Enhancing the *in vivo* detection of cancer by manipulating magnetic fields applied to tumor targeting superparamagnetic iron oxide nanoparticles

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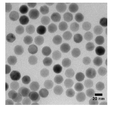
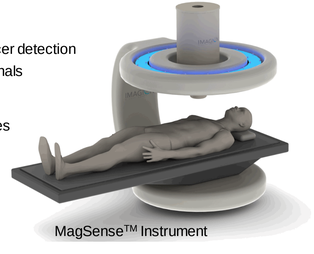
Introduction

- The MagSense™ platform consists of superconducting quantum interference devices (SQUIDs) to detect tumor targeted iron oxide nanoparticles (NPs) that are specifically bound to cancer cells. The detection relies on SQUIDs high sensitivity to magnetic field produced by the superparamagnetic relaxation (SPMR) of the NPs.
- Proof of concept demonstrates specific detection of HER-2 positive breast cancer cells *in vitro* and *in vivo.*
- Current efforts are focused to:
  - Improve the lower limit of SPMR Cancer detection
  - Reduce the influence of off-target signals

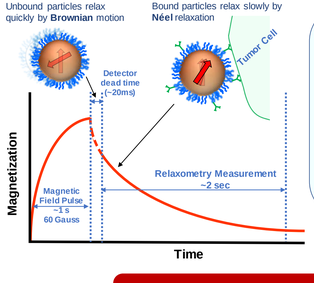
MagSense™ nanoparticles





MagSense™ Instrument

SPMR Background



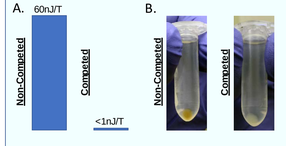
In vivo SPMR Cancer Detection

1. Inject mAb conjugated NPs
2. Apply small magnetizing pulse
3. NPs relax to their equilibrium states
   - **Brownian** motion of unbound NPs [fast and **undetectable**]
   - **Néel** relaxation of NPs bound to cells [slow and **detectable**]

SPMR ONLY DETECTS NPs BOUND TO CANCER CELLS/TISSUES

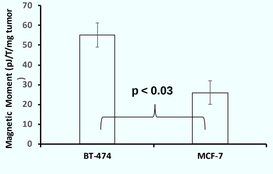
Proof–of-Concept SPMR specific cancer detection

In Vitro Cell Competition



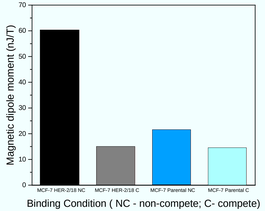
Competitive binding of anti-HER2 conjugated NPs to MCF7/HER2-18 cells as measured by **A.** the MagSense™ instrument and confirmed by **B.** digital photography.

In Vivo Cell Specificity



The strength of the magnetic dipole generated by the MagSense-Anti-HER2 particles is dependent on the level of HER2 expression on the cell surface.

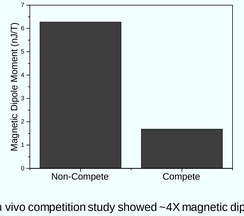
In Vitro Cell Specificity



Binding Condition (NC - non-compete; C- compete)

Competitive binding of anti-HER2 conjugated NPs can be correlated to the expression of HER2 on cells. MagSense™ measurements of MCF7/HER2-18 and parental MCF7cells.

In Vivo Cell Competition

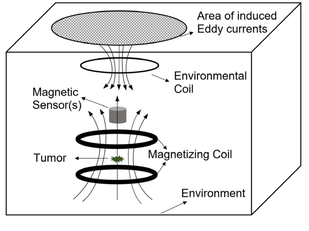


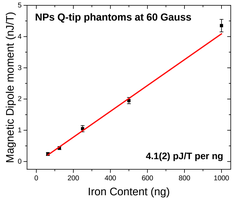
In vivo competition study showed ~4X magnetic dipole signal in non-compete mouse vs. compete mouse.

Reducing the influence of the environmental background

The Problem: The magnetization pulse induces non-specific magnetic fields (Eddy currents in the conductive environment), that increase instrument dead time, limit dynamic range, and lower the sensitivity.

Solution: Generate a field of opposite polarity to cancel Eddy currents



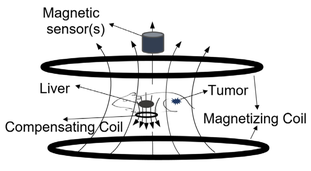


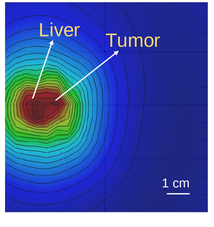
- **4-fold Improvement** on the lower limit of *in vitro* detection from 250 ng to 62.5 ng of Fe
- Reached, *in vitro* sensitivity to **5, 000 BT474 targeted cells** ($5x10^4$ nps/cell (achieved) at $3x10^9$ nps/μg of Fe_3O_4)
- Projected, *in vivo* sensitivity at **100, 000 cancer cells** (e.g., in lymph nodes at 100% delivery at 3-cm depth)
- Projected, detection *in vivo* **tumor size of 2.5 mm³** (at 4% tumor delivery at 3-cm depth, e.g., breast cancer)

Improving tumor detectability

The Problem: SPMR signals at off-target sites (liver and spleen) influence tumor detection

Solution: Compensate the magnetic field at off-target sites





- **6-fold reduction of the Liver signal** from $3.3x10^2$ to $0.56x10^2$ nJ/T
- **Resolving a Tumor of 10% of a liver** at 2cm away from the liver
- Projected, **10-fold reduction of liver signal** with a better coil design

Summary and Conclusion

- We presented the **proof-of-concept SPMR specific cancer detection *in vivo* and *in vitro***
- Demonstrated improvement in tumor detectability *in vitro* by reducing signals at off-target sites
- An improvement of the **lower limit of detection to 5,000 BT474 cells *in vitro*** was presented
- We project sensitivity to **100,000 cells** (100% delivery) and **2.5 mm³ tumor size** (at 4% delivery) at **3-cm depth** - primary breast tumors and sentinel lymph nodes detection
- Future work: Improvements on MagSense™ Instrument and NPs to allow for detection at larger depth