

# POTENZIALE UTILIZZO TERAPEUTICO DI NANOVETTORI MAGNETICI NEI TUMORI CEREBRALI



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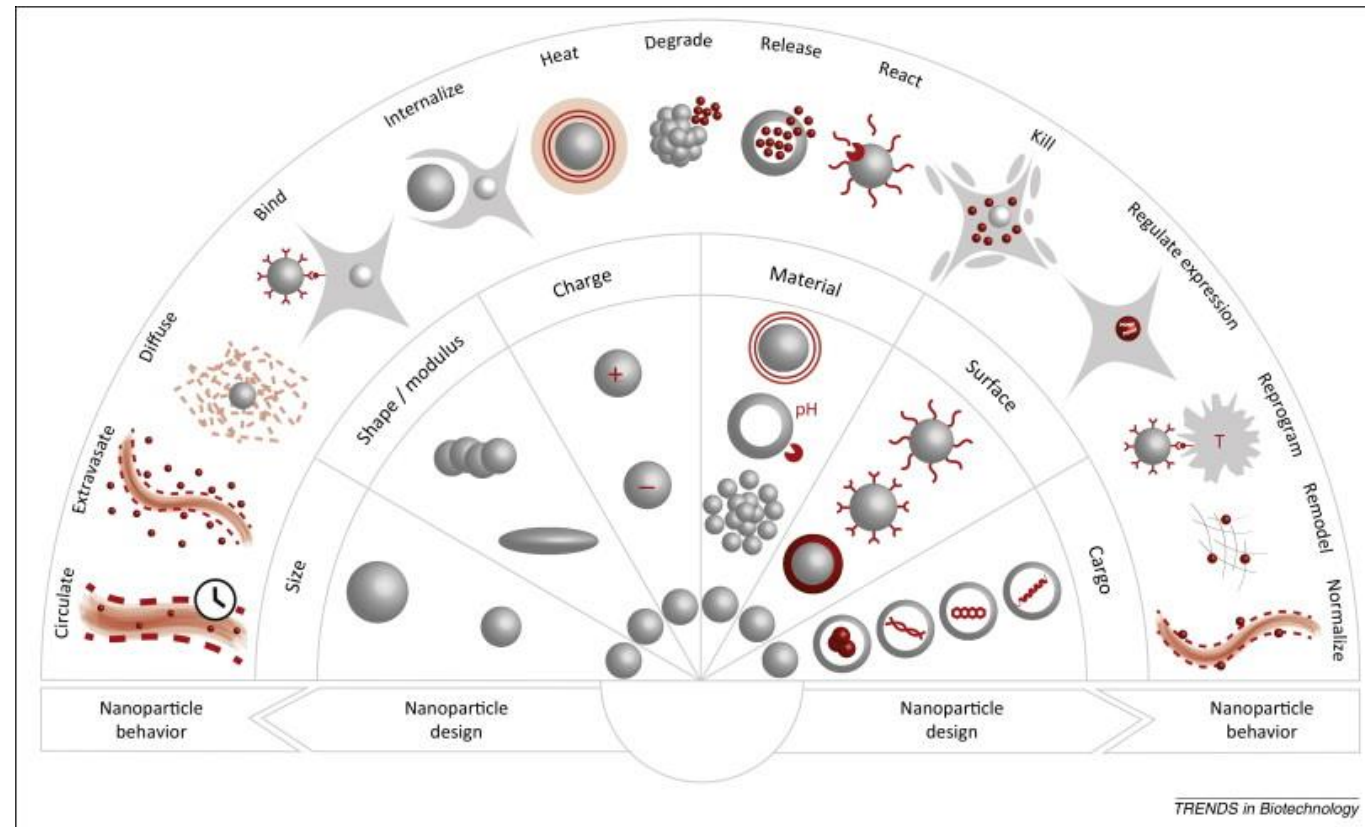
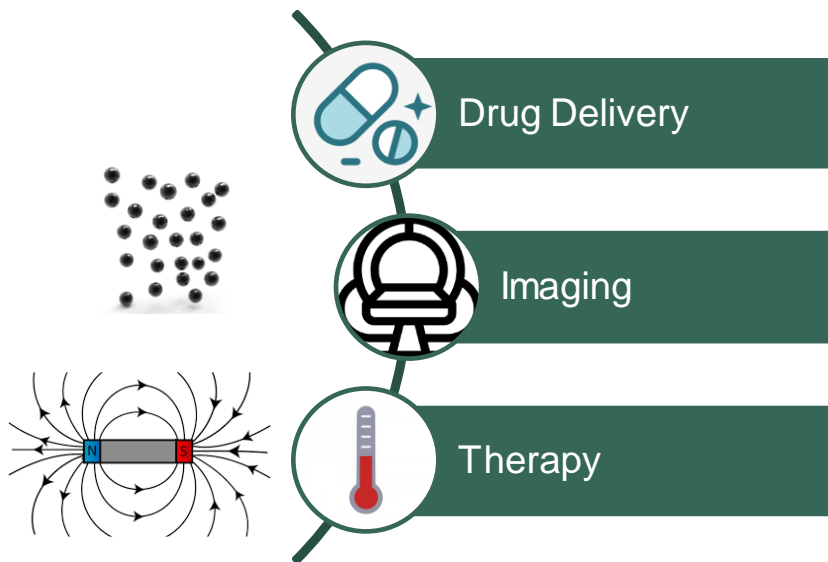
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# NANOMEDICINE: THERANOSTIC MAGNETIC NANOPARTICLES

- **Theranostic:** integration of diagnostic imaging capability with therapeutic intervention
- **Magnetic nanoparticles (MNPs):** high magnetic moment, allowing manipulation by external magnetic fields.

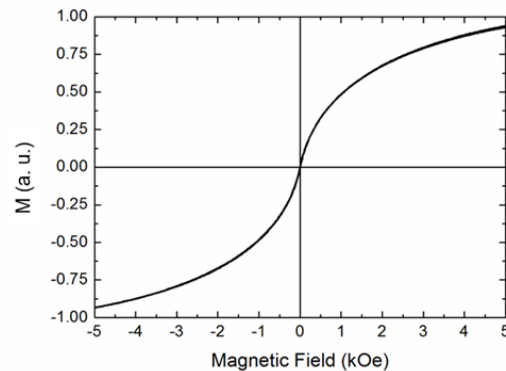


(Hauert and Bathia, 2014, *Trends in Biotechnology*)

# BEYOND ONCOLOGICAL HYPERTHERMIA...

Novel Multipurpose Theranostic Carriers in the Central Nervous System

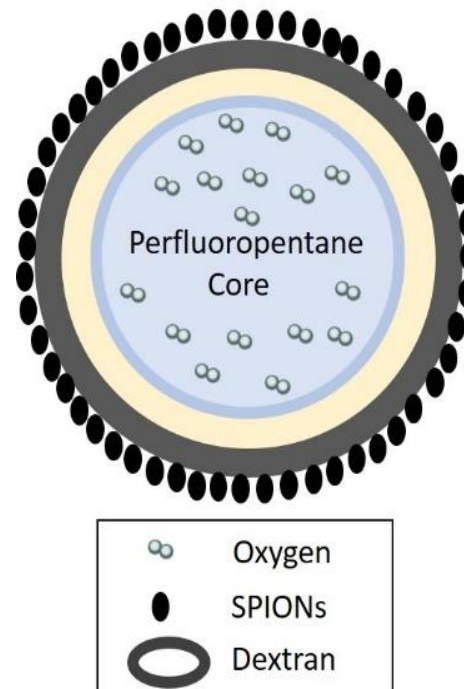
Magnetic Oxygen Loaded Nanobubbles (MOLNBs):  
Dextran NB covered with Superparamagnetic iron  
Oxide nanoparticles (SPIONs)



(Zullino et al., 2019, *Frontiers in Pharmacology*)



Physically Drivable Magnetic Nanobubbles



## US Sonography

- Enhancing of O<sub>2</sub> release by sonication
- Monitoring and Imaging by US

## Magnetic Driving

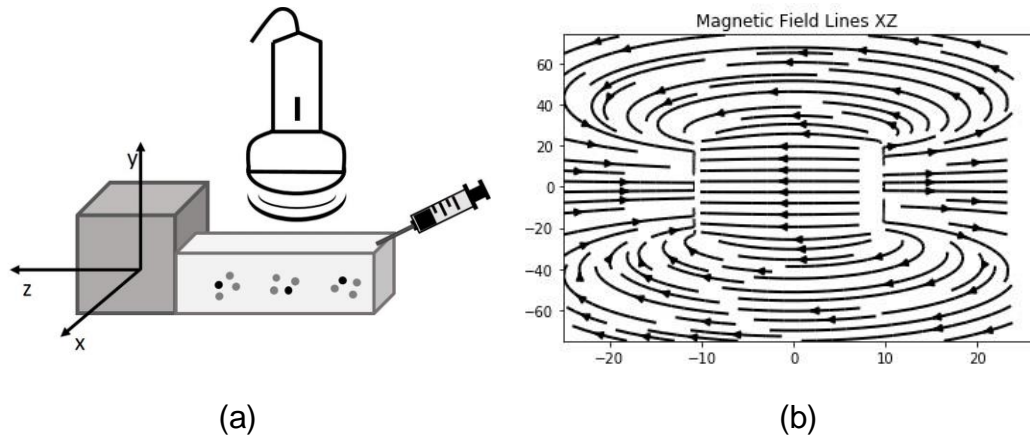
- Targeting of brain tumors by *ad hoc* tailored magnetic fields
- Helping BBB crossing by magnetic force
- Monitoring and Imaging by MRI

## Oxygen and/or Drug Loading

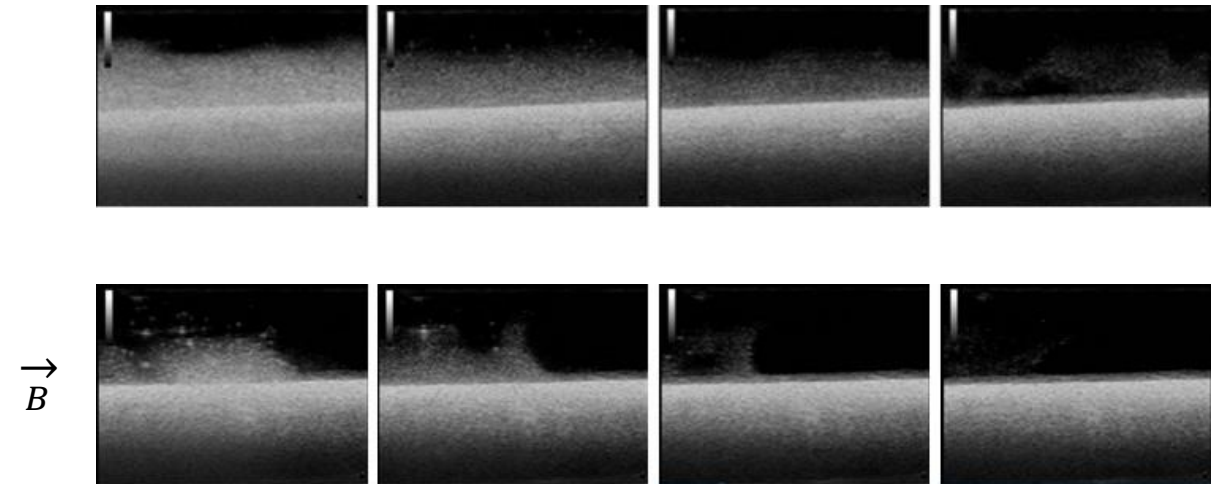
- Loading and delivery of O<sub>2</sub> by diffusion for radiotherapy enhancement in CNS
- Loading and delivery of chemotherapy drugs to target brain tumors

(Ficiarà E. et al., 2020 *Molecules*, 25,2104)

# ULTRASOUND MONITORING OF MOLNBS



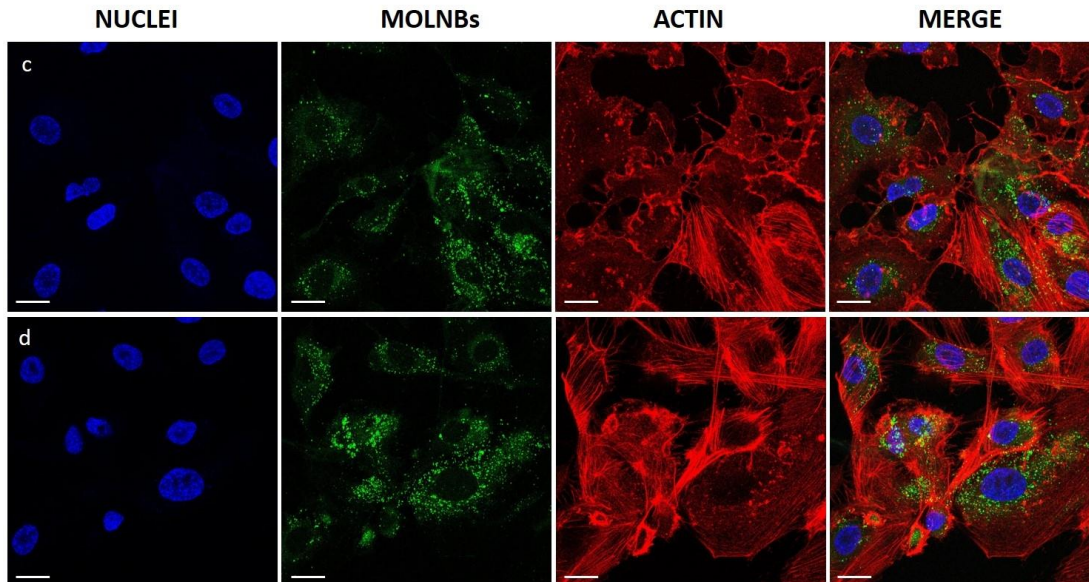
- a) Setup used for the imaging of MOLNBs in absence and presence of the magnetic field produced by the cuboid magnet (1.26–1.29 T).
- b) Projection of magnetic field lines in the XZ plane assessed by the z-direction of the magnetic field.



Snapshots from US imaging of MOLNBs in absence and presence of the magnetic field. Images were recorded at different time frames (5, 15, 25, 55 sec) from the injection.



# BIOCOMPATIBILITY FOR BLOOD-BRAIN BARRIER CELLS



- Confocal microscopy: MOLNBs interact in a non-toxic way with human brain microvascular endothelial cells (hBMECs)
- Absence of hemolytic activity



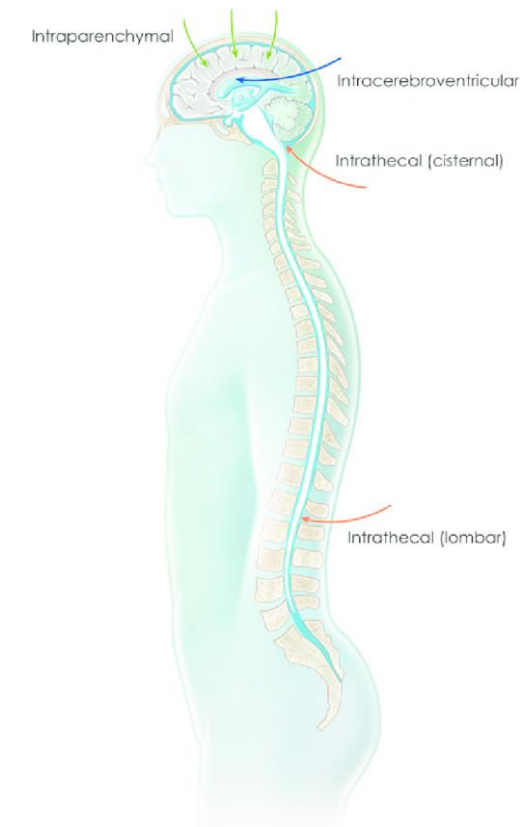
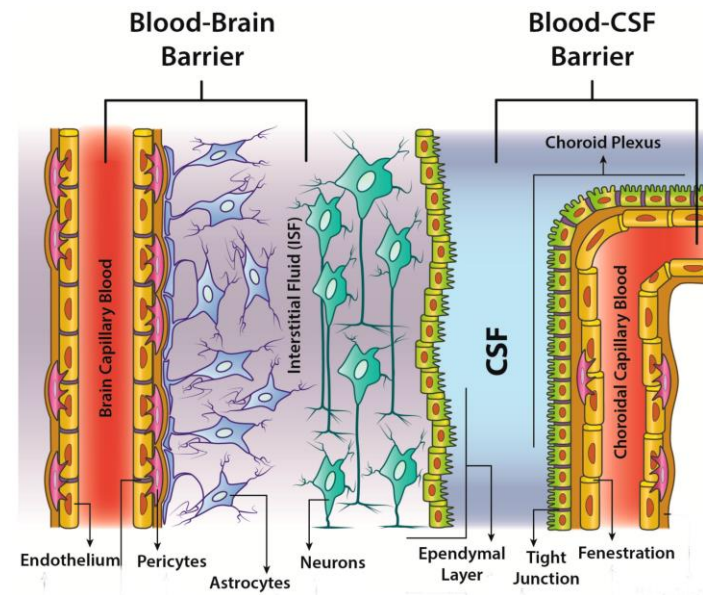
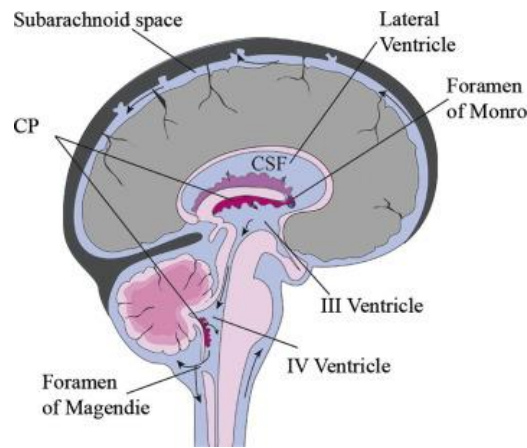
Potentiality of MOLNBs to cross brain barriers from injection in systemic circulation

(Ficiarà E. et al., 2020 *Molecules*, 25,2104)

- Preliminary magnetic investigation: MOLNBs can be magnetically guided using external permanent magnets
- Current problem: NPs overcome brain barriers from systemic circulation?

# FUTURE PERSPECTIVES

- MOLNBs might be safely administrated locally via intravertebral injection in the CSF, monitoring their concentration by MRI or sonography.
- Stability in real matrix fluids, such as serum or CSF
- MOLNBs may be magnetically driven towards blood-CSF barrier (BCSFB) to deliver oxygen and chemotherapy drugs to brain tumors.



# CURRENT WORK: NEW SET UP SIMULATING BRAIN

- Tailoring the driving magnetic field based on the position and dimension of the brain tumor and the brain membranes
- Monitoring by means US
- Tuning of magnetic fields  $B$  using little magnets



**Precisely directing MOLNBs in brain regions in which tumors are located**

Simulations of magnetic field



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

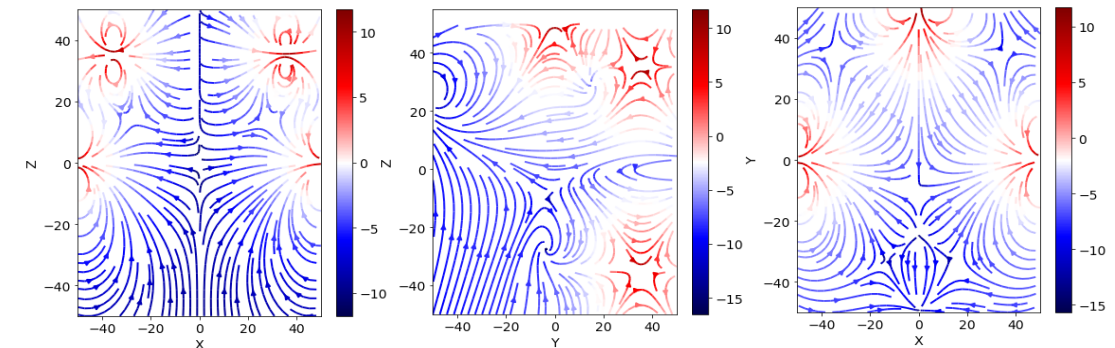
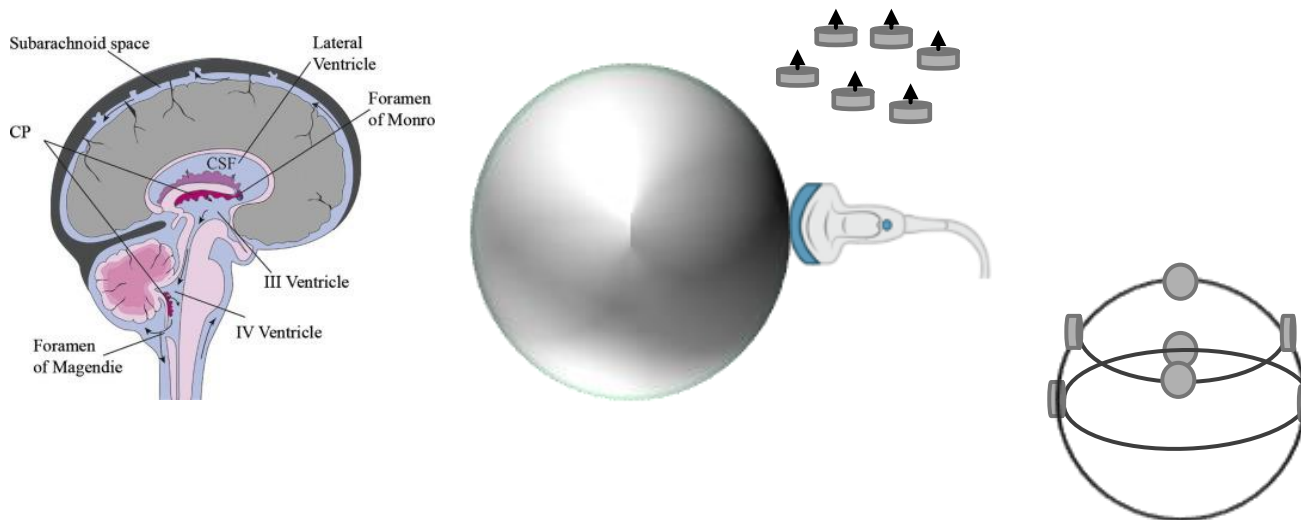
SoftwareX

journal homepage: [www.elsevier.com/locate/softx](https://www.elsevier.com/locate/softx)

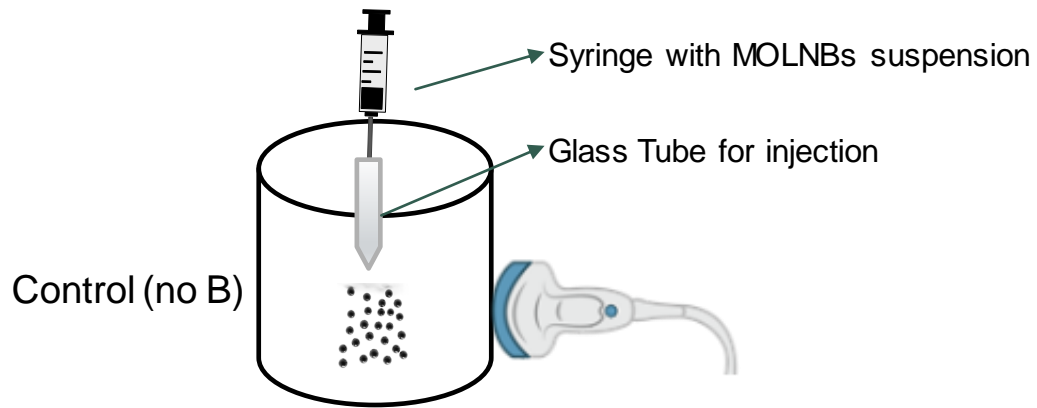
Original software publication

Magpylib: A free Python package for magnetic field computation

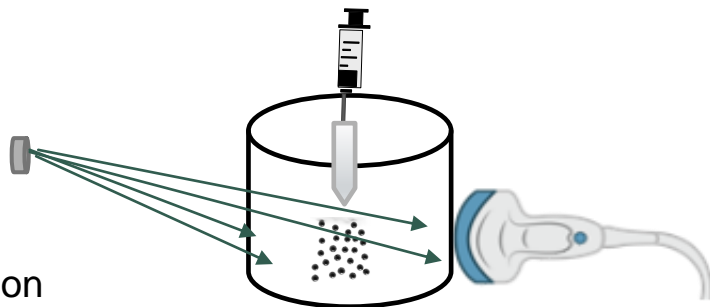
Michael Ortner<sup>a,\*</sup>, Lucas Gabriel Coliado Bandeira<sup>b</sup>



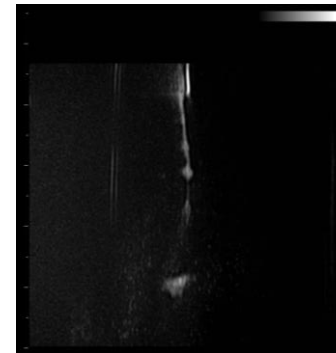
# PRELIMINARY RESULTS



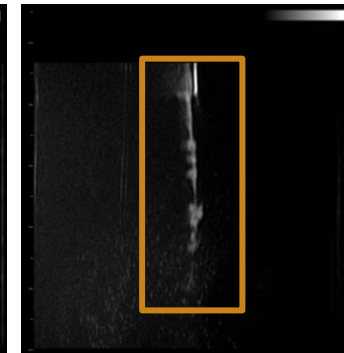
Snapshots from US imaging at 5, 15, 30 s



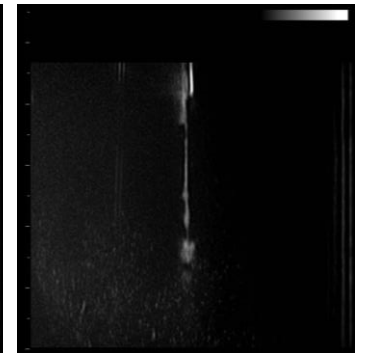
5s



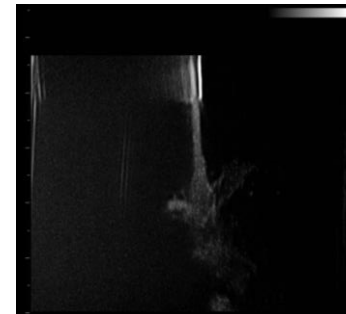
15s



30s



- Homogeneous flow of MOLNBs in vertical direction

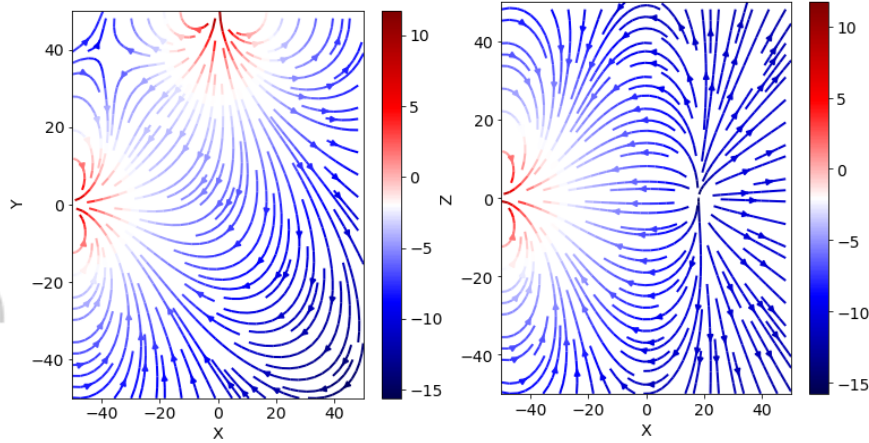
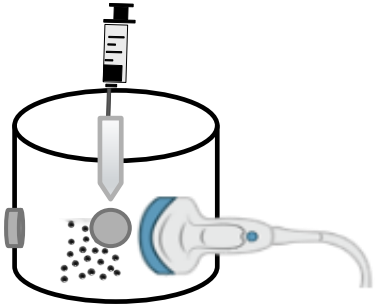


- Spreading of flow

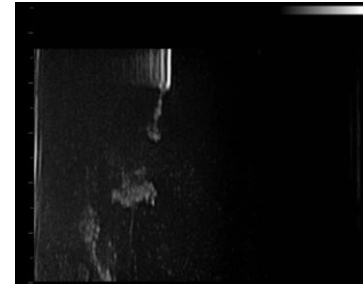


# DIFFERENT CONFIGURATIONS OF MAGNETIC FIELD

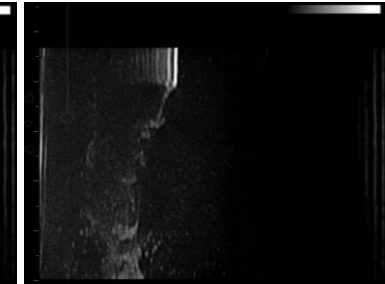
2 magnets



5s



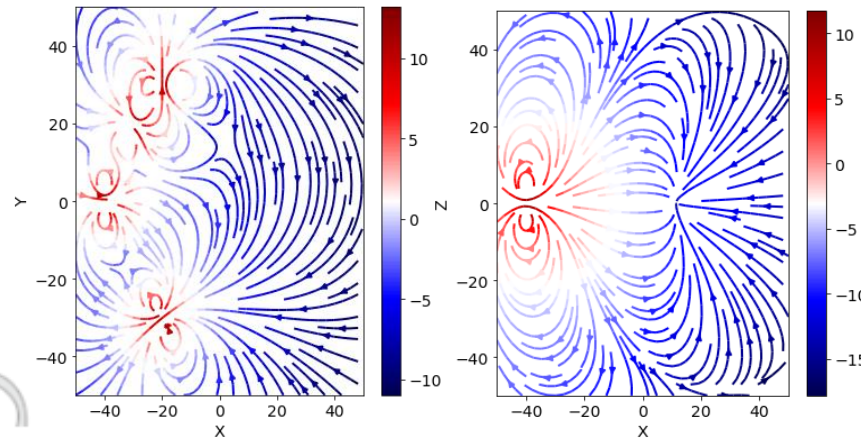
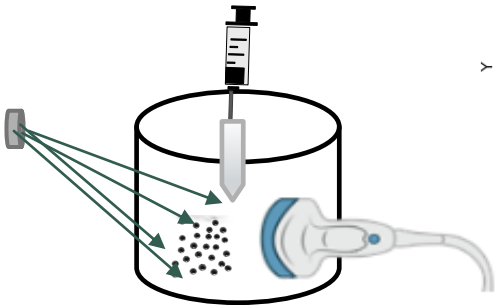
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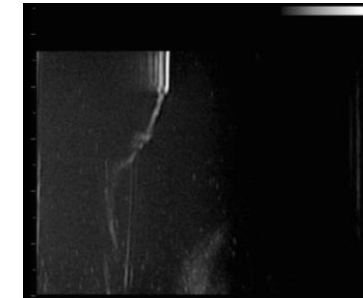
30s



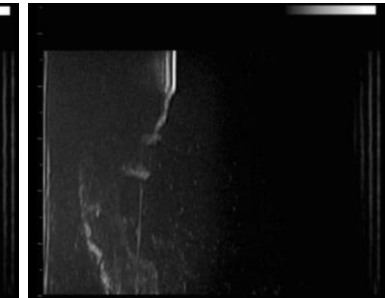
4 magnets  
Distance 2 cm



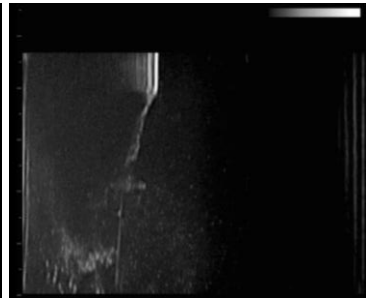
5s



15s



30s



**Deviation of flow toward the magnets**

# CONCLUSIONS

- Physically drivable Magnetic Nanobubbles crossing brain barriers to reach brain tumors
- New setup simulating brain and motion of NBs inside brain fluids
- Tailoring magnetic fields according to position and dimension of tumors
- Monitoring of NBs by sonography
- Future investigation on MRI monitoring