

CONFOCAL ANALYSIS OF FLUORESCENT MRI CONTRAST AGENT BEHAVIOR

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KEY WORDS : MRI, *in vivo* labelling, confocal microscopy, factor analysis,

The usual magnetic resonance imagery (MRI) contrast agents contain Gadolinium (Gd) or Iron (Fe). These products are used to examine the biodistribution process *in vivo* and when they are fluorescent, it is possible to analyze their access to cells by means of confocal microscopy. The purpose of this work is to characterize the fate of magneto-fluorescent products injected *in vivo* in small animals intravenously. To be in the imaging conditions of ultra small particle iron oxide (USPIO) contrast agents, a product which combines nanoparticles of Fe and Texas Red (Institute für Diagnostik Forschung, Berlin) is used. Also, to avoid the need to use MRI contrast agents bearing fluorochromes, Gd is replaced by Europium (Eu). In this regard, Eu-BOPTA is used in this presentation in place of Gd-BOPTA (Multihance, Bracco, Lugano). Also, bi-photon confocal microscopy is used to assess the presence of compounds containing Eu or Fe in the liver and blood vessels of injected mice in similar experimental conditions. To this end, the cell nuclei of samples are counterstained with Syto 13. To characterize Eu-BOPTA and Fe-Texas Red at the cellular level, image analysis is performed on spectral sequences of confocal and bi-photon images to get specific co-localized images of Eu or Fe and nuclei. Sequences of images are investigated by Factor Analysis of Medical Image Sequences (FAMIS). This method uses physical properties of fluorochromes (emission spectra and decay rates), and provides the images corresponding to each fluorochrome [1, 2]. Therefore, detection of Eu and Texas Red of injected compounds in tissues is made possible in samples of livers and blood vessels of mice after administration of these compounds. The characterization of the presence of Eu or Fe in tissues can be performed on the basis of direct fluorescence microscopy analysis but we have made it much more specific and reliable by using spectral bi-photon confocal microscopy and FAMIS image processing. Our investigation also determines the interest to use fluorescent MRI contrast agents as *in vivo* staining tools of cellular sites. As a result, detection of Eu and Fe of injected compounds in tissue is now possible in embedded samples of livers of mice (positive control) after administration of Multihance Eu-substitute compounds and Fe-Texas Red and analysis with multiphoton confocal microscopy and image processing. It opens a way to follow up the fate of MRI products in blood vessels. Analysis of compounds containing Eu or Fe in injected mice determines the specificity of these compounds in blood vessels. By now it results in the detection of Fe nanoparticles in blood vessels. Prospectively, work involving different concentrations of Fe and Eu will be carried out to analyze the capture of these products in different lipomatous situations.

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