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THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

Hand-held OCT probe for transcutaneous use to assess various pathologies in real-time

Nicusor Iftimia*, John Grimble*,Gopi Maguluri*, Aliana Caron*, Rahul Anil Sheth**, Sanjay Gupta**, Amanda Mc Waters**, Savitri Krishnamurthy**

*Physical Sciences Inc., Andover, MA
** MD Anderson Cancer Center, Houston, Tx

Research Motivation

- **Transcutaneous assessment** of tissue morphology is possible with either radiological imaging, or through biopsy
- While radiological imaging can reach any location within the human body, the resolution **of the images is limited to hundreds of microns**, which is nor always sufficient for reliable diagnosis
- Although biopsy provides a good diagnostic yield while inducing minimal tissue morbidity, its sensitivity and specificity vary over a large range, mainly due to tissue heterogeneity, as well as **morphology distortion** during core biopsy collection
- **Minimally invasive optical biopsy** is a newer approach, that can be used to complement either radiological imaging or biopsy, by providing micron-scale tissue morphology images, as well as functional information

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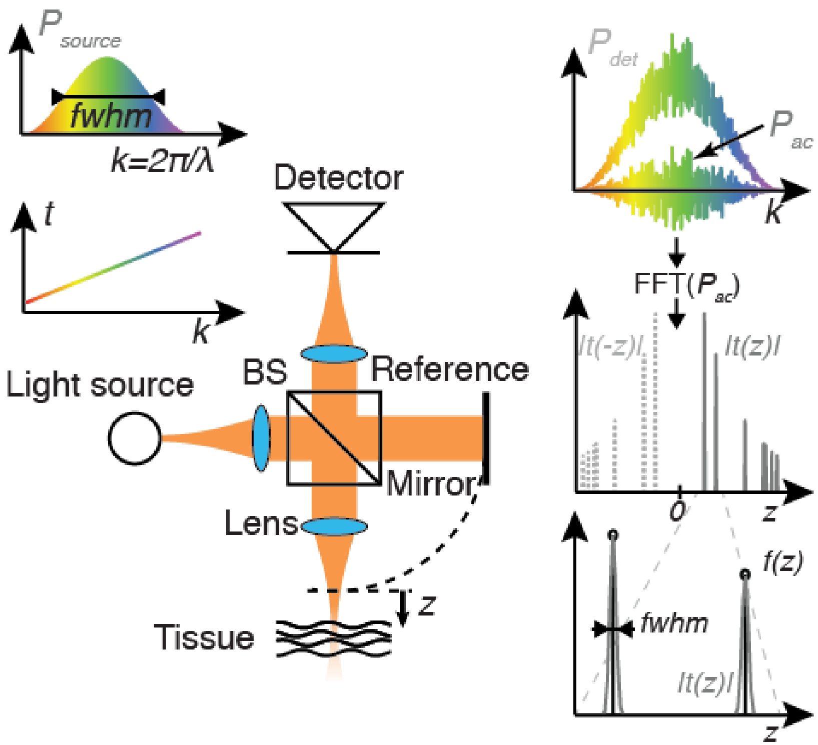
Proposed Approach

Assess tissue Morphology and Function using Minimally invasive Optical Coherence Tomography



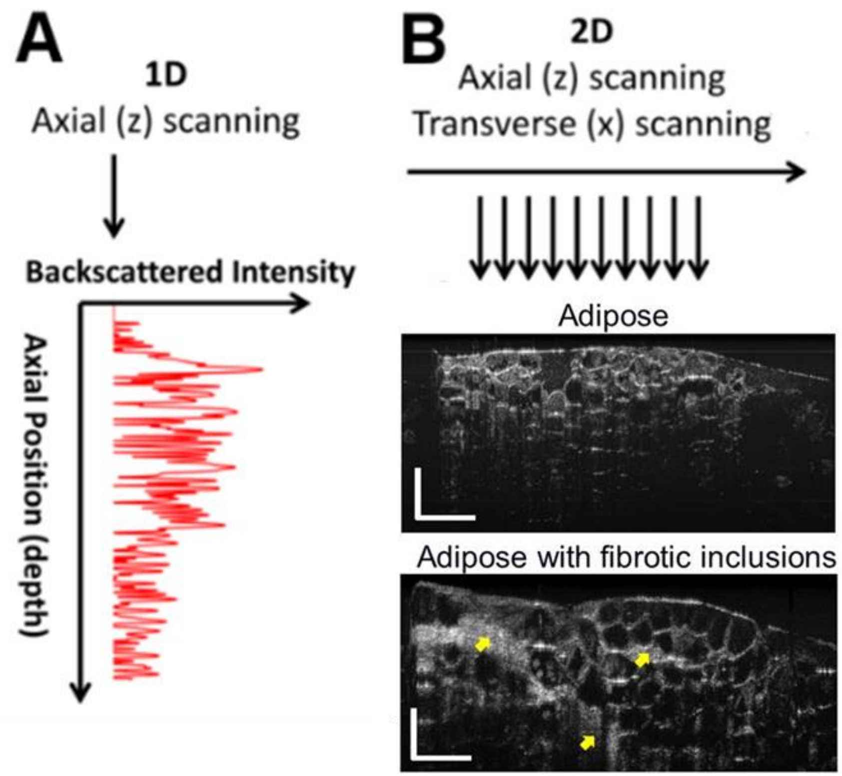
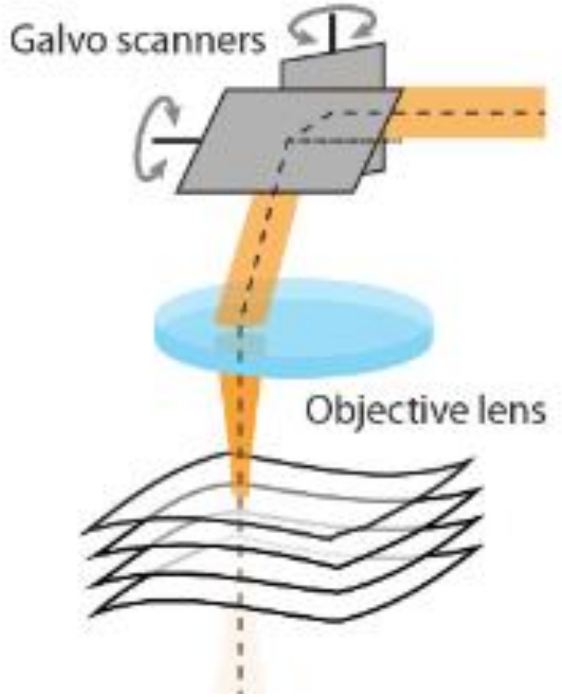


Image Source:

Center for Biomedical OCT Research

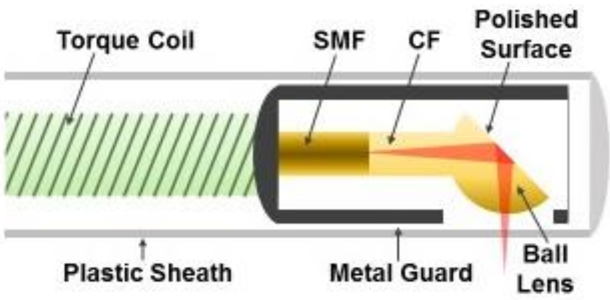
Scanning approaches

A: Raster Scan



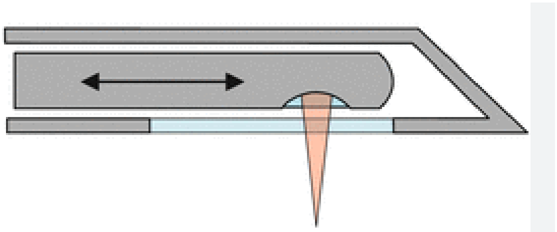
- Requires a high linearity scan
- Cannot be used for deep tissue imaging

B: Rotary Scan



- Requires a high linearity rotary scan

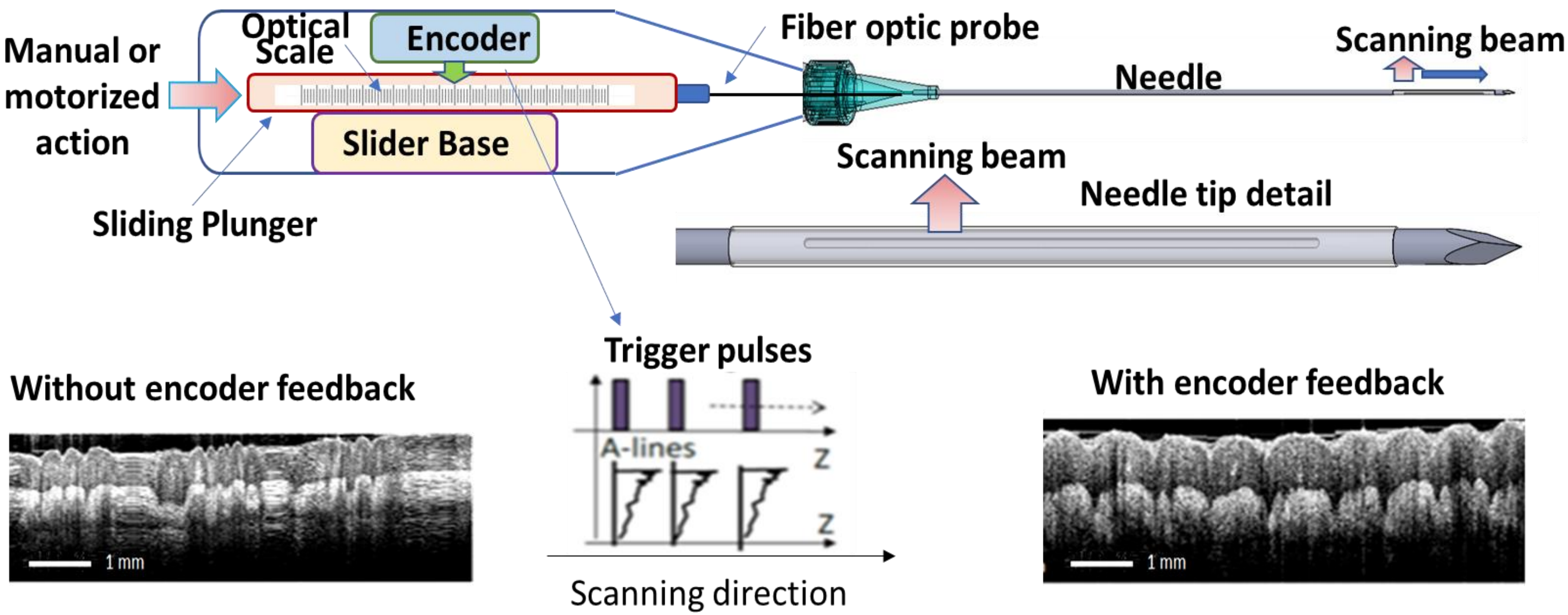
C: Axial Scan



- Requires a high linearity axial scan

Proposed Scanning approach

<Data acquisition based on encoder feedback>



US Patent 11109759: Apparatus and method for assessment of interstitial tissue

Nicusor Iftimia, Gopi Maguluri, Ernest W. Chang, Shing Chang, John Magill, and William Brugge. Hand scanning optical coherence tomography imaging using encoder feedback. Optics Letters Optics Letters 39(24), 6807-10 (2014).

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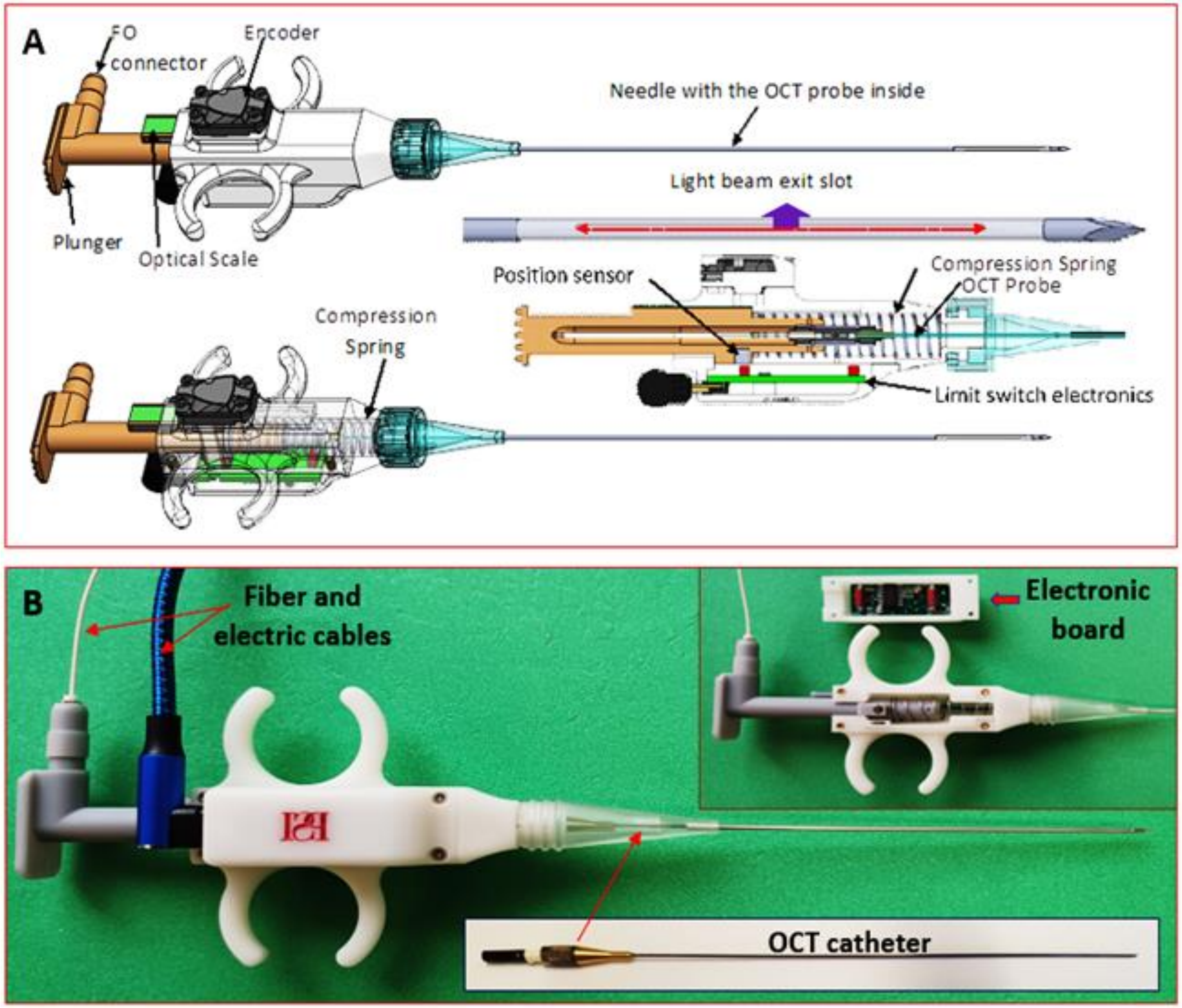
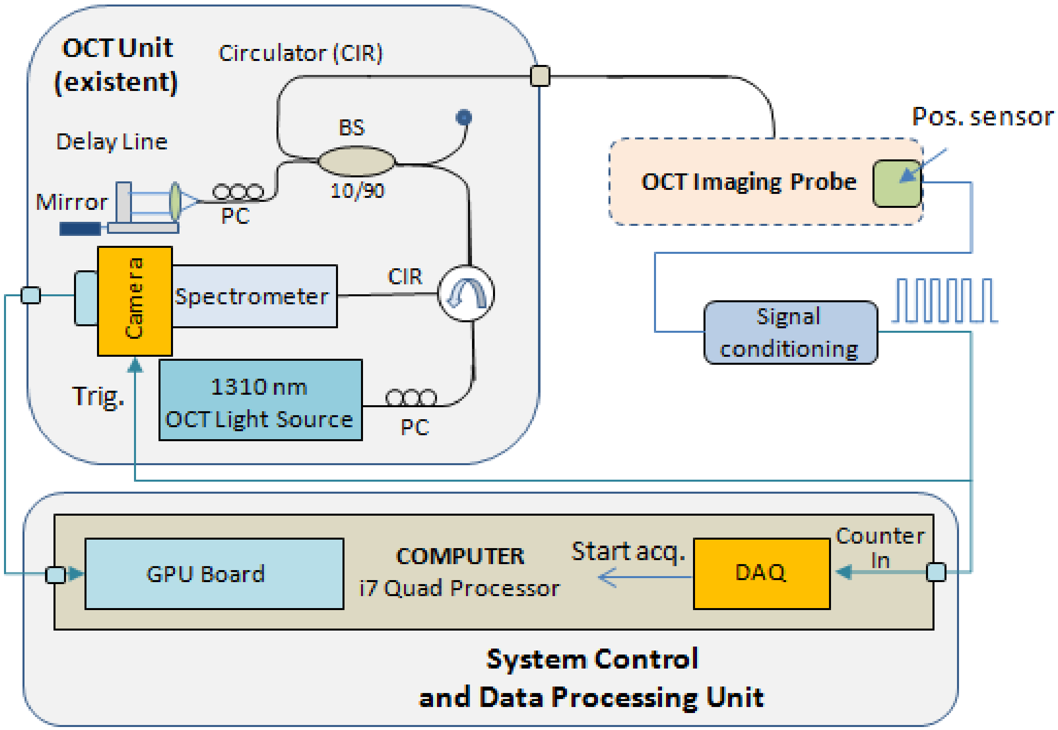
Gen I HH OCT Probe Implementation

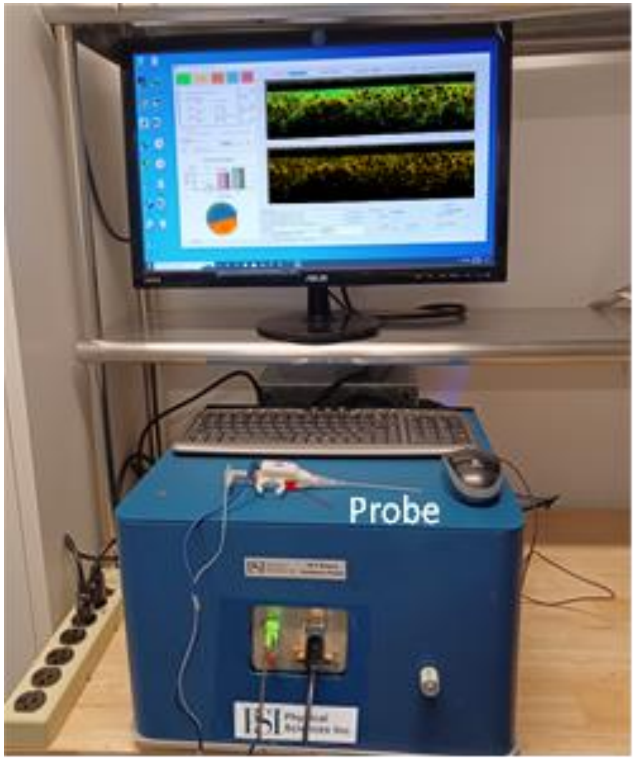


Capabilities

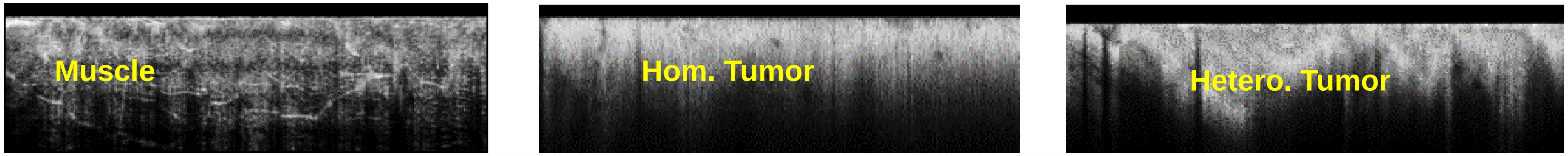
- Provides an axial-scan- 15-20 mm
- Provides high lateral resolution: ~15 um
- Allows for easy replacements of the distal end parts: Needle and OCT catheter
- Can use a magnetic tip - enables needle tracking

Instrumentation Schematic & Implementation





GPU-based Tissue differentiation algorithm



- Calculate <u>mean values</u> of several parameters for each tissue type: homogeneous tumor, heterogeneous tumor, normal tissue i = 1,2,3. (n components vector) <u>for a training set</u>
- Calculate <u>covariance matrices</u>: $S_i = \frac{1}{n_i}\sum_{j=1}^{n_i}\left(x_{i,j}-\overline{x_i}\right)\left(x_{i,j}-\overline{x_i}\right)^T$
- Determine the same parameters for the <u>data to be analyzed</u>;
- Calculate quadratic discrimination score (one for each tissue type):

$$d_i^Q = -\frac{1}{2}\ln\left|S_i\right| - \frac{1}{2}\left(x-\overline{x_i}\right)^T S_i^{-1}\left(x-\overline{x_i}\right)$$

- Assign the maximum score to each area of the image that is being analyzed.

M. Mujat, D. Hammer, R.D. Ferguson, C. Gittins, and N. Iftimia., "Automated algorithm for breast tissue differentiation in optical coherence tomography", J. Biomedical Optics, 14(3) 034040, 2009

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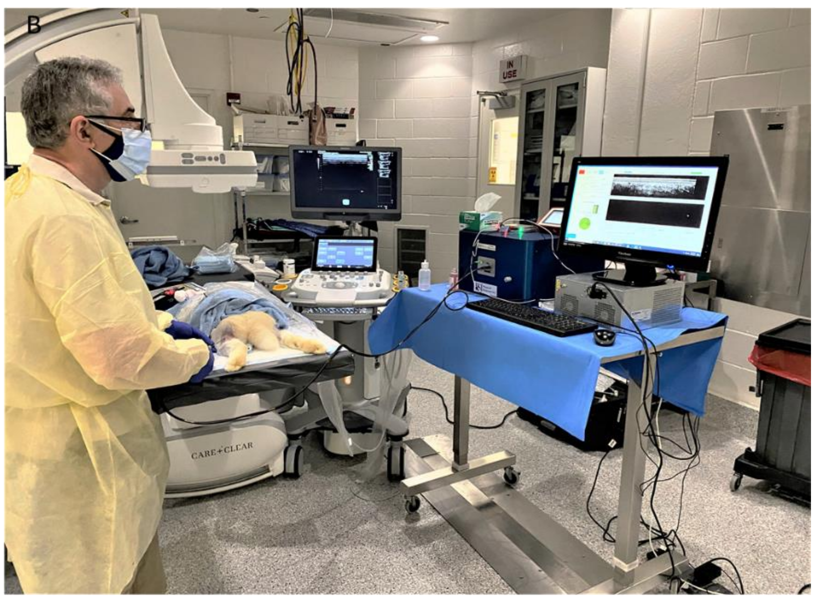
MDACC Biopsy Guidance Study

Study Goals

- Assess technology capability to determine tissue morphology at the tip of the biopsy needle
- Develop *in vivo* training sets for tissue-type differentiation
- Assess algorithm capabilities by comparing the results against histopathology results



Animal model:
Albino New Zealand White (NXW) Rabbits, Strain Code 052

All experiments were performed in agreement with the MDACC IAUCUC approved animal protocol - 00001349-RN00-AR002

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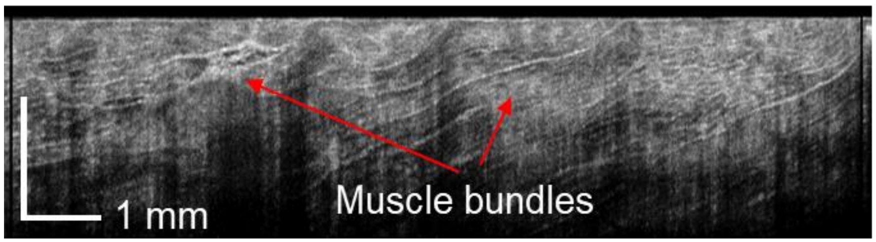
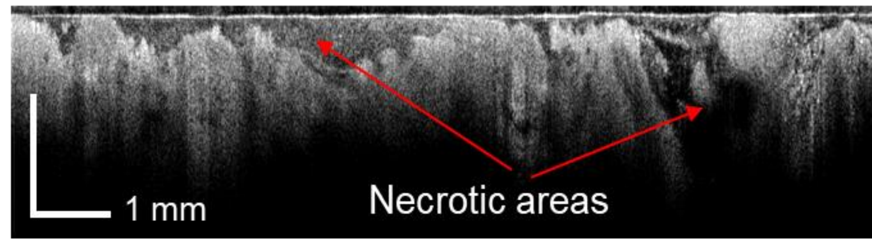
Example of Collected OCT Images

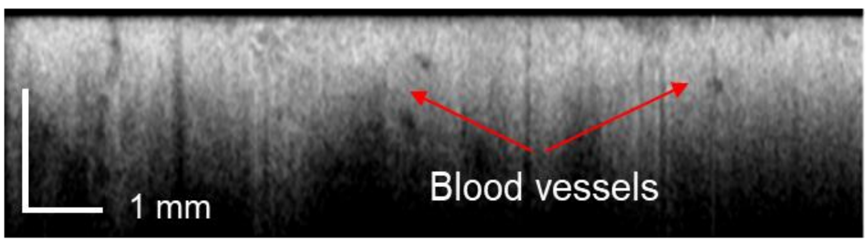
Muscle



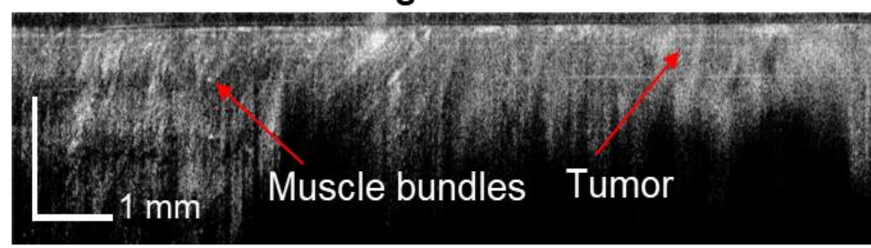
Tumor with necrosis



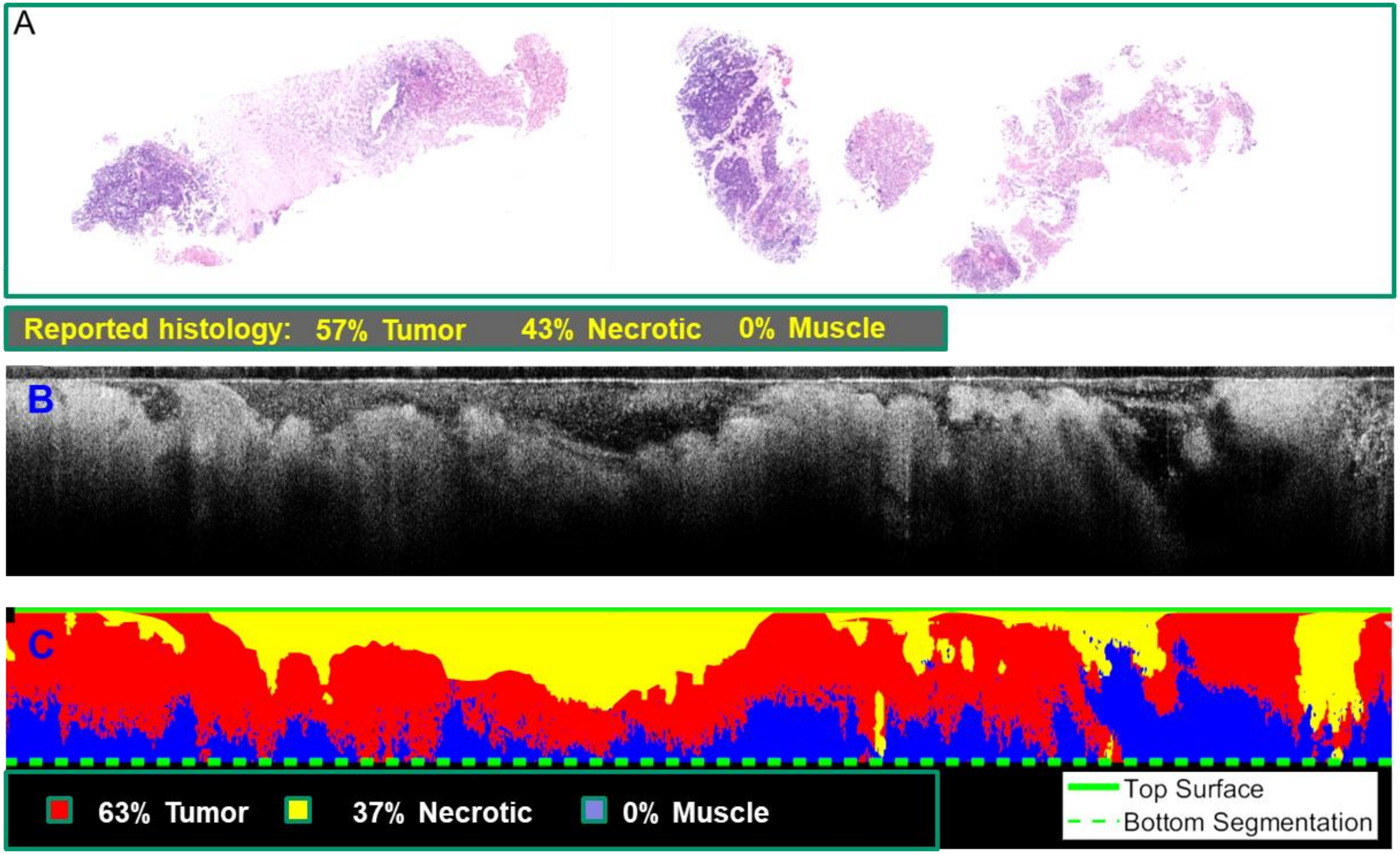
Homogeneous Tumor



Heterogeneous Tumor



Example of Processed Data



Summary of the in vivo Rabbit Study

Animal ID	Investigated site	OCT findings	Histology findings
21L033	Left	Heterogeneous tissue, ~5% tumor (**FP**)	Skeletal muscle
	Right	Mostly Skeletal muscle, ~3% tumor (**FP**)	Skeletal muscle
21L034	Left	Heterogeneous tissue, ~14% tumor	~10% tumor
	Right	Heterogeneous tissue, ~20% tumor	~15% tumor
21L035	Left	Homogeneous tissue~75% tumor	~70% tumor
	Right	Heterogeneous tissue, ~40% tumor	~50% tumor
21L036	Left	Mostly skeletal muscle, ~10% tumor	~10% tumor
	Right	Homogeneous tumor, ~75% tumor	~70% tumor
21L037	Left	Mostly Skeletal muscle, ~ 5% tumor	Skeletal muscle, ~3% tumor
	Right	Mostly Skeletal muscle, ~5% tumor	Skeletal muscle, ~3% tumor

Conclusions: - OCT/ Histology – within 10% agreement
- 2FPs- better tissue differentiation accuracy is needed

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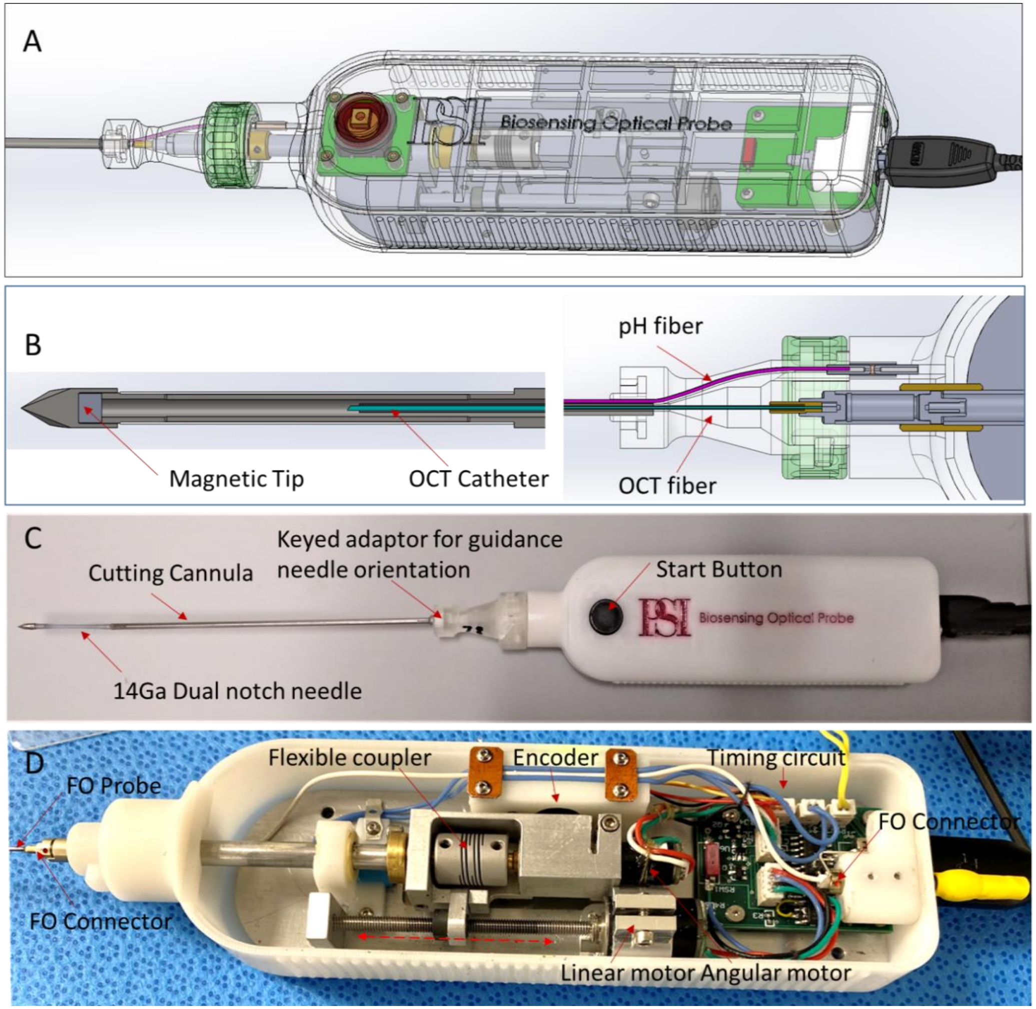
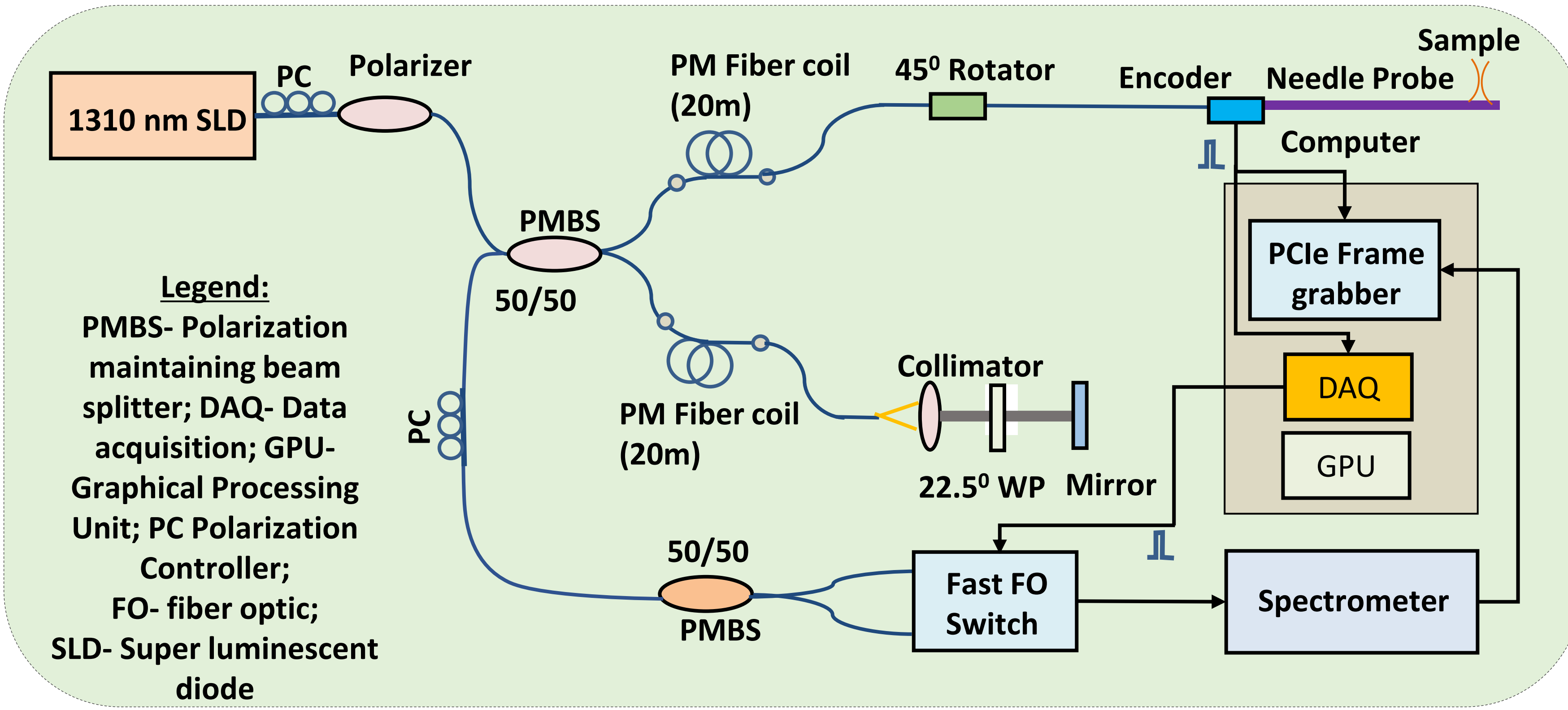
Gen II Biopsy Guidance Probe



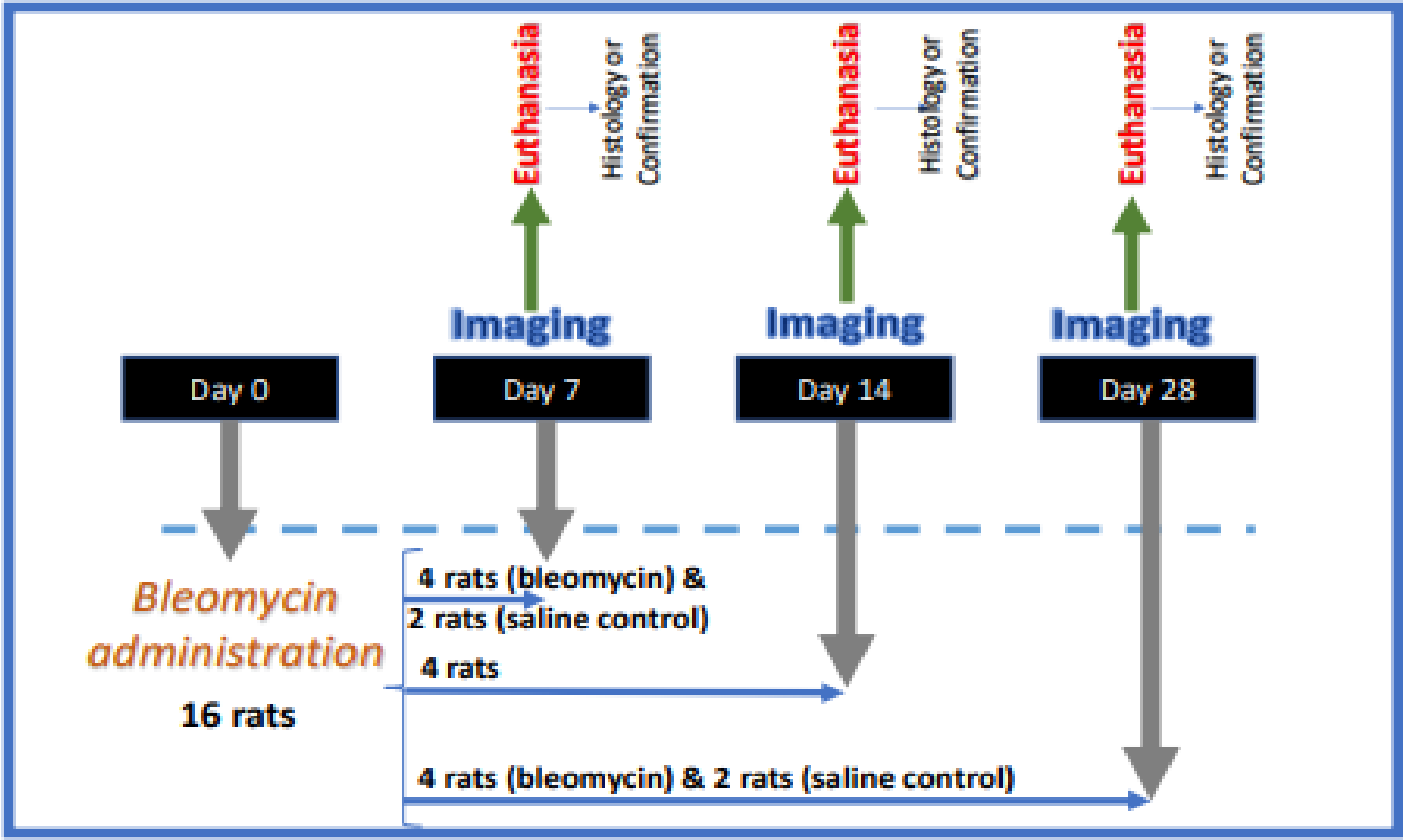
Capabilities

- Provides combined axial- angular scan-scans large volume of tissue (15 mm x 1.5mm)
- Provides improved lateral resolution: ~10 um
- Provides angular co-registration with the biopsy gun – same orientation of collected data with the collected biopsy specimens

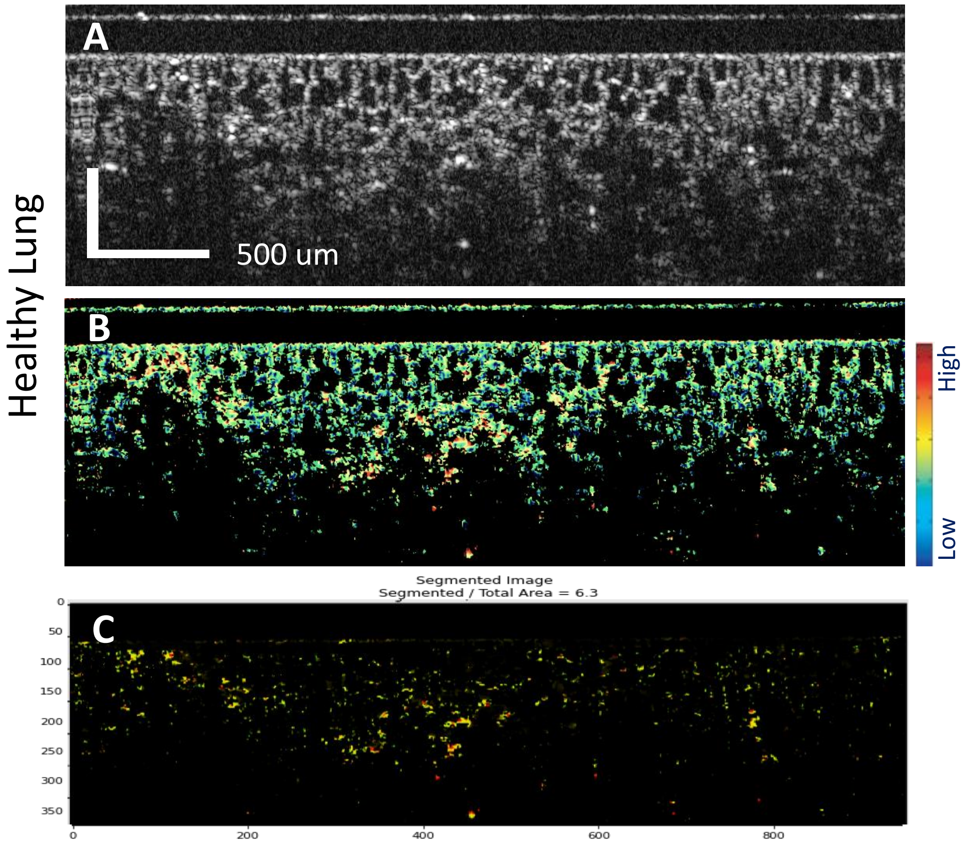
Instrumentation added capability: Tissue birefringence - PS OCT

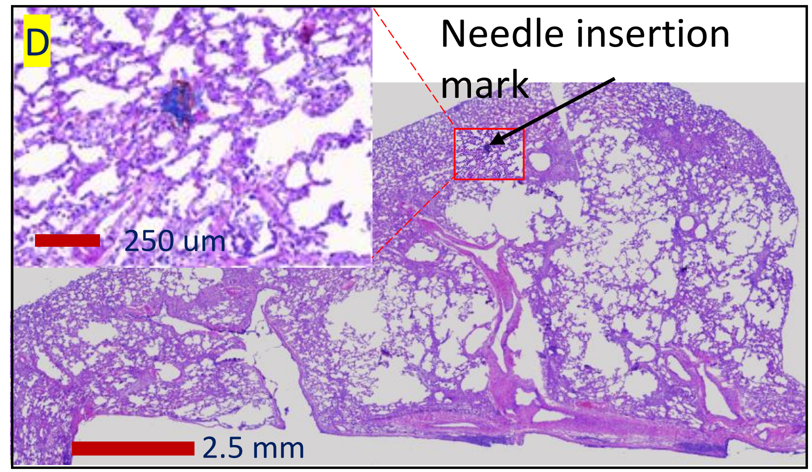


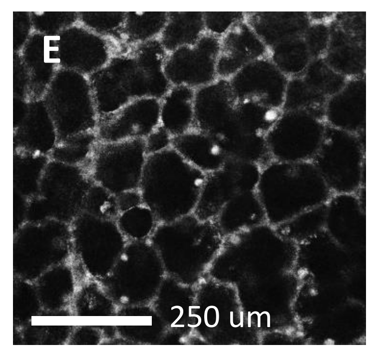
Animal study: Bleomycin rat of lung fibrosis

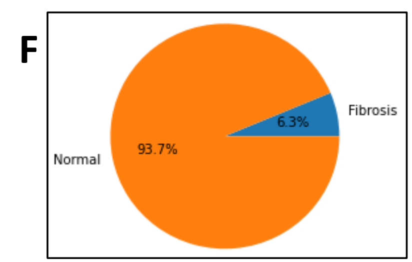


7 days after Bleomycin administration



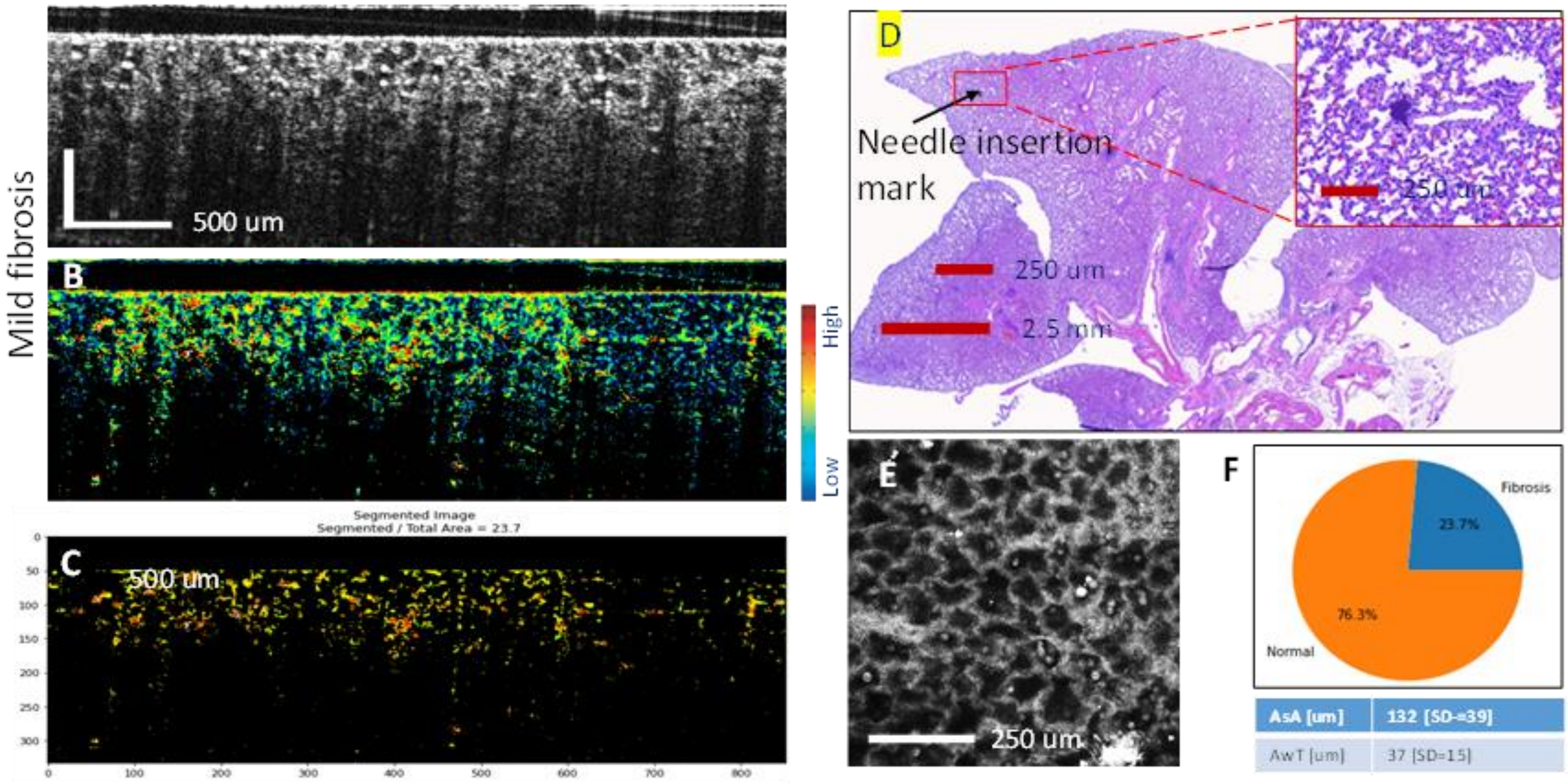




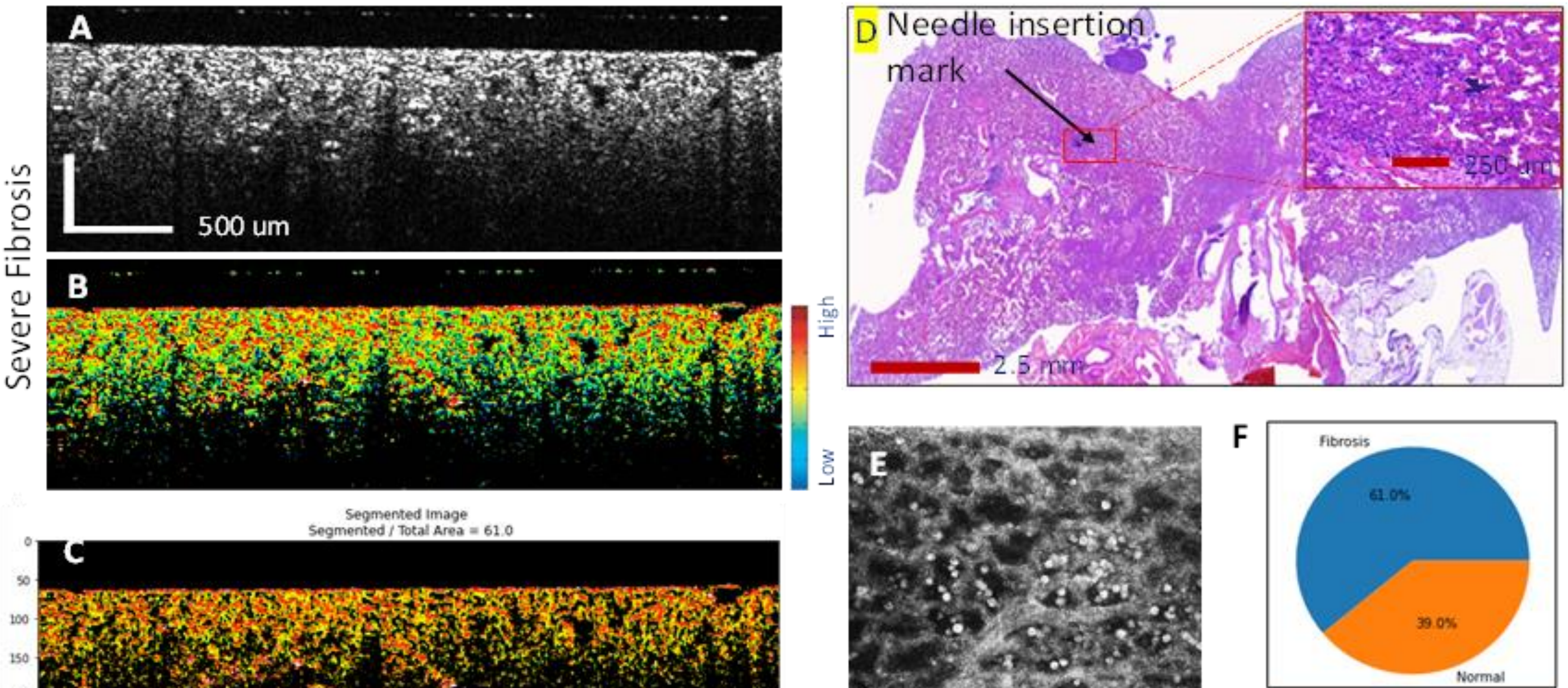


AsA [um]	165 [SD-=45]
AwT [um]	27 [SD=13]

14 days after Bleomycin administration



28 days after Bleomycin administration

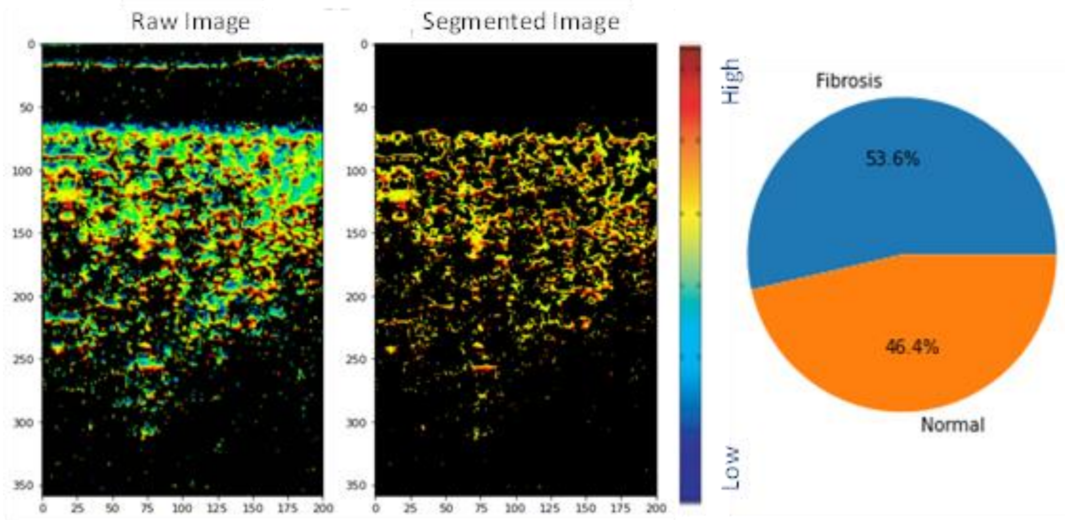


AsA [um]	85 [SD=15]
AwT [um]	65 [SD=12]

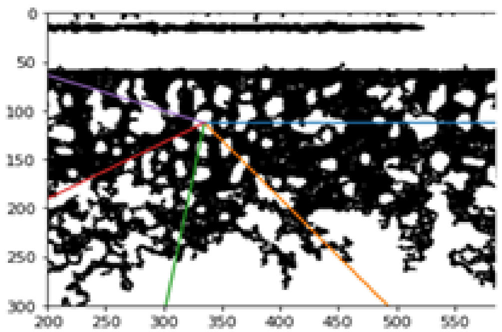
Analysis of OCT images

Parameters

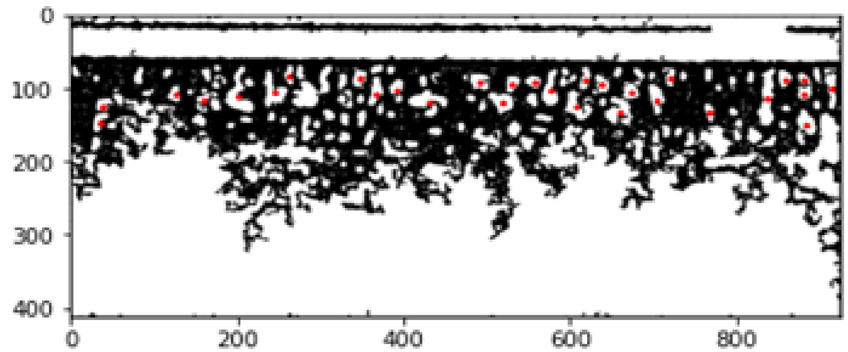
- Area of increased birefringence
- Alveoli average size and wall thickness



Radial search for wall thickness calculation



Alveoli identification and size calculation



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Study Summery

OCT/Histology Correlation Summary

	Day 7		Day 14		Day 28	
	Histology	Algorithm	Histology	Algorithm	Histology	Algorithm
Absence of fibrosis	4(control rats)	4	0	0	4 (control rats)	4
Incipient fibrosis	8	7	2	4	0	0
Moderate fibrosis	x	1	6	4	2	3
Severe fibrosis	x	x	0	0	6	5
Miss correlated Sites		1		2		2

OCT Parameters Summary

	Area of high birefringence	Average thickness of alveoli wall [um]	Average size of alveoli [um]
Absence of fibrosis	<5%	25+/-15	158+/-48
Incipient fibrosis	5% to 25%	35+/-12	112+/-23
Moderate fibrosis	25% to 50%	53+/-16	66+/-17
Severe fibrosis	>50%	>75	<50

Summary

- Designed, fabricated and pre-clinically evaluated a novel biopsy gun and a biosensor probe, enabling one-to-one correlation between the optically investigated site and the collected biopsy cores
- Designed and developed an automated algorithm for real-time data analysis and display, enabling the user to make an informed decision about the best tumor location for acquiring a biopsy specimen
- Demonstrated that the biosensor probe enables the user to reliably assess tissue composition tip of the biopsy needle with less than 10% error and thus improve biopsy success rate
- Added functional capabilities that may enable minimally invasive diagnosis of difficult to diagnose diseases, such as lung fibrosis.

Next steps:

- Improve hardware-software to address current limitations: resolution and image processing speed
- Develop a Gen II device and perform a human study and demonstrate clinical utility
- Develop a regulatory strategy, and attract funding to support technology commercialization

Acknowledgement

Funding:

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NIH/NHLBI: 1 R43 HL150948-01