

Analysis of Gd-based MRI contrast agents and potential transmetallation products in human body fluids

Lena Telgmann¹, Jens Künnemeyer¹, Faruk Tokmak² and Uwe Karst¹;

¹Institute of Inorganic and Analytical Chemistry, University of Münster, Corrensstr. 30, 48149 Münster, Germany;

²Marienhospital, KfH-Nierenzentrum, University of Bochum, Cruismannstr. 37, 44807 Bochum

Contrast agents for magnetic resonance imaging based on Gadolinium (Gd) are complexed with polyaminocarboxylic acid chelating agents. These complexes have very high thermodynamic stability constants, but a connection between the medication with Gd-based contrast agents and a newly observed disease called nephrogenic systemic fibrose has been proposed. It has been postulated that transmetallation reactions with parental iron or oral chromium supplements play a role in its pathogenesis. A separation technique for Gd chelates and potential transmetallation products is presented. The separation efficiency of capillary electrophoresis for ionic compounds is combined with the high resolution of time-of-flight mass spectrometry. In blood plasma three ionic Gd-based contrast agents Gd-DTPA, Gd-BOPTA and Gd-DOTA have each been added to different iron supplements, iron salts or chromium salts respectively. The samples were analysed by CE/ESI-ToF-MS. Iron transmetallation products have been detected in the samples that contained one of the iron salts and either of the contrast agents Gd-DTPA or Gd-BOPTA, but not in the samples with iron supplements. A transmetallation reaction is in general possible, but a direct connection between the medication with parental iron supplements after the treatment with Gd-based contrast agents and NSF cannot be proven. Gd-DOTA showed no transmetallation at all. Its macrocyclic structure leads to a higher stability compared to complexes based on linear ligands (Gd-DTPA and Gd-BOPTA). The samples containing chromium picolinate or chromium chloride did not lead to transmetallation as well. A connection between a medication with chromium in any binding form and NSF cannot be shown at all.