

## The saline bolus as an MR contrast agent

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### Introduction

Gd-DTPA bolus contrast is being used routinely in clinical imaging to make relative cerebral blood volume (rCBV) maps. Is it possible to do the same thing with a saline bolus to obtain useful hemodynamics parameters? Two questions need to be answered about the saline bolus. First, does it cause a detectable MR signal? Secondly, what are the hemodynamic/physiological properties that would be showcased by its MR signal? We hypothesize that the dilution of blood by the saline bolus could lead to a change in T2\* weighted signal. Since the MR sensitivity to deoxyhemoglobin was expected to be small and noisy, we also investigated the  $\Delta R2^*$  signal of a saline bolus diluting monocrySTALLINE iron oxide nanoparticle (MION) already preloaded into the vascular system. MION, a long half-life intravascular MR contrast agent many times stronger in susceptibility effect than deoxyhemoglobins and Gd agents, offers a model system for blood but with much higher contrast to noise.

In the routine use of MION, the increase in  $\Delta R2^*$  post MION injection is used to make rCBV maps. We expect an opposite observation of a smaller  $\Delta R2^*$  in the dilution of either blood or MION by a saline bolus. The  $\Delta R2^*$  of MION dilution is expected to return something similar to rCBV because the MION effect dominates any deoxyhemoglobin effect. The  $\Delta R2^*$  signal generated by the saline dilution of blood, on the other hand, is more complicated in a living system. As blood is diluted by a saline bolus,  $\Delta R2^*$  can be modeled by a multiplication of three terms: CBV, hematocrit (ht) and oxygen extraction fraction (OEF), or  $\Delta R2^* \approx CBV \times \Delta ht \times OEF$  for each voxel. With the assumption of ht being reduced in the same proportion for each pixel by a diluting saline bolus, a map of rCBV x OEF could be obtained from  $\Delta R2^*$ . Since there may be an active neuronal response to blood dilution which causes an abrupt drop in the amount of available oxygen delivered to the tissue, we cannot assume that the OEF value per pixel remains constant in time in response to the bolus passage. We expect a response of a combined rCBV and OEF term in deoxyhemoglobin dilution and will not be able to obtain a simple rCBV measurement from the BOLD data. In this manuscript, we first searched for the detectability of the MR signal when either blood or MION loaded blood is diluted by a saline bolus. Then we compared the reference rCBV maps obtained by the steady states of the pre and post MION contrast with the maps obtained by the saline dilution of blood and of MION, respectively.

### Materials and Methods

Two sprague Dawley rats were scanned using a 9.4T animal MR imaging system (Bruker, Billerica, MA). Animals were free breathing under pentobarbital anesthesia, secured to the imaging cradle through a tooth bar and a pair of ear bars.  **$\Delta R2^*$  measurement of a saline bolus challenge.** A saline bolus challenge (1cc) was carried out on both rats while images were collected with EPI with TR 110ms for 1<sup>st</sup> rat and 200ms for the 2<sup>nd</sup> rat, TE 35ms, and spatial resolution 0.5 X 0.5 X 1.5 mm<sup>3</sup>. Total of 1100 time points were collected, with the saline bolus (1cc) injected at ~40th second of baseline. **Reference rCBF measurement using pre and post MION steady state.** Reference rCBF maps were made with pre and post steady states of MION with a venous injection of a 9mg/Kg body weight of MION.  **$\Delta R2^*$  measurement of a saline bolus challenge with MION preloaded in the vascular system.** A saline bolus was again injected after 40 seconds of baseline data collection, this time with MION already in the vascular system. **Data Analysis.** MR signal was converted to  $\Delta R2^*$ . Reference rCBF maps were made from the post-MION steady state  $\Delta R2^*$  signal. For the bolus data, we made maps two ways: integrating  $\Delta R2^*$  signal under the first pass peak and integrating the steady state after the bolus.

### Results and Discussion

$\Delta R2^*$  signals were detectable and became smaller in a saline bolus dilution of both blood and MION. The reference rCBV maps (Fig 1) shared more similar features with  $\Delta R2^*$  maps made by the saline dilution of MION (Fig 3) than with  $\Delta R2^*$  maps made by the saline dilution of deoxyhemoglobin (Fig 2). As the result of blood dilution is a combination of rCBV and OEF, differences from rCBV are to be expected. One advantage of blood dilution is that contrast agent leakage would not be an issue. Options to separate the rCBV and OEF terms in future research may include the use of the asymmetric spin echo sequence, a technique already utilized in OEF mapping.

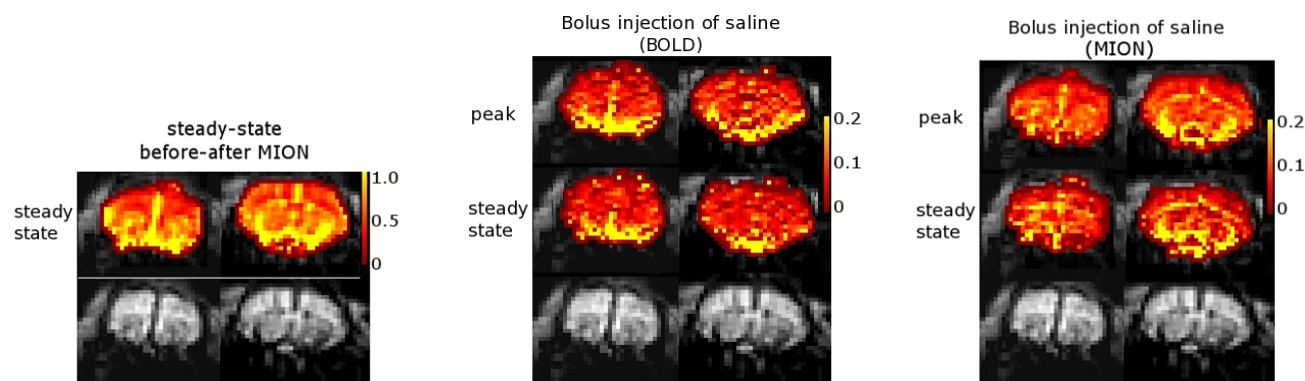


Fig 1. Reference rCBVmap ( $\Delta R2^*$ )

Fig 2. Saline bolus  $\Delta R2^*$  map

Fig 3.  $\Delta R2^*$  map of Saline bolus with MION preloaded