Dosage by synchrotron radiation of gadolinium in the isolated mouse liver perfused with EOB –DTPA- Gd (Eovist®), a MRI contrast agent

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Introduction

MRI (magnetic resonance imaging) is an imaging method providing non invasively anatomic and functionnal pictures of exceptional quality. It uses the fact that nuclei in a magnetic field can absorb (excitation) and emit (return to equilibrium) radio waves which frequency depends on the nature of the nuclei themselves, their environment and the magnetic field. The picture intensity can be modified by changing the parameters of the imaging sequence or by the use of paramagnetic or superparamagnetic contrast agents. The first ones contain gadolinium or manganese ions, while the latter ones are iron oxide nanoparticles dispersed in a biocompatible material.
Contrary to the situation encountered in X-ray imaging like CT, in MRI, the signal intensity is not directly proportional to the contrast agent concentration, partly because its efficiency (relaxivity) changes with the chemical environment.

Objectives

Our project aims at developing an alternative method for *in vivo* dosage of contrast agent. The medical line of the ESRF allows for non-destructive measurement of the gadolinium concentration, hence of the concentration of the contrast agent, from the picture intensity. In this work, we have evaluated the efficiency of the method by measuring the gadolinium concentration in the isolated mouse liver perfused with a chelate of gadolinium.

Methods

The model used is the isolated and perfused mouse liver developing a fulminant hepatitis. The mouses (25-30 g) were anaesthetized by intraperitoneal injection of Nembutal (0,1 ml/kg of body weight). After laparotomy, innards were pushed aside to expose the portal vein in wich a catheter, draining the perfusion liquid, was inserted. The liver was then isolated and the perfusion liquid (Krebs-Henseleit) expulsed from the sus-hepatic vein.
Hepatitis were induced by intraperitoneal injection of D(+)-galactosamine (50 mg/mouse) and intravenous injection of LPS (10 µg/mouse). Hepatitis developed within six hours. The goal was to compare the EOB-DTPA-Gd pharmacokinetics in liver with and without hepatitis by using the following sequence: acquisition of one picture every minute during 5 minutes and afterward one picture every 5 minutes for 25 minutes. The circuit was then rinsed using a one-through perfusion mode. During this time, six pictures were collected. The contrast agent EOB-DTPA-Gd was added to the perfusion liquid (250 µl from a 250 mM solution).

Results and discussion

The pictures clearly show the contrast evolution as a function of time: during the first 5 minutes, the contrast agent accumulates (fig 1), then its concentration stabilizes (fig 2) before decreasing for the last 25 minutes (fig 3).
If the method allows the dynamic follow-up of the liver contrast, it still remains a semi-quantitative dosage. The adequate softwares are currently under development to allow for the allocation of concentration value to each pixels intensity.

Figure 1. These pictures correspond to the five first minutes following the administration of the contrast agent.

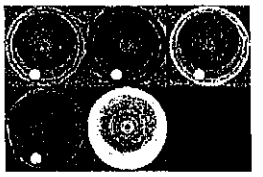

Figure 2. These 5 pictures show the evolution of the contrast agent concentration in the liver during the period covering the 10^{th} to the 30^{th} min. following the administration of the contrast agent. The hyperintense area is a reference containing a known concentration of contrast agent (± 0.5 mmol/l Gd).

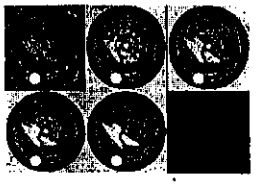

Figure 3: These pictures were collected during the rinsing period (1 picture / 5 minutes). The contrast agent concentration remains constant.