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Machine learning algorithm to classify multiphoton microscopy images of pancreatic neuroendocrine tumors

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BACKGROUND

Surgery is the preferred method of treatment for most pancreatic neuroendocrine tumors (PNETs), particularly functional PNETs or those greater than 2 cm in largest dimension. Existing techniques include intraoperative ultrasound and manual palpation, both of which have inherent disadvantages such as poor resolution and low contrast against normal pancreatic tissue. This results in surgeons performing more demolitive resections, such as the Whipple procedure, when they may not be strictly necessary in order to ensure total removal of tumors. Therefore, improving surgical localization methods could greatly improve patient outcome and quality of life.

Multiphoton microscopy (MPM) is an optical imaging technique capable of visualizing intrinsic biomarkers through two-photon fluorescence, and collagen through second harmonic generation (SHG), notably without the aid of exogenous labels and with increased penetration depth compared to conventional microscopy. Here we test the use of MPM as a new method of microscopic tumor localization by applying this data to novel machine learning algorithms designed to automatically classify tissue types.

METHODS

Formalin-fixed paraffin-embedded PNET (n=36) and normal pancreas (n=21) samples were imaged with a multiphoton microscope at five excitation and emission wavelengths corresponding to four endogenous fluorophore and SHG signals. Images covered an area approximately 4 mm by 4 mm. Texture features were then extracted using Haralick's method, and a computer model trained to classify the samples as tumor or normal tissue using linear discriminant analysis. Sets of one to six features were tested, and models assessed using a leave-one-out-approach. Accuracy of classifiers was evaluated as the ratio of the number of correctly identified samples.

RESULTS

As the number of features increases, accuracy of the classifiers increases until plateauing at n=5 features.

Number of features	Accuracy of classifier
1	78.9%
2	82.5%
3	89.5%
4	93.0%
5	93.0%

CONCLUSIONS

We have demonstrated that using n=4 features, we are able to distinguish between PNETs and normal pancreatic tissue to 93.0% accuracy. By building this model, we can begin to test which imaging wavelengths and texture features are optimal for distinguishing the two tissue types, which in turn provides guidelines for the development of new surgical guidance instruments. This supports the continued investigation of MPM as a clinical imaging technique, and lays the groundwork for the integration of machine learning methods to real time imaging.

ABSTRACT ID 23691