Chemistry for Magnetic Resonance Imaging

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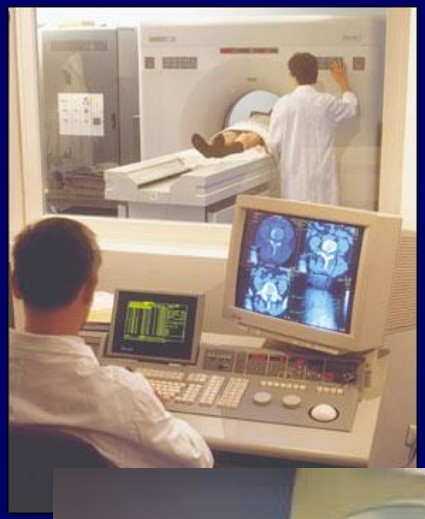
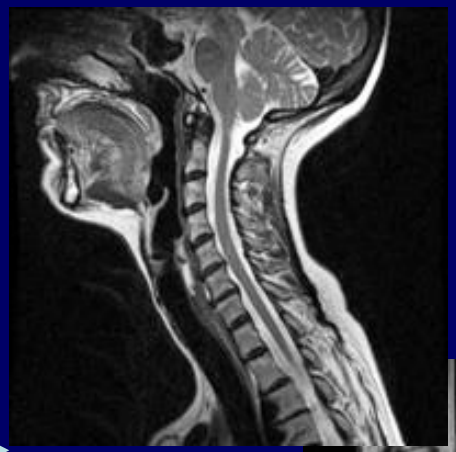
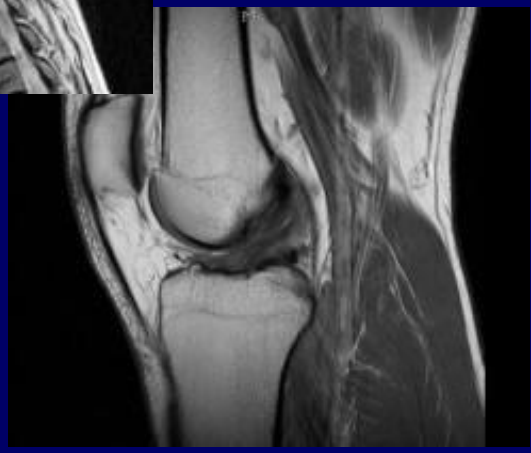
MRI

Based on magnetic resonance of water protons



B = 0.5 – 3.0 Tesla





3-dimensional image

excellent resolution

no depth limitation

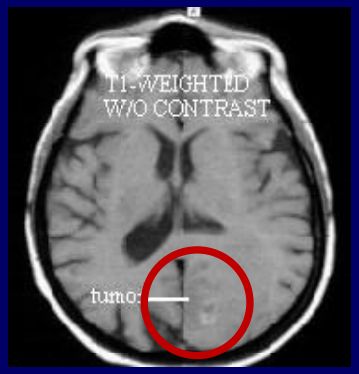
though low sensitivity

MRI contrast agents:

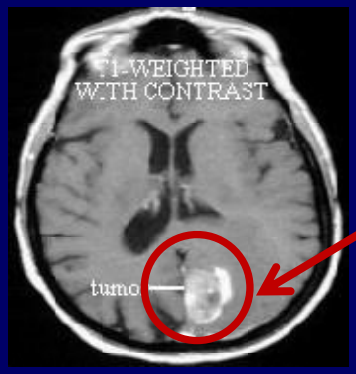
Injected into patients to improve image contrast

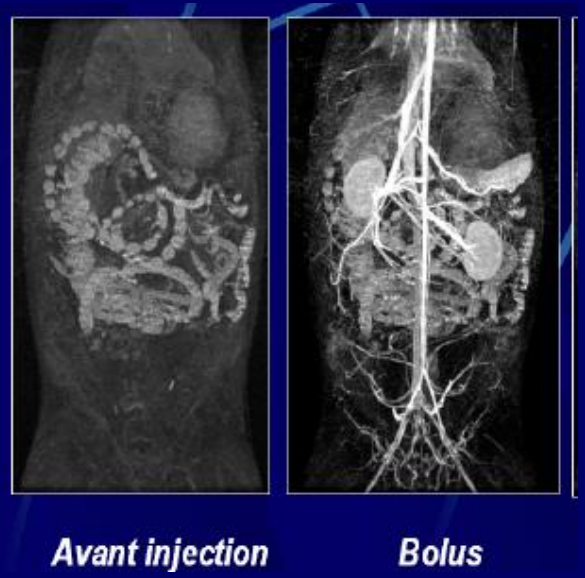
Reduce the relaxation times of water protons

Without CA



With CA

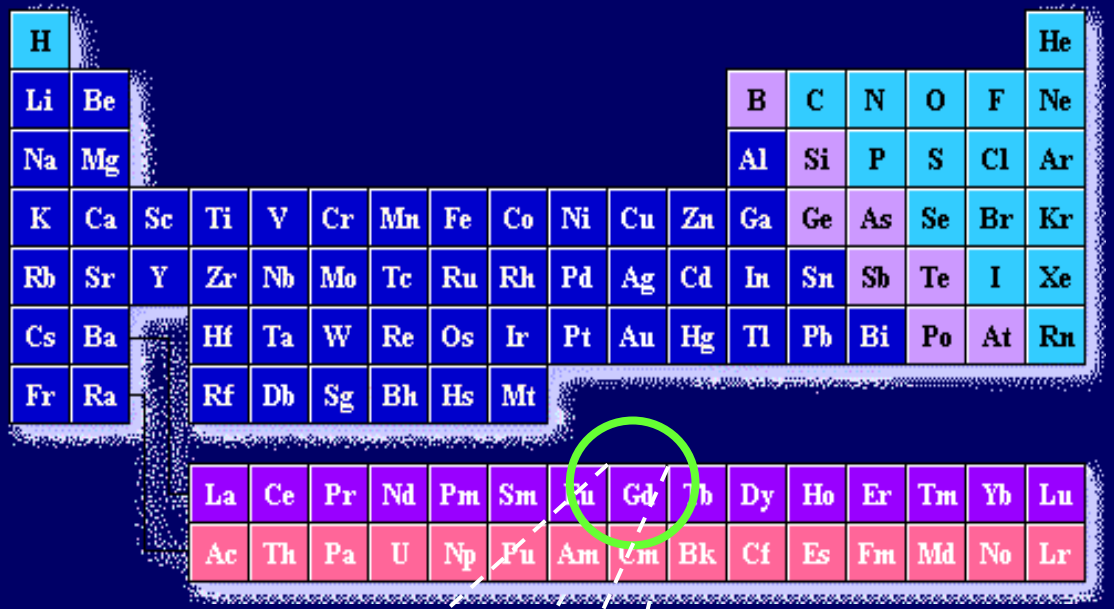


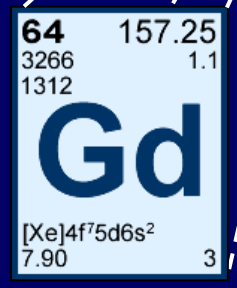


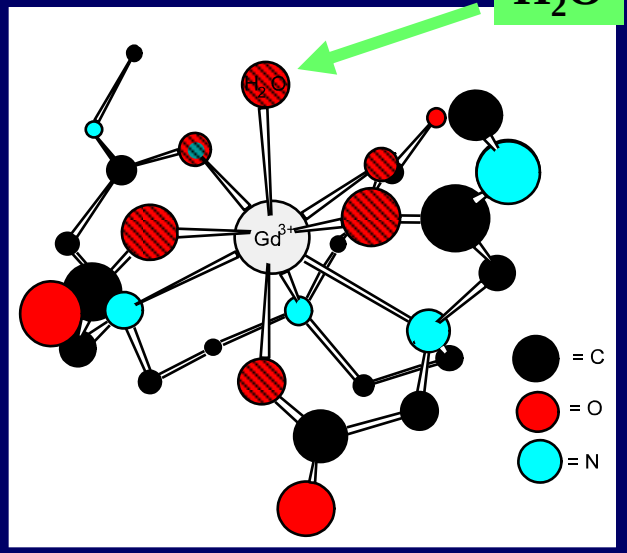
~40 % of clinical MRI examinations

MRI contrast agents:

➡ Paramagnetic metal ion







lanthanides

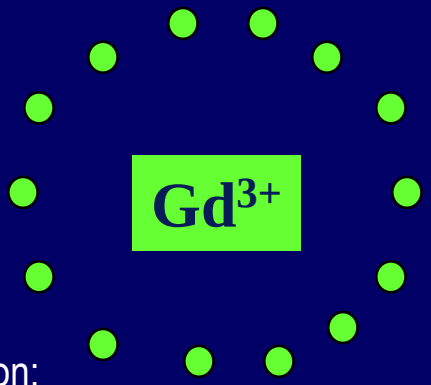
GADOLINIUM

How to make them safer?

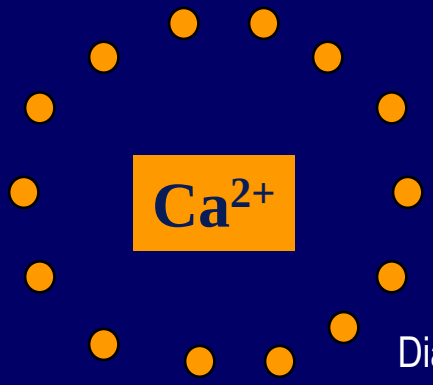
How to increase MRI efficiency ?

How to make them more specific?

Gd^{3+} alone would be toxic…



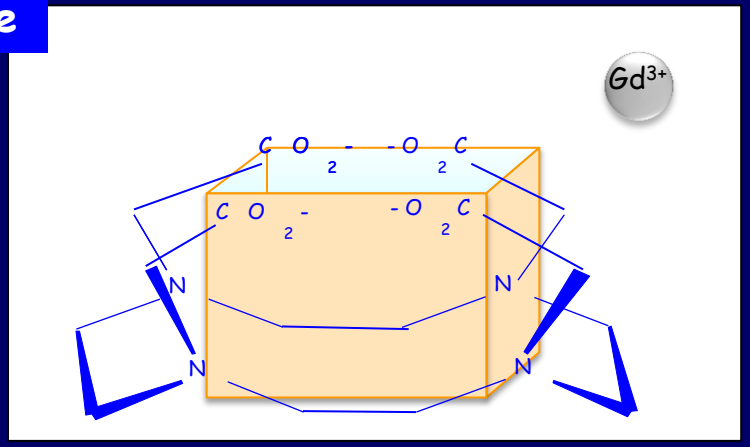
Diameter of the ion:
1.02 A



Diameter of the ion :
0.99 A

would replace Ca^{2+} in the biological medium

Has to be wrapped up in a non-toxic molecule



- How strong is the interaction ?
- How fast the metal can eventually come out ?
- Could we replace Gd^{3+} with the biogenic metal ion Mn^{2+}?

Make it specific: molecular imaging

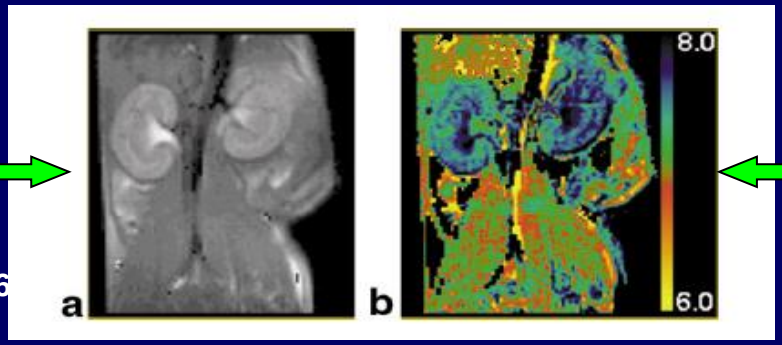
New applications for refined analysis:

in vivo visualisation of molecules or molecular processes at the cellular level, ***signatures of a given pathology***

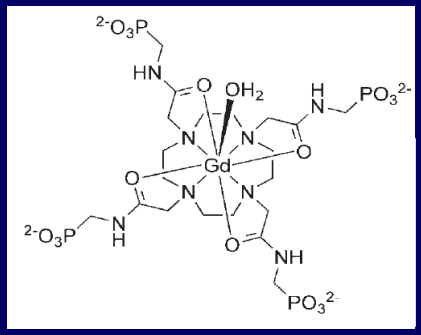
- targeting to receptors or other biomarkers
- reporting on physical-chemical parameters of tissues (pH, pO_2, T, concentration of metabolites-, ions etc.) – responsive imaging

Smart MRI probes: capable of giving a specific MRI response depending on the tissue parameter to be detected.

Anatomical image



pH map

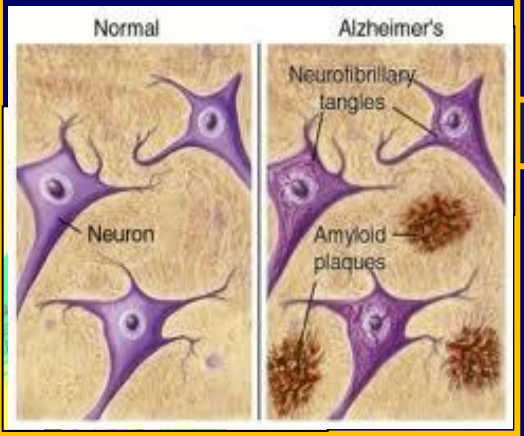


Sherry et al,
***Magn. Reson. Med.* 2003, 2006**

Molecular Imaging – towards personalized medicine

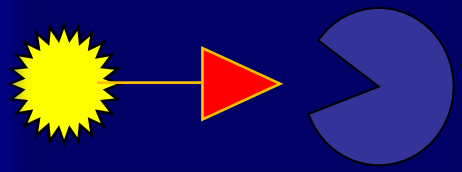
- Detect the disease before morphological signs appear (tumors)
- Predict patient response to treatment
- Follow drug delivery in vivo

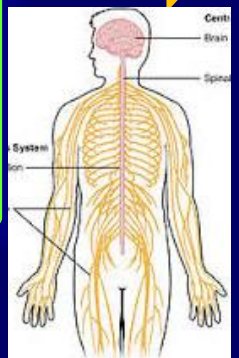
Identify appropriate biomarkers



Chemistry

Create probes that recognize biomarkers and "light up" when they bind them in vivo





Imaging

High sensitivity, high specificity

Lanthanide-based molecular imaging agents

- responsive agents for functional brain imaging (detection of Ca^{2+}, neurotransmitters)
- detection of Zn^{2+}
- enzymatically activated agents
- detection of amyloid peptides (AD, diabetes)
- theragnostic approaches (combining therapy and diagnostics)

In the future, imaging will become more molecular.

We will be able to visualize molecules that are the signatures of a given pathology.

It will facilitate early diagnosis before morphological signs of the disease appear.

Cooperation between Debrecen and Orléans

- **Joint PhD** (Z. Palinkas, 2012)
- **PHC Balaton** 2012-2013 (student exchange in both directions)
- **TET** (S. Laine, PhD student in Debrecen – 2 months)
- **COST short term scientific missions** (1 French student to Debrecen and several Hungarian students to Orléans : few days - 3 months)
- **Studium fellowship** : 1 year stay in Orléans for Gyula Tircso (2015); Ferenc Kalman (2016)
- **Campus Hungary Placement** (K. Pota, 2014, 3 months; Z. Garda, 2015, 5 months)
- **Master 2 internship** in Orléans (R. Botar, 6 months, 2016)
- **8 joint publications** since 2010; at least 5 more in preparation