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TITLE: Electromagnetic-Optical Coherence Tomography Guidance of Transbronchial Solitary Pulmonary Nodule Biopsy

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14. ABSTRACT

We present a novel high-resolution multimodality imaging platform utilizing CT and electromagnetic (EM) navigation for spatial guidance to targeted lung nodules, and OCT for microscopic volumetric imaging. The OCT optic fiber probe and EM sensor were incorporated into a single flexible catheter. The catheter was designed to be compatible with a custom peripheral transbronchial aspiration needle to enable both imaging and specimen collection. The EM sensor guides the catheter and biopsy needle to the spatial location of the pulmonary nodules and OCT images are obtained to microscopically assess the tissue.

15. SUBJECT TERMS

Electromagnetic Optical Coherence Tomography, Biopsy Guidance, Lung Cancer, Optical Microscopy

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1. INTRODUCTION

Lung cancer is the leading cause of cancer related death accounting for more deaths than breast, prostate and colon combined. Early diagnosis is critical to patient survival, however the vast majority of lung malignancies are detected only once symptoms arise and the cancer has spread, at which time patients have little chance of cure. Macroscopic imaging modalities including CT and bronchoscopy have made significant strides in increasing early detection, however they do not have the required specificity to diagnose malignancy. Diagnosis must be made on the microscopic level, which at present can only be accomplished with excisional biopsy. Unfortunately, low-risk bronchoscopic techniques for retrieving biopsy samples are hampered by low diagnostic yields, and trans-thoracic and surgical approaches carry higher intrinsic risk of complications. Given the very high false positive rates of these macroscopic imaging platforms it is imperative that high-risk procedures are avoided and the diagnostic accuracy of lower-risk approaches are greatly improved. In this proposal we aim to dramatically increase the diagnostic yield of low-risk bronchial biopsy using a novel multimodality electromagnetic and optical coherence tomography (EM-OCT) biopsy guidance platform to provide not only macroscopic spatial guidance to the lesion (using CT and EM) but to additionally confirm the needle placement within the lesion on the microscopic scale (OCT) ensuring that the needle is positioned within the target lesion prior to biopsy acquisition. Specifically we will (Aim 1) develop and fabricate an EM-OCT catheter, rotary junction and system software to facilitate real-time 3D imaging of, and navigation to, SPN for transbronchial biopsy, and (Aim 2) conduct a preclinical study to demonstrate the feasibility of EM-OCT biopsy guidance of artificial SPN (aSPN) in living swine.

2. KEYWORDS

Electromagnetic Navigation, Biopsy Guidance, Optical Microscopy, Optical Coherence Tomography, Lung Cancer, Optical needle.

3. OVERALL PROJECT SUMMARY

***Aim 1:* Develop and fabricate an EM-OCT catheter, rotary junction, and system software to facilitate real-time 3D imaging of, and navigation to, peripheral pulmonary lesions for transbronchial biopsy.**

Task 1: Construct and electro-optical rotary junction

In year 1 we successfully completed this task.

Task 2: Design and construct EM-OCT catheters that are compatible with standard TBNA

In year 1 we fabricated 2 prototype EM-OCT catheters. The design of these catheters is shown below.

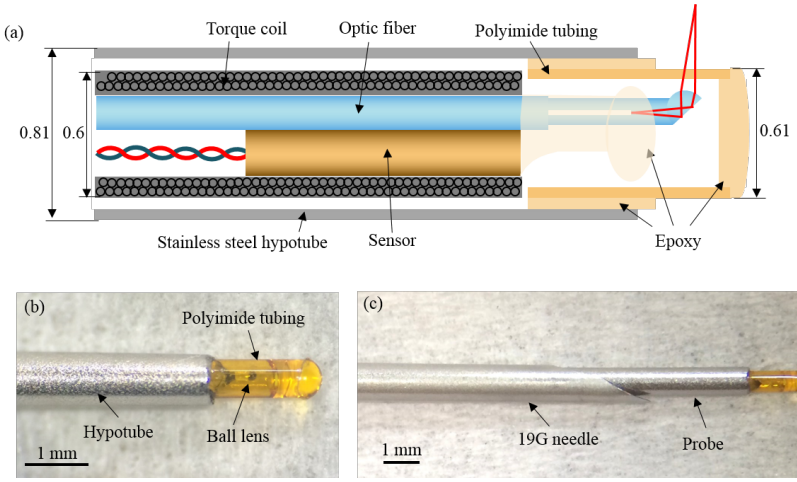
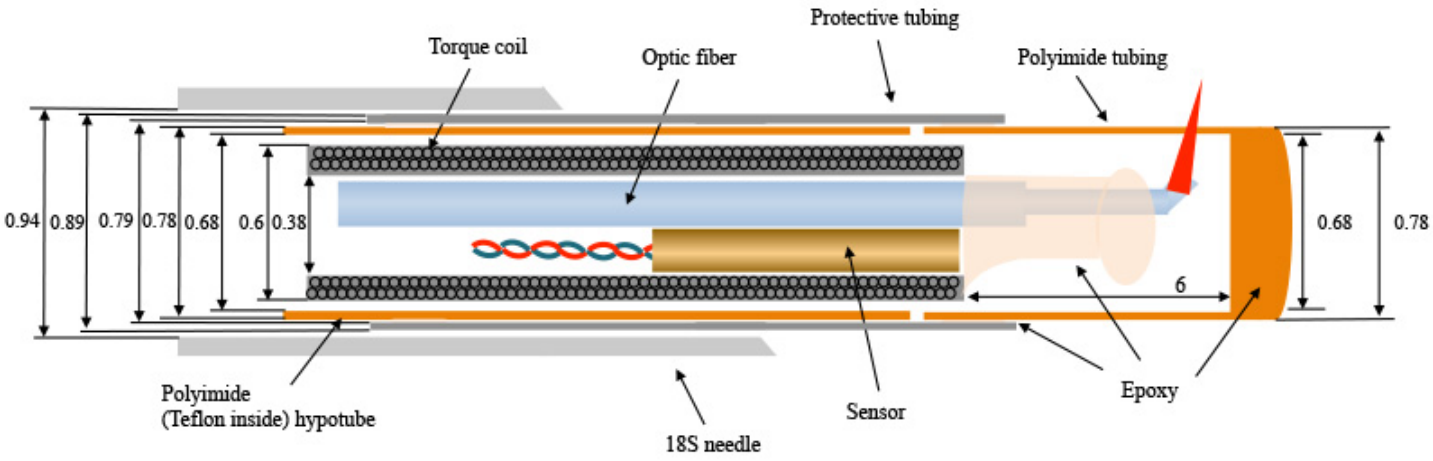


Figure: Schematic of EM-OCT probe design at the distal end, both the sensor and fiber optic probe were incorporated inside a double layer torque coil for rotational scanning. Stainless steel hypotube was used to protect the probe, and a sealed polyimide tubing was epoxied to hypotube as optical window. (b) Photograph of the distal end of the probe, the ball lens is visible through the polyimide tubing. (c) Photograph of the distal end of the probe inside 19G TBNA needle. (unit: mm)

Upon testing we found that although the catheters met all optical and electro-magnetic specifications, the completed catheter was insufficiently flexible causing issues when used transbronchially, the protective hypotube retained shape memory once used through the bronchoscope and therefore greatly increased the NURD experienced by the optical core. We have since further redesigned the EM-OCT catheters to incorporate only a short hypotube to protect from needle damage and to instead extend the polyimide tubing the length of the catehter. We will also teflon coat the outer surface of the torque coil and the inner surface of the polyimide sheath to reduce NURD.



We have recently fabricated 1 catheter prototype and are in the process of thoroughly testing this design.

- *Current prototype optical parameters: ball lens radius: r_s=106 µm, r_t=136 µm; Focus length: f_s=791 µm, f_t=868 µm; Spot size: D_s=17.8 µm, D_t=16.5 µm; Polished angle: 41 degree; Optical length: 2070 mm; Output power: 29 mW*

Task 3: Design and develop navigational software to provide real time tracking of the catheter position within the tracheobronchial tree

In year 1 we successfully completed this task.

***Aim 2:* Conduct a preclinical study to demonstrate feasibility of EM-OCT biopsy guidance of artificial SPN (aSPN) in living swine (n=6).**

Task 4: Validation and refinement of catheter tracking within fixed lungs

Rather than using fixed lungs that would degrade over time, we elected to do our testing using a rubber airway phantom. We performed the EM navigated OCT imaging in the airway phantom. The figure below is a photograph of the experimental set-up. The airway phantom with the fiducial markers were placed on top of tabletop field generator. Both the airway phantom and sensor were registered with the virtual volume model and virtual sensor respectively by following steps described in section 2.4. The probe was placed inside the airway phantom and connected to both EM system and OCT systems in the proximal. There was 7 mm offset between the optical beam and the sensor and was compensated in the navigation software. Both the EM navigation and OCT imaging were updated in real-time. The volume model on Slicer was set with transparency of 0.6 so that the sensor model can be visualize through the airway. The navigation screen was recorded by screen recorder (Camstasia Recorder 8, TechSmith) at the same time when saving OCT raw data.

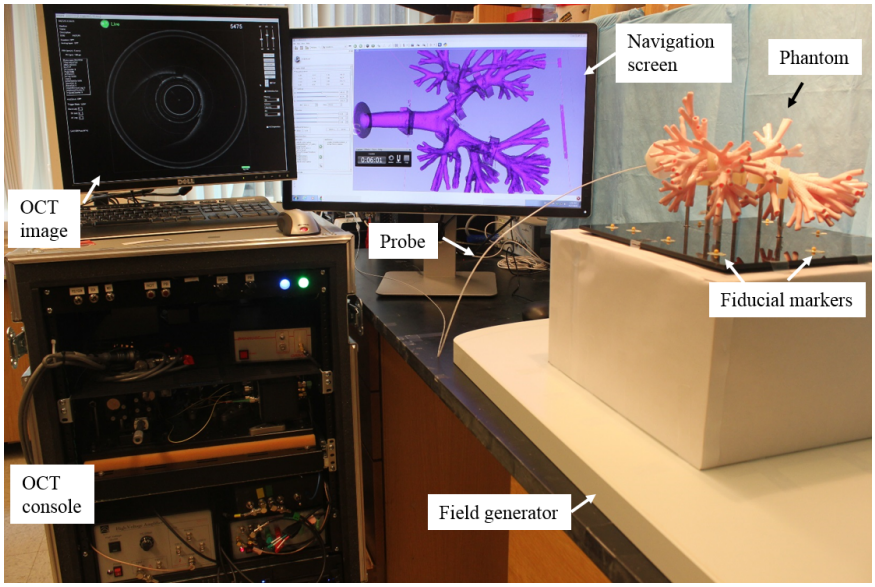


Figure: Experimental set-up. Airway phantom was placed on top of tabletop filed generator. The endobronchial EM-OCT probe was placed within the lung phantom and connects to EM system and OCT system in the proximal. EM navigation and OCT imaging are running simultaneously on two different screens.

At each fiducial marker location as determined by the EM navigation, all the markers were additionally visible by OCT. As expected we found that the sensor was sensitive to fast movement or spinning of the catehter which caused a loss of EM signal, thus navigation to targets were performed prior to spinning the OCT catheter.

Task 5: Conduct swine studies to demonstrate the feasibility of EM-OCT transbronchial biopsy guidance and to determine the potential increase in the diagnostic yield over conventional biopsy approaches.

Due to delays in obtaining preclinical animal study approval from ACURO for our MGH approved Protocol 2013N00053 we have not yet commenced the preclinical studies necessary to complete this proposal. We have formally requested and received a No Cost Extension of 9 months in order to complete these studies.

Prior to conducting the in vivo studies we conduced a number of tests with our initial EM-OCT catheter in freshly excises human lungs however, we found that the revised design of the EM-OCT catheter was too rigid and thus retained shape memory when working tortuous paths to peripheral nodules. These mechanical limitations were unaccaptable for seemless integratation into current TBNA clinical procedures and therefore we have since redesigned the EM-OCT catheter for a 3rd time (see Task 2).

Although mechanical issues with the catheter design were noted, we were able to successfully navigate and obtain images from human lungs obtained at autopsy and were able to successfully identify features according to our previously published OCT image interpretation criteria (see figure below).

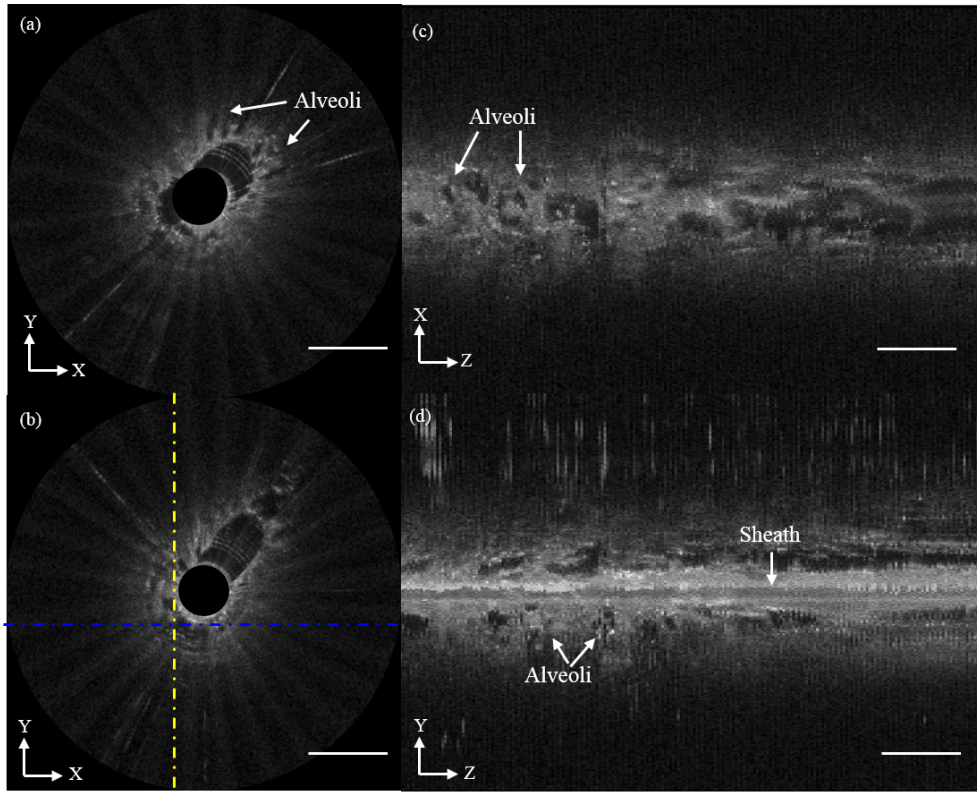


Figure: Ex vivo OCT images of human lung parenchyma acquired with the EM-OCT catheter. Alveoli show as the signal void pockets in the images. (a) and (b): Cross sectional images; (c) and (d): longitudinal images along pullback, in XZ and YZ plane respectively. Longitudinal slices is (c) and (d) were taken from the blue and yellow lines in (b) respectively. Scale bar: 1 mm.

4. KEY RESEARCH ACCOMPLISHMENTS

Nothing to report.

5. CONCLUSION

We have accomplished many of the milestones outlined above for this research proposal and do not expect any difficulties completing the tasks as outlined in the statement of work.

Our objective is to develop, test and validate an EM-OCT biopsy guidance platform that is compatible with standard bronchoscopy techniques and greatly increases the diagnostic yield of bronchial biopsy. This objective is in line with the following LCRP Area of Emphasis: ***"Identification or development of non-invasive or minimally invasive tools to improve detection of the initial stages of lung cancer."*** Increasing the diagnostic yield of transbronchial biopsy approaches may reduce the number of high-risk surgical diagnostic procedures performed, and when coupled with CT screening may increase the early detection of lung cancer.

Specifically we envision that following the identification and gross localization of a nodule by CT, a low-risk transbronchial biopsy will be acquired for diagnosis using EM-OCT guidance rather than a higher-risk transthoracic or surgical diagnostic procedure. The EM-OCT biopsy guidance platform will (1) provide spatial guidance to the lesion through real-time tracking the location of the biopsy needle within the lung using the previously reconstructed CT roadmap of the tracheobronchial tree, and (2) will provide microscopic OCT guidance to ensure that the needle is positioned within the lesion prior to biopsy acquisition.

6. PUBLICATIONS, ABSTRACTS AND PRESENTATIONS

Abstract/Oral Presentation:

1. Wang Y, Shishkov M, Vosburgh KG, Hariri LP, Adams DC, Miller AJ, San-Jose Estepar R, Lanuti M, Bouma BE, **Suter MJ.** Electromagnetic optical coherence tomography guided needle biopsy of lung nodules. SPIE Photonics West; 2015 February, San Francisco, CA, USA: 9304-120.

7. INVENTIONS, PATENTS AND LICENSES

Nothing to report.

8. REPORTABLE OUTCOMES

Nothing to report.

9. OTHER ACHIEVEMENTS

Nothing to report.

10. REFERENCES

None

11. APPENDICES

None

SUPPORTING DATA

None