Intraoperative optical coherence tomography of the human thyroid: Feasibility for surgical assessment

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Thyroid nodules assessed with ultrasound and fine-needle aspiration biopsy are diagnosed as "suspicious" or "indeterminate" in 15%–20% of the cases. Typically, total thyroidectomy is performed in such cases; however, only 25%–50% are found to be cancerous upon final histopathologic analysis. Here we demonstrate optical coherence tomography (OCT) imaging of the human thyroid as a potential intraoperative imaging tool for providing tissue assessment in real time during surgical procedures. Fresh excised tissue specimens from 28 patients undergoing thyroid surgery were imaged in the laboratory using a benchtop OCT system. Three-dimensional OCT images showed different microstructural features in normal, benign, and malignant thyroid tissues. A similar portable OCT system was then designed and constructed for use in the operating room, and intraoperative imaging of excised thyroid tissue from 6 patients was performed during the surgical procedure. The results demonstrate the potential of OCT to provide real-time imaging guidance during thyroid surgeries. (Translational Research 2017;■■:■■–■■)

INTRODUCTION

Thyroid cancer is the most common cancer of the endocrine system, and the National Cancer Institute predicted 56,870 new cases of thyroid cancer and 2010 deaths in the United States in 2017.[1] The thyroid gland consists of 2 connected lobes located at the front of the neck, which wrap around the trachea. The gland produces the hormones L-thyroxine (T4) and L-triiodothyronine (T3), which regulate metabolic physiological processes, cellular respiration, total energy expenditure, growth and maturation of tissues, and turnover of hormones, substrates, and vitamins. Parathyroid glands, located at the back of the thyroid, produce parathyroid hormone, which, along with calcitonin, is involved in regulating the amount of calcium in the blood and bones.[2]

After manual palpation of the neck as part of the physical examination, ultrasonography is often the first imaging modality employed to evaluate the presence of a thyroid nodule because it is readily accessible, inexpensive, noninvasive, and requires no radiation exposure. Ultrasound imaging is also effective at delineating intrathyroidal architecture, distinguishing cystic from solid lesions, determining if a nodule is solitary or part of a multinodular gland, and accurately locating and measuring the dimensions of a nodule. However, ultrasonography is dependent on an ultrasonographer for the quality of images, regions of the neck covered, and interpretation. Other

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AT A GLANCE COMMENTARY

Erickson-Bhatt SJ, et al.

Background

About 15%–25% of thyroid nodule cases are found to be "cytologically indeterminate." Partial or total thyroidectomy is recommended in most indeterminate cases because of the possibility of carcinoma; however, only about 25%–50% of the cases are found to be cancerous by postsurgical histologic analysis.

Translational Significance

Optical coherence tomography has demonstrated the ability to distinguish normal, benign, and malignant thyroid tissue on ex vivo specimens. From benchtop to the operating room, this article demonstrates the feasibility and potential of optical coherence tomography as a tool for intraoperative surgical guidance during thyroid procedures, which can reduce patient morbidity.

less common methods include radionuclide imaging, positron emission tomography, single-photon emission computed tomography, x-ray computed tomography, and magnetic resonance imaging, but these clinical imaging modalities are usually insufficient to provide accurate diagnosis of malignant nodules. Therefore, fine-needle aspiration biopsy (FNAB) is currently used as the gold standard for deciding whether to proceed with surgical treatment of thyroid nodules. FNAB results in 4 possible diagnoses: (1) benign nodule (occurs in ~70% of the cases; the recommended procedure is usually to follow the nodule without surgery); (2) malignant nodule (occurs in 4% of the cases; the recommended procedure is usually partial or total thyroidectomy); (3) suspicious nodule (occurs in 15%–25% of the cases; the surgeon determines case-by-case how to proceed—typically total thyroidectomy or possibly lobectomy with frozen section analysis to determine malignancy); (4) nondiagnostic (which occurs in 5%–10% of the cases when insufficient cytologic material is present to make a diagnosis; the typical procedure is to repeat the FNAB or proceed with surgery).[2-4]

About 15%–25% of thyroid nodule cases are found to be "cytologically indeterminate" and termed as follicular neoplasm, suspicious for carcinoma, or atypical.[5-7] This finding may be due to various benign cellular or nuclear changes, which can be indistinguishable from papillary carcinoma, which can be metastatic. Additionally, features such as capsular penetration and vascular structures indicative of follicular carcinoma cannot be discerned in aspiration cytology because of disruption of the tissue architecture. The American Thyroid Association and the European Thyroid Association have recommended partial or total thyroidectomy in most indeterminate cases because of the possibility of carcinoma; however, only about 25%–50% of the cases are found to be cancerous by postsurgical histologic analysis. Hemithyroidectomy is preferred when possible because of lower morbidity,[8] and many patients will not require exogenous levothyroxine if half of the thyroid is functional.[6]

Optical coherence tomography (OCT) is the optical analogue to ultrasound imaging, but uses broadband near-infrared light to produce much higher-resolution images with the tradeoff of reduced imaging depth penetration[9] (1). OCT has been widely used for clinical ophthalmic imaging[10] (2) and has demonstrated clinical translation in other areas as well, including gastroenterology,[11,12] dermatology,[13,14] cardiology,[15,16] and primary care.[17] OCT has also been used for cancer imaging and demonstrated the capability of imaging breast cancer intraoperatively[18-20] and in vivo within the surgical cavity[21] for real-time surgical guidance. OCT has demonstrated the ability to distinguish normal, benign, and malignant thyroid tissue on ex vivo specimens,[22,23] as well as to identify thyroid and parathyroid glands on ex vivo specimens and intraoperatively.[24,25] However, none of these studies have demonstrated the ability to image in vivo. From benchtop to the operating room, this article demonstrates the feasibility and the potential of OCT as a tool for intraoperative surgical guidance during thyroid procedures.

MATERIALS AND METHODS

Benchtop OCT system. The benchtop OCT system (Fig 1) consisted of a superluminescent diode source with 1310-nm center wavelength and 170-nm bandwidth. A 50/50 fiber coupler was used to split the beam between the reference and sample arms. The axial and transverse resolutions of the system were 6 and 16 µm, respectively. The optical power at the sample was less than 10 mW. Reflected light was detected using a spectrometer in this spectral-domain OCT configuration. The tissue was placed in a dish and noncontact imaging was performed in the *x*-*y* lateral directions (using 2 computer-controlled galvanometer-scanning mirrors), as well as in the axial (*z*) direction to generate 3-dimensional (3D) image data, which were immediately displayed on the computer monitor.

Ex vivo imaging using the benchtop OCT system. The ex vivo human tissue studies were approved by the Institutional Review Boards at the University of Illinois at Urbana-Champaign and the Carle Foundation Hospi-