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Optical coherence tomography imaging for cancer diagnosis and therapy guidance

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Abstract—Optical Coherence Tomography (OCT) is an emerging optical technology that has shown great promise for early cancer detection. Using backreflected light to visualize tissue microstructure, OCT can provide information on nuclear size and shape, nuclear-to-cytoplasmic ratio, and the organization and structure of glands. It can also provide functional information, like blood flow, tissue birefringence, etc. These capabilities could potentially be employed in three ways: as a primary diagnostic test to replace biopsy, as a screening tool to direct biopsy, and as a diagnostic tool to guide therapy and monitor therapy response. In this paper we present an application of OCT for pancreatic cancer diagnosis and therapy guidance.

I. INTRODUCTION

Optical coherence tomography (OCT) imaging is a very attractive technology, which can be used to perform both structural and functional investigation of the biological tissue [1-3] and complement the findings of the current clinical imaging technologies, like endoscopy or ultrasound. Very similar to ultrasound technology, OCT performs cross-sectional imaging by measuring the magnitude and echo time delay of backscattered light.

Image resolutions on the order of several microns can be achieved, and imaging can be performed in situ and in real time. The incident light beam is directed at the object to be imaged, and the time delay and magnitude of backreflected light is measured in the axial or longitudinal direction. The beam is scanned in the transverse direction, and rapid successive axial measurements are performed. The result is a two-dimensional data set image, which represents the optical reflection or backscattering in a cross-sectional plane through the material or tissue.

OCT has evolved very fast within the last five-six years. The traditional time-domain approach has been almost totally replaced by the Fourier domain approach, which can be implemented in the either spectral-domain (SD) or swept source (SS) versions. [4] The SD-OCT approach uses individual spectral components of broadband low coherence light, which are detected separately by use of a spectrometer and a charge-coupled device (CCD) array. The swept SS-OCT approach uses a sweeping wavelength light source and a single detector to analyze individual spectral components. Both approaches enable very high speed/high signal-to-noise-ratio OCT imaging. They also allow for more than an order of magnitude increase in imaging speed and sensitivity compared to the standard time domain OCT approach (TD-OCT). [5] Another significant advantage of these two approaches, compared to the more traditional TD approach, is that they provide direct access to the spectrum of the optical signal, which enables more accurate retrieving of the Doppler signals generated by the motion of the scattering particles present within the imaged biological sample (e.g.: blood cells). [6]

In this paper we demonstrate that OCT imaging shows a high potential for pancreatic cancer diagnosis, biopsy guidance, and therapy monitoring. The results of a preliminary ex vivo study are presented.

II. STUDY MOTIVATION

Cystic lesions of the pancreas represent an increasingly common diagnostic and therapeutic challenge. [7-9] A significant number of pancreatic cysts are detected incidentally when noninvasive abdominal imaging is performed for unrelated diagnosis. However, a challenging problem for gastroenterologists is to differentiate between benign pancreatic cysts (pseudocysts and serous cystadenomas or SCAs) and malignant or potentially malignant cystic neoplasms (mucinous cystic neoplasms or MCNs) because the majority of the latter cysts should be excised, whereas most benign pancreatic cysts do not require surgical resection and can be treated with observation or drainage depending on symptoms, size, and growth rate. MCNs can range in atypia form low grade (adenoma, borderline) to in-situ and invasive carcinomas. Although all of these lesions can potentially progress to an invasive carcinoma, the low grade lesions can be observed radiologically. However, the distinction of low grade from high-grade MCNs cannot be definitively made with the currently available technology.

Traditionally, computed tomography (CT) has been used as a first line of diagnosis for cystic neoplastic lesions of the pancreas. More recently EUS has been used to image the pancreas. Either of these techniques can be supplemented by the use of fine needle aspiration cytology. EUS imaging allows for identification of pancreatic lesions as small as 2 to 3 mm. [10] However, EUS alone cannot be used to differentiate benign from malignant lesions because the limited resolution makes it difficult to see specific features of these lesions. In a study of 98 cystic lesions of the pancreas, Ahmad et al. [11] showed that EUS features alone could not be used to differentiate reliably between benign and malignant cystic lesions of the

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pancreas. The accuracy of FNAB has recently been questioned. In addition, good lines of communication between the cytopathologist and the endoscopist, adequate sampling, adequate sample processing, accurate interpretation by the cytopathologist, and the ability to determine the need for additional samples required for ancillary studies are all needed for effective diagnosis. All these make the accuracy of EUS-FNA vary over a relatively large range (69% to 100%). [12-14] The inability of distinguish benign cysts from neoplastic cysts of the pancreas frequently results in unwarranted surgical intervention. A higher resolution imaging technology capable of distinguishing between these cystic neoplasms will significantly alter our current paradigms, and spare many of these patients from the morbidity associated with pancreatic surgery.

III. MATERIALS AND METHODS

We have recently developed an OCT instrument and minimally invasive probe that are suitable for pancreatic cysts investigation under EUS guidance. Photographs of the OCT-laser therapy system and benchtop/catheter probes are shown in Fig. 1.

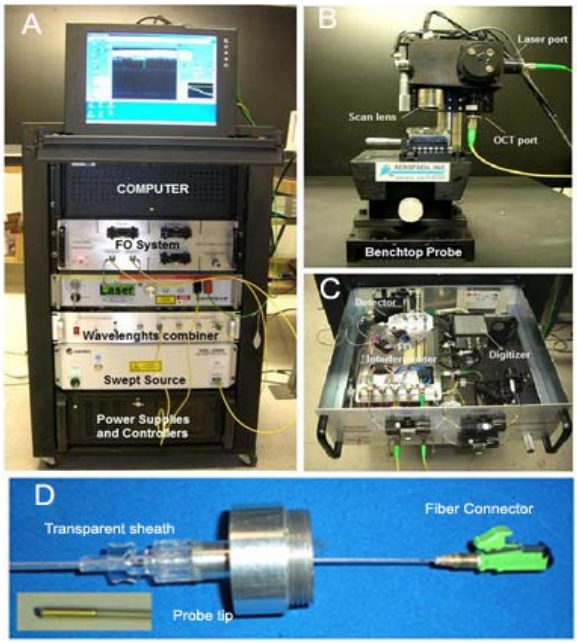

Figure 1. Photographs of the SSOCT System (A,C), benchtop probe (B), and minimally invasive needle-type probe(D).

The capability of the OCT technology for pancreatic cancer diagnosis and laser therapy guidance was preliminarily tested on freshly excised pancreatic tissue specimens. This work has been done in collaboration with Massachusetts General Hospital (MGH), gastroenterology and pathology departments. Pancreatic tissue specimens were obtained from patients undergoing surgery. The identity of the patients was not disclosed to our team of investigators. An IRB protocol for this study was approved by the MGH IRB. OCT data were analyzed and compared against tissue histology to assess the ability of OCT imaging to detect detailed morphology of the pancreatic cystic lesions. Following data collection, each OCT imaging site of the tissue was marked with India ink. Then tissue was fixed in formalin and histological examination was performed. The results of histology findings were correlated with OCT findings.

Representative OCT images for the three major cystic lesions are shown in Fig. 2. The back-to back nature of the microcysts in serous cystadenomas is illustrated in Fig. 2A. Mucinous cystadenomas are illustrated in Fig. 2B. The OCT images of SCAs show the delicate septae that separates the individual microcysts. In contrast, MCNs OCT images show multiple large and dominant cysts with small daughter cysts. However, unlike SCAs, the cysts are separated by solid non-cystic tissue and the mucin secretion is highly scattering.

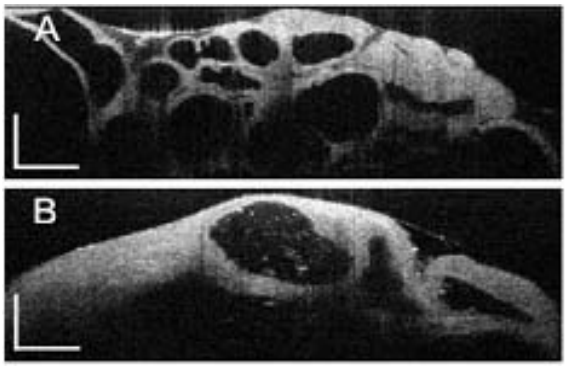

Figure 2. Representative OCT images of SCAs (A), and MCNs (B). OCT scale bar- 500 microns.

Following this preliminary study, a more detailed study was performed to determine the consistency of these findings. Therefore, we first established OCT criteria to differentiate between SCA, MCN, as well as between these lesions and normal tissue, and then we tested these criteria on a relatively large number of tissue specimens. In total, about 60 excised tissue specimens (SCAs, IPMNs, MCNs, and normal adjacent tissue) were used in our study. A "training set" of 20 specimens, 5 of each tissue-type, was used to develop criteria for tissue differentiation, and the remaining 40 specimens were used as a validation set to test these criteria.

An overall specificity of 92% and sensitivity of 88% was found. A very good differentiation between serous and mucinous cystic lesions was possible as well. An overall 97% accuracy for differentiation between SCAs and MCNs was found.

The capability of the OCT system for real-time monitoring of tissue morphological changes during laser therapy was tested as well. Since the laser therapy beam is sent through the same catheter on exactly the same position on the tissue with the OCT imaging beam, the OCT image can be used to monitor the laser irradiation effect on tissue.

An example of OCT images taken before and after laser exposure is shown in Fig. 3. The OCT/laser beams were scanned to generate a 5x5 mm raster on an SCA tissue surface. After one minute of continuous irradiation with 1W/1620 nm laser beam, an obvious damage of the tissue was observed. The microcyst had totally collapsed and the aqueous content of the mucin was practically evaporated. Although only morphologic changes were monitored at this time, we are planning to measure physiological changes as well.

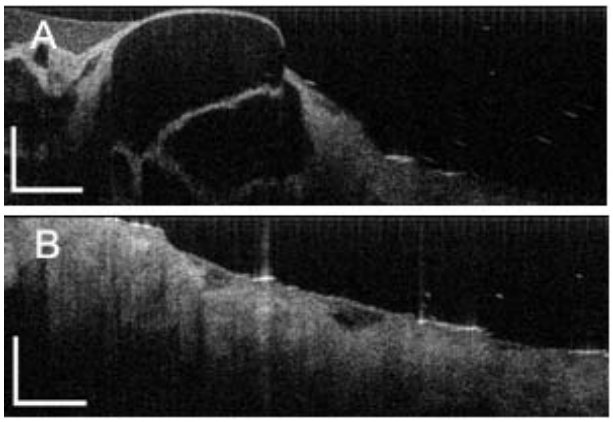

Figure 3. OCT for laser therapy monitoring
A. SCA before therapy; B -SCA after therapy. OCT scale bar- 500 microns.

IV. CONCLUSIONS

We have demonstrated in this study that OCT is the suitable technology for cancer diagnosis and therapy monitoring.

A preliminary testing the OCT technology for pancreatic cancer diagnosis and therapy guidance was performed ex vivo on human tissue specimens. An expanded in vivo study on is planned. The very preliminary results suggest that OCT might be a good tool for in vivo differentiation between various cystic lesions of the pancreas. Since fiber optic-based catheters can be used under EUS or MR CT guidance to reach suspicious masses within the pancreas, in vivo OCT imaging of pancreatic lesions seems feasible and could become an important imaging modality for pancreatic cancer diagnosis. By helping the gastroenterologists to differentiate between benign and cystic neoplasms, a better management of the pancreatic cancer patients will be possible. The elimination of unnecessary surgeries of the benign lesions of the pancreas would have an important emotional impact on patients and family members, and would reduce healthcare costs.

OCT use for laser therapy guidance or monitoring of the therapeutic response seems to be a feasible approach as well. However, a very detailed study has to be performed on an animal model to determine the outcome of this therapy procedure.

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