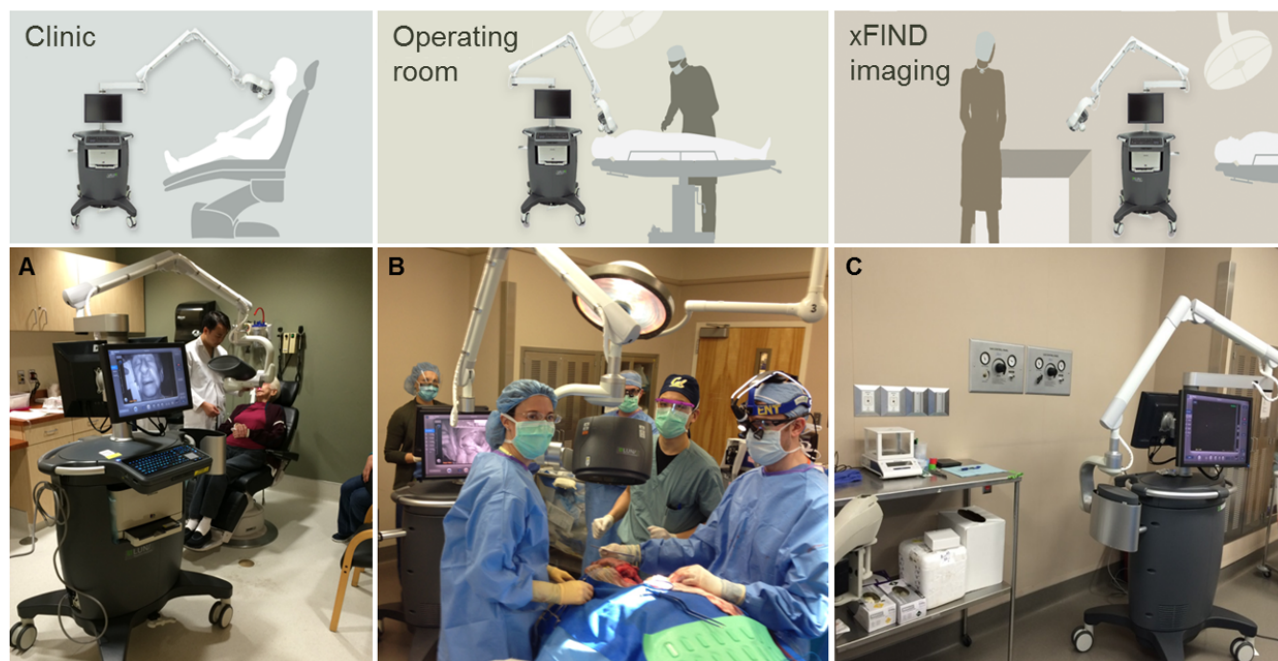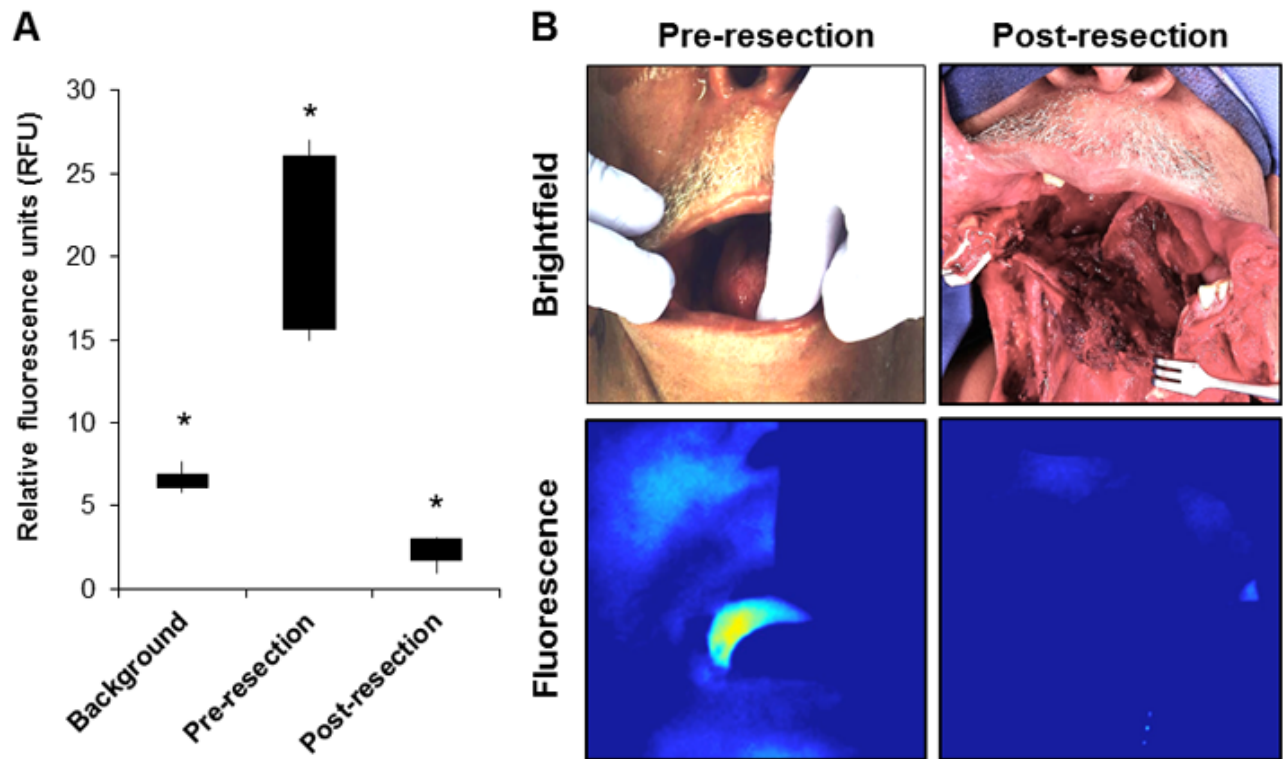**Supplemental Figure 1. Optical characteristics and standardized performance comparisons.** (A) Optical spectral range of the open-field imaging device. (B) Signal-to-noise ratio for the open-field device and an optimized, closed-field device after imaging the same standard containing 4 decreasing concentrations of IRDye800 (pictured below the graph). (C) Tumor-to-background ratios of the same ex vivo specimen on the open-field and optimized closed-field devices for three representative patients.

Supplemental Figure 2. Workflow of the LUNA system repurposed for fluorescence-guided surgery. Real-time imaging of head and neck cancer patients was performed before surgery in the preoperative clinic (A), in the surgical field (B), and using the ex vivo x-FIND imaging system in the operating room (C).

Supplemental Figure 3. Fluorescence imaging of the postresection wound bed. (A) Quantification of the background, preresection, and postresection wound bed fluorescence of three representative patients. (B) Bright-field and corresponding fluorescence images of the pre- and postresection wound bed of a patient who underwent total glossectomy.