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Assessment Skin Cancer Margins Using Raman Spectroscopy

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ABSTRACT

Accurate delineation of skin cancer margins is essential for effective treatment planning, yet current clinical assessment relies primarily on visual examination and biopsy, which cannot provide real-time information regarding microscopic tumor extension. This study investigates the feasibility of using in vivo Raman spectroscopy as a non-invasive optical biopsy technique to characterize molecular differences between skin cancer and surrounding healthy tissue.

Distinct biochemical differences were observed between malignant and normal tissue. Tumor spectra exhibited increased Raman peaks associated with DNA, phenylalanine, lipids, amide bands, and tryptophan, while collagen-related peaks were reduced. Intensity heat maps further demonstrated increasing signal intensity toward the center of the lesion and asymmetric gradients extending into surrounding tissue, suggesting heterogeneous microscopic tumor infiltration beyond the visible lesion boundaries. These findings demonstrate the potential of handheld Raman spectroscopy to provide rapid, non-invasive assessment of skin cancer margins. With further validation in larger patient cohorts, this technology could support real-time target volume definition and treatment planning for skin cancer radiation therapy while reducing reliance on invasive diagnostic procedures.

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INTRODUCTION

This work presents the development of a novel cancer diagnostic system based on a handheld Raman spectroscopic probe capable of acquiring in vivo spectra from skin lesions within seconds of contact.

Serving as a non-invasive optical biopsy, the approach has the potential to reduce reliance on tissue excision and conventional biopsy procedures while enabling immediate, evidence-based clinical decision-making during a patient's initial visit.

RESULTS

As shown in Figure 1, relative to normal appearing tissue, tumors had increased peaks of DNA (~700 cm^{-1}), phenylalanine (~1100 cm^{-1}), lipid (~1000, 1300, 1700 cm^{-1}), amide (~1200, 1600 cm^{-1}) and tryptophan (~700 cm^{-1}) and decrease in peak collagen (~900 cm^{-1}). In analysis of heat maps for the peaks mentioned above, there was an asymmetric intensity gradient when moving lateral from the lesion in different directions, indicating possible nonsymmetric infiltration of the cancer into adjacent tissue. Moreover, intensity heat maps demonstrated increased signal intensity toward the center of the visible tumors, which is consistent with expectations.

DISCUSSION

We consider this study to be innovative because it investigates if Raman Spectroscopy can be used as a tool to assess molecular changes that can distinguish skin cancers from surrounding normal skin.

Further characterization of this technology may allow for in-vivo, real-time, nondestructive assessment of skin tumors to define target volumes for radiation therapy treatment.

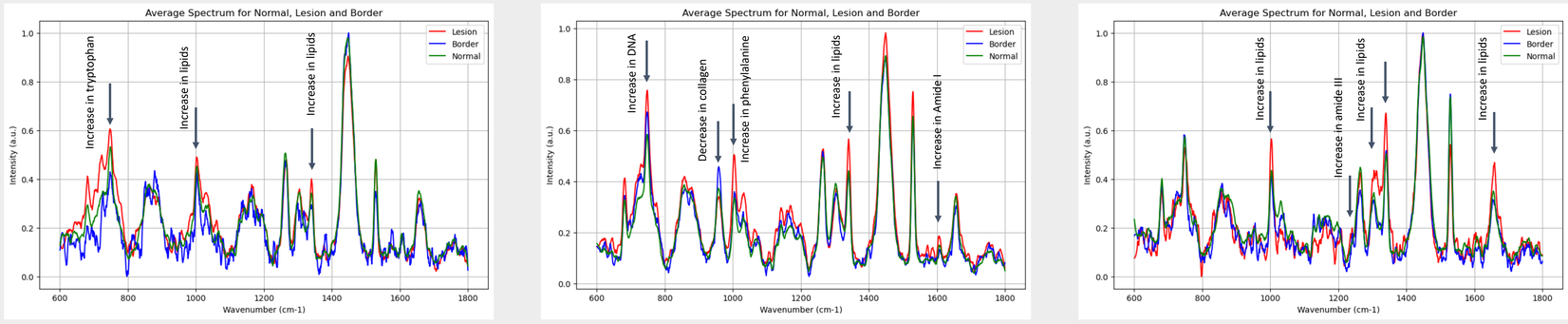

Figure 1. Average processed Raman spectrum for tumor (red), normal appearing skin (green), and border tissue between tumor and normal skin (blue) for each patient.

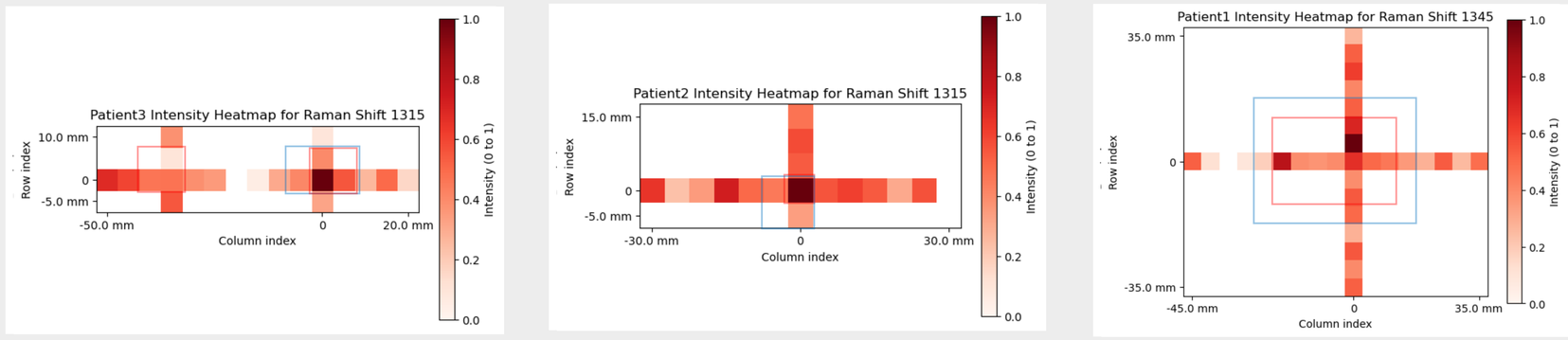

Figure 2. Intensity heat maps of the Raman spectra peak near wave number 1300 (lipid component). The red box indicates the visible tumor, while the region between the blue and red boxes represents the border between normal and tumor tissue, as determined by visual assessment by a radiation oncologist.

METHODS AND MATERIALS

Three subjects with biopsy-proven basal or squamous cell carcinoma were enrolled for clinical trial under IRB2023-00602. Spectra were acquired using a handheld Raman probe (EmVision) and spectroscope (Hubner Photonics Inc) using 785nm wavelength and 25 mW power. Measurements were taken of malignant lesions and surrounding skin at predefined grid spacing (5 mm). Data were labeled as normal appearing skin, lesion border and lesion by radiation oncologist visual assessment. Each Raman spectrum underwent baseline correction and median filtering to remove cosmic ray artifacts. Noise smoothing was performed using a Savitzky-Golay filter, and each spectrum was normalized to a range of 0 to 1. Spectra were averaged to observe peak differences of tissue classes.

Intensity heat maps were generated for specific peaks, based on the literature and observations from our data.

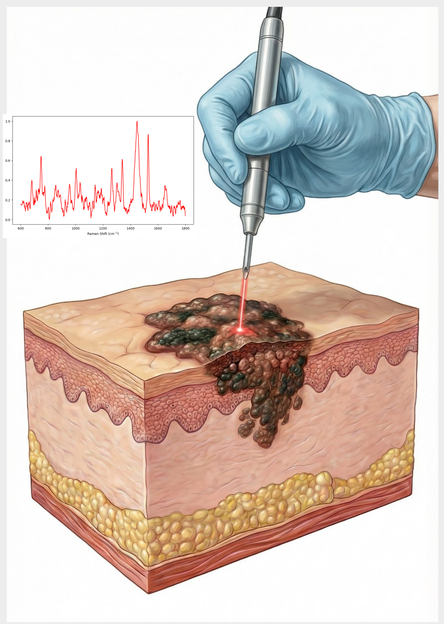

Figure 3. In-vivo Raman Spectroscopy on skin cancer lesions using a handheld Raman spectroscopic probe.

CONCLUSIONS

There is no reliable tool in our clinical practice that can provide in-vivo, real-time guidance to determine the margins of skin cancer for brachytherapy. Raman spectroscopy showed differential signal intensity between the tumor and adjacent normal tissue.

It has potential to estimate the accurate extent of microscopic infiltrating tumor and guide skin cancer brachytherapy with informed margin assessment.

REFERENCES

1. Cattell, R., et al. “Skin Lesion Subtype Classification Using Lesion and Border Radiomic Features: SU-330-GPD-D-26.” Medical Physics, vol. 52, no. 10, Oct. 2025, e7005959-e7005960.

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