Feasibility of Magnetic (FerroTrace™) and Indocyanine Green (ICG) Sentinel Lymph Node Mapping in Colorectal Cancer (MAGICSENT Trial)

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BACKGROUND

In theory, localised colorectal cancer should be cured by surgery alone. However, the 5-year relative survival rate is as low as 80%*. Lymphatic spread in colorectal cancer is associated with a reduction in overall survival, and **accurate lymph node (LN) status can inform therapeutic treatment and/or surveillance strategy**.

Sentinel lymph node (SLN) mapping has the potential to identify involved LNs for subsequent resection and ultra-staging. However, **successful application relies on accurately identifying the SLN from other lower-yield lymph nodes**.

While conventional use of blue dye or indocyanine green (ICG) dye alone can provide sensitive and detailed intraoperative lymphatic mapping, **they are less suited to identifying SLNs** as within minutes; they rapidly flow beyond SLNs to lower echelons.

A new magnetic tracer **FerroTrace™ has been developed by Ferronova to overcome these issues** as it possesses high accumulation in SLNs, reduced flow-through and is retained in SLNs for several weeks, allowing **preoperative MRI localisation of draining LNs**, which helps identify high risk LNs outside of standard surgical field.

THE TECHNOLOGY

Four key technologies are used for an advanced SLN mapping approach:

- **FerroTrace™** (Ferronova, Australia) – injected during surgery or 24hrs before
- **ICG dye** ('Verdye'; Diagnostic Green, Germany) – injected during surgery
- **Fluorescence imaging camera** ('Image1 S Rubina'; Karl Storz Endoskope, Germany) – used to visualise lymphatic basin containing ICG during surgery
- **Handheld magnetometer probe** ('Sentimag'; Endomag, UK) – used to identify SLNs in tissue specimen based on magnetic signal







Left: Vials of FerroTrace and ICG

Middle: Endoscopic fluorescence camera

Right: Handheld magnetometer probe

*Siegel RL et al. Colorectal cancer statistics, 2017. CA Cancer J Clin. 2017 May 6;67(3):177–193. Newland RC et al. Pathologic determinants of survival associated with colorectal cancer with lymph node metastases. A multivariate analysis of 579 patients. Cancer. 1994 Apr 15;73(8):2076–82.

SUMMARY

This paper demonstrates an enhanced method of lymphatic mapping, which is **applicable to colorectal and upper gastrointestinal cancers**.

FerroTrace is highly specific to the SLN, and a magnetometer probe **easily differentiates the SLN** from other LNs based on signal strength.

Fluorescent ICG provides **sensitive visual identification** of the draining lymphatic basin (vessels and LNs) during surgery.

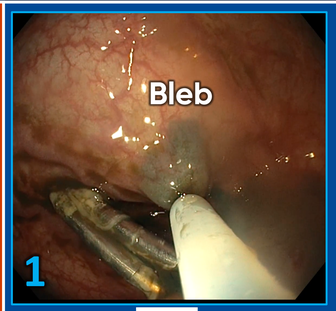
FerroTrace remains active in LNs for weeks following injection, and can be identified on MRI for a **non-radioactive approach to preoperative lymphatic mapping**.

Preoperative MRI facilitates **identification of high-risk LNs** outside of the conventional surgical field.

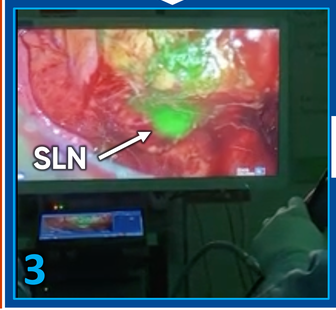
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WORKFLOW and TECHNIQUE

1. A 25-guage endoscopic needle is used to inject the tracers in 4 equal-volume 1 mL quadrants positioned ≤10mm from the primary tumour periphery. FerroTrace and ICG can be combined or injected independently. At each site a small volume is initially injected to confirm bleb and check the needle is correctly positioned in the submucosa.
2. MRI can be performed after FerroTrace injection to define regions containing magnetic LNs, e.g. in rectal cancer patients prior to surgery.
3. ICG dye is visualised with the fluorescence camera during surgery, highlighting draining lymphatic pathways and providing real-time surgical guidance.
4. After dissection of the tumour and lymphatic tissue, the magnetometer probe is used to scan the specimen to find the highly-magnetic SLNs.

To date, 10 patients have been successfully enrolled (3 sigmoid colon, 1 left colon, 4 right colon, 2 rectal).

End point: Clear identification of SLNs allows for detailed pathology (ultra-staging) on a small number of targeted LNs. This results in more accurate diagnosis of micro-metastases and isolated tumor cells in patients assessed to be clinically node-negative.



A multimodal approach to improve accuracy of SLN localization