Development of an ICG polymeric nanoformulations for fluorescence-guided surgery

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Fluorescence-guided surgery (FGS) utilizes fluorescent agents to enhance tissue contrast, aiding intraoperative anatomical and/or tumour visualization. However, current FGS agents suffer from limitations in specificity, selectivity, and bioavailability.[1] This study aims to develop a fluorescent nanoformulation of indocyanine green (ICG) to improve circulation time and specificity, enhancing visual distinction between healthy and malignant tissues and ultimately improving surgical outcomes.[2]

PEG-PLGA nanoparticles (NPs) were synthesized using a 3D-printed microfluidic platform for precise size control. To enhance ICG loading and stability, hydrophobic ion-pairing strategies, including tetrabutylammonium bromide (TOAB), were explored. The nanoprecipitation process was optimized for uniform size and low polydispersity. Nanoparticle properties were characterized via dynamic light scattering (DLS) and transmission electron microscopy (TEM). ICG quantum yield was optimized by modifying the pairing agent and nanoprecipitation conditions. Pharmacokinetics were evaluated in murine and swine models following intravenous injection. Lymphatic and vascular biodistribution were assessed via fluorescence imaging using a Karl Storz endoscope.

Uniform nanoparticle formulations were successfully synthesized, as shown by DLS and TEM (Fig. 1A). Toxicity and circulation half-life were influenced by the hydrophobic pairing agent used for ICG encapsulation (Fig. 1B), which also significantly impacted ICG's quantum yield. Imaging was achieved in a large animal model using a clinical FGS endoscope.

Encapsulating ICG in PEG-PLGA nanoparticles shows promise for enhancing vascular and lymphatic bioavailability, improving precision and efficacy in fluorescence-guided surgery

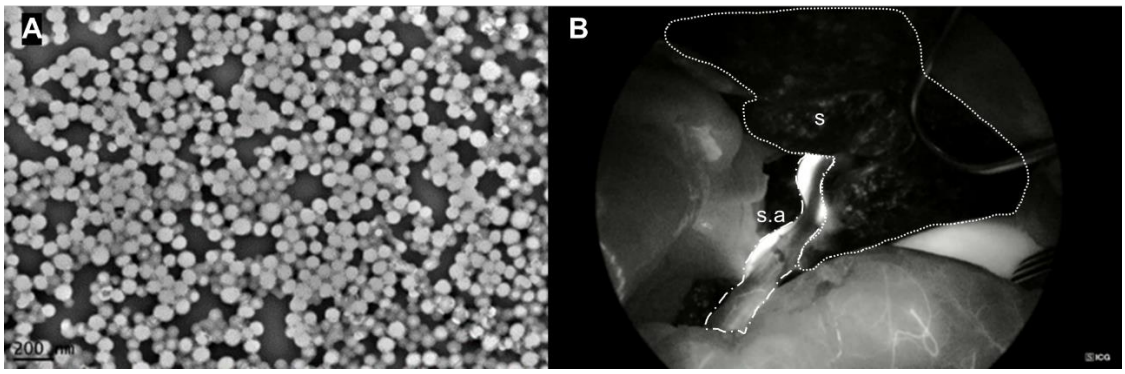

Figure 1. A. TEM image of ICG-TOAB loaded PEG-PLGA nanoparticle. B. A near-infra red endoscopic still image of the spleen(s) and splenic artery (s.a) depicting the circulating ICG-TOAB PEG-PLGA nanoformulation in a swine model.

References

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2. Olson, M. T.; Ly, Q. P.; Mohs, A. M., Fluorescence Guidance in Surgical Oncology: Challenges, Opportunities, and Translation. *Mol Imaging Biol* **2019,** *21* (2), 200-218.