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ASO Author Reflections: Fluorescent Anti-CEA IR800 for Tumor Labeling

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PAST

A critical issue in the surgical treatment of solid gastrointestinal malignancies is difficulty in direct, real-time, intraoperative visualization of the lesion or its metastases. An unacceptable number of curative-intent surgeries performed for pancreatic cancer are seen, with early recurrence at the surgical site or at distant locations. This indicates the weakness of our ability to completely remove the tumor at the resection bed, as well as our ability to recognize radiographically occult metastatic disease. Intraoperative imaging modalities such as ultrasound or image guidance with non-specific contrast-enhancing agents such as fluorescein, methylene blue, or indocyanine green (ICG) have been useful adjuncts, but they are limited in their specificity. There is a need for a tumor binding probe to provide real-time oncologic surgical guidance.

PRESENT

Enhancement of visualization using tumor-specific fluorescent probes can increase tissue contrast to more accurately stage disease, and, when localized, increase rates of oncologically complete resections. This study described a novel antibody–fluorophore conjugate as a potential solution.¹ The antibody is humanized, which decreases the risk of human anti-chimeric antibodies. The dye is a near-infrared fluorophore, which improves tissue depth penetration compared with visible wavelength dyes. A signal is seen in 6 h, but peak fluorescence and highest contrast is seen at 48 h, consistent with the kinetics of other antibody–fluorophore conjugates being evaluated in this field. The biodistribution shows initial non-specific accumulation primarily in the liver, but this washes out rapidly to give a strong tumor-specific signal in 48 h. Carcinoembryonic antigen (CEA) is an ideal target for fluorescence-guided surgery (FGS) of solid gastrointestinal malignancies as it is expressed on the membrane of most of these tumors with a high antigenic density compared with other markers.² Both antibody and dye have been shown to be safe in initial clinical trials, and the combined probe is a promising one for FGS.

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FUTURE

A wide array of probes and fluorophores are being evaluated for fluorescence guidance. The ideal fluorescent probe would be efficient and cost effective to synthesize, with rapid pharmacokinetics, and high sensitivity and specificity.³ Due to the heterogeneity in probe design, there is variability in dosing, timing of imaging, and choice of imaging devices. Further studies are necessary to optimize these variables and determine the definition of an adequate signal for FGS. As clinical trials with probes progress, there will be a need for modifications based on patient's tumor biology. Studies to determine minimal antigenic density necessary for an adequate tumor signal are underway, as well as the dose and distribution of the probe needed for patients whose target antigens are shed in the serum or are altered due to neoadjuvant chemotherapies.^{4,5} Tumor-specific probe development is a rapidly developing field, with the potential to greatly enhance intraoperative decision making and improve rates of oncologically complete resections.

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