Characterization of nonmelanoma skin cancer with multimodal imaging

Ulas Sunar 1,2, Dan Rohrbach1, Dan Muffoletto2, Rolf Saager3, Weirong Mo1, Andrew Kowalczewski1, Janet Morgan4, Anne Paquette2, Bruce J. Tromberg3 and Nathalie Zeitouni1

Dept of Cell Stress Biology & Oncology, Roswell Park Cancer Institute, Buffalo, NY
Dept of Biomedical Engineering, University at Buffalo, Buffalo, NY
Dept Dermatology, Roswell Park Cancer Institute, Buffalo, NY
Beckman Laser Institute, University of California Irvine, Irvine, CA

Abstract: To guide intervention planning of nonmelanoma skin cancer (NMSC), information about the tumor depth and thickness as well as functional contrast is desired. The results indicate that ultrasound and spatial frequency domain imaging can provide accurate structural and enhanced contrasts in NMSC.

OCIS codes: General (170.0170) Medical optics and biotechnology; (170.3660) Light propagation in tissues; (170.3880) Medical and biological imaging.

1. Introduction

Treatment of NMSC is usually by excision or Mohs micrographic surgery [1]. Any tool that can help to delineate the depth/thickness of the tumor and assess the margins would guide surgery or therapy and lead to improved treatment planning.

Several noninvasive imaging modalities have been applied to skin cancer. Among them, high frequency ultrasound (HFUS) provides high resolution (~50 µm) as well as deep penetration depth (>2 mm)[2]. However, the technique relies on mechanical contrast rather than functional contrast. Optical imaging can complement high resolution ultrasound with its high functional contrast and sensitivity. Spatial frequency domain imaging (SFDI) can provide optical (absorption and scattering), vascular (tissue oxygen saturation, blood volume) and fluorescence contrasts [3].

In this work, we will present preliminary results from our recently developed clinical multi-modal imaging instrument. Our results indicate that multimodal approach can map optical and ultrasound contrasts to enable clinicians to better discriminate the tumors for treatment planning.

2. Materials and Methods

2.1 Clinical study

An IRB approved clinical trial (protocol #I226912) was initiated at Roswell Park Cancer Institute. Patients with biopsy-proven NMSCs, which were scheduled to be removed with Mohs micrographic surgery were enrolled. Informed consent was obtained from all subjects before the measurements. The primary objective was to validate non-invasive assessment of tumor thickness with ultrasound imaging by comparing them with the thickness measured by Mohs micrographic surgery. Secondary objective was to obtain optical contrasts for improved characterization of the tumor tissue.

2.2 Spatial frequency domain and ultrasound imaging

The details of our custom spatial frequency domain imaging (SFDI) instrument is described elsewhere [4]. Briefly, the instrument consisted of four high-power, compact LEDs as light sources and light was directed through a liquid light guide to a projector with a DMD module. The DMD module generated the appropriate sine wave patterns with three different phases (0, 2π/3, 4π/3) and eleven spatial frequencies from 0 to 5cm⁻¹. The patterns were projected onto the skin surface and reflected light was collected with the CCD cameras. We utilized a commercial grade HFUS imaging system (40 MHz, Episcan, Longport Inc.) for imaging NMSC structure. The HFUS probe allowed a 15 mm line scan (A-scan) with a single element transducer and 1 second of full B-scan acquisition in both forward
and backward directions. The system had an approximately 5 mm signal penetration depth and ~45 µm axial (depth) resolution.

![Clinical instrument, Detailed picture of SFDI, and schematic diagram of the imaging head.](image)

**Fig. 1.** (a) Clinical instrument. (b) Detailed picture of SFDI and (c) schematic diagram of the imaging head showing the projector module, two CCD cameras, beam splitter, polarizer and analyzer.

The Mohs surgeon (N. Z.) performed the histopathological measurements. Tumors with a minimum diameter of 0.5-10 mm were excised as per the standard of care for Mohs surgery. Frozen sections were cut from excised tumors in the Mohs laboratory and the sections were stained with hematoxylin & eosin (H&E) for morphological assessment.

### 3. Results

![Histology results, ultrasound contrast, and histology results for an SCC case.](image)

**Fig. 2.** (a) Histology results for an SCC case, (b) ultrasound contrast. Green circles highlight areas of tumor, red line shows lesion thickness.

Figure 2 shows the results from a patient with an SCC tumor, which was visible in the H&E staining image showing darker purple areas (Fig.2(a)) and in the HFUS image (2b) showing hypoechoic regions defining a tumor of roughly 0.73 mm in thickness.

![White light picture, Reflectance image, Absorption map, Scattering map, StO2 map, and Total Hb map.](image)

**Fig. 3.** (a) White light picture of the lesion and (b) Reflectance image at 590 nm. (c) Absorption map at 590 nm. (d) Scattering map at 590 nm. (e) and (f) show the StO2 and Total Hb maps, respectively. Scale bar corresponds to 2mm.
Figure 3 summarizes the SFDI results. Figure 3a is a clinical picture and 3b is the reflectance raw image. Figure 3c and 3d are the extracted 2D maps of optical absorption and scattering, respectively. Scattering map showed the lesion more clearly. Figure 3e and 3f shows the blood oxygen saturation and blood volume, respectively. The tumor showed more oxygenation and more blood volume compared to surrounding tissue.

In summary, we performed SFDI and HFUS measurements for mapping NMSCs before Mohs surgery. We showed that HFUS is capable of providing high-resolution structural images such as the thickness of NMSCs and SFDI can provide a complementary optical contrast.

Acknowledgements. This research is partially supported by P30CA16056 and by the American Society for Dermatologic Surgery Cutting Edge Research Grant (CERG).

4. References


