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A multinuclear MR study of Gd-EOB-DTPA: comprehensive preclinical characterization of an organ specific MRI contrast agent.

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The characterization of the hepatobiliary contrast agent Gd-EOB-DTPA (gadolinium 3, 6, 9-triaza-3, 6, 9-tris(carboxymethyl)-4-(4-ethoxybenzyl)-undecandicarboxylic acid) in various media (water solution, protein containing solution, phosphorylated metabolites solution, and excised and perfused liver) was performed using different NMR approaches: water 1H nuclear magnetic relaxation dispersion profiles, 2H NMR longitudinal and transverse relaxation rates of labeled complex, water 17O transverse relaxation rates and chemical shifts, 31P relaxation rates and peak area of phosphorylated metabolites. The higher proton relaxivity of Gd-EOB-DTPA in water compared with Gd-DTPA is related to a shorter distance (r) between the water proton and the gadolinium ion and to a longer rotational correlation time (tauR) of the hydrated complex. Although the thermodynamic stability of Gd-EOB-DTPA is identical to the one of Gd-DTPA, its kinetic stability in solutions containing phosphorylated metabolites (ATP, phosphocreatine, and inorganic phosphate) as measured by 31P relaxation rates analysis is higher than for the parent compound. Gd-EOB-DTPA binds noncovalently to serum proteins. Its interaction with human serum albumin is characterized by a dissociation constant of 1-4.1 mM as calculated from proton and deuterium relaxation rates and equilibrium dialysis. This noncovalent interaction involves the subdomain IIA of human serum albumin. 31P spectroscopy of the excised and perfused rat livers was used to monitor the uptake of Gd-EOB-DTPA by the hepatocytes where it enhances the nuclear relaxation of the intracellular metabolites without impairing the adenosine triphosphate metabolism of the cells.

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