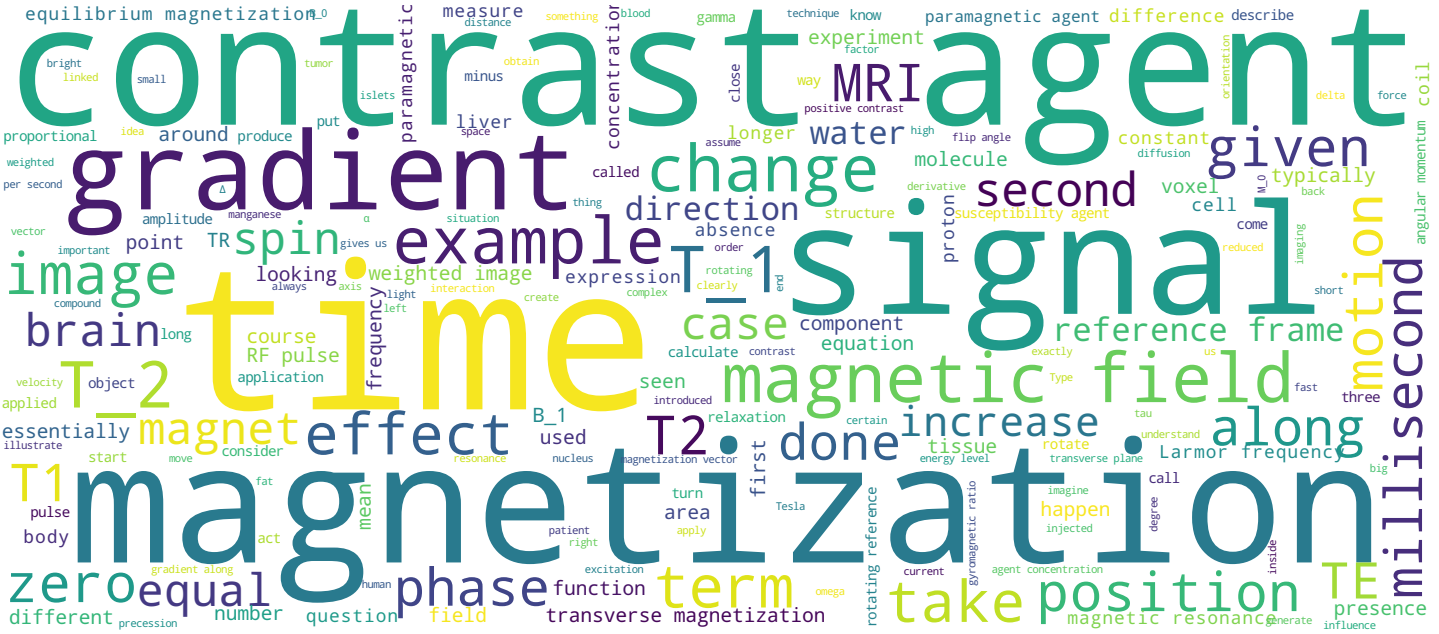
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

12.5 MR contrast agents

Fundamentals of Biomedical Imaging

Prof. Rolf Gruetter



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EPFL

12-5. What are the mechanisms of MRI Contrast Agents ?

Relaxation times are shortened by relaxivity r_1, r_2^*

1) T_1 – Paramagnetic agents

Mechanism: (interaction with water & molecular tumbling)

Contrast agent w. concentration. [CA] shortens T_1:

$$\frac{1}{T_1^{CA}} = \frac{1}{T_1} + r_1[CA]$$

12-18

So how do contrast agents work for MRI? Remember, we had discussed contrast agents for computed tomography that they change the effectiveness of tissue and therefore the linear continuation coefficient. And so how does a contrast agent MRI work? And essentially we distinguish two classes of contrast agents. The one are those that act on *T_1*, it's paramagnetic agents. These paramagnetic agents-- the interaction as it is done is very complex. It's difficult to understand, but essentially the picture that we have is, it is an interaction of the contrast agent with surrounding water, it's own molecular tumbling and how fast the water diffuses and how close the [lot] diffuses close to that paramagnetic agent. So, that's the molecular picture. Phenomenologically, the way they are scribed is that one over *T_1* in the presence of the contrast agent is given by one over *T1* in the absence of the contrast agent plus a term that is the contrast agent concentration times this factor *r_1*, and this factor *r_1* is the relaxivity of the this contrast agent on *T_1*. It, in a way, describes what concentration of contrast agent one needs to generate a change in *T_1*.

Notes

Summary

0m 04s

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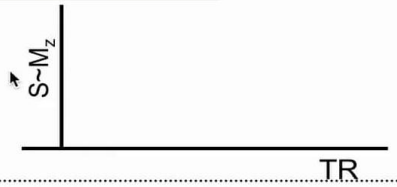
$$\frac{1}{T_1^{CA}} = \frac{1}{T_1} + r_1[CA]$$

Example:

[CA]=1mM, r_1=3 $mM^{-1}s^{-1}$ and T_1=1s:

$1/T_1^{CA}=1+3=4 \rightarrow T_1^{CA}=0.25s$



12-18

So it is a phenomenological equation, and we'll stick with this. So, to give you an idea for a typical parameter here, if you take a contrast agent concentration of a millimolar, relaxivity of 3 per millimolar per second and *T_1* of the tissue in the absence of the contrast agent one second then we can plug these numbers in, and we'll actually calculate that the *T_1* in the presence of one millimolar of this particular contrast agent changes from one second to 250 milliseconds followed by a factor of four. This is huge change in *T_1*. Imagine you're doing your image at a *TR* of 250 milliseconds, the *T_1* of one second, this will create a very dark image but then you're close here to the optimal repetition time at this point and the image, the signal intensity, will increase drastically. So if we look at the signal and now in this case we need to take some *T_1* weighted images proportional to *x* magnetization, so it's *T_1* weighted. We're looking at this expression here and we have assumed here for the experiment that the *TE* is much shorter than *T_2*.

Notes

Summary

1m 25s

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brighter signal on T_1-weighted images

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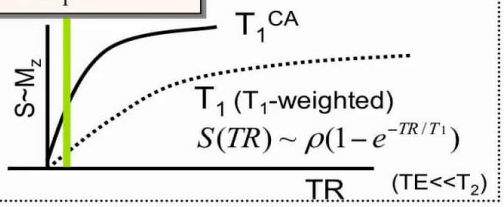


2) T_2 – Paramagnetic and Susceptibility agents

[T_2* – Susceptibility agents]

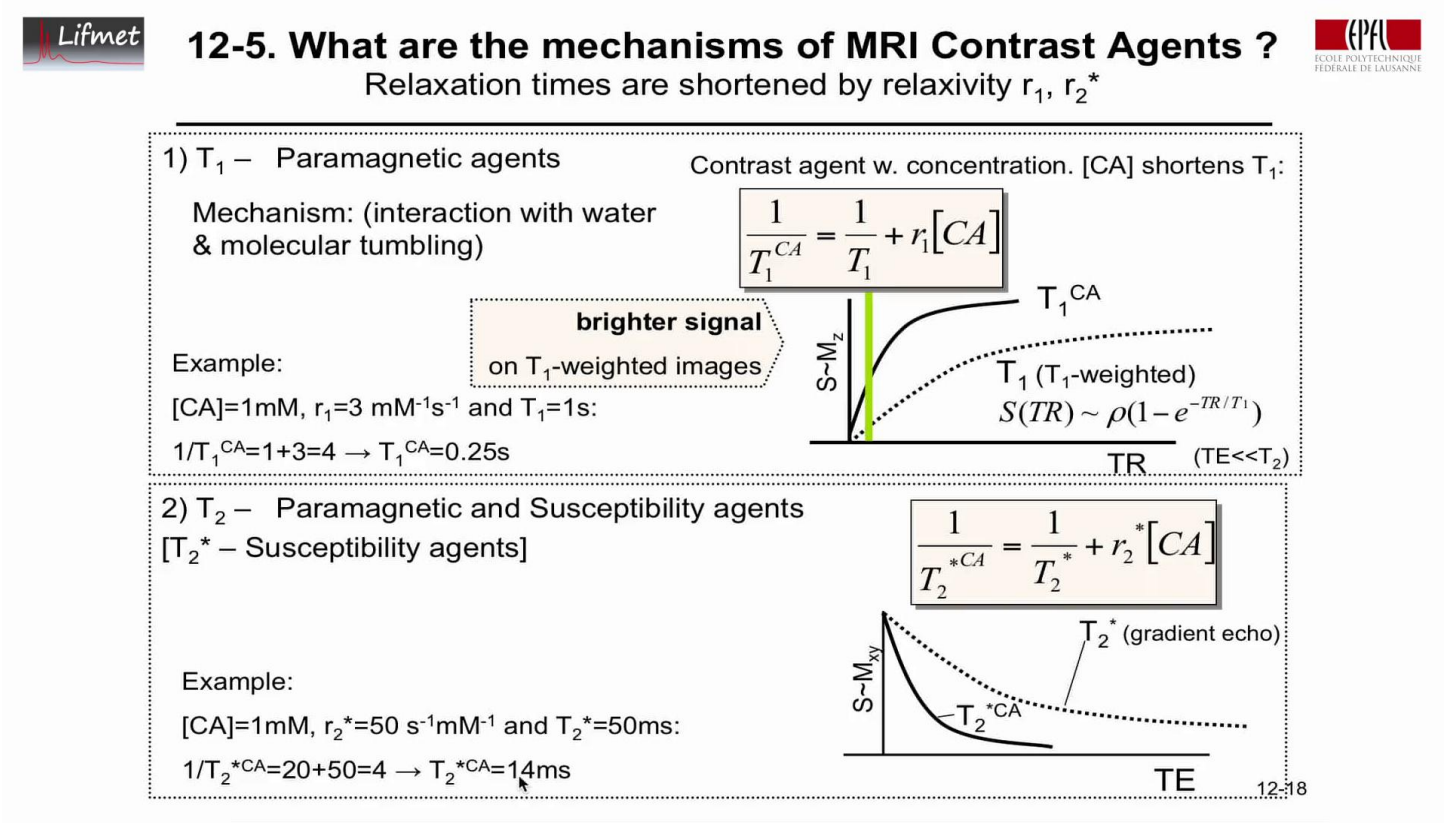
12-18

This is in the absence of the contrast agent and in the presence of the contrast agent, the recovery to thermodynamic equilibrium is much faster, so if we measure at a relatively short *TR* the signal becomes bright in the presence of the contrast agent. So this paramagnetic agents, they lead to a brighter signal of *T_1* weighted images. The other class of contrast agents are paramagnetic and susceptibility agents, they act on *T_2* and *T_2**, and the *T`-2** agents are called susceptibility agents. So if we look here-- actually the expression that describes the effect on *T_2** has the same expression that we have for *T_1*, it's the effect of the contrast agent concentration but now we have the proportionality here is the relativity of *r_2** So what happens with the signal as a function of *TE*, the signal is proportional to the transverse magnetization, this is in the absence of a contrast agent, that's *T_2** with a gradient angle and in the presence of the contrast agent we have *T_2 for* CA, *that's this* T2** here, a faster decay.

Notes

Summary

2m 34s



So, to give you an idea, we take, again, a contrast agent concentration of a millimolar typical relaxivity of 50 per second per millimolar and a *T_2** of 50 milliseconds. We calculate now, and with this concentration we calculate that now the *T_2** is 14 milliseconds. So we go from 50 milliseconds to 14 milliseconds.

Notes

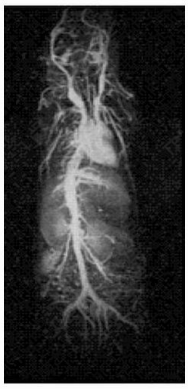
Summary

3m 44s

Examples I

MRI contrast agents

Typically restricted to blood
- Ideal to image vessels
- Leaky vessel walls
  - » Tumours
  - » Inflammation



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Now imagine what happens, you're measuring at a *TE* of 50 milliseconds, now, the contrast agent comes in at a concentration of a millimolar, the *T_2** is reduced to 14 milliseconds, at the *TE* of 50 milliseconds we no longer have a signal. So while you were optimal for the absence of a contrast agent, now the signal has decayed. And this basically leads to a reduced signal in the presence of the contrast agent for the paramagnetic and susceptibility agents on *T_2* or *T_2** weighted images, and that is because we are measuring somewhere here, at a more prolonged *TE*. So, paramagnetic agents produce a brighter signal because they act on *T_1*, paramagnetic and susceptibility agents which act on *T_2* and *T_2**, they produce reduced signal. So let's look at some examples of contrast agents. First, some properties, they are typically restricted to blood, they are ideal to image vessels, or leaky vessel walls, such as what we see in tumors and inflammation. So here we have an example of the mouse vasculature. We have an MRI of the mouse trunk, so this is before contrast agent application and this is after, we can see a change here, clearly in the trunk where the contrast agent has gone.

Notes

Summary

4m 05s

Examples I

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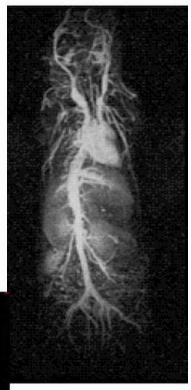
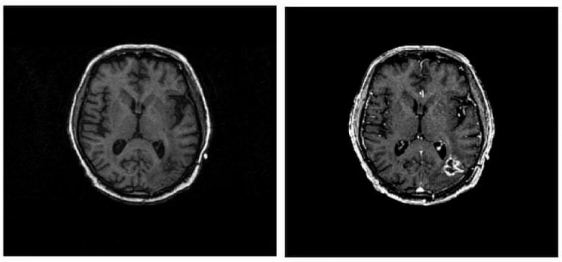
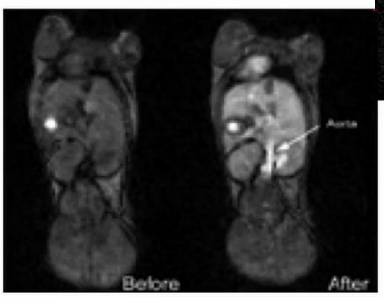
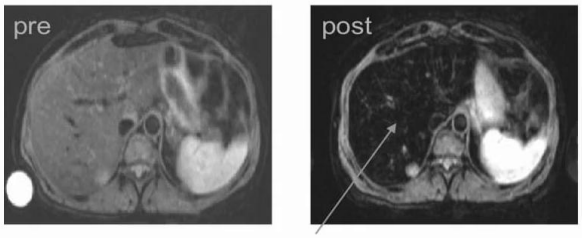




Gd Enhanced Brain Malignancy



MRI of mouse trunk



Negative Contrast From Iron Oxide (T_2* agent)

This is an example of brain; there's a malignancy in the brain, before the contrast and after the contrast. We can see difference we can see here the ring that lights up, this tells us that there is a breakdown of blood/brain barrier, which is typical for the tumoral edge, still very well vascularized breakdown of blood/brain barrier. You can also see here a lots of the vessels, the bright stuff that lights up, these are vessels that carry the contrast agent. So this is a predominant way of enhancing leaky tissue. Here is now an example of contrast agent application-- before contrast and after the contrast, and we see here the liver, and the liver is now suddenly becoming dark. This is a susceptibility agent, it's a *T_2** agent, that's iron oxide in this particular case, and it has produced negative contrast. So here we have positive contrast, positive contrast, positive contrast, and here this example of a *T-2*-based paramagnetic and susceptibility contrast agent like iron oxide is producing negative contrast, so signal is reduced.

Notes

Summary

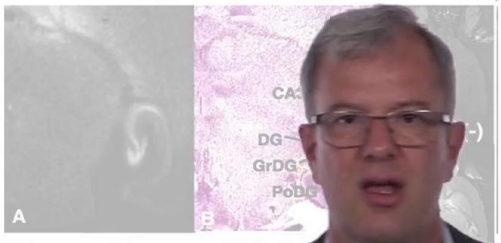
5m 21s

Examples II: Intracellular contrast agents

Mn-enhanced MRI (MEMRI)

Mn-enhanced MRI (synaptic activity imaging)

Manganese (paramagnetic):
- Transported by Ca channels
- Shortens T_1



Imaging stem cells, transplanted cells

Cells pre-loaded with contrast agent

The second example that I want to talk about are intracellular contrast agents. They are much harder. One is manganese. Manganese is paramagnetic, it shortens the *T_1*. It has the interesting feature that is transported by calcium channels and therefore shortens the *T_1*. So this has been used in, among others, in brain imaging. This is an image of a rodent brain, and we can see here very nicely the structure of the hippocampus, the different areas, *CA3*, the dendrite areas, etc. corresponding to the structure seen in histology. Prior to manganese, this *T_1*-weighted image look fairly uninteresting after the application of manganese, one can see a very substantial contrast which reflects the activity, the differential activity of calcium channels in the brain by region. Now manganese as a contrast agent is not used in humans, it has issues of toxicity, but in neuroscience it has become a very interesting and promising tool to look at fundamental neuroscience questions and also other questions. Now, another thing for intracellular contrast is a bit particular that I want to mention. That is the imaging of transplanted cells, or stem cells.

Notes

Summary

6m 35s

Examples II: Intracellular contrast agents

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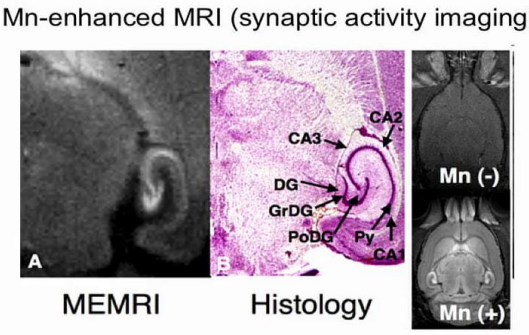
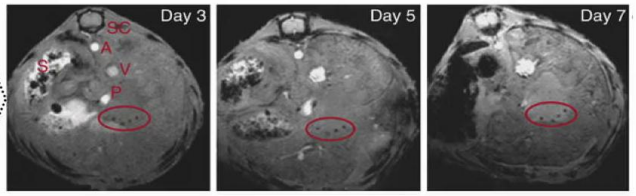


Imaging stem cells, transplanted cells

Cells pre-loaded with contrast agent



Transplanted Langerhans islets in liver

12-20

So, what is done here is, for example, that the cells that are injected are preloaded with contrast agent. So within them, they contain the contrast agent and then one looks at the change in MRI signal as the cells are being injected and then migrate within the body. And this is an example of transplanted Langerhan cells in the liver, so lung transplantation of islets is a recent form of treatment for Type I diabetes. These islets are injected into the patient, and one of the questions here was that where do these transplanted islets go in the body? There has been a suspicion that they would end up in the liver and, indeed, what these images show here, here are the islets, they show up as dark because they are, in this case, they were used with a susceptibility contrast agent, so a *T_2* contrast agent or *T_2** and they are, indeed, showing up here dislodged in the liver where they are making their action on the body by helping to secrete insulin and therefore reduce the effects of Type I diabetes in these patients.

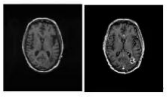
Notes

Summary

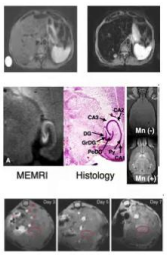
7m 56s

Credits

MR Angiogram of a Mouse, fig 3.
Dr. Peter Choyke, Molecular Imaging Program
http://andremartins.yolasite.com/Biochemistry.php



“Ressonancia magnetica nuclear », fig 2_9.
http://www.ebah.com.br/content/ABAAAAp9gAJ/ressonancia-magnetica-nuclear?part=2



Zdravka Medarova et al. Nature Protocols 2006; 1: 429

Notes

Summary

9m 17s