PARAMAP: an Automated Imaging Analysis Tool for Quantitative CEST Molecular Imaging: Validation in vitro

J. Flament1, B. Marty1, S. Mériaux1, J. Valette1, C. Medina2, C. Robic3, M. Port4, F. Lethimonnier1, and F. Boumezbeur1

1NeuroSpin, I2IBM, Commissariat à l’Energie Atomique, Gif-sur-Yvette, France, 2Research Division, Guerbet, Roissy-Charles de Gaulle, France

Introduction

Recently, a new class of paramagnetic contrast agent has been developed for Chemical Exchange Saturation Transfer (PARACEST) magnetic resonance imaging [1-3]. Since visualizing CEST contrast requires two measurements with $B_0$ saturation applied on-resonance (at $\delta$, frequency of the shifted bound water) and off-resonance (at $-\delta$), CEST imaging is sensitive to inhomogeneities in both $B_0$ and $B_1$ fields. Therefore, in order to generate quantitative CEST maps, it is important to elaborate correction algorithms to get rid of errors induced by $B_0$ and $B_1$ fields. In this study, we proposed to use a numerical simulation of the CEST contrast mechanism based on the Bloch equations modified for chemical exchange incorporating $B_0$ and $B_1$ dependencies [4]. The efficiency of our analysis tool was verified in vitro.

Materials and Methods

MRI acquisition. Experiments were realized on a 7 T small animal MRI scanner (Bruker, Ettlingen, Germany) using a bird-cage 3-cm-diameter $^1$H coil for acquisition and reception. CEST images were acquired with a RARE sequence (TE/TR=80/5500 ms; turbo factor 32) preceded by a CW saturation pulse being applied at ± 50 ppm ($T_{sp}=400 ms$, $B_{sat}=20 \mu T$). $B_0$ and $B_1$ maps were acquired separately using a GE sequence (TE=5, 7.5, 10, 15 ms; TR=300ms, flip angle of 30° and 60°). In vitro tests were performed on a 6-tubes phantom each containing $[\text{Eu}^{3+}]$DOTAMGly (Guerbet, Roissy, France; concentrations of 0.5, 1, 2.5, 5, 7.5, 10 mM) [3] embedded in a low-gelling point 4% agarose matrix.

Z-spectra Simulation and Image Analysis with PARAMAP. Our image analysis tool designed as PARAMAP is a Matlab (The MathWorks Inc., Natick, MA) based program aiming at correcting the $B_0$ and $B_1$ induced errors on the native CEST image ($I_0$) and $B_1$ induced errors on the native CEST image ($I_0$). Briefly, PARAMAP simulates for each pixel $r$ a series of asymmetric Z-spectra using $B_0(r)$ and $B_1(r)$ values with the concentration C as a variable ($aMTR(C,r)$). The others parameters of the simulation ($k_1$, $\delta$, $T_1$ and $T_2$ of both pools) are extracted from experimental Z-spectra of $[\text{Eu}^{3+}]$DOTAMGly (data not shown). The concentration map $C(r)$ is then calculated from the minimization of the cost function: $|I_0(r)-aMTR(C,r)|$.

Results and Discussion

As illustrated by the figure 1, field inhomogeneities manifest themselves strongly on the amplitude of the observed CEST effect for a given concentration. Therefore a 10% error on $B_{sat}$ leads to a 4% over- or under-estimation. Similarly, a 100Hz frequency error leads to a 1% over- or under-estimation. In our experiment, $B_0$ and $B_1$ inhomogeneities were quite modest as illustrated (standard deviations: $\sigma_{\text{REF}}=21 \text{Hz}$ and $\sigma_{\text{REV}}=0.5 \mu T$). Yet without correction, the calculated CEST effect (Fig.2, open red dots) is quite different to the CEST effect expected (blue dots). If not corrected, discrepancies between the known and the estimated concentrations are on average of 0.8mM. The $B_0$ and $B_1$ corrections (green line) improve significantly the quantitativity of the established PARACEST concentration map with an averaged over-estimation of 0.3 mM (See Fig.3).

Conclusion

CEST agents are promising new contrast agents for MR molecular imaging since they allow to reach nanomolar sensitivity [5]. Yet, their susceptibility to parameters such as $B_0$, $B_1$ is a real issue to achieve truly quantitative CEST imaging. In this study, we validated in vitro PARAMAP, a home-made software aimed at correcting not only for $B_0$ and $B_1$ field inhomogeneities. Ultimately, quantitative PARACEST concentration maps were obtained within a reasonable margin. To move further toward in vivo quantitative CEST imaging, we are actually extending the simulation to a 4-site chemical exchange model similar to the one described by Li et al. [6].

The software will be available at: http://groups.google.com/group/paramap.

Acknowledgments

Grant sponsor: Isel/Innac French-German Project.

References

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