Mid-IR Label-Free Digital Pathology for the Identification of Biomarkers in Tissue Fibrosis

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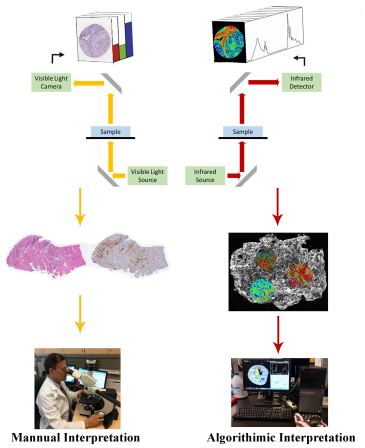
Introduction

- Infrared (IR) spectroscopic imaging is an emerging approach for rapid label-free imaging of biomolecules in cells and tissues.
- Biomolecules in tissue absorb different regions of the infrared giving rise to a biochemical 'signature'.
- This 'signature' has been shown to be altered between different cell types and disease states.
- Our lab at the University of Illinois at Chicago is geared towards;

1) Identifying areas where current techniques fails
2) Identify where there is a need for additional diagnostic/prognostic information.

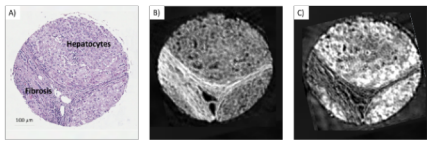


- IR imaging permits extracting IR signatures from multiple cells types and tissue structures to determine which has the best diagnostic/prognostic value.
- Paradigm has been to focus directly on cells involved in disease processes however bystanders may hold clinically useful information.
- Stromal changes and fibrosis in multiple organs can occur due to insults to the tissue (e.g. viral, alcohol, rejection).
- Excessive fibrosis ultimately leads to organ dysfunction and even failure.
- Regions of stroma and fibrosis represent a novel target to identify biomarkers of disease.

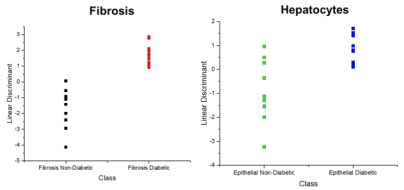
Nazeer et. Al. "Infrared Spectroscopic Imaging: Label-Free Biochemical Analysis of Stroma and Tissue Fibrosis" Invited review in Journal of Biochemistry and Cell Biology. 92:14-17 (2017).

1. QCL-IR Imaging Can Rapidly Visualize and Assess Liver Tissue Fibrosis

- Recent advances in broadband Quantum Cascade Laser (QCL) technology in the mid-IR has allowed for new QCL based imaging instruments.
- QCL imaging offers two major benefits over conventional Fourier-Transform infrared imaging systems – 1) Ability for live real-time imaging of tissue and 2) Rapid single frequency data collection.



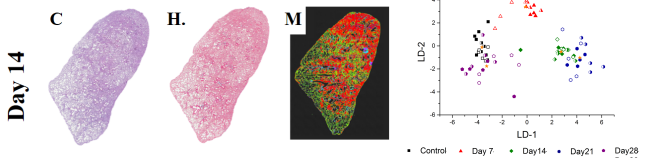
- QCL imaging has been shown to allow for real-time visualize and quantification of liver fibrosis using only single spectral frequencies.
- Focusing on areas of fibrosis may avoid regions such as hepatocytes that have a large degree of non-diagnostic spectral variance which swamps the diagnostic signal such as detecting diabetic damage.



Sreedhar et. Al. "Infrared spectroscopic imaging detects chemical modifications in liver fibrosis due to diabetes and disease" Biomedical Optics Express. 7:2419-2424 (2016).

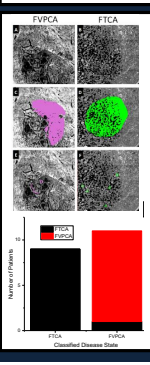
2. IR imaging Can Track Fibrosis Progression and Remission

- There is a need for tools that can track progression of fibrosis. In particular, there is a strong focus on developing anti-fibrotic drugs and identifying the effect it has on the organ.



- A mouse model of pulmonary fibrosis demonstrated biochemical changes associated with fibrosis progression (progresses to maximum fibrosis at day 21) followed by remission (day 28).

3. Fibrosis May Aid in Diagnoses

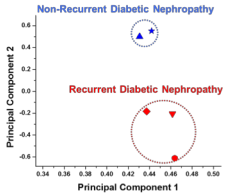


- Follicular variant of papillary thyroid carcinoma (FVPCA) continues to be a challenging entity for clinicians to diagnose, given its morphological mimicry of follicular thyroid carcinoma (FTCA).
- Regions of fibrosis are found within the tumors
- Global ROIs allowed for accurate diagnosis however fibrosis specific ROIs were unable to discriminate.

Martinez et. Al. "Accounting for tissue heterogeneity in infrared spectroscopic imaging for accurate diagnosis of thyroid carcinoma subtypes". Invited manuscript in Vibrational Spectroscopy. 91:77-82 (2016).

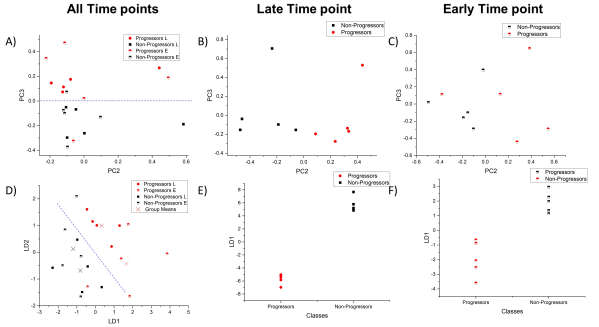
4. Biochemical Signatures in Regions of Fibrosis can Predict Outcome

- Biochemical changes can be detected before histological changes of the development of diabetic nephropathy in renal transplant patients.
- Another complication that can affect renal transplant is development of tubulointerstitial fibrosis.



Varma et. Al. "A label-free approach by infrared spectroscopic imaging for interrogating the biochemistry of diabetic nephropathy progression" Kidney International. 89:1153-1159 (2016).

- There is currently no method to predict development of tubulointerstitial fibrosis and thus intervene.
- Patients were tracked over 12 months post-transplant to determine those who would undergo rapid fibrosis progression.

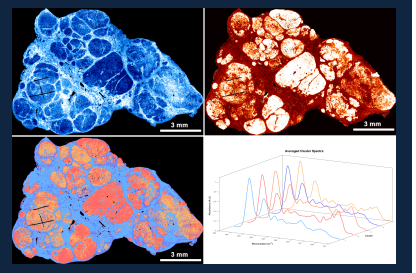


- A biochemical signature in the earliest biopsies could predict those patients that would undergo rapid tubulointerstitial fibrosis.

Varma et. al. "Predicting Fibrosis Progression in Renal Transplant Recipients Using Laser-Based Infrared Spectroscopic Imaging " Scientific Reports. 8 (2018).

Discussion

- IR imaging allow for rapid biochemical imaging of tissues and permits visualization of fibrosis.
- Fibrotic regions may hold additional diagnostic and prognostic information that can guide clinical decisions.



Acknowledgments

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