A dual-modality approach to sentinel node biopsy of the stomach:
Combining highly specific mannose-coated magnetic nanoparticles with ICG dye

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BACKGROUND

Application of the **sentinel lymph node (SLN)** concept has transformed the surgical approach in which breast cancer and melanoma are routinely treated, and has provided a 'gold standard' over more invasive procedures (such as axillary lymph node dissection).

SLN biopsy provides benefits by reducing patient morbidity, simplifying surgical workflow and reducing surgery time, and facilitates more detailed pathological processing on fewer removed nodes. However, **successful application relies on accurately identifying the SLN from other lower-yield lymph nodes**.

This can be challenging in complex environments such as gastric cancer, where using conventional tracers such as blue dyes and radioactive colloids is not convenient or practical, because tracing blue dye through perigastric tissue is technically difficult and radioactive colloids require special handling, with a short window of use.

We propose a novel dual-tracer SLN technique utilizing magnetic and fluorescent agents for gastric cancer, as tested in a large animal model. This approach uses a mixture of **mannose-labelled magnetic nanoparticles (FerroTrace)** and **fluorescent dye indocyanine green (ICG)**.

The mannose-labelled FerroTrace has been designed to be highly specific to the SLN with minimal flow-through to lower echelon nodes, while ICG provides sensitive mapping of lymphatic vessels and nodes with tissue penetration through perigastric tissue to guide SLN identification.

METHODS

All procedures were performed via exploratory laparotomy. For this pilot study, one pig was injected into the stomach submucosa with a single **0.1 mL dose consisting of a 50:50 ratio of FerroTrace (50 mg/mL) and ICG (2.5 mg/mL)**. Lymphatic mapping was performed immediately after injection. Dissection was guided by a Stryker *1688 AIM 4K* infrared camera. Magnetic tracer was detected in the nodes using a Ferronova *FerroMag* magnetometer probe. The animal was humanely euthanized following the procedure.

SUMMARY

Feasibility of using a combined magnetic-ICG tracer for SLN biopsy in a gastrointestinal model was confirmed.

Indocyanine green (ICG) dye effectively guided identification of lymph node basin containing SLN via use of an infrared camera.

Our novel mannose-labelled magnetic tracer (FerroTrace) was 100% specific to the SLN, with no flow-through detected to lower echelon nodes.

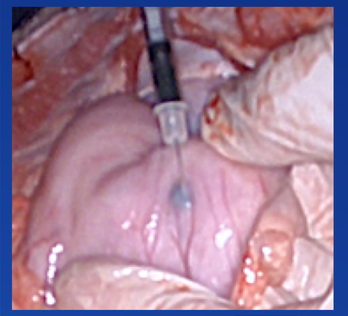
This proof-of-principle study provides evidence and confidence to support future trials exploring the feasibility of a fluorescent-magnetic dual tracer for SLN biopsy in gastrointestinal cancers.

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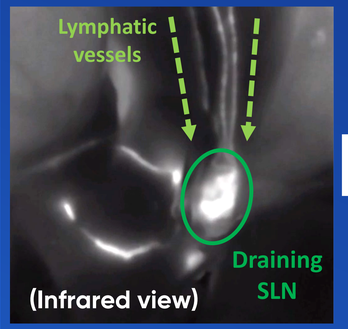
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Mix and Inject



Identify LNs



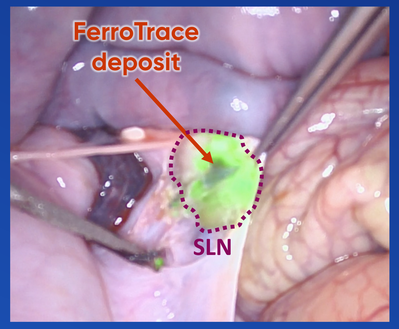
RESULTS

The procedure took approximately 12 minutes to complete. The Stryker camera successfully identified fluorescent vessels leading from the injection site into lymph nodes in real time. These pathways were followed until all fluorescent lymph nodes were found. In total, **7 ICG-positive lymph nodes were identified and removed with the aid of the Stryker camera**.

After removal, each lymph node was imaged again with the Stryker camera to confirm ICG signal. The FerroMag probe was then used to detect accumulations of FerroTrace.

Only one node - the SLN - gave a positive magnetic signal. In addition, **the SLN showed a dark discolouration** due to the accumulation of magnetic particles, providing an additional mode of confirmation (visual).

There were no ICG-negative nodes containing magnetic signal, indicating **highly-specific accumulation of FerroTrace in the SLN.**



Fluorescent and brown / magnetic SLN