

# Point-of-care optical imaging and guidance for breast cancer surgery

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*High-resolution imaging and guidance using optical coherence tomography (OCT) can transfer diagnostic capabilities from the pathology lab to the operating room, enabling real-time tissue visualization and point-of-care decisions.*

Optical coherence tomography (OCT) is a rapidly emerging technology with potential to impact many areas of clinical medicine and human biology.<sup>1</sup> The optical analogue to ultrasound, in which reflected light is detected rather than sound, OCT forms images based on spatial variations in an index of refraction. Thus, exogenous contrast agents are unnecessary, although ongoing research aims to determine whether, as in other medical imaging modalities, they can be beneficial.<sup>2</sup> OCT can be used to perform optical biopsies, generating images that resemble histological sections but without removal and staining of tissue. OCT has potential for use with a variety of tumors, and we have investigated how it may be applied to intraoperative surgery with respect to breast cancer.

Surgery has traditionally relied only on visual macroscopic assessment to differentiate between normal and tumor tissue during an operation. After resection, tissue is sent to the laboratory, where a pathologist further visually assesses suspicious areas, carefully slices thin sections, then stains and views them under a high-resolution microscope to confirm the presence of tumor cells and to determine if any are located along the surgical margin. These techniques are time-consuming and, more importantly, tend to significantly under-sample tissue, leaving many areas microscopically uninspected.

Surgeons and patients could dramatically benefit from knowing intraoperatively if resection is complete such that no tumor cells remain. To date several methods have been devised to provide more real-time information. For example, cryosectioning is commonly performed in small pathology labs adjacent to the operating room, but achieving adequate sampling remains



**Figure 1.** Intra-operative optical coherence tomography (OCT) in surgical oncology. A portable system (lower left) was used for imaging tumor margins and lymph nodes (top middle) as well as needle-biopsy placement (top right). In representative images of tumor margins (bottom right panels), in contrast to abundant adipose cells on the negative margin, the positive margin exhibits highly heterogeneous scattering regions. Highest scattering regions (arrows) correspond to foci of tumor cells, as confirmed by histology. (Photos and images courtesy of Carle Foundation Hospital and Beckman Institute for Advanced Science and Technology.)

problematic. Additionally, touch-preparation methods attempt to sample cells at tumor margins for rapid staining and visualization, and real-time polymerase chain reaction is used on specimens that are pulverized and fractionated for analysis. These and other techniques have not been effective in providing either cellular diagnostic information or spatial localization in real time.

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Moving diagnostic capabilities from the pathology lab to the operating room for point-of-care decisions thus remains highly desirable. High-resolution OCT may be an effective solution for rapid intraoperative assessment of tumor margins, lymph nodes, and tissue masses. This modality can be engineered to provide a cellular view of tissue over large areas without the need to physically disrupt, process, section, and stain tissue.<sup>3-5</sup> In addition, recent advances in OCT technology, image reconstruction algorithms, and automated classification enable rapid acquisition of microscopic images, making feasible rapid sampling of more tumor margins, lymph nodes, and masses in real-time at the cellular level.

We constructed a portable OCT system and imaged human tissue intraoperatively during lumpectomy and mastectomy surgeries for breast cancer (see Figure 1). Freshly resected tumor masses and lymph nodes were scanned over the surgical margins and capsules, respectively. Three-dimensional OCT data sets were acquired, and areas that appeared suspicious, indicative of a positive tumor margin, were identified and marked. Normal-appearing margins were also tagged as controls. The tissue was then transferred to the pathology department, in accordance with the standard of care, where they were subjected to corresponding histology in addition to standard evaluation. These ongoing studies to date have involved more than 65 patients. Approximately 15% of the tissue masses showed evidence of positive tumor margins, and corresponding histology confirmed the presence of residual tumor cells. Lymph node features correlated well with histology. Intraoperative imaging with OCT and refractive index needles also showed strong correlations. This suggests, in addition, that these techniques may be used in the future to guide biopsy needles to abnormal tissue during outpatient procedures.

OCT can provide high-resolution, label-free imaging at higher sampling rates for intraoperative assessment, not only of resected tissue but also of residual tumor cavities and lymph node tissue. Our experience with breast cancer surgery is a representative illustration. The techniques and principles we describe may be adapted and applied to any type of solid tumor resection, or to optical guidance of needle biopsies for most solid tumors, including those resectable from a brain, lung, liver, thyroid, or kidney. Future developments will include handheld probes for *in situ* patient imaging and refinement of reconstruction and classification algorithms<sup>6,7</sup> to automatically identify suspicious regions from large volumes of OCT data.

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