories of recurrent urticarial eruptions accompanied by systemic symptoms including arthralgias, intermittent fevers, sore throat, and fatigue. Associated hyper-ferritinemia and elevations of CRP were also noted. Several patients had histories of recurrent thrombophlebitis. Some skin biopsies showed variably perivascular lymphocytic infiltration without dermal mucin and neutrophils, while others showed more prominent diffuse neutrophilic infiltrate of the reticular dermis. Leukocytoclastic debris was noted in some cases, but no fibrinoid necrosis of vessel walls, which would be expected in active vasculitis, was seen. Many of the patients' symptoms typically responded to elevated doses of prednisone, but they failed therapeutic trials of several medications including antimalarials, methotrexate, mycophenolate mofetil, and dapsone. A few patients have been started on tocilizumab, and after several years have finally achieved control of symptoms, with recurrence on therapy interruption. Tocilizumab represents a potential novel therapeutic option for this patient population, which may represent "atypical adult-onset still's disease". Clinical images, clinical course, pathology and laboratory investigations will be presented for discussion.

Category: (2) Early experiments with well-defined objectives/hypotheses

8:50 a.m.

GRANZYME B CONTRIBUTES TO BLISTER FORMATION IN AUTOIMMUNE SUBEPIDERMAL BLISTERING DISEASES THROUGH HEMIDESMOSOME PROTEIN DEGRADATION

Sho Hiroyasu[1,2,3], Matthew R. Zeglinski[1,2,3], Hongyan Zhao[1,2,3], Peter A. Lennox[4], Nancy Van Laeken[4], Nick J. Carr[4], Angela Burleigh[5], Richard I. Crawford[2,5], Chiharu Tateishi[6], Daisuke Tsuruta[6], Anika Kasprick[7], Ralf J. Ludwig[7], and David J. Granville[1,2,3]

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Granzyme B (GzmB) is a pro-apoptotic protease that plays a pathological role in several inflammatory skin conditions through an extracellular proteolytic mechanism. GzmB-positive neutrophils are abundant in lesional skin in autoimmune subepidermal blistering diseases (ASBDs); hence, GzmB may contribute to ASBD pathology. In the current study, the function of GzmB in blister formation was assessed in a murine model of the ASBD, epidermolysis bullosa acquisita (EBA), using both wild type C57Bl/6 (WT) and GzmB knockout (GzmBKO) mice. After 12 days, GzmBKO mice exhibited reduced affected body surface area compared to WT mice (n=8 for each, $P<0.01$). Moreover, ears from GzmBKO mice with EBA had lower histological blister scores compared to the WT mice with EBA (n=7 for each, $P<0.05$). Further, the loss of hemidesmosomal proteins, collagen XVII and α6 integrin, was reduced in ear extracts from GzmBKO mice with EBA compared to WT mice with EBA (n=6 for each, $P<0.01$). In support, primary human keratinocytes exposed to GzmB *in vitro* showed reductions in both cell attachment strength and collagen XVII protein level. The *in vitro* results were rescued with a newly developed GzmB inhibitor (n=3). In addition, high levels of GzmB and collagen XVII fragments were detected in blister fluid from bullous pemphigoid patients (n=3), further indicating that GzmB may contribute to the blistering of ASBDs by cleaving collagen XVII. In summary, GzmB contributes to blister formation in ASBDs through the cleavage of hemidesmosomal proteins. Our study provides evidence validating GzmB as a therapeutic target for the treatment of ASBDs.

Category: Applied/functional experiments

9:00 a.m.

ASCERTAINMENT OF ATOPIC DERMATITIS USING HEALTH INSURANCE CLAIMS AND PRESCRIPTION RECORDS IN FAMILY PRACTICE

Thomas J.X. Zhang[1,2], Harvey Lui[1,2,3], Tim K. Lee[1,2,3], Jan Dutz[1], Martin Dawes[4], Janet McKeown[4],Sunil Kalia[1,2,3]
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[3]Departments of Cancer Control and Integrative Oncology, BC Cancer
[4]Department of Family Practice, The University of British Columbia

Background: Atopic dermatitis (AD) is a chronic and recurrent inflammatory skin condition associated with diminished quality of life and significant financial burdens. There are limited validated methods for ascertaining AD patients who access the healthcare system. ***Objective***: To propose and test the validity of claims- and prescription-based models for AD ascertainment. ***Methods:*** Our nested cohort study uses chart records and BC provincial insurance claims data from 6 family physicians providing general care in an urban Canadian metropolitan center. The charts of patients with AD were abstracted for their diagnostic codes and prescription medications. AD diagnostic standards are based on the United Kingdom Working Party, the Hanifin and Rajka criteria, with physician diagnosis as a secondary confirmation. Patient cases with uncertain diagnoses of AD are excluded from analyses. ***Results:*** To date, 138 patient cases have been abstracted. Among 51 patient cases with ICD-9 diagnostic code 691 (atopic dermatitis and related conditions), 32 (62.7%) had a diagnosis of AD; for 96 cases with diagnostic code 692 (contact dermatitis and other eczema), 21 (21.9%) had a diagnosis of AD. "Non-atopic dermatitis" and "non-eczematous" skin cases constituted 52 (37.7%) and 33 (23.9%) of the total abstracted cases, respectively. ***Conclusion:*** Next, we plan to obtain additional patient cases and to incorporate other factors including demographics and prescription treatments to develop algorithmic models as an ascertainment method for AD patients.

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

9:10 a.m.

MOTION-TOLERANT HIGH-RESOLUTION EXTENDED FIELD VOLUMETRIC MULTIMODAL OPTICAL BIOPSY VIA VERTICAL PLANE TISSUE IMAGING

Zhenguo Wu[1,2], Yunxian Tian[1,2], Jianhua Zhao[1,2], Yimei Huang[1,2], Harvey Lui[1,2], Sunil Kalia[2], Haishan Zeng[1,2]
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Optical biopsy using reflectance confocal and multiphoton techniques greatly facilitates *in vivo* evaluation of tissue by providing morphologic, biochemical, and physiologic information. As the most accessible organ, the skin is often the initial target for these optical biopsy applications. To date microscopic *in vivo* skin imaging has primarily been oriented and displayed in the horizontal, X-Y plane. However, horizontal optical sections can be difficult to correlate with conventional histology, vulnerable to involuntary body motion, hard to stitch efficiently, and lack three-dimensional cellular and tissue information. To address these challenges, we developed an instrument for vertical plane-based multimodality and volumetric optical biopsy. With a relatively rapid vertical plane scanning speed of 15 frames per second, tissue information according to depth and skin surface position can be recorded in near real time. This device features XZ-Y volumetric imaging with motion correction, thereby enabling contiguous three-dimensional *in vivo* tissue exploration over several millimeters. Furthermore, integrated and co-registered multimodality microscopy can be performed according to reflectance confocal, two photon fluorescence, and second harmonic modalities to provide three separate contrast methods for examining a tissue volume of interest. *In vivo* data acquired from normal and cancerous skin has shown that optically biopsied tissue yields wide fields of view, high contrast, and multilayered tissue architecture when viewed in XZ-plane, and high-resolution cellular morphology when displayed in the XY-plane.

Category: early experiments with well defined objectives

9:20 a.m.

INPATIENT DERAMTOLOGY CONSULTS AT TWO VANCOUVER TERTIARY CARE HOSPITALS

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Introduction

Dermatology consultations provide valuable clinical information for healthcare teams in hospitals. Because skin conditions affect up to 24% of the population, patients with skin disease are seen in hospitals by non-dermatologists leading to a considerable amount of consultations. Studies show consultations by dermatologists result in changes to diagnosis, treatment, and length-of-stay in hospital.

Objective and Method

We aim to describe dermatology consultations seen at two Vancouver hospitals over a five-year period. The primary purpose of this study is quality assurance. We used data collected from January 1, 2011, to December 31, 2015 from dermatology consultations seen at Vancouver General Hospital (VGH) and St. Paul's Hospital (SPH). Information collected include diagnosis and referring department.

Results

Over 5 years, 2,150 distinct dermatology consults were seen. The top 10 diagnoses included drug eruptions (16.7%), eczemas other than contact dermatitis (16.3%), cutaneous infections (15.1%), skin conditions associated with connective tissue disease and vasculitis (6.1%), contact dermatitis (4.4%), bullous diseases (4.0%), malignant skin conditions (3.9%), psoriasis (3.8%), ulcers (2.9%), and urticaria (1.7%). A literature review demonstrated similar findings in common diagnoses at other institutions around the world. The majority of consultations originated from Internal Medicine and Subspecialties (35.0%), Emergency Medicine (14.8%), Surgery (12.7%), Blood & Marrow Transplantation (12.6%), and Family Medicine (10.6%).

Conclusion

The Dermatology consult service teams at VGH and SPH provide insight into diagnosis and management for a broad range of skin conditions. The large scope of dermatologic presentations provides for substantial learning opportunities for students and residents alike.

Category: Early experiments with well-defined objectives/hypotheses

11:00 a.m.

TRACKING CELLULAR DYNAMICS OF HUMAN SKIN RESPONSES TO UV EXPOSURE USING *IN VIVO* MULTIMODAL MICROSCOPY

Giselle (Yunxian) Tian[1,2], Harvey Lui[1,2], Jianhua Zhao[1,2], Zhenguo Wu[1,2], Sunil Kalia[1,3], Vincent Richer[1], InSeok Seo[4], Hao Ou-Yang[4], Haishan Zeng[1,2]

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Background: Serial analysis of cellular dynamics over time offers new insights into human skin responses to solar radiation. However, most of the previous studies are based on multiple biopsies and *ex vivo* analysis which precludes the monitoring of the same sites and cells over time. *In vivo* microscopy enables the possibility of real-time live cell imaging. Here we report a robust non-invasive method to achieve repeated and precise access to the same micro-locations over a two weeks observation window.

Methods: The technique is based on affixing a temporary skin "surface marker" as a landmark to help locating the same microstructures between imaging sessions. At baseline, the region-of-interest (ROI) is determined and imaged; at follow up sessions, the ROI can be readily revisited using the external marker. Using this method, we were able to monitor the same cells in human skin after ultraviolet B (UVB) radiation over two weeks. Skin microscopic responses were studied with a multimodality *in vivo* microscopy system capable of co-registered video rate reflectance confocal microscopy (RCM), two-photon fluorescence (TPF) and second harmonic generation (SHG) imaging.

Results: Quantitative analysis of TPF signal revealed that the melanin distribution pattern changed with time after UVB exposure with melanin appearing to migrate upwards towards the skin surface. Blood flow was monitored within the same capillaries over two weeks. Multimodal analyses enabled accurate thickness calculation of the viable epidermis, and stratum corneum as well as cell density variations over time, thus demonstrating evolution of tissue edema and cell proliferation induced by UVB.

Category: Early experiments with well defined objectives/hypotheses

11:10 a.m.

RISK OF SKIN CANCER DEVELOPMENT IN PATIENTS TREATED WITH ULTRAVIOLET THERAPY

Elle Wang[1,2], Yi Ariel Liu[5], Richard Crawford[1,5], Harvey Lui[1,2,3], Tim Lee[1,2,4], Sunil Kalia[1,2,4]
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[5]Department of Pathology and Laboratory, University of British Columbia, Vancouver, Canada.

Background: Although ultraviolet (UV) phototherapy is an important treatment option for skin diseases such as psoriasis and atopic dermatitis, specific safety thresholds for cumulative therapeutic UV exposure and long-term effects of UV therapy remain unclear.

Objective: To determine the long-term skin cancer risk in patients being treated with UV.

Methods: A retrospective chart review was conducted on patients receiving UV therapy from 1970 to 2018. Patients were identified via patient medical charts at VGH Skin Care Centre. Demographic and treatment covariates that were analyzed included age, gender, skin type, diagnosis, and details of phototherapy. Endpoints included pathological confirmation of basal cell carcinoma (BCC), squamous cell carcinoma (SCC), or melanoma.

Results: A total of 2,291 patients without a prior cancer history (1,256 male and 1,035 female) were followed-up for 15,765 person-years. Three melanoma, eleven SCC and twenty-one BCC were detected during the follow-up period. The range of BB-UVB and NB-UVB cumulative dose was 0.01-1502.39 J/cm^2 (median 3.14, interquartile range (IQR): 0.80-11.34) and 0.03-4975.00 J/cm^2 (median 11.96, IQR: 2.53-42.76), respectively. The median (IQR) value of BB-UVB and NB-UVB total session was 32 (14-85) and 31 (11-76), respectively. The Cox-regression analysis results suggested there was no correlation between cumulative dosage, total session and the development of cancer (NB-UVB cumulative dose: Hazard Ratio (HR): 0.999, p=0.78; BB-UVB cumulative dose: HR: 0.998, p=0.13; NB-UVB total session: HR: 1.00, p=0.40; BB-UVB total session: HR: 1.00, p=0.012).

Conclusion: We found that there was no risk of skin cancer with higher number of treatment sessions or cumulative dosage.

Category**:** Applied/functional experiments

11:20 a.m.

TOPICAL IMMUNOMODULATION FOR THE TREATMENT OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE)

Paulina Piesik[1], Jan P Dutz[1,2]

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Introduction: Multiple sclerosis (MS) is an autoimmune disease characterized by T-cell mediated destruction of myelinated axon sheaths in the central nervous system. Topical application of the vitamin D analogue, calcipotriol, can abrogate the generation of contact hypersensitivity. We aim to test whether topical calcipotriol or tretinoin (vitamin A), a similarly immunomodulatory compound, can restrain the pathogenicity of a mouse model of MS.

Hypothesis: We hypothesize that topical treatment with calcipotriol or tretinoin reduces EAE disease severity by reducing the generation of encephalitogenic T cells and increasing the number of regulatory T cells.

Methodology: We used the experimental autoimmune encephalitis (EAE) mouse model of MS. Mice were pre-treated with tretinoin, calcipotriol, or vehicle for 2 days once daily before induction of EAE. Mice were monitored for 28 days, scored and weighed daily. Lymph nodes and spleens were harvested for flow cytometric analysis of T cell subsets and cytokine expression. Brain and spinal cord sections were collected in fixative for histological study.

Preliminary results: Topical pre-treatment with tretinoin, but not calcipotriol, reduced the severity of EAE as reflected by lower clinical disease scores and sustained maintenance of body weight. Immune cell phenotype analysis showed reduced expression of interferon-γ in CD4 and CD8 T cell compartments from lymphoid organs of animals pre-treated with tretinoin.

Outro: 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 systemic immunity.

Category: Early experiment with well-defined objectives/ hypotheses

11:30 a.m.

SUNSCREEN PROPERTIES, PREFERENCES, AND UTILIZATION

Rebeca Pinca[1], Nick Bansback[2], Sunil Kalia[1,3,4]
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Background: Skin cancer is the most common type of cancer and its incidence is increasing, yet it is one of the most preventable cancers. Sun protection and sun exposure avoidance can prevent over 90% of skin cancer. Sunscreen is one of the most common modalities used for sun protection; however, there is limited understanding of individuals' decisions regarding sunscreen usage.

Objective: The objective of this study is to understand how different properties of sunscreen affect usage amongst dermatology patients.

Methods: We developed a discrete choice experiment to understand the importance of different sunscreen attributes: cosmetic aspects (unpleasant smell, mild skin side-effects, greasiness, white film); effectiveness (lifetime risk of sunburn and cancer), and cost. Experimental design theory was used to develop 40 different, hypothetical sunscreen profiles. Respondents were randomly assigned to answer 10 questions, each comparing one of the sunscreen profiles with no sunscreen use. Preferences were examined using conditional and latent class models.

Results: 244 respondents completed the survey, providing 4834 responses. Model results suggest that cost was not a major deterrent to using sunscreen some days but was a deterrent to using it every day. Cosmetic aspects were important deterrents to any sunscreen use, and were more important, or equal, deterrents compared to cancer risk and sunburn, respectively.

Conclusion: Participants' stated sunscreen preferences indicate that its effectiveness in decreasing skin cancer risk was not an important factor for sunscreen usage. Further work on helping individuals understand this risk, by providing salience to other risk taking behaviours, may help increase sunscreen use.

Category: Early experiments with well defined objectives/hypotheses

11:40 a.m.

INCORPORATING PATIENT DEMOGRAPHICS INTO RAMAN SPECTROSCOPY ALGORITHM IMPROVES DIAGNOSTIC PERFORMANCE

Jianhua Zhao,[1,2] Haishan Zeng,[1,2] Sunil Kalia [1,3] and Harvey Lui [1]
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Background and objective:
Raman spectroscopy is a non-invasive optical technique that provides finger-print information on molecules within biological tissue. We developed a real-time in vivo Raman system for skin cancer diagnosis. In this study we evaluate if incorporating patients' demographics improves diagnostic accuracy.

Patients and methods: Raman spectra of 731 cases were measured, which were divided into skin cancers (including malignant melanoma, basal cell carcinoma, squamous cell carcinoma and precancerous lesion - actinic keratosis, n = 340) and benign skin lesions (including pigmented nevi and seborrheic keratosis, n = 391). Patient age, gender, skin type and location of the lesion were incorporated into the analysis. Multivariate statistical analysis including principal component and general discriminant analysis (PC-GDA) and partial least squares (PLS) are used for skin cancer discrimination based on leave-one-out cross-validation.

Results: The posterior probability of being a cancer is significantly dependent on gender, age and location of the lesion ($p < 0.05$) but independent of skin type ($p > 0.05$). Based on PLS analysis, the area under the receiver operating characteristic curve (ROC) can be improved from 0.913 (95%CI: 0.892-0.933) to 0.934 (95%CI: 0.917-0.952) after taking into account demographics. The specificity is increased from 33.5% to 44.5% at sensitivity of 99%; and from 76.0% to 82.1% at sensitivity of 90%.

Conclusions: Diagnostic accuracy of real-time Raman spectroscopy for skin cancer detection is improved by incorporating patients' demographics.

Category: Applied/functional experiments (in vivo studies)

1:00 p.m.

COMPARISON OF DIFFERENT SUN-SAFETY EDUCATION INTERVENTIONS IN CHANGING SUN EXPOSURE AND PROTECTION PRACTICES IN A GENERAL DERMATOLOGY CLINIC: A PILOT STUDY

<u>Panteha Eshtiaghi</u>[1], Touraj Khosravi-Hafshejani[1], Gulaab Sara[1], Harvey Lui[1,2], Sunil Kalia[1,2]

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Sun safety education is a strategy to reduce the risk of skin cancer. Active learning, compared to passive learning, has demonstrated superior knowledge acquisition. The aim of this study was to compare the effectiveness of different education modalities in changing patient reported sun-exposure, sun-protective behaviors, and skin colour. From May to June 2018, 73 participants recruited at a general dermatology clinic were arbitrarily allocated to receive sun-safety education through one of 3 modes: interactive online module, video or no education. A baseline Sun Exposure and Behaviour Inventory (SEBI) questionnaire was administered and colorimetry readings of sun-exposed and sun-protected areas were taken. Patients were followed 8 and 16-weeks after the initial visit where a modified SEBI was administered and serial L*a*b* measurements were taken. The change in SEBI scores and L*a*b* measurements (Euclidean distance = ΔE) between the initial and follow-up visits were analyzed. At 8 weeks post intervention, participants in the online module and video groups had significantly improved SEBI scores compared to control ($p < 0.05$, Kruskal-Wallace). At 16 weeks, only the module group showed significant improvement in SEBI scores compared to control ($p < 0.05$, ANOVA). There was no statistical difference in skin-colour (i.e. ΔE or ΔL) between the three groups at 8 or 16-week follow-up time points. Self-reported sun-protective behavioral changes were only maintained at 16 weeks with online module education. These changes did not correlate with significant skin color changes. Interactive strategies should be explored further to promote patient behaviour that translates to long-lasting objective changes in sun-protection.

Category: Pilot/exploratory experiments

1:10 p.m.

DEVELOPMENT OF A NOVEL APPROACH IN INDUCTION OF AA AND EVALUATING THE POTENCIA; ROLE OF MYELOID CELLS IN HAIR LOSS IN C3H/HEJ

Yunyuan Li, Ruhangiz T. Kilani, Aziz Ghahary

Burn and Wound Healing Research Lab, Department of Surgery, UBC

Alopecia areata (AA) is an autoimmune skin disease characterised by hair loss and local skin inflammation. In this study, we have developed a novel approach in inducing both the patchy and alopecia universalise in C3H mice. We simply isolated a mixture of skin cells from AA affected skin of mice and showed that intra-dermally injection of these cells into healthy mice caused AA. In addition to skin fibroblasts and keratinocytes, the mixture of isolated cells contained lymphocytes and myeloid cells. We then cultured this mixture of cells for two days. The attached and suspended cells were separately intradermally injected in healthy mice. Surprisingly, the induction rate of AA in mice received either attached cells or suspended cells were almost the same. However, mice received attached cells developed patchy while mice received suspended cells developed universalise. Examination of attached cells indicated they mainly included fibroblasts, keratinocytes and CD11b+ myeloid cells. To exclude the possible skin fibroblasts and keratinocytes can induce AA, we isolated skin cells from normal mice and injected the same number of cells to healthy mice. Result showed that none of mice developed to AA. Interestingly, intradermally injection of splenocyte-derived myeloid cells could also induce AA in C3H/HeJ mice and C57/BL mice. These findings confirmed the reproducibility of inducing AA in C3H/HeJ mice by our new approach without previously used AA skin grafting or injecting a cocktail of cytokine treated T cells. Further, CD11b+ myeloid cells from AA-affected skin may play a potential role in induction of alopecia areata.

Category: applied/functional experiments (animal models of disease and *in vivo* studies).

1:20 p.m.

A PROSPECTIVE STUDY OF TREATMENT SATISFACTION AND ASSOCIATED FACTORS FOR ADHERENCE TO PHOTOTHERAPY

Ian Tin Yue Wong, Abdulmohsen Altaleb, Harvey Lui, Vincent Richer, Sunil Kalia
Department of Dermatology and Skin Science, University of British Columbia, Photomedicine Institute, Vancouver Coastal Health Research Institute

Treatment satisfaction, patient/clinical factors have not been prospectively studied in relation to phototherapy adherence. We aim to describe patient satisfaction and to identify positive and negative aspects related to phototherapy adherence. We aim to compare the baseline demographic and clinical characteristics of adherent versus non-adherent patients undergoing phototherapy for psoriasis (Ps) or atopic dermatitis (AD). From July 2017 to August 2018, patients with either Ps or AD receiving phototherapy at the Skin Care Centre were enrolled. Adherence was defined as attendance at phototherapy sessions twice weekly for a minimum of 20 sessions. Over 12 weeks, treatment satisfaction, clinical data, including mPASI, mEASI and DLQI, patient-specified factors related to phototherapy were collected. In total, 76 patients (53 Ps, 23 AD) were enrolled; 40 patients (24 Ps, 16 AD) were adherent; 23 patients were non-adherent (20 Ps, 3 AD) and 13 patients withdrew (9 Ps, 4 AD). At 12 weeks, our findings show that adherent patients' treatment satisfaction may be related to the tolerability of phototherapy side effects. Amongst adherent patients, access to "parking" and "time" appear to be the most negative aspects, whereas "getting better" from their skin condition is the most positive factor. Multivariate analysis of Ps patients identified baseline DLQI as being associated with phototherapy adherence (p=0.03), when controlling for gender, age, children count, education, travel distance and mPASI. Preliminary analysis suggests baseline disease severity as an associated factor in adherent patients receiving phototherapy. Phototherapy satisfaction amongst adherent patients may be related to its tolerable side effect profile.

Category: Early experiments with well defined objectives/hypotheses

1:30 p.m.

SKIN CANCER DETECTION THROUGH COMPLETE OPTICAL POLARIZATION SPECKLE ANALYSIS

Daniel C. Louie[1,2,3], Yuheng Wang[1,3], Lioudmilla Tchvialeva[2,3], Sunil Kalia[2,3], Harvey Lui[2,3,4], Shuo Tang[1], Tim K. Lee[1,2,3,4]
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[3]Photomedicine Institute, Vancouver General Hospital
[4]Departments of Cancer Control Research and Integrative Oncology, BC Cancer

Background and Objectives: The polarization of light waves refers to the orientation of their intrinsic oscillations. In a previous study, a prototype low-cost optical probe was constructed in which the polarization signals it measured from the skin were found to have diagnostic use for cancer detection. This abstract proposes a new device and clinical study to further explore the diagnostic uses of polarization. This device aims to completely analyze the phenomenon of polarization speckle which is a noise-like optical interference pattern with statistical properties that are related to the morphology of an illuminated target. This project is the next iteration towards achieving low-cost and non-invasive optical skin cancer detection.

Hypothesis: We hypothesize that the dysplasia present in skin cancer will exhibit significantly different polarization speckle patterns than benign lesions. This diagnostic information will be extracted from speckle images in two ways. The first will be with previously validated statistical interpretations of speckle. The second will be through a deep learning classification technique.

Proposed Methods: Complete polarization characterization of a target requires understanding of how the polarization of light changes as it interacts with the target. This is mathematically modelled by a Mueller matrix, which requires four different polarization illuminations and four polarization detection channels to measure completely. The previous prototype used two illuminations and had four detectors separated in space. This new device will separate detectors in time, using automatic optical filters in front of a single laser and camera.

Category: Pilot/Exploratory Experiments

1:40 p.m.

INVESTIGATING THE ROLE OF GRANZYME SERINE PROTEASES IN PSORIASIS

Katlyn C. Richardson[1,2], Christopher T. Turner[1,2], Sho Hiroyasu[1,2], Matthew R. Zeglinski[1,2], David J. Granville[1,2,3]

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Psoriasis is a common skin disease characterized by skin inflammation and epidermal hyperplasia forming thick, scaly 'plaques', which often limit affected individuals' daily activities. Current therapies are not completely effective and present with a number of side effects. Thus, a deeper understanding of the immunopathological mechanisms associated with psoriasis are necessary and new therapeutic options are required. Granzymes (Gzms), a family of serine proteases, are drastically elevated in numerous inflammatory skin conditions including atopic dermatitis, alopecia areata and diabetic wounds, functioning to increase inflammation, cleave extracellular matrix and impair barrier function. Despite also being elevated in psoriasis, the patho/physiological role of Gzms in this disease remains unknown. In the present study, we *hypothesize* that Gzms contribute to the onset and progression of psoriasis through the augmentation of inflammation and/or skin barrier dysfunction. The objectives of our study are: 1) characterize Gzm expression and tissue localization in human psoriasis using immunohistochemistry, ELISA and qPCR; 2) induce psoriasis with imiquimod in Gzm knockout and wild-type mice then compare psoriasis onset and severity, and 3) investigate biological pathways linked to Gzm-mediated pro-inflammatory activity and skin barrier dysfunction using immunohistochemistry, cell culture permeability assays, cytokine ELISA and *in vitro* cleavage assays. The demonstration that Gzm elevation in psoriasis contributes to increased disease severity would project important insights into disease mechanisms and provide key rationale for pursuing Gzm-targeted inhibitors for the improved treatment of psoriasis.

Category: Early experiments with well-defined objectives/hypotheses