New Perspectives in Magnetic Resonance Molecular Imaging

Carmen Burtea, Sophie Laurent, Luce Vander Elst, Robert N Muller
Department of Organic and Biomedical Chemistry, NMR and Molecular Imaging Laboratory
University of Mons-Hainaut, 24 Avenue du Champ de Mars, B-7000 Mons, Belgium
Robert.Muller@umh.ac.be

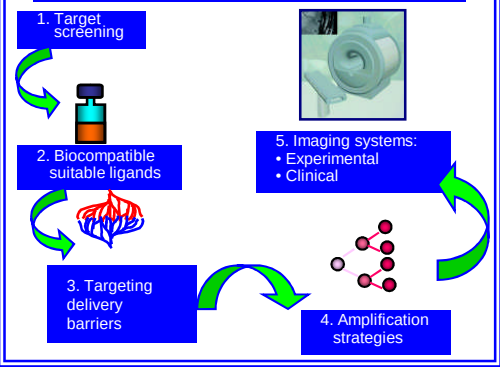
INTRODUCTION

Molecular imaging = characterization and measurement of biologic processes at the cellular and molecular level (*Weissleder R, Mahmood U, Molecular imaging, Radiology, 219, 2001, 316-333*).

Criteria to image specific molecules in vivo (Figure 1):

- ⇨ availability and reasonable pharmacodynamics
- ⇨ ability to overcome biologic delivery barriers (vascular, interstitial, cell membrane)
- ⇨ use of amplification strategies (chemical or biological)
- ⇨ availability of sensitive, fast, high-resolution imaging techniques

Figure 1. Criteria to image specific molecules in vivo.



Molecular contrast agents for MRI

Conventionally accepted:

⇨ tissue concentration of receptors (moles/g): 10^{-9} - 10^{-13} M

⇨ minimum concentration for visibility by MRI:

- 6^{th} generation dendrimer with max relaxivity (moles/g): 5.2 x 10^{-12}
- superparamagnetic iron oxide (moles of particles/g): 1.6 x 10^{-11}

MR contrast agents as biochemical reporters:

- enzyme activated
- calcium activated
- pH-activated
- pO_2 activated
- protein bound
- T_2 activated
- chemical exchange saturation transfer

MRI applications of molecular contrast agents

In vivo applications:

⇨ diagnosis of a particular pathology:

- atherosclerosis (cathepsin B, fibrin)
- inflammation (E-selectin)
- cancer (angiogenesis)

⇨ monitoring of gene therapy and chemotherapy:

- detection of apoptosis
- gene expression as a reporter of gene therapy

In vitro applications: :

- contrast agents as magnetic relaxation switches (sensing of molecular interactions)
- high throughput screening

MR molecular contrast agents developed by our team

In vitro applications:

⇨ **C-MALISA:** application of C-ELISA for MRI

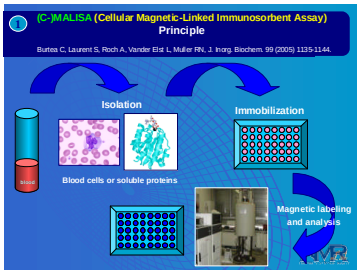
⇨ **Streptavidin-biotin** interaction as an amplification system:

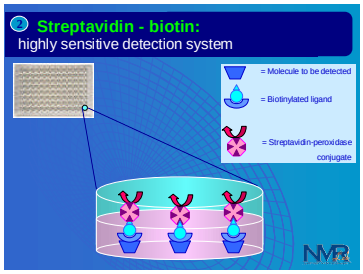
- MR relaxometry
- MALISA

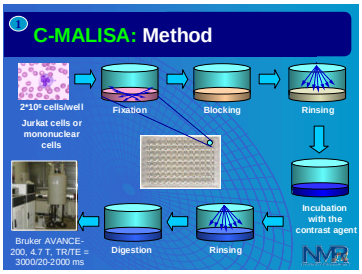
In vivo applications:

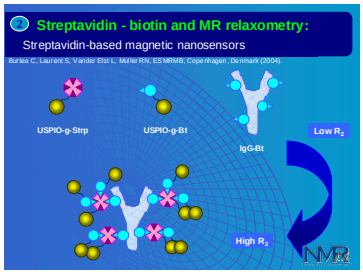
⇨ **Molecular targeting of atherosclerotic plaque** with a small molecular weight non-peptidic **RGD mimetic** grafted to:

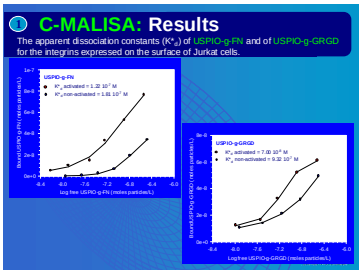
- USPIO
- Gd-DTPA

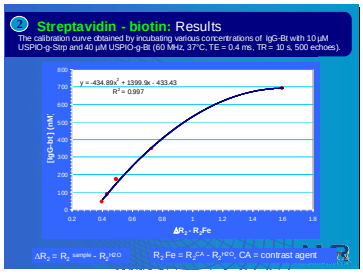


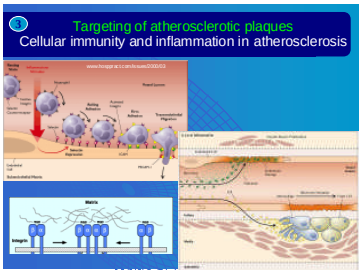


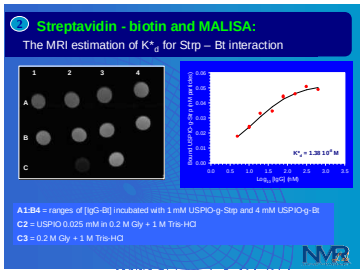


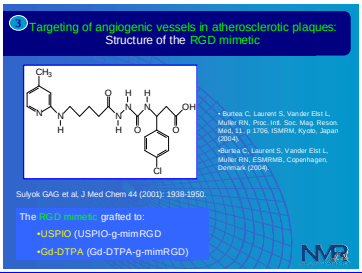


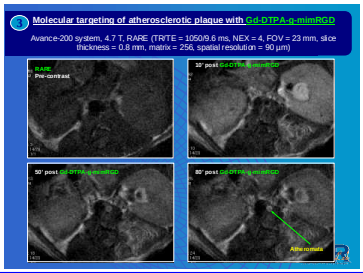












CONCLUSIONS

C-MALISA:

- ⇨ high-throughput setting
- ⇨ allows the accurate detection and quantification of the cell surface receptors
- ⇨ offers a second application for the contrast agents

Streptavidin-based magnetic nanosensors (MRI and relaxometry):

- ⇨ highly sensitive to IgG-Bt concentrations in the nanomolar range
- ⇨ can be used to sense various molecular interactions

MRI detection of vulnerable atherosclerotic plaques:

- ⇨ mimRGD-based contrast agent contributes to the high-resolution *in vivo* molecular imaging and visualisation of unstable atherosclerotic lesions

ACKNOWLEDGEMENTS

This work was financially supported by the ARC program of the French Community of Belgium (research contract no. 00-05/258), by the DGTRE (Region of Wallonia, NOMADE project), and by the project of co-operation CNRS/CGRI-FNRS (research contract no. 12/02/2003-022-5, ref. PV/EJ/FR/1522/ng dossier 03/007).