Physical Principles of Transient T1-Lengthening by Hemodilution: Applications to Perfusion MRI with Normal Saline Injections (NSI)

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Purpose: Normal saline (NS) has recently been demonstrated as a safe and promising T_1-lengthening contrast agent for dynamic-MRI of the head and brain; with the potential for tissue perfusion mapping by hemodilution analysis (see **Fig.** 1a). In these preliminary studies, a dynamic inversion-recovery turbo-spin-echo (*dynIR-TSE*) pulse sequence was run during and after an NS injection for up to five minutes, thus generating four-dimensional (4D) spatio-temporal image datasets. The purpose of this work is to model the magnetization dynamics of blood and perfused tissues during and after transient hemodilution as observed in dynamic-NSI.

Experimental Methods: In this prospective, IRB-approved, and HIPAA complaint study, 17 patients were imaged using a 1.5T MRI unit (Philips Achieva-XR, Best, The Netherlands) using the quadrature body coil and a 16-channel phased array head coil for TX and RX respectively. The dynIR-TSE scans were run repeatedly for up to five minutes with the NS injection (duration 25s) given after a short delay post pulse sequence start. Up to 100cc of NS were injected through an antecubital vein at rates of 3-4ml/s: 3ml/s employed in patients with a 22 Gauge needle; 4ml/s in those with a 20 Gauge needle) using a power injector (Medrad Spectris Solaris, Bayer Healthcare, Warrendale, PA). The key imaging parameters of the *dynIR-TSE* pulse sequence were in the following ranges: TI=600-900ms, TR=1.6-2.1s, TEeff=4.6-10ms, voxel 1 x 1.5 x 7-10 mm^3 leading imaging volumes of 7-14 slices and temporal resolutions in the 16-20s.

Theory: Blood is modeled as a two-compartment system with very rapid exchange between the intra- and extra-cellular compartments. In the fast exchange limit, the spin-lattice relaxation rate ($R_1=1/T_1$) of blood is the weighted sum of the plasma and intra-cellular red blood cell (RBC) longitudinal relaxation rates, *i.e.*: $R_1^{(blood)} = f_{(plasma)}\, R_1^{(plasma)} + f_{(RBC)}\, R_1^{(RBC)}$ where $f_{(plasma)}$ and $f_{(RCB)}$ are the fractions of extra- and intra-cellular water respectively, and where the blood plasma and RBC longitudinal relaxation rate values are known at 1.5T, specifically: $R_1^{(plasma)} = 0.49 \pm 0.04\ s^{-1}\ and\ R_1^{(RBC)} = 1.1\ s^{-1}$. In addition, $f_{(plasma)} + f_{(RCB)} = 1$ and therefore, the longitudinal relaxation time can be written as a function of the intra-cellular water fraction, which is function of *Hct*: $T_1^{(blood)}(Hct) = \left[\frac{1}{T_1^{(plasma)}} + f_{(RBC)}\left(\frac{1}{T_1^{(RBC)}} - \frac{1}{T_1^{(plasma)}}\right)\right]^{-1}$.

Results: By denoting the NS injection temporal profile by $p(t)$ (see **Fig.** 1b), the transient T_1 of blood can be modeled in terms of instantaneous water RBC water fraction (see Eq. 3 below). Computer modelling of Eq. 3 leads to T1 modulation by hemodilution secondary to NS injection.

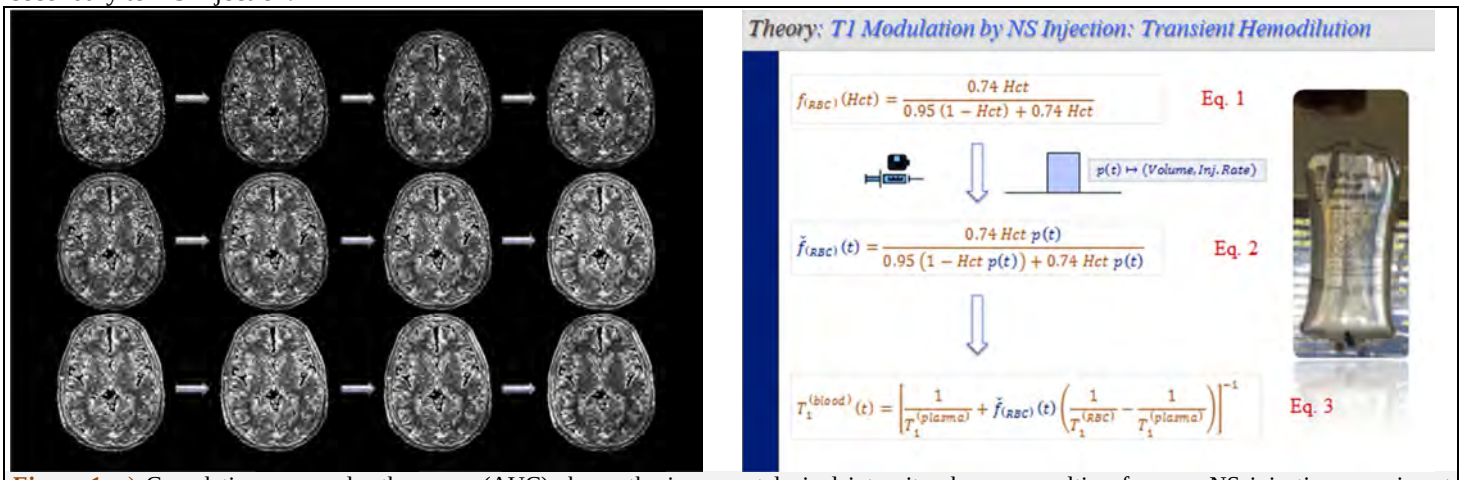

Figure 1: a) Cumulative area under the curve (AUC) shows the incremental pixel intensity changes resulting from an NS injection experiment showing a transient change in T1 that is more prominent in expected regions of higher perfusion (e.g. gray matter, basal ganglia, and skin). **b)** Equations are shown that model the T_1 modulation in terms of the temporal profile of the NS injection.

Conclusion: This work further demonstrates the viability of NS as a measurable, safe, practical, and inexpensive T_1 contrast agent for dynamic perfusion MRI. The described theoretical developments, which are based on a two-compartment model with rapid exchange, could be useful for quantifying brain perfusion in patients with Gd contraindications such as renal insufficiency and pregnant patients.