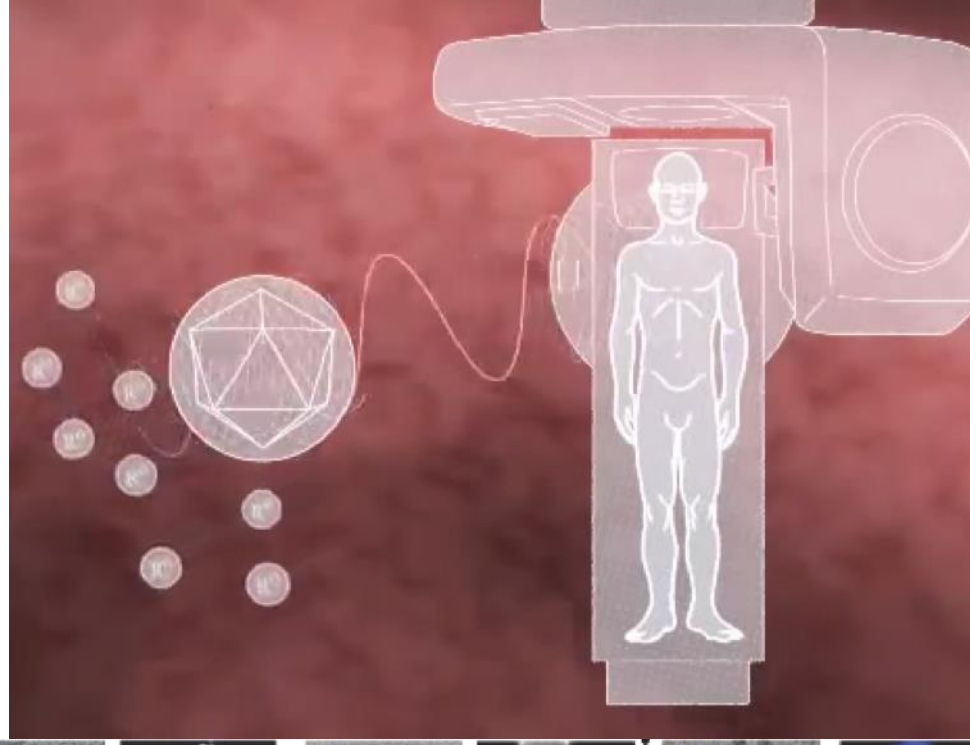
Nanoparticle theranostics with PET and MRI

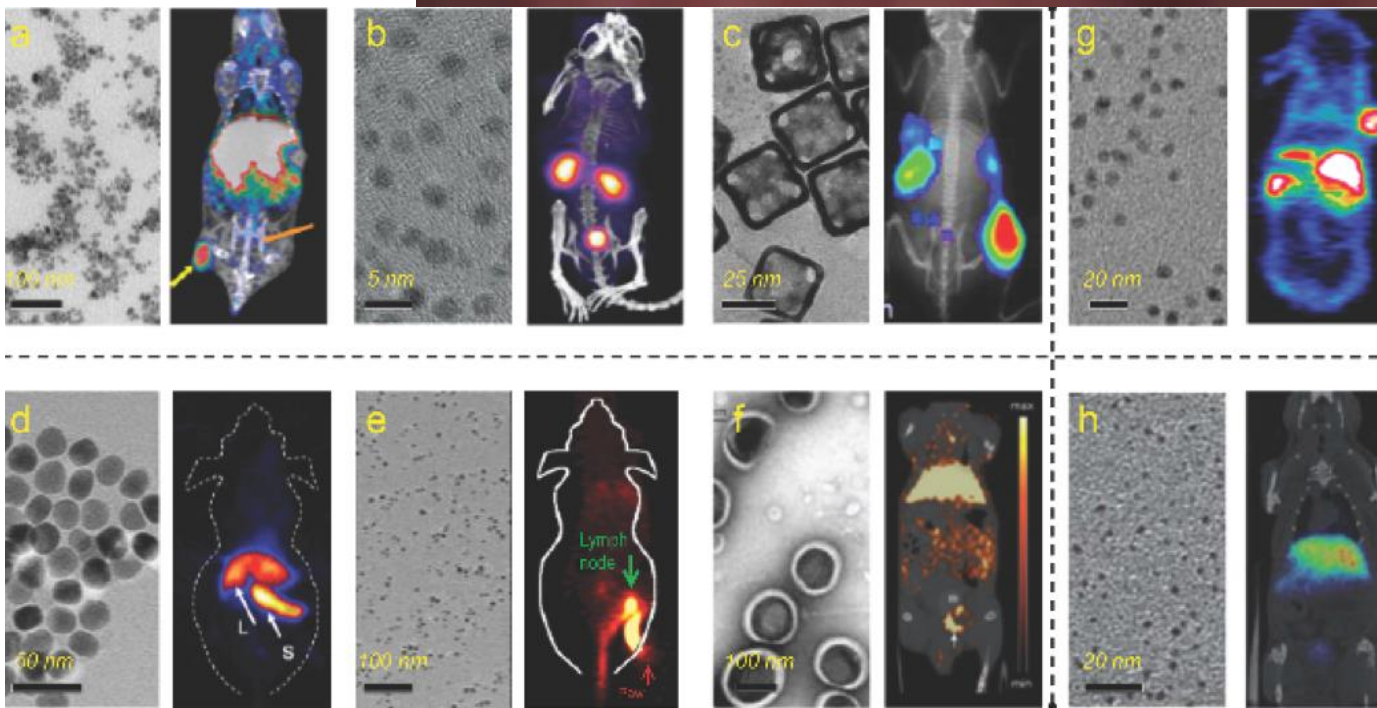
International workshop

"Positronium – from quantum physics to medical applications"

26-28 April 2023, Split

Zdenka Kuncic
School of Physics
and
Sydney Nano Institute,
Australia





THE UNIVERSITY OF SYDNEY

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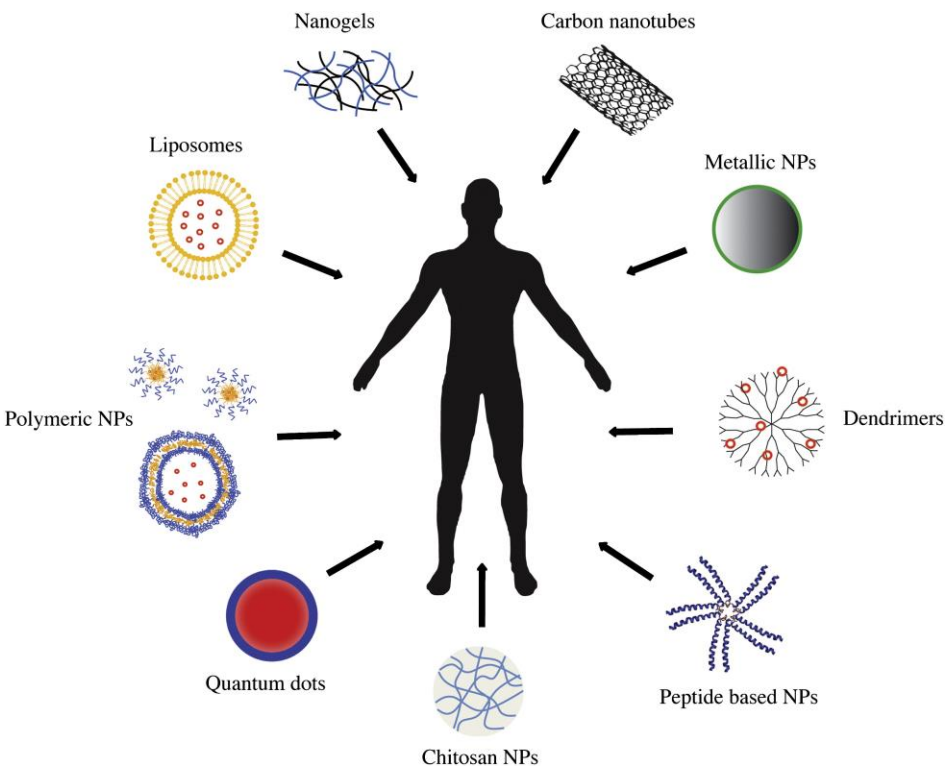
- Prof Matt Rosen, Athinoula A. Martinos Centre for Biomedical Imaging, MGH and Harvard Medical School

I. Introduction: nanotechnology for medicine

Geometric confinement on nanoscales induces unique physical properties:

1) Large surface area–to–volume ratio;
2) Mechanical, optical, electrical, magnetic behaviour;
3) Non-trivial quantum effects.

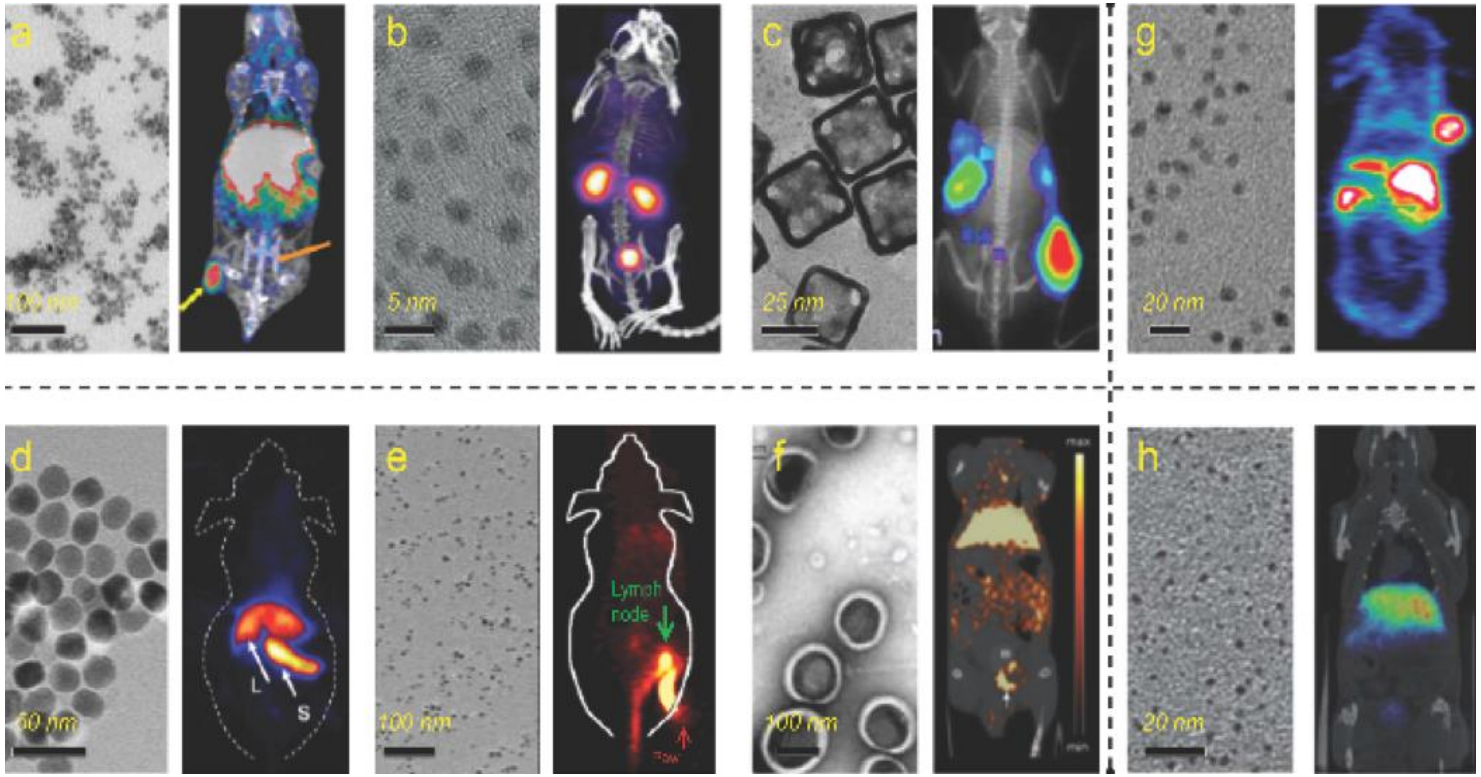


Challenge 1: *how can we harness these properties for novel theranostic applications?*

Challenge 2: *how can we maximise opportunities for clinical translation?*

I. Introduction: radio-nanomedicine

- Nanoparticles labelled with radio-isotopes for diagnostic imaging (e.g. PET, SPECT) and targeted radionuclide therapy
- Better selectivity/specificity, tumour cell targeting



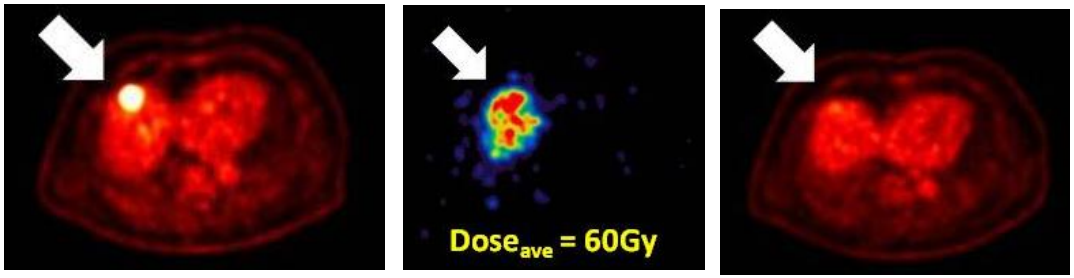
Goel et al. *Small* (2014)

I. Introduction: radio-nanomedicine

- Commonly used radio-isotopes:

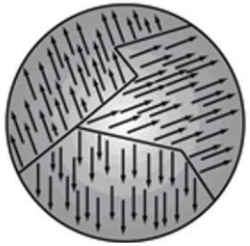
isotope	Particle type	Half-life	use
^{64}Cu	β^+	12.7 hrs	PET
^{89}Zr	β^+	3.3 days	PET
^{68}Ga	β^+	68 mins	PET
^{90}Y	β^+ and β^- (3.7 mm)	2.7 days	PET and therapy
^{99}Tc	γ	6.0 hrs	SPECT
^{177}Lu	γ and β^- (0.67 mm)	6.7 days	SPECT and therapy
^{223}Ra	α (42 μm)	11.4 days	therapy

Y-90 PET CRC mets in liver

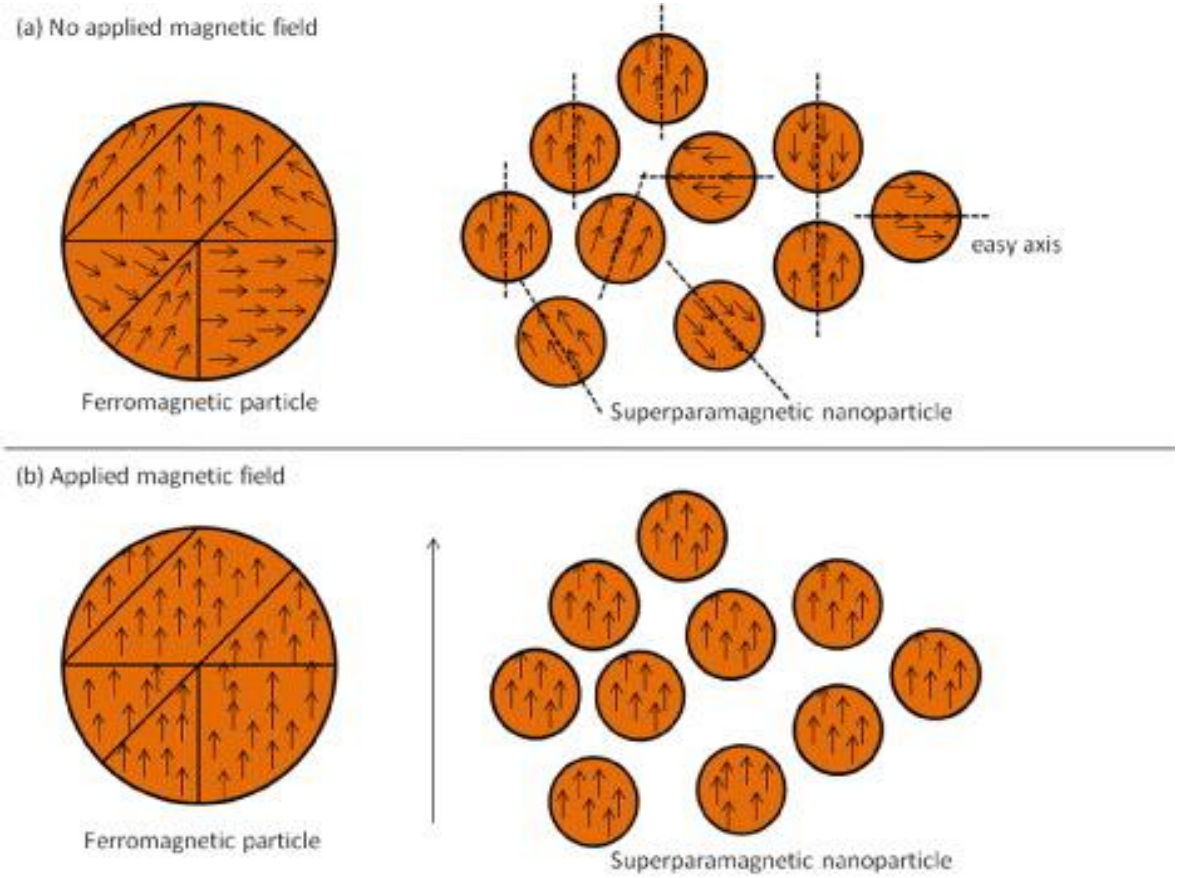


Willowson *et al.* (2017)

II. SPIONs for MRI

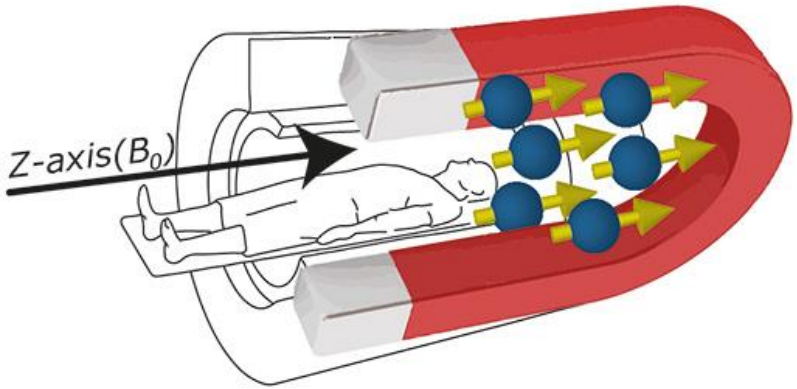


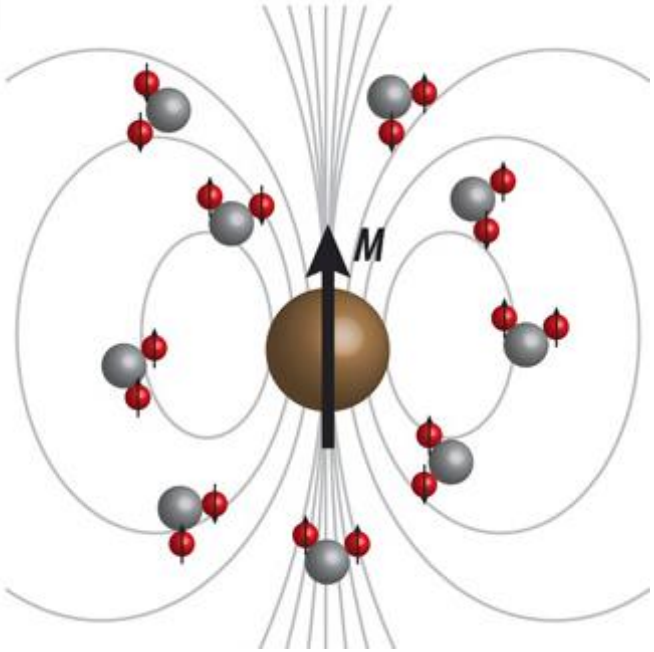
- **SPION** = **S**uper**P**aramagnetic **I**ron **O**xide **N**anoparticle
  - Strong magnetic susceptibility in an external B-field:



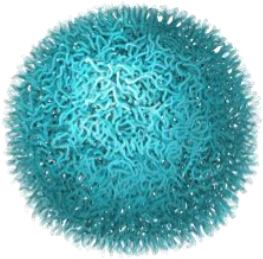
II. SPIONs for MRI

- In MRI (B_0 = 1-3 T), SPIONs interact with ^1H spins, shortening relaxation times, and inducing a strong nanoscale B-field inhomogeneity:





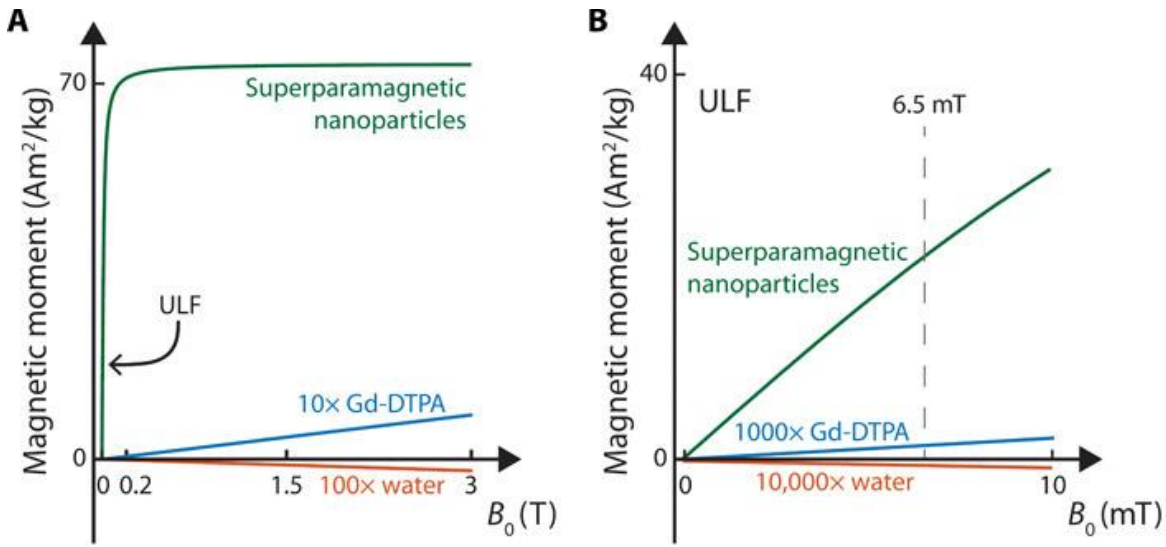
II. SPIONs for Ultra-Low-Field (mT) MRI



RESEARCH ARTICLE | APPLIED SCIENCES AND ENGINEERING

High-sensitivity in vivo contrast for ultra-low field magnetic resonance imaging using superparamagnetic iron oxide nanoparticles

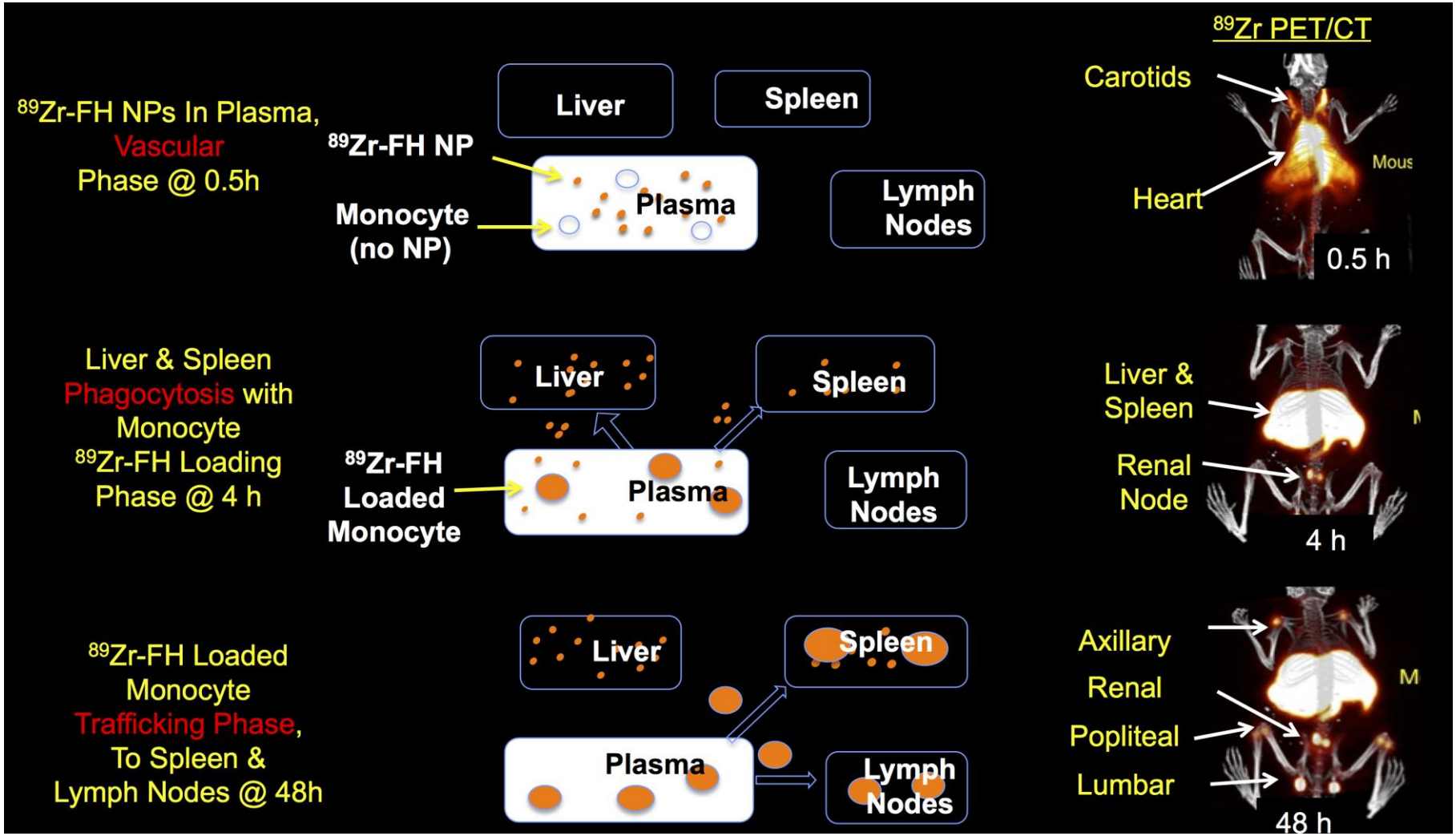
David E. J. Waddington[1,2,3,*], Thomas Boele[2,4], Richard Maschmeyer[1], Zdenka Kuncic[1,5] and Matthew S. Rosen[2,6,7]



Science Advances (2020)

HYPERFINE
Portable MR Imaging

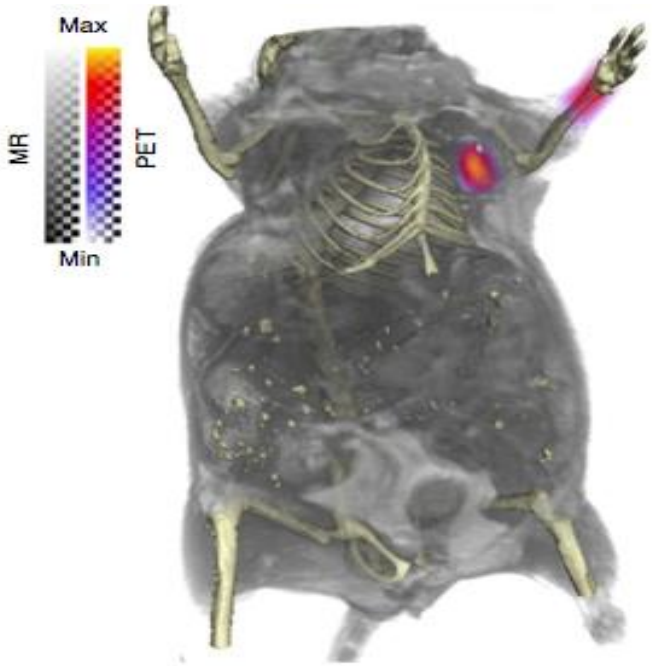
II. Detecting inflammation with SPIONs



Normandin et al. IJNM (2015)

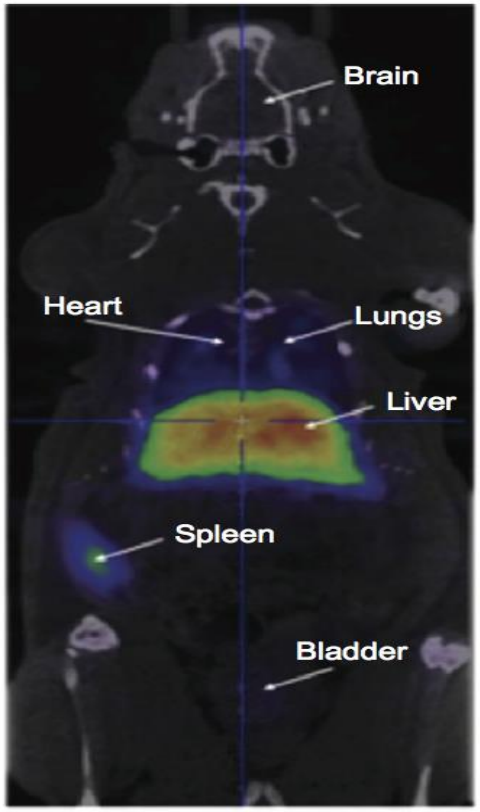
Radiolabelled SPIONs: PET-CT + MRI

^{89}Zr-SPIONs: invasion status of tumor draining lymph nodes critical for cancer staging



Thorek et al. *Nature Commun.* (2013)

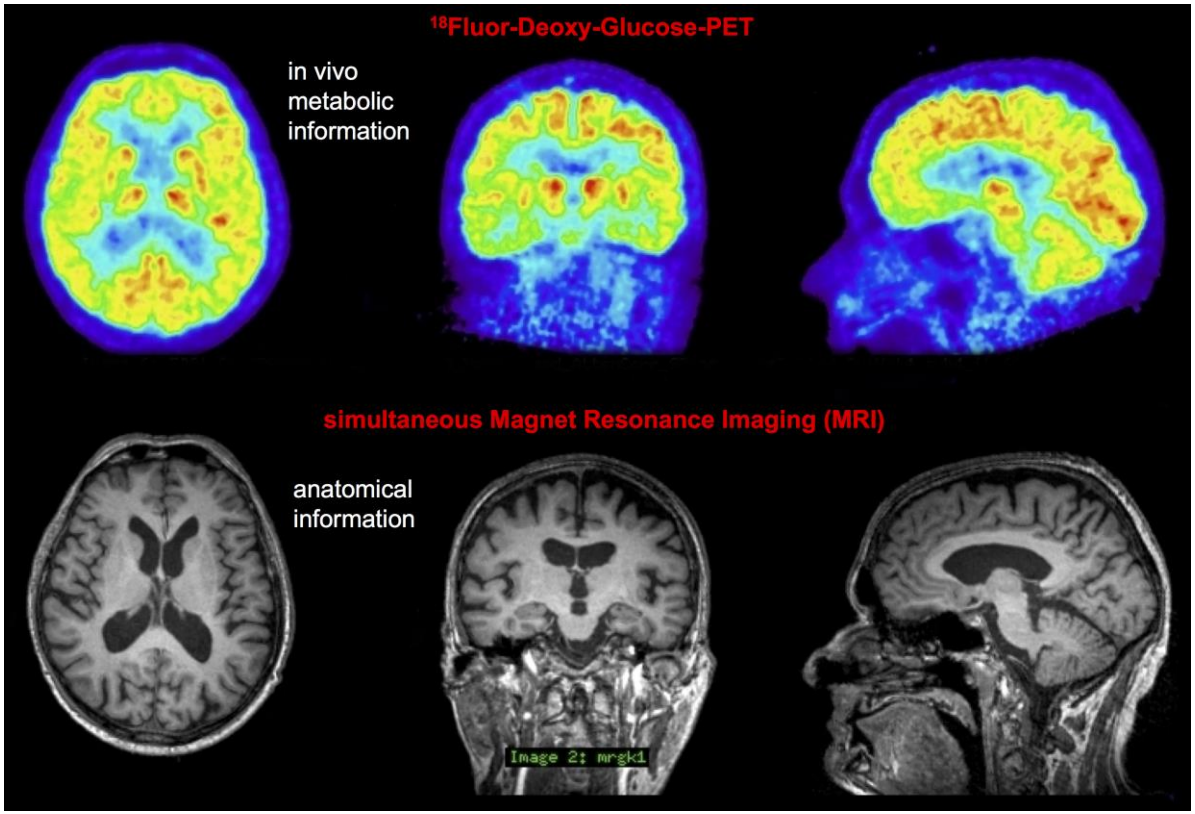
^{68}Ga-SPIONs: PET-CT biodistribution



Locatelli et al. *IJNM* (2012)

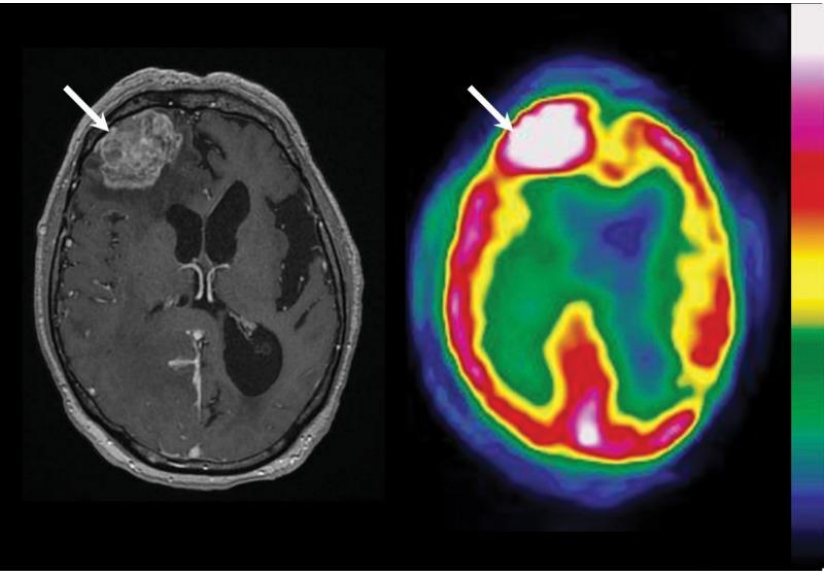
III. Radiolabelled SPIONs: PET and MRI brain imaging

- **PET** → High sensitivity biological imaging
- **MRI** → Superior soft-tissue contrast and spatial resolution

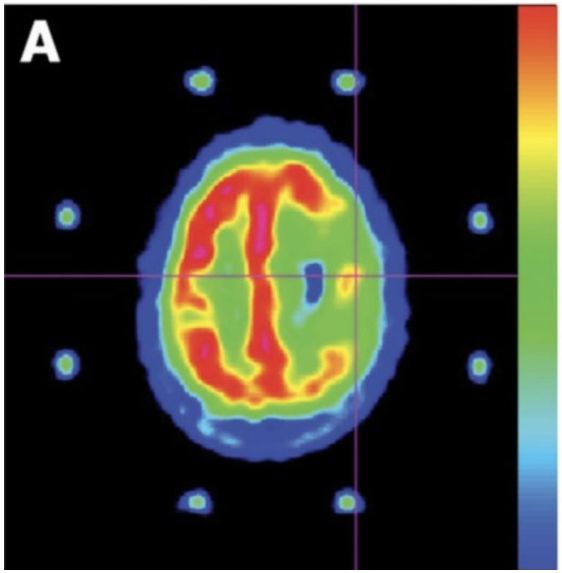


III. Radiolabelled SPIONs for glioblastoma

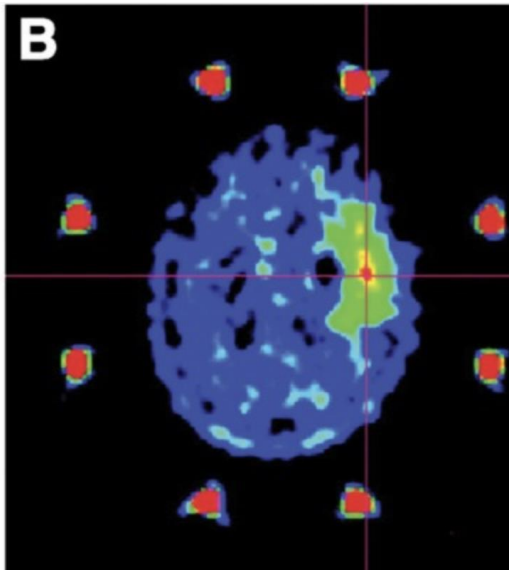
- MRI: limited glioma grading, treatment response
- ^{18}F-FDG-PET: insufficient differential uptake (non-targeting)
- amino acid PET tracers are better, but isotopes are short-lived



Gd-enhanced T1W ^{18}F-FDG PET



^{18}F-FDG PET

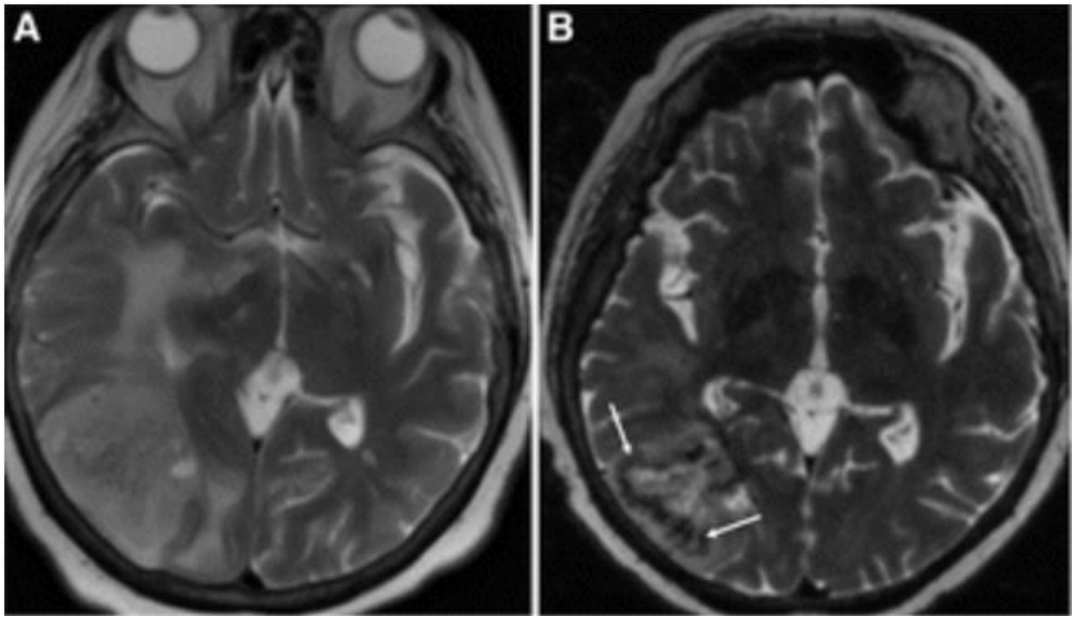


^{11}C-MET PET

Verger & Langdon 2017

III. SPIONs for glioblastoma

- SPIONs: can target neuroinflammation sites and provide diagnostic MRI tool for macrophages in gliomas – BUT only if it crosses blood-brain barrier (BBB)

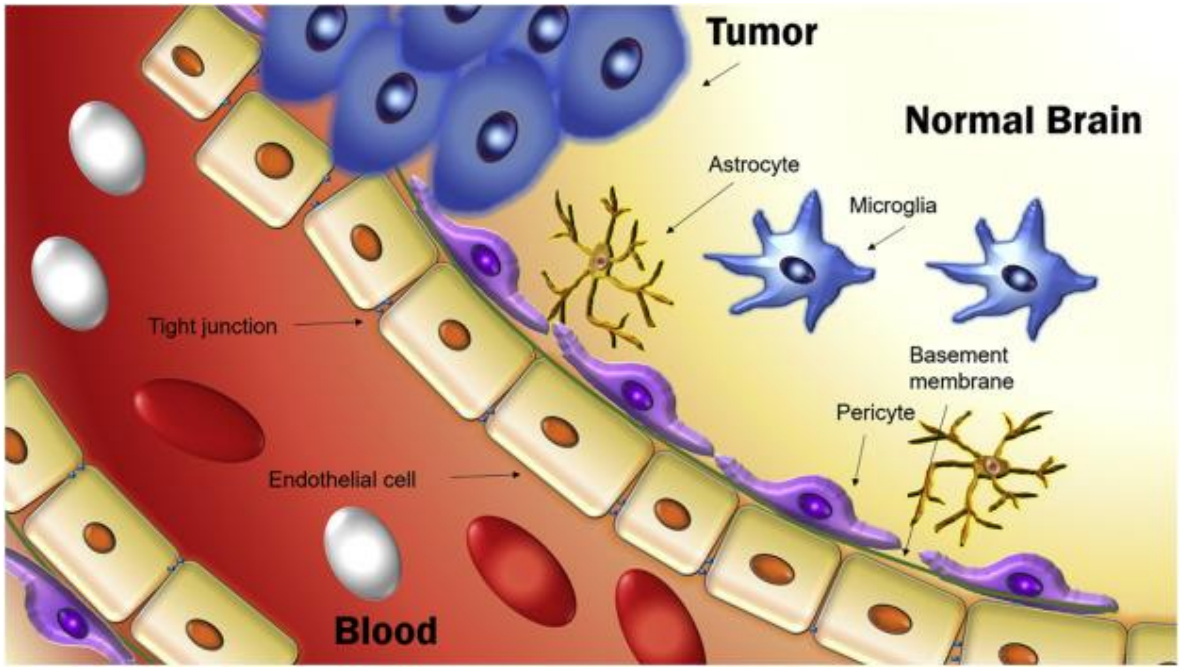


T2W MRI w/o SPIONs T2W MRI w SPIONs

Iv et al. 2018

III. SPIONs for glioblastoma

- BBB remains intact in regions of tumour infiltration → *inaccessible to MRI & PET diagnostic agents and treatments*

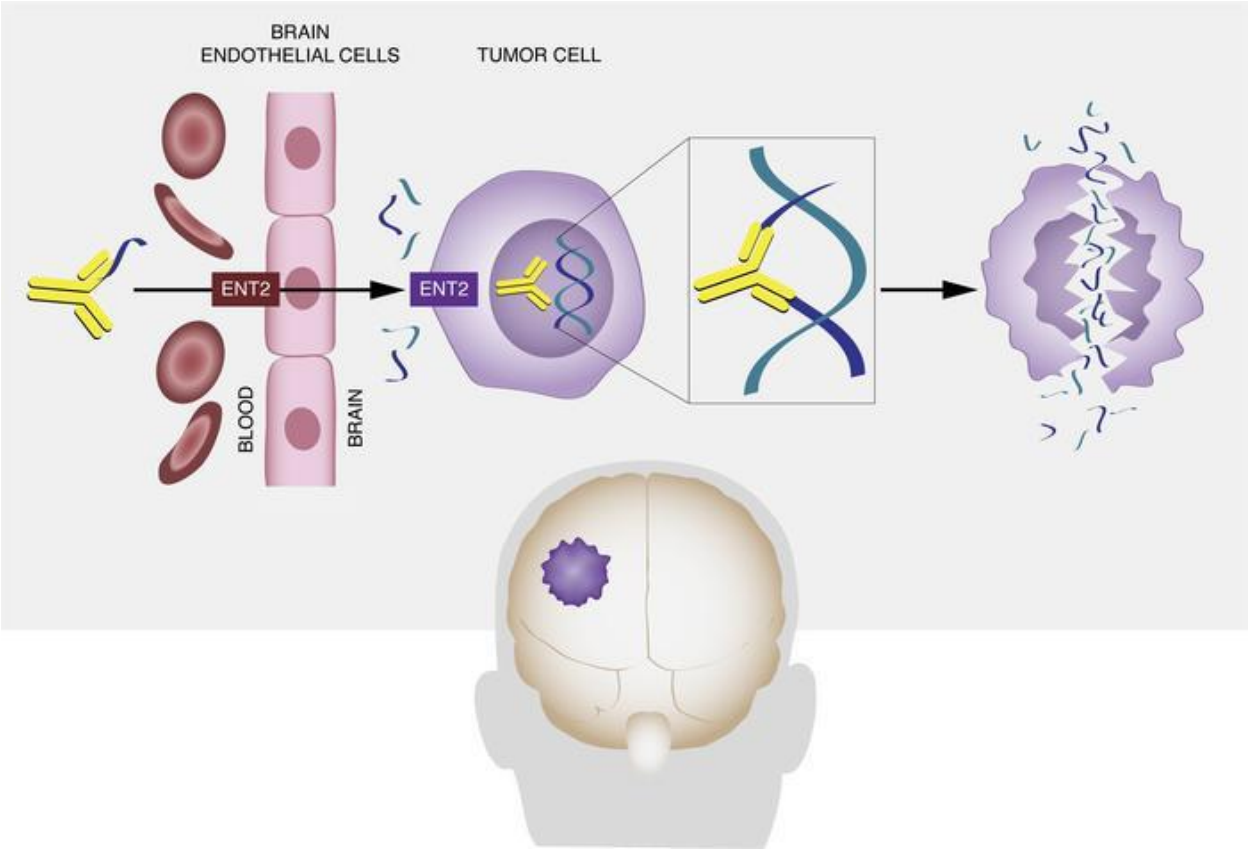


Israel et al. 2020

III. SPIONs for GBM (in progress)

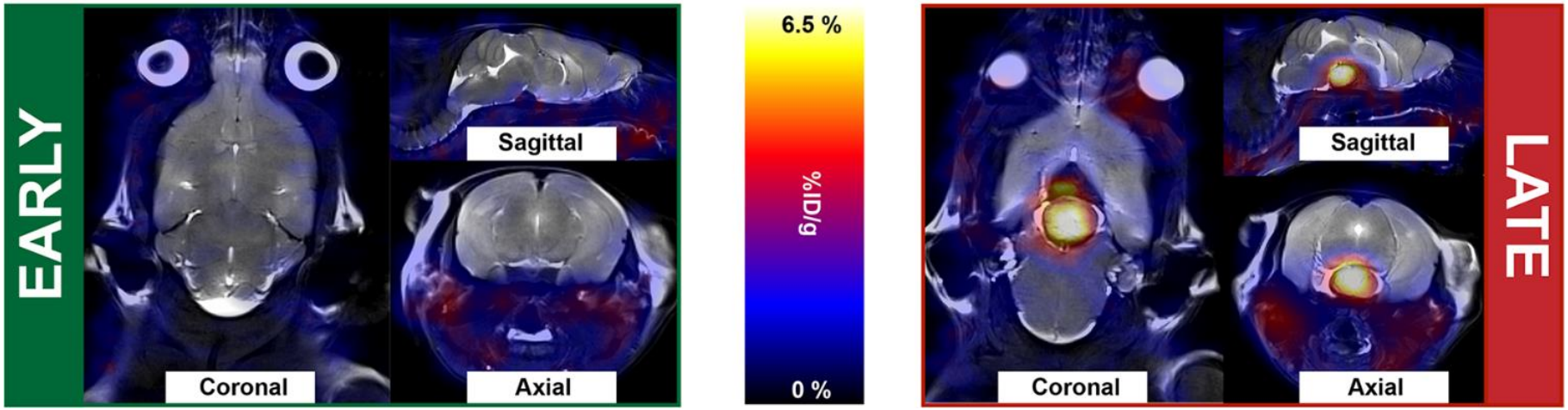
- Hypothesis: SPIONs functionalised with novel DNA-damaging antibodies can cross intact BBB, accumulate in infiltrative GBM tissue, and enhance contrast in MRI scans

Rattry et al. *JCI Insight* 2021
ENT2 facilitates brain endothelial cell penetration and blood- brain barrier transport by a tumor-targeting anti-DNA autoantibody



III. Radiolabelled SPIONs for GBM (next study)

- SPIONs radiolabelled with a PET tracer can enable physiological monitoring of GBM response to anti-DNA



Gd-enhanced T1W MRI + PET imaging of ^{64}Cu-labelled NPs in GBM mouse model (Houston et al. 2020)

- SPIONs labelled with a targeting radiotherapeutic (Pb-212) can enhance anti-DNA action, which sensitizes tumour cells to radiation

IV. Towards MRI and PET-MRI nano-theranostics

nature > scientific reports > articles > article

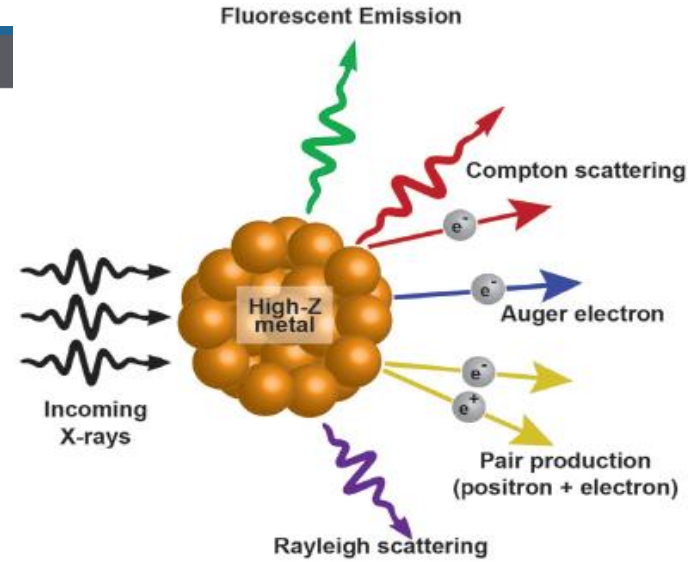
MENU

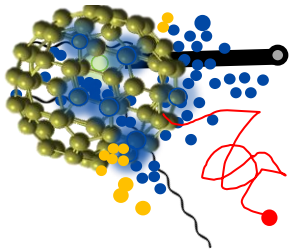
SCIENTIFIC REPORTS

Article | Open Access | Published: 04 October 2019

Radio-enhancement effects by radiolabeled nanoparticles

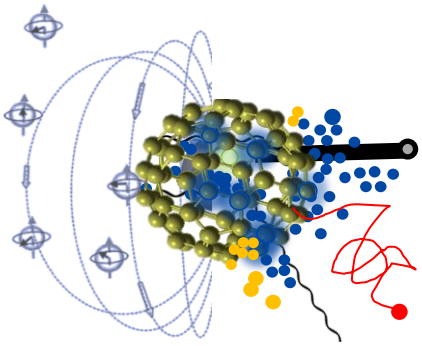
Yaser Hadi Gholami, Richard Maschmeyer & Zdenka Kuncic





Atomic dose enhancement effect in radionuclide therapy, up to 20%

^{212}Pb (α)
^{213}Bi (α, β^-, γ)
^{177}Lu (β^-, γ, Auger)
^{89}Zr (β^+, γ, Auger)
^{67}Cu (β^-, γ, Auger)
^{64}Cu (β^+, β^-, γ, Auger)
^{90}Y (β^-)



Magnetic dose enhancement in radionuclide therapy, up to ~ 60%

magnetised SPION

New Australian industry - university partnership funding! (2023-27)

Australian Research Centre
Research Hub for **A**dvanced **M**anufacture of **T**argeted **R**adiopharmaceuticals

UQ's new hub to develop manufacturing of radiopharmaceuticals

MIGNON D'SOUZA
September 19, 2022, 4:36 pm