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Contrast agent for early diagnostics and monitoring of progression of liver cancer.

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SEVENTH FRAMEWORK PROGRAMME

Patient need

HCC

- the most frequently diagnosed type of liver cancer
- the second most common liver lesion
- Size and staging

Currently	With new type of targeted CA
Not possible to mix different CA	All exams (US+PET+MRI+US guided biopsy) made in a single day
Diagnostic tests made in different days	Immediate response
Not possible to detect lesions <1 cm	Attach ligands binding to HCCs
	Improve specificity of the diagnosis
	Detect sub-cm lesions
	Long term stability
	Narrow size destribution

Business opportunity & Goal

According to the report by Global Industry Analysts:

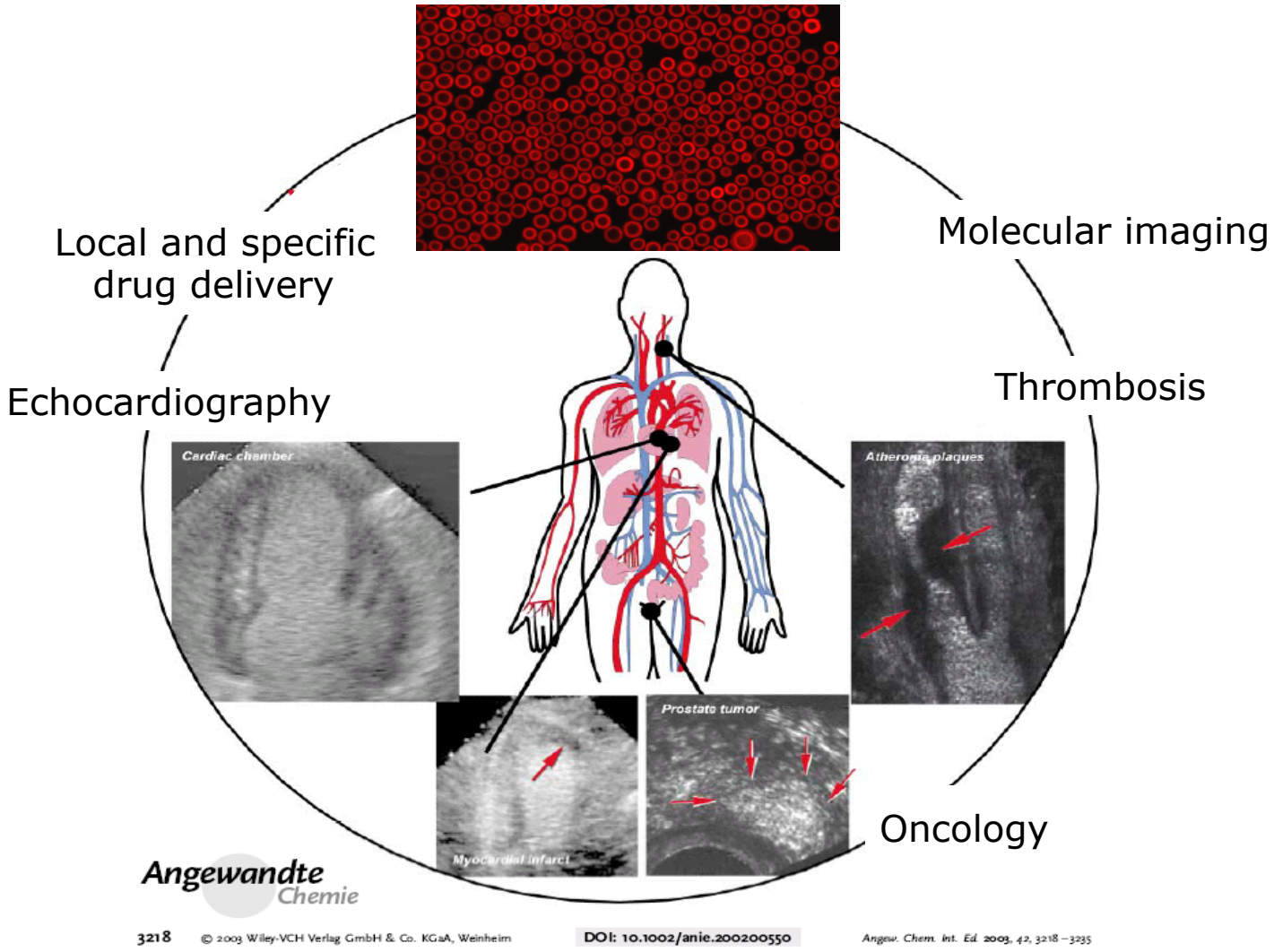
- Medical device market (336 billion euro in 2008) is expected to grow 9% annually.
- World imaging agents market is assumed to exceed 11 billion euro by 2015.
- The market is driven by increasing amount of diagnostic examinations and broadening areas of applications.
- The US is still the largest market for contrast agents worldwide
- Developing countries, China and India, are considered to play major role in the growth of the contrast agent market.

HCC is widely diagnosed in Asia, the current project can meet healthcare needs with market possibilities and trends.

The goal of the project is to develop targeted multimodal contrast agent
that supports several imaging approaches,
with special reference to ultrasound, MRI and SPECT
for
early diagnostics and monitoring of progression of liver cancer (HCC).

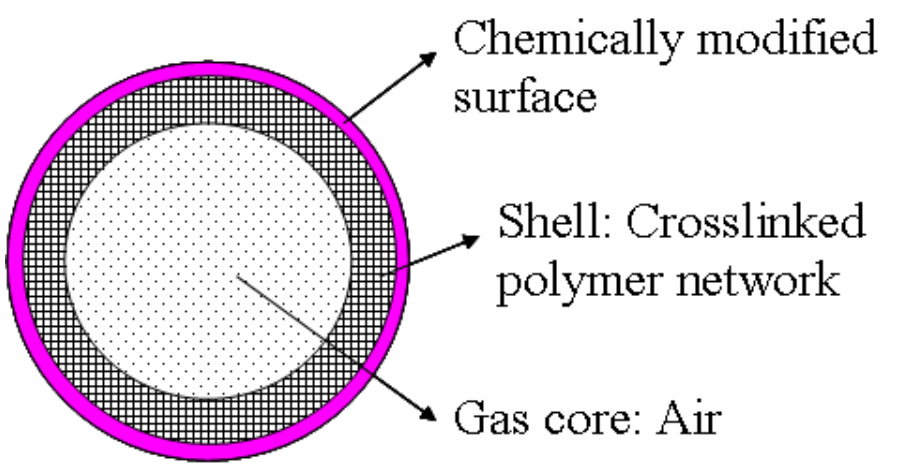
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Intended final product



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Intended final product



Local or specific drug delivery

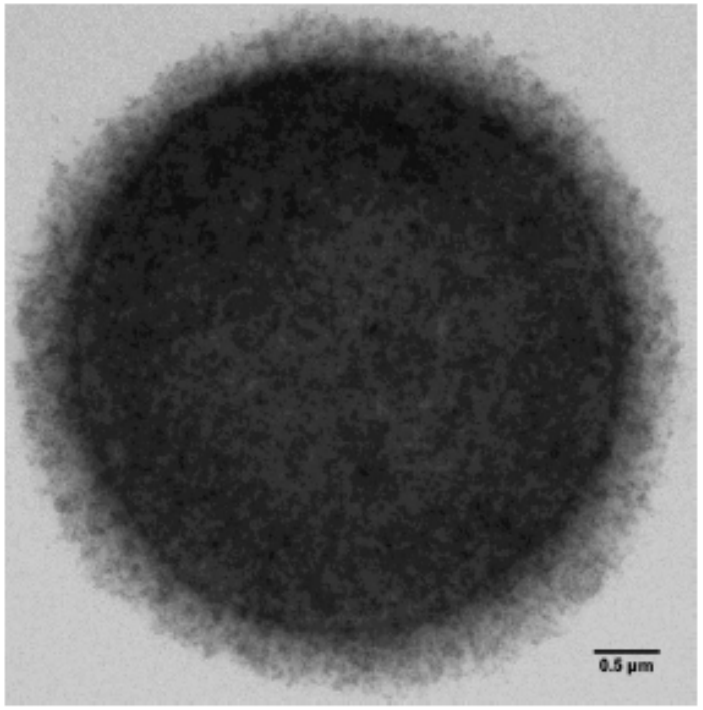
Ligand binding

Average Diameter (μm)	Average Shell Thickness (μm)
3.0 ± 0.5	0.4 ± 0.1

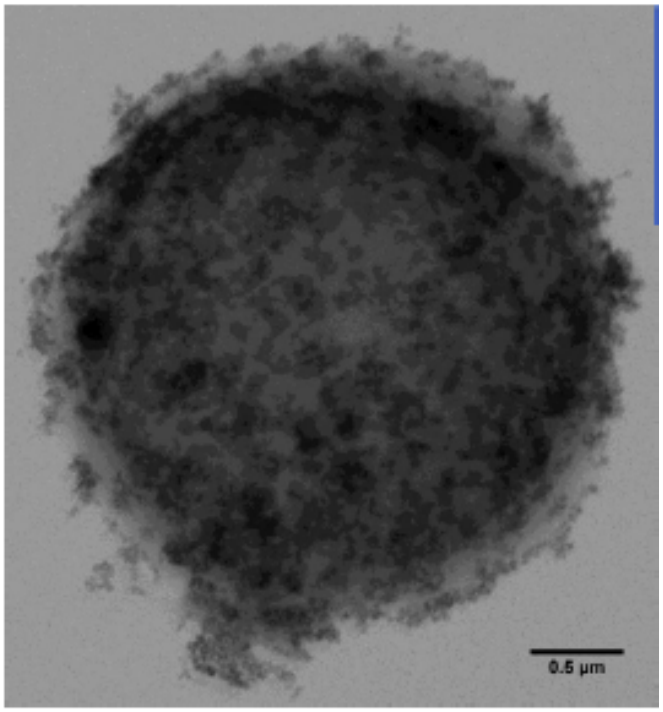
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Structural Characterization

SuperparamagneticIron Oxide Nanoparticles(SPIONs)
introduce magnetic properties



SPIONs added **during** fabrication
Homogenous distribution

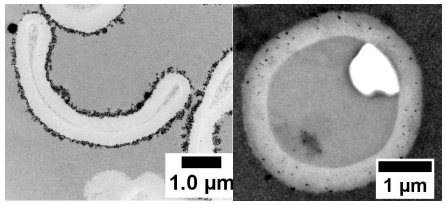


SPIONs added **after** fabrication
Less homogenous distribution

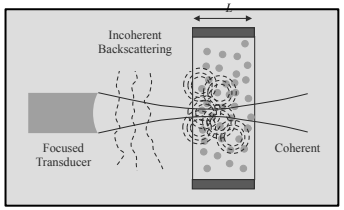
From characterization to *in vivo* imaging

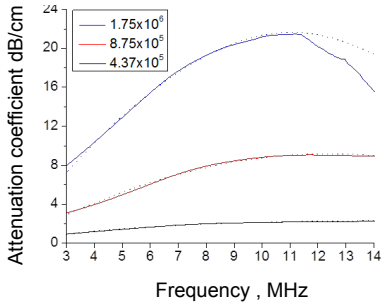
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TEM

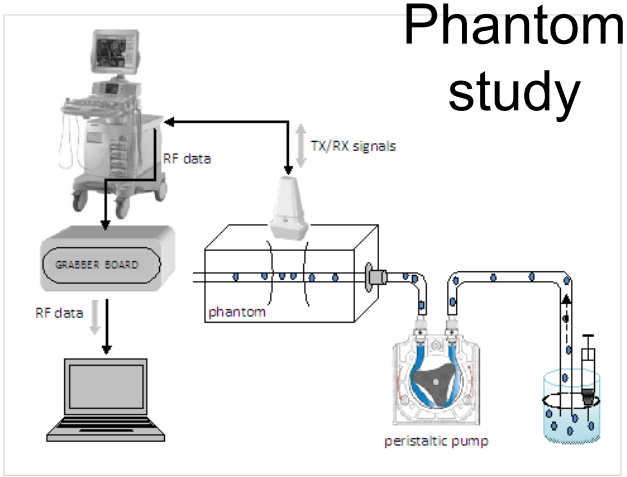


US

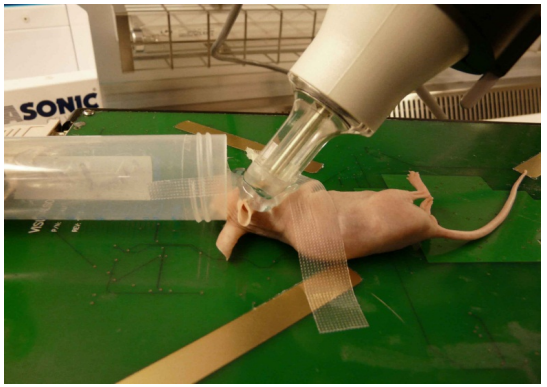


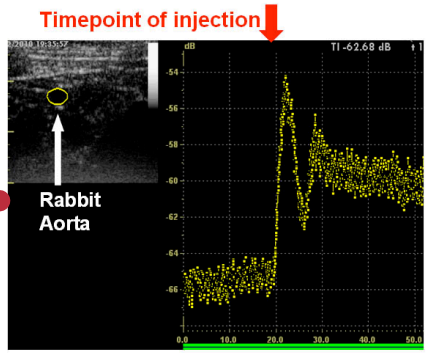


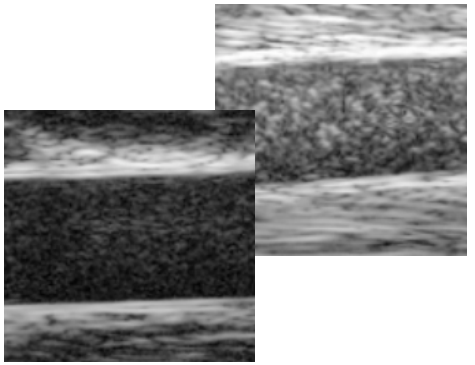
Phantom study











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Intended final product

Air filled MBs stabilized by a biocompatible PVA shell

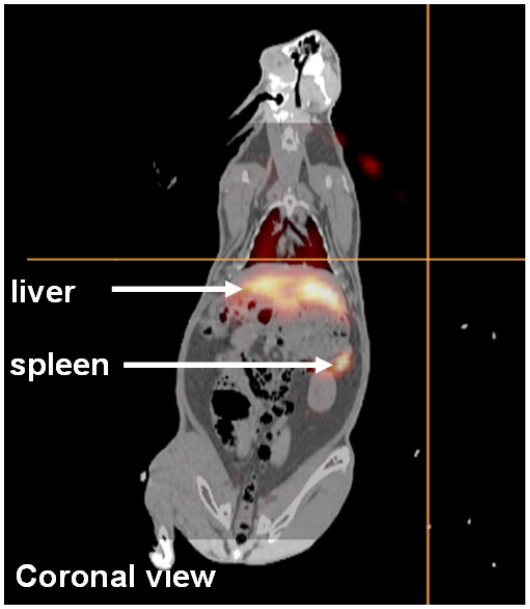
- Gas core => ultrasound scattering
- SPIONs => MRI
- Tc99m => SPECT
- Ligand => molecular imaging

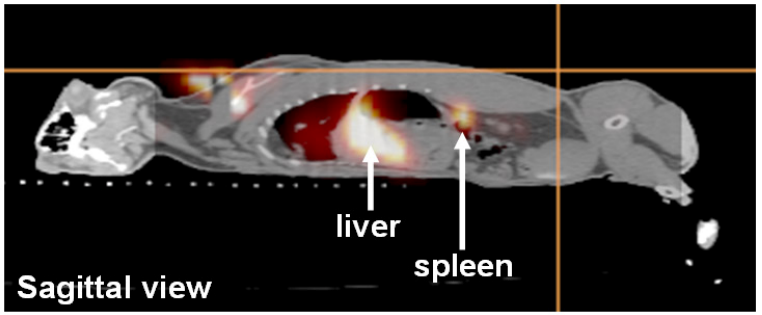
Multimodal CA can be used for cardiac and vascular applications:

- inflammation in vascular wall
- ischemia
- thrombotic events
- evaluation of angiogenesis

HCC has been selected for proof-of-concept purpose.

Contrast enhancement SPECT
^{99m}Tc-labelled chitosan coated MB in rabbit

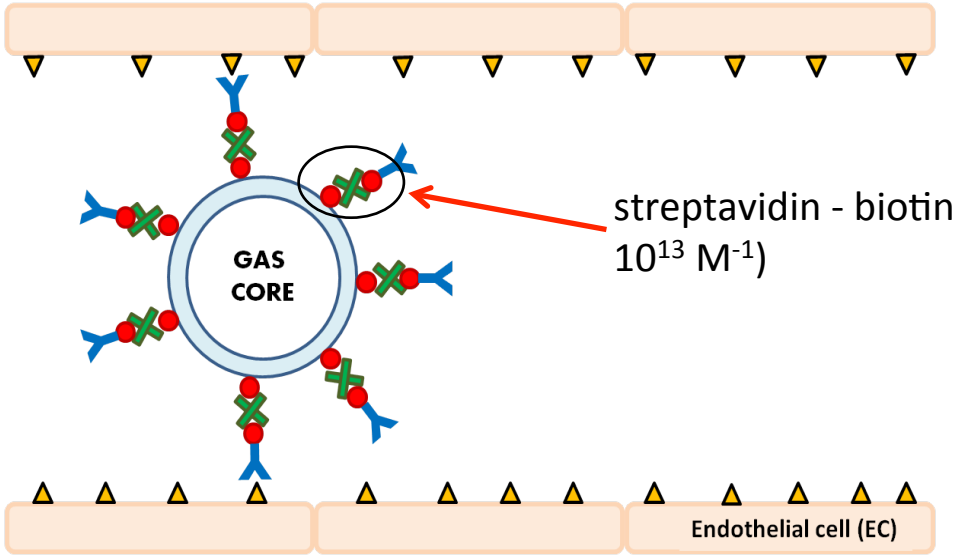




SPECT/CT imaging of rabbit over 37 min post injection of 25 MBq ^{99m}Tc labelled chitosan coated MB in 2.5 ml injection volume (ear vein) using a Siemens Symbia T16 SPECT-CT.

- Accumulation of MB could be observed in rabbit liver and spleen
- Little activity can be seen in the lung
- No activity could be found in the bladder

Synthesis and surface modifications of MB



Y Antibody (anti P-selectin, anti-ICAM-1, anti-VCAM-1)

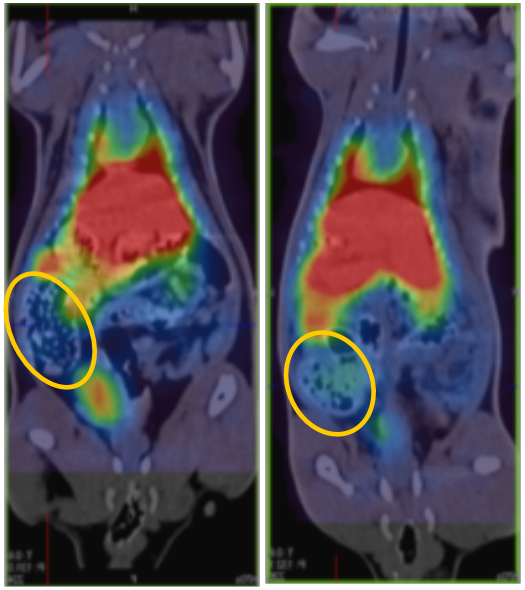
Antigen (P-selectin, ICAM-1, VCAM-1)

Biotin

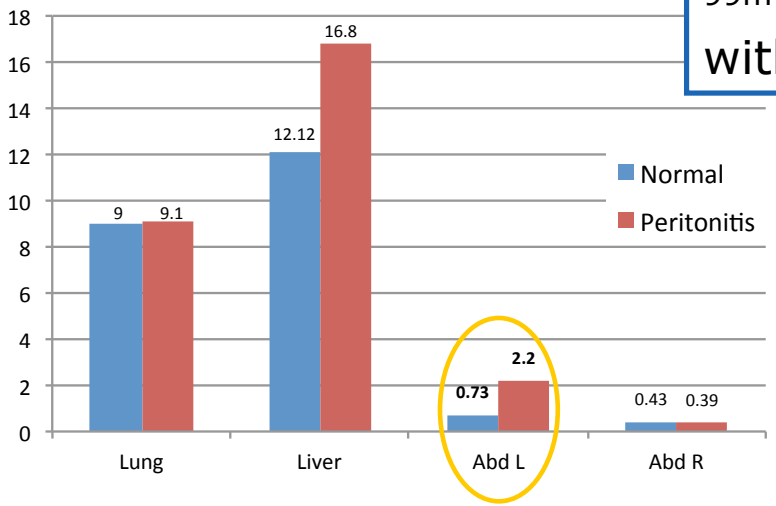
Streptavidin

Imaging of inflammation with targeted MBs SPECT/CT:

Normal rat



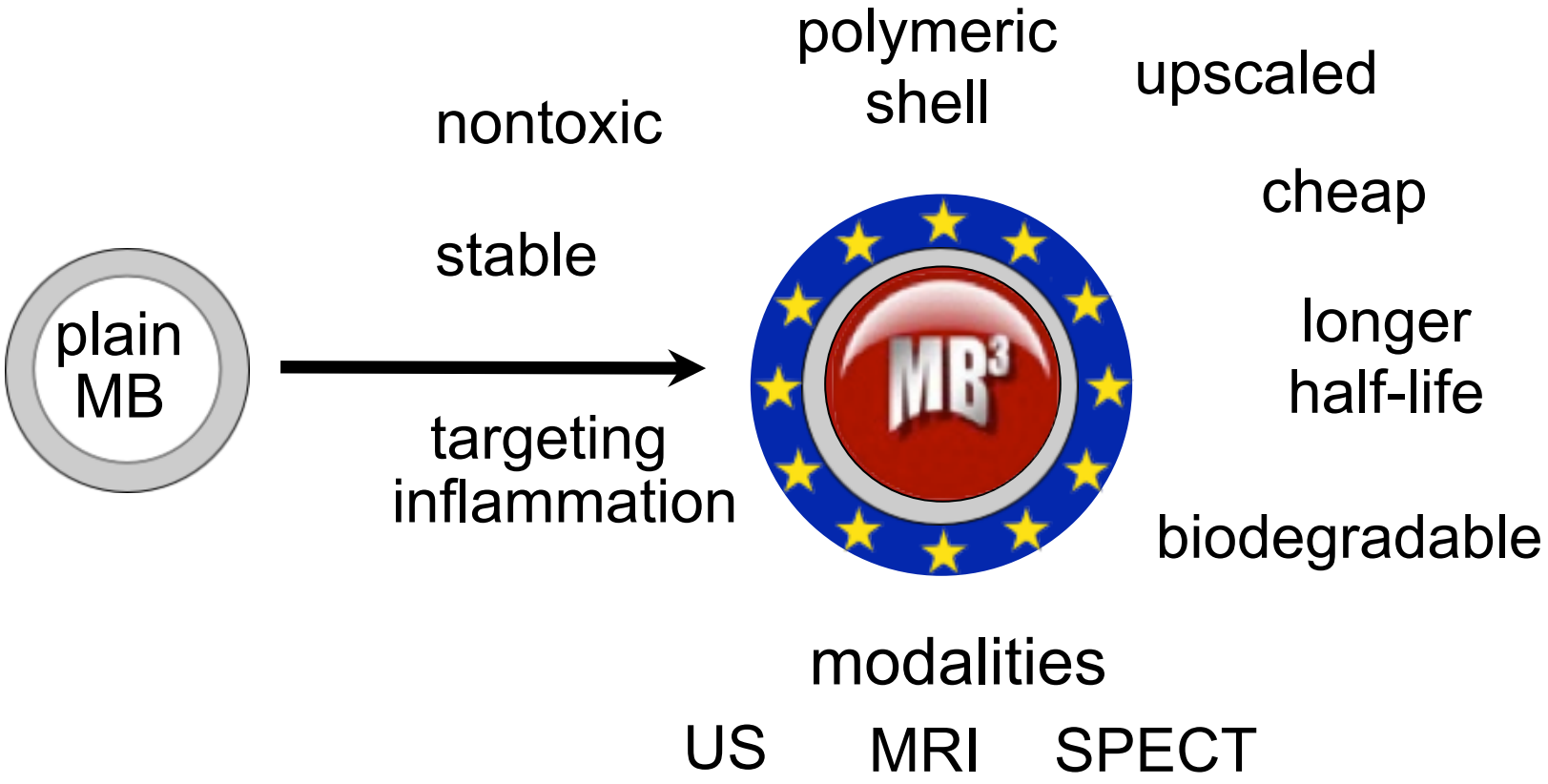
Rat with left sided peritonitis



^{99m}Tc-labelled Type C MBs with *anti*-ICAM-1 (relative counts)

Inflamed side shows **3** times as high relative counts compared to healthy animal

Why polyvinyl alcohol MBs ?





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Thank you!