

# Noninvasive Infrared Imaging for quantitative assessment of Tumor Vasculature and Response to Therapy

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**Abstract:** In this study we are investigating three infrared imaging techniques, thermography, multispectral imaging and Laser Doppler imaging (LDI) to assess parameters of vascularity in lesions of Kaposi's sarcoma (KS) and response to therapy. Thermography, multispectral imaging and LDI were recorded over the lesion and compare to normal skin either adjacent to the lesion or on the contralateral side. The KS lesions generally had increased temperature, blood volume (as measured by multispectral imaging) and blood flux (as measured by LDI) as compare to normal skin. After the treatment with experimental anti-KS drug, temperature, blood volume and blood flow of the lesion were significantly reduced from the baseline. These techniques hold promise to assess physiological parameter in KS lesion and their changes with therapy.

**Keywords**—Infrared imaging, angiogenesis, kaposi's sarcoma, anti-KS therapy.

## I. INTRODUCTION

It is well recognized that new vessel formation is an essential component in tumorigenesis and there is currently a substantial interest in developing therapies to treat cancer through inhibition of this process. To monitor such therapy, it is desirable to establish techniques to assess tumor vasculature and its changes with therapy. There are currently no standard non-invasive techniques to assess parameters of angiogenesis in lesions of interest and to monitor changes in these parameter with therapy.

Kaposi's sarcoma (KS) represents a useful model to study angiogenesis. KS is a highly vascular tumor that is a frequent cause of morbidity and mortality among people infected with acquired immunodeficiency syndrome (AIDS). Angiogenesis and capillary permeability can play an important role in the development and progression of KS [1, 2].

In an attempt to develop and assess non-invasive methods to assess KS lesions, we have evaluated three

methods: infrared thermal imaging (thermography), near infrared (NIR) multispectral imaging and Laser Doppler imaging (LDI). Here we describe techniques for the assessment of these three modalities in patient with KS. In addition, we describe the use of these techniques to monitor patients undergoing experimental anti-KS drug.

## II. METHOD

### 1 Subject:

The protocol for this study approved by the institutional review board of the National Cancer Institute, and written consent was obtained from all subjects. Twenty patients have been investigated. All were male with mean age 37.04 and standard deviation 6.4 years. Lesions that were considered for the measurement were at least 0.2 cm in diameter. Most of the lesions studied were nodular. Immediately prior to imaging, each patient removed sufficient garments and accessories to expose the entire area to be recorded including the contralateral side. Prior to, and during imaging, the subjects are seated, at rest, in a closed room at a room temperature around 23 °C.

### 2. Measurement:

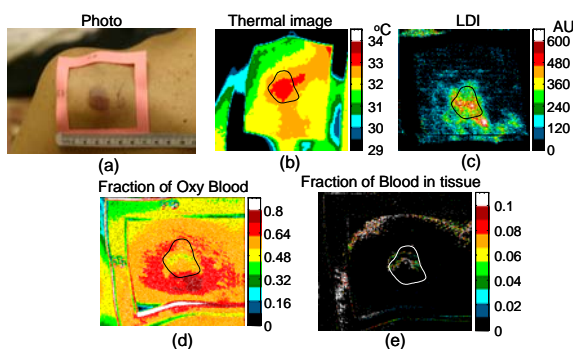
Before starting the measurement a 5 cm x 5 cm square mask was placed around the lesion and the contralateral side to assist in registering the multi-modal images obtained.

#### 1. Thermography:

Thermography provides a two-dimensional image of superficial skin temperatures [3]. The concept is that higher temperatures occur in the skin superficial to veins that are involved in active transport of blood. Thermal patterns were recorded using an infrared camera (Bioyear, USA) with a uniform sensitivity in the wavelength range 8 to 12 μm and temperature resolution of 0.05 °C. The instrument is sensitive to heat changes resulting from changes in blood flow.

Thermograms were recorded immediately after uncovering the lesion area including contralateral side. The experiment was repeated after 15 minutes when the body temperature has stabilized with ambient temperature.

The mean values and standard deviations of temperature in lesion area and adjacent skin including contralateral side were calculated by placing a region of interest (ROI). The position of the lesion and the adjacent skin area are located by matching the mask in the images with photograph of the lesion area. Temporal changes in lesion area are also investigated by placing the ROI in the images obtained immediately and after 15 min uncovering lesion area.



**Fig. 1.** Typical example of images obtained from a KS patient using multi-imaging modality imaging technique: a) Photograph; b) Thermal image; c) LDI image; d) Fraction of oxy blood and e) Fraction of blood in tissue.

## 2. Near Infrared Multi-spectral Imaging

Near infrared multi-spectral imaging technique is a non-contact spectral imaging system that capture images with a high-resolution charge coupled device (CCD) portable camera (Princeton instruments) at six wavelength in the near infrared. A white light held approximately 50 cm from the patient skin illuminates the lesion uniformly. Using optical filters, images are obtained at six specially selected wavelengths, including 700, 750, 800, 850, 900 and 1000 nm. Using a multivariate analysis we are able to monitor changes in concentrations of oxy- and deoxyhemoglobin observed from absorption coefficients determined at these wavelengths.

Spectral images were recorded after uncovering the lesion area including contralateral side.

## 3. Laser Doppler Imaging:

LDI provides two dimensional image of blood velocity over a define area [4]. LDI flux value is assessed in the lesion area and contralateral sides using LDI (MoorLDI Inc. UK). The LDI images are acquired by scanning the marked area consecutively with thermographic imaging and the LDI values (flux) are obtained by placement of a ROI in the marked area.

Measurements were obtained prior to therapy and after receiving an experimental drug for 18 weeks.

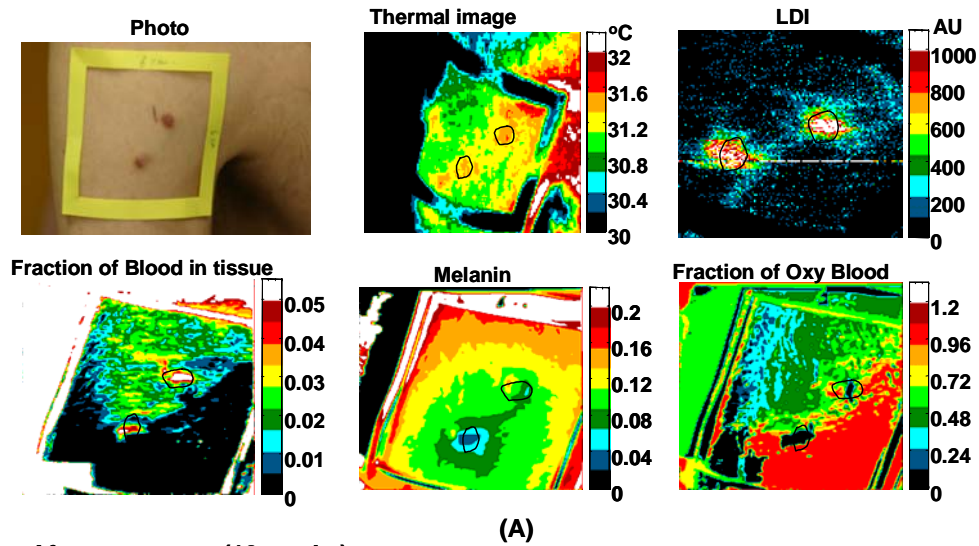
## III. RESULTS

Typical example of images obtained from a tumor before the start of treatment using different imaging modalities is shown in fig. 1. Skin temperature is significantly elevated in the skin overlaying the tumor. Similarly, hyper-perfusion is also observed in LDI. Relatively high contrast of blood volume and oxy-blood are observed in the tumor region, which is expected for metabolically active tumor. Comparative images of three modalities before and after the treatment are presented in fig. 2. Tumor region is not clearly distinct in the image of thermal. But the activity of superficial vein surround the tumor is clearly observed in the thermal image. However, tumor is clearly observed in the image of LDI. The activity of tumor at the tumor site is clearly observed in the image of blood volume. However, the oxy-blood level is not uniformly distributed in the image of oxy-blood. After the treatment significant changes of functional behaviors are observed in the images of different modalities.

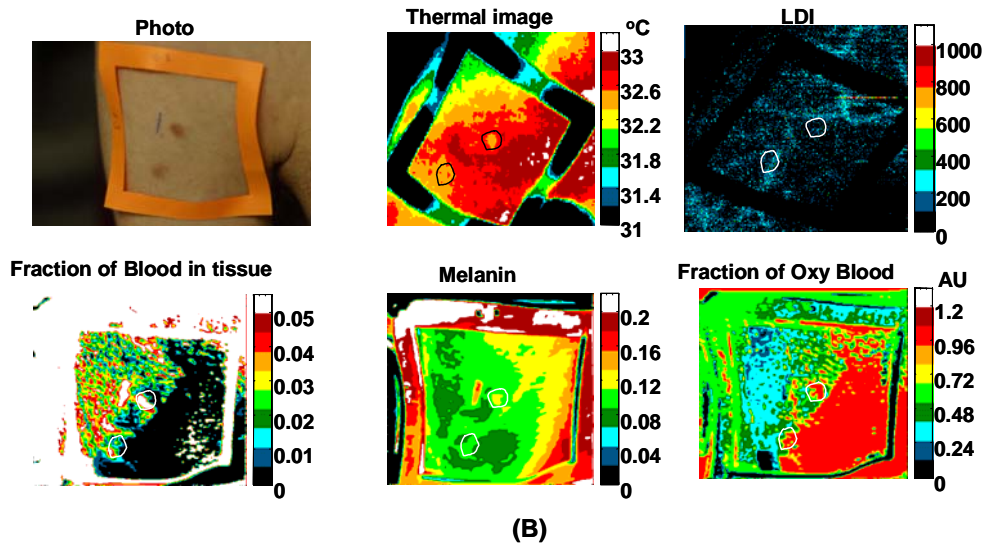
## IV. DISCUSSION

KS is a highly vascular tumor predominantly involved in the skin. Therefore, it can be investigated by non-invasive methods to evaluate vascularity and vascular changes. The thermal signature of skin not only reflects superficial vascularity, but also provides deep tissue activity. Whereas, LDI enable detailed analysis of blood flow patterns in skin up to an approximately depth of 1 mm. NIR multi spectral images provide local variation of oxy- and deoxy hemoglobin in tissue. In this study, pre and post drug patient at week 18 appears significant and may be an indication of drug treatment. The present study demonstrates that thermography, LDI and NIR multi spectral images can be used to detect functional vascular abnormalities in KS lesion and to document improvements with therapy.

**Before treatment (Base line)**



**After treatment (18 weeks)**



**Fig. 2.** Typical example of lesion (A) before (baseline), (B) 18 weeks after the treatment obtained from a subject with KS lesion.

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