11279 - Real-time tissue discrimination during soft tissue sarcoma surgical resection with Raman spectroscopy

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Level of Evidence: Diagnostic Studies – Investigating a Diagnostic test II: Development of diagnostic criteria on consecutive patients (with universally applied reference "gold" standard). Systematic review of Level II studies.

Background:

Soft tissue sarcomas are aggressive, heterogeneous mesenchymal cancers that are extremely challenging to treat. Due to their compartmental growth, they are best treated through complete surgical resection, but almost certainly recur unless resected with a margin of normal tissue. However, sarcoma margins are definitively assessed postoperatively, and intraoperative methods are strongly hindered by time and sampling restrictions. Postoperatively positive margins are a primary cause of local recurrence, less effective secondary treatment, physical and emotional morbidity, and financial burden, emphasizing the need for real-time margin assessment for complete sarcoma removal that minimizes tissue loss.

Raman spectroscopy has the potential to provide real-time and automated intraoperative assessment of sarcoma cells within the surgical bed without the removal of any tissue for analysis. This method measures energy shifts of light scattering based on tissue composition. The resultant Raman spectrum functions as a biochemical fingerprint of the sample's molecular structure that can be used to detect changes representative of neoplastic transformation.

2-4 Questions/Purposes:
The purpose of this study is to evaluate the utility of Raman spectroscopy for real-time assessment of tissues in the sarcoma bed. Such a tool would allow us to combine margin evaluation and surgical guidance so the surgeon receives rapid feedback while choosing the extent of the sarcoma mass removal. The overall goal is to enhance the surgeon's ability to completely remove the sarcoma within a sheath of normal tissue while minimizing normal tissue loss.

Patients and Methods:
We present a preliminary *in vivo* study evaluating Raman spectroscopy for the stated purpose. Raman spectroscopy data was collected from 40 patients undergoing soft tissue sarcoma resection. Upon excision of the sarcoma mass, a portable near-infrared Raman spectroscopy system was used to evaluate control tissues in the surgical bed. Then, the sarcoma itself was evaluated through small incision(s) of the excised mass. Each measurement was standardized for day-to-day variation, and the resultant spectra were correlated to intraoperative and postoperative surgical pathology performed as part of routine surgical care. A classification model utilizing multinomial logistic regression analysis was developed to evaluate the Raman spectroscopy data from sarcoma and non-sarcoma tissues. The model utilized a leave-one-patient-out assessment to evaluate these data.

All patients over the age of 18 undergoing soft tissue sarcoma resection were included. Postoperatively-identified benign soft tissue masses for which spectroscopy data was collected were excluded from data analysis.

Results:
Raman spectroscopy displays the ability to identify individual Raman spectra for the various normal tissues in the surgical bed. It also displays the ability to characterize Raman spectra for individual sarcomas that are distinct from those of normal tissues. Moreover, Raman spectroscopy displays the sensitivity to correlate histological properties

and biochemical composition with Raman signature of sarcomas and surgical bed tissues. Analyses of these Raman data reveal a strong ability to discriminate between normal tissues and sarcomas, with sensitivities and specificities greater than 85%.

Figure 1: Distinct Raman signatures of surgical bed tissues

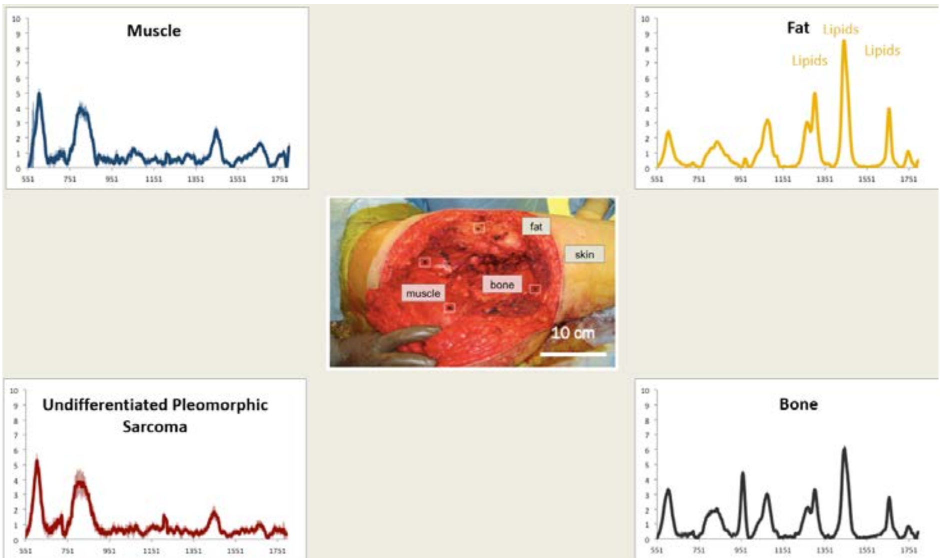
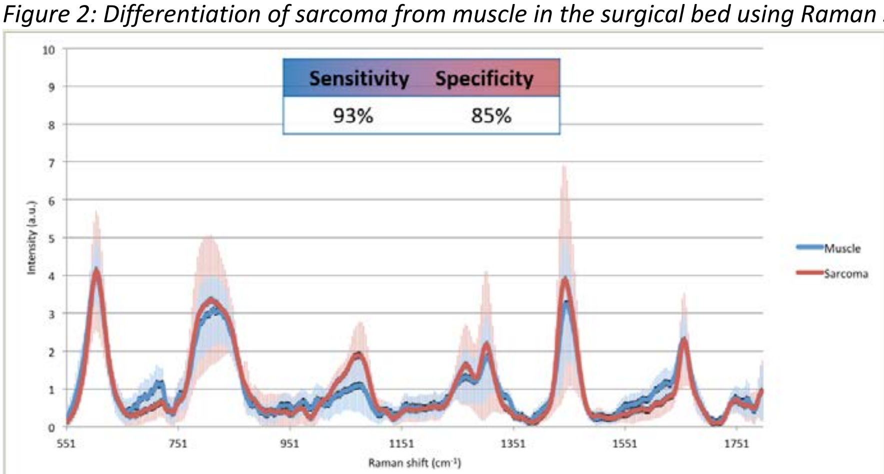


Figure 2: Differentiation of sarcoma from muscle in the surgical bed using Raman spectroscopy



Conclusions:
This study establishes the ability of Raman spectroscopy to achieve tissue-type differentiation between soft tissue sarcomas and the normal tissues of the surgical bed. Moreover, it displays the ability of Raman spectroscopy to characterize sarcomas and account for inherent sarcoma variability. This study serves as a critical primary step for the utilization of Raman spectroscopy for real-time intraoperative margin evaluation during soft tissue sarcoma resections. It also serves as the first primary Raman spectroscopy databank for individual sarcoma subtypes for the utilization of Raman spectroscopy for precise intraoperative identification and differentiation of sarcomas.