Title: MRI Imaging of Liver Fibrosis with Vitamin A Functionalized Magnetoliposomes in Rats

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Abstract:

Introduction

Hepatic fibrosis is the result of the wound-healing response of the liver to repeated injury. After an acute liver injury (e.g., viral hepatitis), parenchymal cells regenerate and replace the necrotic or apoptotic cells. This process is associated with and inflammatory response and limited deposition of extracellular matrix (ECM) proteins. In advanced stages, the liver contains approximately 6 times more ECM than normal. Hepatic Stellate Cells (HSCs) are the main ECM-producing cells in the injured liver. In the normal liver, HSCs reside in the space of Disse and are the major storage sites of vitamin A. Following chronic injury, HSCs activate or transdifferentiate into myofibroblast-like cells, acquiring contractile, proinflammatory and fibrogenic properties. Although liver biopsy is still the 'golden standard' used to stage most cases of liver disease, there is a need for reliable, simple, and noninvasive methods to detect changes in the liver parenchyma in less advanced stages of fibrosis. In order to overcome this problem, we have used Vitamin A-functionalized magnetoliposomes (vit A-MLs) as MRI contrast agents, which were designed to specifically be taken up by HSCs. Changes of MRI contrast with the onset of HSC activation and development of liver fibrosis were monitored to develop a method for non-invasive monitoring of this disease and/or potential evaluation of therapy in the future.

Methods

Fibrosis was induced in the liver of Sprague-Dawley rats (Charles River, Germany) by repeated administration of a 'test compound' used as a model to follow activation and proliferation of HSCs. Hereby, a MRI contrast agent was used to target specifically this cells. This contrast agent consists of in-house Magnetoliposomes functionalized with vitamin A residues (vit A-MLs) to target the vitamin A storage capacity of HSC. Due to the paramagnetic iron in the vit A-MLs core, it also acts as an MRI contrast agent.

Results

We could identify the presence of 'cobbled stone' (or granular structures) appearance on the liver tissue post contrast administration indicating an accumulation of Vit. A MLs in the lipid droplets of HSCs. Changes in the signal intensity represented in the form of histogram can provide an indication about the loss of anatomical structure (wich is a direct indication of disease progression) of the liver allowing to identify fibrosis positive animals. Histopathological staining for activated stellate cell marker and iron specific staining further indicate the uptake specificity in the liver.

Conclusions

Preliminary results indicate the possibility to detect the onset (and progression) of liver fibrosis in vivo, using MRI imaging with Vit. A functionalized MLs. There was a consistency in the reduction of the SI for pre and post-MLs animals indicating that Vit. A MLs can be used as MR contrast agent in liver disease research.

Acknowledgement/References

This research project was supported by a grant from the Flemish agency for innovation by science and technology.

Abstract category:

☐ Cancer

☐ Neurology

x Novel technologies, methodologies and modalities

☐ Other