INTERNATIONAL SOCIETY FOR DIGITAL IMAGING OF THE SKIN NEWSLETTER ©2007

"Migrating skin imaging technology into clinical practice"

ISDIS invites you to attend its 2nd Annual U.S meeting on Thursday February 1, 2007. See below and page 4 for more details.

Editor-in-chief: Alon Scope, MD **www.i-s-d-i-s.com**

ISDIS SOCIETY AND THE UPCOMING 2ND ANNUAL MEETING AT AAD-WASHINGTON, DC

The goal of the International Society for Digital Imaging of the Skin (ISDIS) is to promote the migration of new and evolving digital imaging technologies into clinical practice. The ISDIS provides a knowledge sharing platform for clinicians and investigators to advance the use of imaging technologies in dermatology. To this end, the ISDIS promotes the peer-reviewed journal Skin Research and Technology, circulates this periodic newsletter and organizes scientific meetings.

In 2006, the ISDIS held its 1st United States annual meeting in San Francisco. Prominent experts presented outstanding reviews on imaging modalities that have achieved significant milestones in acceptance into clinical practice, such as automated diagnosis (Ralph Braun), total body photography (Allan Halpern), tele-dermoscopy (Peter Soyer), tele-Medicine (Anne Burdick) and migration of imaging technologies to the bedside (Harold Rabinovitz and Rox Anderson).

We are very excited to announce the upcoming 2nd annual U.S. meeting of the ISDIS. The meeting, held in conjunction with the AAD annual meeting at Washington DC, will have research and clinical sessions. In the research session, we will focus on a few imaging modalities that show potential for high impact on translational research. In the clinical session, we will focus on imaging modalities that are likely to impact future clinical practice. Abstracts of the reviews are included in this newsletter.

To contact us, please email Doris Munroe at munroed@mskcc.org

Allan C. Halpern, MD
President of ISDIS

Alexander Zemtsov, MD
Secretary/Treasurer of ISDIS

Clinical Dermatology

INTEGRATING TOTAL BODY PHOTOGRAPHY, DERMOSCOPY AND CONFOCAL MICROSCOPY INTO CLINICAL PRACTICE

By Josep Malvehy, MD

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A true revolution in the dermatologist's diagnostic armamentarium is at our doorstep. Imaging techniques that allow a detailed, immediate, noninvasive evaluation of the skin at the bedside are becoming available. Total body photography, already recognized for its usefulness in the early detection of melanoma, has been subject to technological improvement. Systems for the automated detection of new or changing lesions **(Fig 1)** are becoming commercially-available and may impact skin cancer surveillance in primary dermatology settings. Such systems can facilitate clinical follow-up of patients at high-risk for melanoma.

The incorporation of higher magnification microscopes to the practice of dermoscopy allows for studying skin lesions in-vivo in greater detail. This technique has applications beyond discrimination of malignant tumors from benign lesions; it can have wider impact on clinical research

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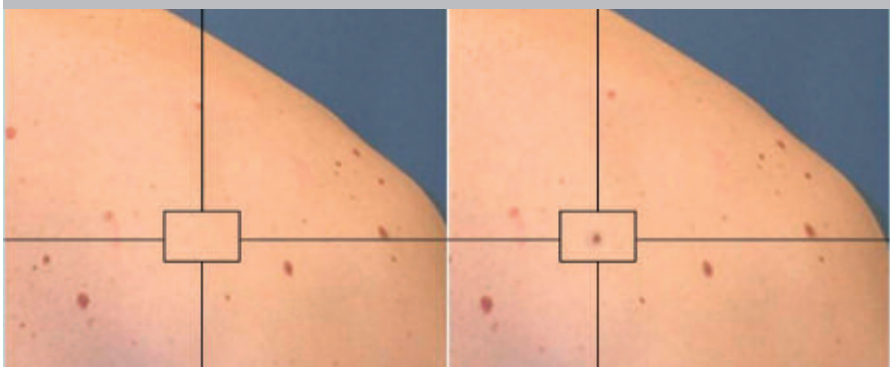
Figure 1: Detection of a new melanocytic lesion during follow-up total body photography.



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fields, such as the study of the natural evolution of melanocytic lesions, correlation of dermoscopic structures with histopathological findings and in-vivo and ex-vivo mapping of tumors.

In addition, reflectance confocal microscopy (RCM) gives us the possibility to study the skin in cellular-level detail at the bedside. Now we can detect amelanotic melanoma (Fig 2) or subclinical recurrence at the surgical site, select the best area for skin biopsy or validate the preoperative clinical diagnosis by RCM.

Currently, all the imaging techniques are restricted to University Centers, but with further development will become increasingly available to the practicing general dermatologist. To that end, the imaging modalities need to become more affordable and user-friendly, and the improvement in diagnostic accuracy attributable to imaging validated by clinical research. Dermatologists should be open-minded and prepared for the tremendous foreseen change that will take place in preoperative diagnosis. □

Dermatological Surgery

ADVANCES IN RESOLUTION-BASED ("MICRO") CANCER MAPPING: INTEGRATING CONFOCAL MICROSCOPY INTO MOHS SURGERY

By Kishwer Nehal, MD

Mohs surgeon, Dermatology Service, Memorial Sloan-Kettering Cancer Center, New York, NY

Recent studies have shown that reflectance confocal microscopy (RCM) can image basal cell carcinoma (BCC) in freshly excised Mohs surgery specimens without routine histologic tissue processing. Rapid brightening of nuclei and enhanced detection of BCC are achieved with acetowhitening: immersing the excision specimen in acetic acid for a short time. The acetic acid condenses the chromatin, which increases chromatin backscatter and brightens the nuclei in BCC.

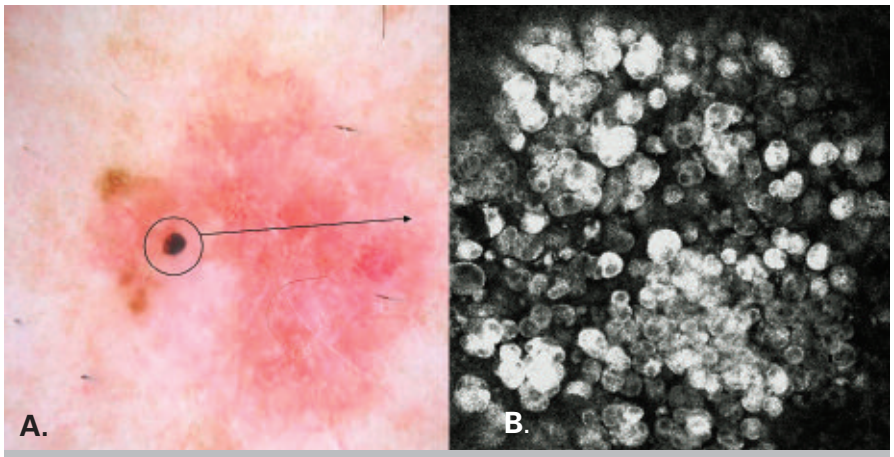

Figure 2: The pigmented focus seen in the dermoscopic image of this hypomelanotic lesion (A, circle) was imaged using reflectance confocal microscopy (RCM, B). RCM showed a multitude of large nucleated pleomorphic bright cells, suggesting the correct diagnosis, melanoma.

Experiments to optimize the acetowhitening technique and enhance detection of BCC were conducted using various acetic acid concentrations (1%-10%) and immersion times (30 seconds to 5 minutes). Two percent acetic acid for 2 minutes provides optimal acetowhitening while minimizing acetic acid concentration and immersion time.

To improve the detection of BCC, confocal reflectance instrumentation and imaging software were refined. Confocal instrumentation developments include a microscope mount for the Mohs surgical specimen which stabilizes the tissue analogous to Mohs embedding. Confocal imaging software has been enhanced and now displays a field-of-view of 15 mm which is comparable to 2x magnification typically used for examining Mohs frozen histology. At present, this RCM imaging technique requires 9 minutes compared to the 20-45 minutes typically required for processing of Mohs frozen histology. The ability to detect superficial, nodular, and micronodular BCC using RCM is comparable with that of Mohs frozen histology. However, small tumor aggregates of infiltrative BCC are not consistently visualized by RCM and tend to be obscured by surrounding dermal structures.

Continued improvements in instrumentation, image quality, and detection of BCC suggest that RCM can potentially expedite tumor mapping during Mohs surgery. Further work is necessary to enhance detection of small foci of BCC relative to the surrounding dermal structures and may require a multimodal imaging technique. □

MAPPING NONMELANOMA SKIN CANCERS USING MULTIMODAL MACRO-IMAGING

By Anna N. Yaroslavsky, PhD

Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Recent advances in optical imaging have made intra-operative guidance of tumor excision surgery technically feasible. Several competing techniques targeting delineation of cancer margins are being developed into practical clinic-ready systems. Real-time imaging capability and sufficient accuracy are the major criteria for evaluating these techniques. The development and clinical application

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Online Links

The use of confocal microscopy in the clinic was recently presented in the popular media (Today Show, NBC, 11.2.2006)

http://video.msn.com/v/us/msnbc.htm?g=fd52b660-01bb-47a7-8f93-7ec7c617096d&f=00&fg=email

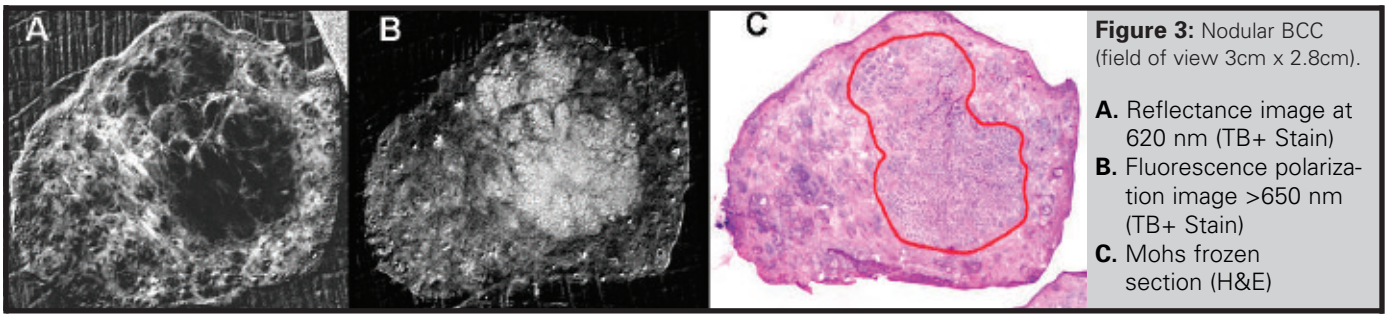

Figure 3: Nodular BCC (field of view 3cm x 2.8cm).

A. Reflectance image at 620 nm (TB+ Stain)
B. Fluorescence polarization image >650 nm (TB+ Stain)
C. Mohs frozen section (H&E)

of reflectance and fluorescence imaging in the context of nonmelanoma skin cancer will be discussed at the ISDIS meeting.

Nonmelanoma skin cancer is the most common form of human cancer, often resulting in high morbidity. Low visual contrast of these tumors makes their intra-operative delineation a challenge. During the last several years, we have been developing a powerful approach based on fundamental differences between cancerous and normal cell interactions with exogenous fluorophore molecules.

The theoretical basis, instrumentation, data-acquisition technique and image-processing algorithms for multi-spectral reflectance and exogenous fluorescence polarization imaging of the nonmelanoma cancers will be discussed.

Comparative advantages of using various exogenous stains, such as toluidine blue (TB) and tetracycline derivatives for the contrast enhancement of cancerous lesions will be analyzed. Clinical results yielded by reflectance (Fig 3A) and fluorescence polarization imaging (Fig 3B) will be presented and compared with histopathology (Fig 3C). Advantages of combining these imaging techniques in a single modality for increasing the sensitivity and specificity of the resulting method will be demonstrated. □

Cosmetic Dermatology

MULTIMODAL IMAGING OF HUMAN SKIN

By Nik Kollias, PhD

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Multimodal imaging refers to the recording of a series of images obtained by different optical modalities. The common modalities include reflectance and fluorescence. In reflectance there is image capture with overhead illumination as well as polarized light illumination and image capture in parallel and perpendicular orientation of the camera polarizer. In fluorescence there are options as to the excitation and the emission wavelengths under which image capture is performed.

Good image registration allows comparison of the information obtained under each of the modalities to confirm features or to obtain elucidation of depth distribution and concentration of absorbing and fluorescing species.

In reflectance with overhead illumination the image corresponds to what one sees in the mirror (Fig 4A). Polarization of source and detector allows enhancement of surface or subsurface features such as wrinkles, texture, pores and colors including erythema and brown pigmentation.

In fluorescence with UVA the fluorescence of collagen cross-links is obtained on which the distribution of superficial melanin pigmentation may be markedly enhanced. fluorescence with blue light (Fig 4B) the fluorescence of elastin cross-links is prominent together with fluorescence of keratin and coproporphyrin. The assembly of these images provides information overload,therefore the need for reduction and summary of the total information becomes essential.

The presentation at the ISDIS meeting will address methods for image capture and registration and approaches to efficient information extraction.

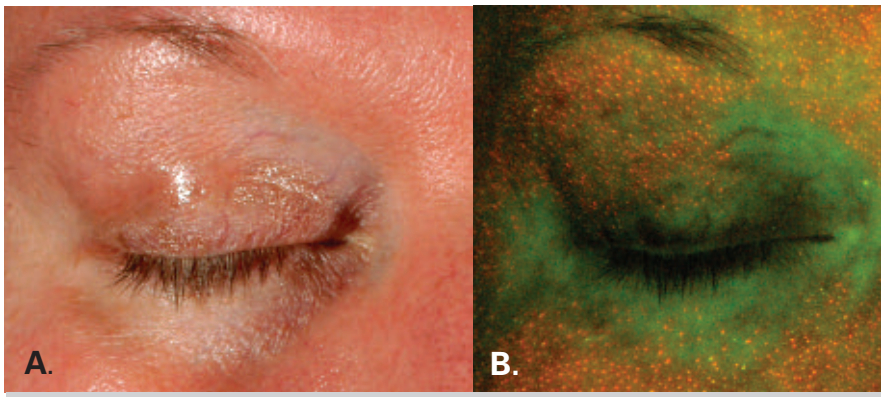

Figure 4: A. Reflectance image with visible light illumination.
B. Fluorescence image with blue light illumination.

Investigative Dermatology

MOLECULAR INSIGHTS INTO SKIN PERMEATION FROM INFRARED IMAGING SPECTROSCOPY STUDIES

By David J. Moore, PhD

ISP, Wayne, NJ

The development of true mid-infrared (IR) spectroscopic imaging presents the opportunity for new applications in investigative dermatology and related disciplines such as pharmaceutics. With these new spectroscopic imaging measurements it is possible to generate spatially resolved molecular images of exogenous molecules in skin without the use of fluorescent labels or histological stains. While the initial biomedical studies of spectroscopic imaging centered on other tissues, we have recently demonstrated that spectroscopic imaging can be used to image skin. The presentation will briefly review the imaging infrared technology and outline the preparation of skin relevant samples, such as designing experiments to probe drug active delivery, deposition or release. Selected examples of applying IR imaging to drug delivery via skin will be presented, illustrating the unique molecular information provided by this technique to research dermatology and skin biophysics. □

SKIN PHOSPHOCREATINE

By Alexander Zemtsov, MD

Indiana University School of Medicine, Muncie, IL

The skin has the unique ability to survive ischemia associated with skin grafts, flaps, and hair transplantation procedures. Spectroscopic data later confirmed by chromatography, immuno-histochemistry and molecular biology techniques identified the presence of large quantities of phosphocreatine in human skin. Phosphocreatine molecules regenerate ATP cellular reserves during ischemia. This reaction is mediated by creatine phosphokinase (CPK) enzymes that were also isolated and studied in normal and abnormal skin.

Serum CPK levels are elevated in burn victims and patients with toxic epidermal necrolysis. Phosphocreatine concentration and CPK activity are elevated in psoriatic skin and in non-melanoma malignancies in comparison with normal skin. Furthermore, skin phosphocreatine and CPK enzymes are localized almost exclusively within the epidermis and in hair follicles. Finally, phosphocreatine and CPK help to protect the skin from UV damage.

This area of research is only beginning to be appreciated by the scientific community. Topical and systemic phosphocreatine administration appears to reverse photo damage and improve wound healing. Spectroscopic monitoring of phosphocreatine and related phosphomelabolites can be potentially used to monitor disease activity and respond to therapy in psoriasis, leg ulcers, skin malignancies, and other skin conditions. □

VISUALIZATION OF DYNAMIC BEHAVIORS OF LANGERHANS CELLS IN MOUSE SKIN

By Akira Takashima, MD PhD

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Langerhans cells (LC) represent an immature member of the dendritic cell family of antigen presenting cells. Although recent studies have demonstrated functional properties of LC, their dynamic motility in their natural habitat (i.e., epidermis) remains relatively unknown. To begin to understand the behavioral biology of LC, we have developed two intravital confocal imaging systems using knock-in mice expressing the endogenous MHC class II I-Ab chain tagged with an enhanced green fluorescence protein (EGFP). This allows for real-time in-vivo tracking of LC. First, we visualized LC movement in the steady-state and under pathological conditions by recording three-dimensional images of the tagged LC in the anesthetized I-Ab-EGFP knock-in mice every two minutes; this "time-lapse" imaging approach has revealed unique behavioral responses of LC to environmental stimuli. Second, we assessed the turn over rates of LC by comparing two sets of images of EGFP+ LC recorded in the same microscopic fields at a 24 hour-interval; this intermittent imaging approach has revealed an extremely long half-life of epidermal LC. The two experimental systems will be presented at the ISDIS meeting with high-resolution images of LC movement. □

Calendar of Events

2nd annual meeting of the ISDIS at the AAD 65th Meeting

Thursday, February 1st, 2007
Time: 1:30-4:30 pm

Renaissance Ballroom West B at the Renaissance Washington, DC Hotel

Please confirm participation by email to Doris Munroe, munroed@mskcc.org

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Sponsors of Meeting

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