Increasing importance of imaging in skin cancer prevention clinical trials

Steven P. Stratton
University of Arizona, Arizona Cancer Center, Tucson, AZ 85724, USA

Skin cancer is the most common malignancy diagnosed in the US. American Cancer Society data indicate that more than one million new cases will be diagnosed in the US this year. Approximately 60,000 of these will be new melanoma cases. Overall mortality rates for non-melanoma skin cancer are very low, but skin cancer morbidity can be high, with a large economic impact. Most deaths due to skin cancer are caused by melanoma (7,700 expected in 2005). Thus, strategies to prevent melanoma are desperately needed, especially considering that the incidence of this disease is increasing yearly. Non-melanoma skin cancers, the majority of which include basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are commonly treated by surgical excision. Precursor lesions such as actinic keratoses are normally treated with cryotherapy or topical medicines for disseminated occurrence. Melanoma treatment depends on stage of disease and ranges from surgical excision to chemotherapy. Chemoprevention strategies for skin cancer are a subject of intense research, and imaging plays an increasingly important role in detection of early lesions, as well as detection of markers for response to an intervention. In the context of a chemoprevention drug development program, imaging modalities include epiluminescence microscopy (dermoscopy) and optical coherence tomography of intact skin, as well as digital karyometric analysis of skin biopsy tissue. The application of these techniques in clinical trial design is becoming an essential component of skin cancer chemoprevention research.

Confocal reflectance microscopy: Image-guided mapping and surgery of melanomas

Milind Rajadhyaksha
Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA

Since the pigment melanin is a strong source of signal and contrast in confocal reflectance images of human skin, melanocytic nevi (moles) and cancers (melanomas) image well. Previous research shows that the nuclear, cellular, and tissue architectural morphology of nevi and melanomas seen in confocal images correlates well to routine histology. Thus, a potential clinical application for confocal reflectance imaging is to guide the mapping and surgical excision of melanomas. Pre-surgical mapping of melanomas is important for two reasons. Despite the good cure rates of excision, the high rate of local recurrences may relate to incomplete excision. Also, subclinical (subsurface) margins may not be visible, may vary significantly, and may extend for several centimeters beyond the clinically visible edge. In a Phase I study (in progress), the margins of three amelanotic melanomas, one large primary, and one recurrent lentigo maligna melanoma were confocally mapped, followed by biopsy and excisional surgery. In all cases, the confocal maps of these large, complex and subsurface melanomas correlated well with the pathology, with the surgically excised margins subsequently confirmed to be clear. Two other cases of lentigo maligna melanomas (on the face) were topically treated with a drug, and the treatment efficacy (i.e., clearance of the cancer) is being successfully monitored with confocal imaging. Thus, confocal reflectance microscopy may enable real-time mapping of melanomas (and other skin cancers such as basal cell carcinomas) in vivo, to guide pre-surgical planning, biopsy and excision, or non-surgical topical treatments.
Imaging, characterization, and analysis of skin lesions

Atam Dhawan
New Jersey Institute of Technology, Department of Electrical and Computer Engineering, Newark, NJ 07102, USA

Skin cancer is the most common malignancy of mankind and represents about one-half of all new cancers detected. Approximately 1.2 million new cases of skin cancer are detected in the US each year. BCC and SCC are the most common types of skin cancers. Melanoma is the deadliest of the skin cancers, accounting for 75% of all skin cancer deaths. It is estimated that one in five Americans will develop at least one skin cancer and one in 75 Americans will develop at least one malignant melanoma. Over 100,000 new cases of melanoma are predicted to be diagnosed in 2006, causing over 8000 deaths.

Optical imaging of skin lesions for early detection and management of skin cancers has been of significant interest in health care sciences. Current imaging methods, such as the dermoscope for imaging skin lesions to detect skin cancer, use predominantly surface illumination and rely heavily on the pattern, texture, and color of the skin lesion. Although clinicians found that dermoscopy can improve diagnostic accuracy by approximately 10–20%, significant room remains for improvement in in vivo diagnosis of skin cancer. The dermoscope using the epiluminescence light microscopy (ELM) imaging method can only measure two-dimensional surface pigmentation features through surface illumination which provides limited information about subsurface lesion architecture. We have developed a novel non-invasive optical instrument called the Nevoscope for in situ imaging of skin lesions through side-transillumination that can be augmented with surface illumination using white light or polarized light. Side-transillumination such as that used in the Nevoscope device has been found more sensitive in visualizing the superficial vascular network and increased blood volume associated with malignant melanoma and BCC. The current clinical prototype version of the Nevoscope imaging system is available from a small business company, Translite. A preliminary database of pathologically validated images of skin cancers, including malignant melanoma, has been developed with computerized feature extraction, analysis, and classification methods for identifying early and potentially malignant lesions, prior to development of a semi-automated screening procedure.