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## **LOVARS** in Central Nervous System Diseases

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A length and offset varied saturation (LOVARS) is a novel Chemical exchange-dependent saturation transfer (CEST) technique with variable length of saturation for 1 pair of offsets, which can detect endogenous macromolecules (e.g. Tumor associated glycoprotein MUC-1) and metabolites. Some preliminary studies have showed that LOVARS is not only helpful in grading glioma, evaluating the therapy effect and even differentiating treatment effect from tumor reoccurrence. Furthermore, it can also detect and differentiate cerebral ischemia from intracranial hemorrhage at very early stage. So it may have the potential to improve the diagnostic flow for early stroke.

Keywords: LOVARS, MRI, STROKE, GLIOMA

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## Dynamic contrast-enhanced MR Imaging: Utility in BBB Imaging and Baffling Issue of Gadolinium Retention

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Dynamic contrast-enhanced (DCE) MR imaging is a noninvasive perfusion MR imaging technique using gadolinium-based contrast agents (GBCAs), from which numerous quantitative pharmacokinetic parameters that reflect microcirculatory structure and function can be derived. Of the various parameters, Ktrans, ve, and vp are more commonly used ones, where Ktrans is defined as the volume transfer constant between the plasma and extravascular extracellular space (EES), ve (also known as the leakage space) as EES and vp as blood plasma volume per unit volume of tissue. Ktrans and ve are considered as imaging biomarkers for permeability or blood-brain barrier (BBB) disruption, while vp is thought to reflect angiogenesis. There is increasing awareness that BBB disruption comprises an important part of the pathophysiology for various CNS diseases, including tumors, epilepsy, stroke, demyelinating disease, small vessel disease, and traumatic brain injury.

GBCAs in contrast enhanced MR imaging have been increasingly used in routine clinical practice because of their added value in the differential diagnosis of various diseases. Because of the high toxicity of gadolinium ions in their free form, gadolinium ions are chemically bonded with non-metal ions, polyaminocarboxylic acid chelating agents, to prevent the exposure of the free gadolinium to the tissue prior to their renal excretion. Based on the chemical structures of the chelating agents, GBCAs are grouped into two main classes, macrocyclic (mGBCAs) and linear (lGBCAs). mGBCAs differ from lGBCAs in that gadolinium ions in mGBCAs are isolated from their surroundings within a preorganized cavity formed by a rigid cage, unlike those in lGBCAs. The previous study by Frenzel et al. found that the difference in the chemical structures could have a major influence on the stability of the compounds by demonstrating that a significant amount of the free gadolinium was released into the serum in lGBCAs, but not in mGBCAs.

Despite the relatively higher stability of the mGBCAs shown in the preclinical study, both mGBCAs and IGBCAs have been used in routine practice because both types of chelates have been shown to be sufficiently stable in the body in patients with normal renal function. Recently, however, concern has been raised about the safety of using IGBCAs because Kanda et al. reported that the repeated use of IGBCAs, namely, gadodiamide and gadopentetate dimeglumine, could cause high signal intensity (SI) in the dentate nucleus (DN) on unenhanced T1-weighted MR images due to gadolinium retention regardless of patients' renal function. A few other subsequent studies on gadodiamide, gadopentetate dimeglumine, and gadobenate dimeglumine also reported similar results. In contrast, a number of previous studies on mGBCAs, gadoterate meglumine and gadoteridol, and gadobutrol reported that no significant T1 hyperintensity was observed in the DN and globus pallidus (GP) even after the repeated administration of the mGBCAs, in keeping with their high in vivo stability. Despite the concordant results between our study and several previous studies, the possibility remains that the amount of gadolinium is small and below the detection threshold to cause a hyperintensity on unenhanced T1-weighted images.

Keywords: Dynamic contrast-enhanced (DCE) MR imaging, Blood-brain barrier (BBB), Gadolinium Retention

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## Printing technology in MR signal detection and device tracking

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Signal excitation and detection device is critical in determining the performance and applicability of MR imaging. Development of such devices with high efficiency can be challenging, particularly at high and ultrahigh fields. Conventional method is usually based on the designs with rigid circuits and fixed geometry to ensure the reasonable operation performance. That is often not optimized in filling factors and geometries matching to anatomy, resulting in reduced detection sensitivity and imaging performance in in-vivo applications. Additionally, in catheter-based interventional MRI procedures, the conventional design and fabrication decreases the flexibility and increase the profile of catheters, making the interventional MRI unpractical or impossible in some circumstances.

In this work, we discuss two printing methods that our research lab is investigating in designing and fabricating RF devices for MR imaging and interventional wireless catheter tracking. Printing technology would be expected to provide a solution to design and construction of efficient MR devices that are flexible, wearable, miniature and cost efficient.

- 1) Screen Printing technique. This technique is based on silk-screen printing from solution that all the electrical components can be printed onto flexible substrates. In the screen printing, the operator squeezes ink through a screen mask to pattern a substrate, which is then annealed. To obtain good conductivity and relatively low temperature during the printing process, silver nano-particle inks are often used. This new technology enables printing on cloth-like substrates that are conforming and provide an excellent fit to the varying patient anatomies, leading to improved filling factor and thus elevated signal detection sensitivity. Possible substrates for the screen printing technique in MR applications are Nylon, PET and PEEK plastics. These polymers are flexible, strong and exhibit relatively high melting temperatures, stiffness and printability. The screen printing technique is particularly suitable for making regular- and large-size MR imaging coils and devices. Due to much reduced cost in making MR devices, this printing technique also makes disposable wearable imaging coils and devices possible.
- 2) Aerosol jet deposition technique. Aerosol jet deposition is a new additive manufacturing process used to create 3D, conformal, micron size electronics and is CAD-file driven, making design practical and customizable. This method can be used to print capacitors, inductors and necessary conductors in the circuit structure of detection devices. Given the unique feature of the aerosol jet deposition printing, this printing technique is particularly suitable for making small size MR devices, e.g. imaging or tracking catheters in interventional MR procedures. To validate the method, in our lab various imaging or tracking catheters for interventional MR procedures have been designed and fabricated by depositing a water-based silver flake ink on 6Fr catheter polymer catheters (polytetrafluoroethylene base and polyethylene ether ketone braiding) using the aerosol jet deposition printing technique. Numerical simulation, standard RF bench testing and MR imaging experiments at 3T were conducted, demonstrating the feasibility of the aerosol jet deposition printing technique in fabrication of miniature imaging and tracking catheters for interventional MRI applications.

Keywords: Printing technology, Wearable MR devices, Interventional MRI, Catheter tracking