Innovations in Intraoperative Tumor Visualization

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KEYWORDS

- Intraoperative tumor imaging • Surgical margin assessment • Optical imaging
- Near-infrared fluorescent imaging • Targeted fluorescent probes

KEY POINTS

- Intraoperative tumor visualization has the potential to significantly improve surgical cancer care by improving adequacy of resection, decreasing resection of normal tissue and structures, and directing adjuvant therapy.
- Various techniques for intraoperative tumor imaging exist, including optical fluorescent imaging, high-frequency ultrasound, optical coherence tomography, optoacoustic imaging, confocal microscopy, elastic scattering spectroscopy, Raman spectroscopy, and radiofrequency spectroscopy; however, no single technique has yet been perfected.
- Optical fluorescence imaging has been further refined with the use of near-infrared techniques and selective probes, improving the sensitivity and accuracy of intraoperative images.

INTRODUCTION

The surgical oncologist is tasked with a great responsibility, with little margin for error. One must localize the tumor and resect it, preferably en bloc, with as little morbidity and contamination to surrounding tissues as possible. Adequacy of resection has implications on local recurrence[1] and survival for many tumor types. Incorrect estimation of tumor resection margins may result in incomplete excision of disease, or increased morbidity with resection of excess normal tissue. Various methods of intraoperative tumor visualization have been, and are being, developed to aid in the real-time assessment of tumor extent and adequacy of resection. Better understanding of the resection margins has implications for adjuvant treatment as well. Knowledge of an increased or decreased risk of local recurrence may inform decisions about adjuvant therapies, such as radiation.

Assessment of the margins of resected tumor is a surrogate measure for the ultimate question: whether or not tumor remains in the patient. Analysis is performed via gross and histologic evaluation of the resected tissue, and is a lengthy and imperfect process. The standard and most widely used method of intraoperative identification of tumor margin is frozen section pathologic analysis. Although it is an accurate way of identifying tumor in the sampled tissue,[2,3] only a small percentage of the margin of resected tissue is actually analyzed. Thus, there is great potential for sampling error both from random sampling of the resected tissue, as well as heterogeneity of the tumor itself. Furthermore, the process is time-consuming and correlation of orientation/localization between the tumor and tumor bed are distorted after excision.[4] Final histologic analysis of complete tumor margins can take up to 5 to 7 days. If margins are found to be positive, the patient may be subjected to reoperation, adjuvant treatments, or both.

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Multiple methods for intraoperative tumor visualization have been developed and continue to be refined. Many of these advances have been driven by brain and head and neck cancers due to the morbidity associated with tissue resection, as well as breast cancers with the increase in breast-conserving surgical techniques. However, a mature technique for intraoperative tumor visualization would benefit surgeons and their patients across all disciplines, guiding accuracy of biopsies, increasing adequacy of resections, and in some instances even providing diagnostic information.

TRADITIONAL IMAGING TECHNIQUES

Traditional imaging techniques, such as MRI and ultrasound. have been studied in brain tumor resection and breast-conserving surgery, respectively. Studies have shown increased rates of complete tumor resection without increased neurologic deficits, and improved survival rates with intraoperative MRI-guided resection of gliomas.[5–7] Although safe and effective, there are disadvantages to this technique. For one, it requires the surgeon to interpret the imaging and correlate the location of the lesion from the image to the tumor bed. Second, previously treated areas may have treatment effects or postoperative changes that affect the MRI image and decrease the accuracy of this technique. Third, obtaining an MRI can be time-consuming, resulting in significant surgical disruptions and prolonged operative time. Finally, there is considerable investment required to create operative suites with the ability to accommodate the logistical needs of the MRI magnet. Ultrasound has fewer logistical pitfalls than MRI, and has been used to localize the tumor, guide resection, and confirm completeness of excision. Studies show ultrasound-guided resection of breast lesions to have improved resection margins and decreased excision volumes than traditional techniques, such as palpation guided, wire localization, or quantitative radionucleotide-guided localization.[8–11] However, the resolution of ultrasound is poor, and similar to other structural imaging modalities, the accuracy is affected by previously treated surgical fields.

Computer-assisted navigation using fiducial markers that are calibrated to the patient's anatomy and cross-sectional (computed tomography [CT] or MRI) imaging can be used for indirect tumor imaging. Calibrated pointers, or surgical instruments (ie, osteotome, burr, cautery) can localize the instrument within the patient's cross-sectional images on a monitor in real time. This can be used to correlate to the planned resection margin, to the tumor, or to other vital anatomic structures. Computer-assisted navigation systems have gained popularity in pelvic resections for technically demanding, complex multiplanar osteotomies, and joint-preserving excisions.[12,13] They have been shown to improve excision accuracy[14] with adequate resection margins (**Fig. 1**). However, accuracy with navigation of soft tissue tumors is poor because of inability to place a stable fiducial, and disruption of the localizers may result in misguided navigation.

OPTICAL FLUORESCENT IMAGING

Optical imaging is based on fluorescence variation between normal and tumor tissue, which may be driven by intrinsic tissue properties or exogenously

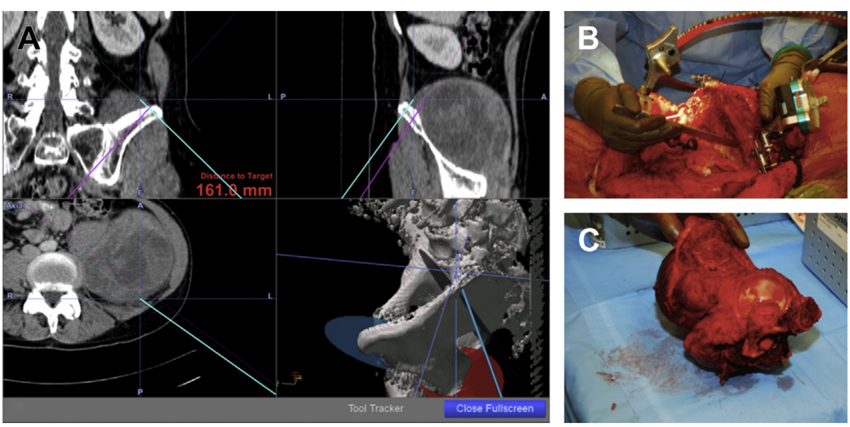

Fig. 1. Computer navigated resection of a large pelvic tumor. (*A*) CT cross-sectional and 3D reformatted images with lines representing anatomic correlate of instruments within the patient. (*B*) Calibrated localizer on an osteotome displays location and trajectory of bone cuts in real time on the patient's cross-sectional imaging. (*C*) Resected pelvic tumor en bloc. (*Courtesy of* Stryker Inc. Kalamazoo, MI, USA; with permission.)