

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

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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.