Correcting Susceptibility Artifacts in Arterial Input Function (AIF) for Dynamic Contrast Enhancement Magnetic Resonance Imaging (DCE-MRI) at 3T.

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Introduction:

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) technique has the potential for estimating a number of key properties of tumor vasculature. Knowledge of these features could be used to provide indicators of tumor grade and surrogate markers of therapeutic response. Several physiological kinetic models have been proposed to model these signal dynamic curves in order to extract functional parameters that could quantify the tumor vascular environment. For most kinetic models, in order to estimate reliable kinetic parameters, the knowledge of the contrast agent concentration time course in blood vessels, also referred to as the arterial input function (AIF) is crucial. However, in high field imaging, the susceptibility effect in DCE-MRI studies is pervasive even with a very short TE time of 1-2 msec. Nonetheless, most traditional methods being used to convert signal intensity in blood pools to contrast agent concentration time curve today assume that the image signal is T1 dominated. When T2* effects cannot be overlooked, they will be unable to provide accurate AIF estimation. Here we propose a novel method that could fully compensate the susceptibility effects for AIF estimation. It allows us to estimate AIF when DCE-MRI data are seriously corrupted by T2* effects.

Methods:

A. Theory

According to the Ernst formula, gradient-echo image intensity could be written as:

$$\frac{S(t)}{S(0)} = \exp\left(-TE\cdot\left(\frac{1}{T_2^*}-\frac{1}{T_{20}^*}\right)\right)\cdot\frac{1-\exp\left(-\frac{TR}{T1}\right)}{1-\cos\alpha\cdot\exp\left(-\frac{TR}{T1}\right)}\Big/\frac{1-\exp\left(-\frac{TR}{T10}\right)}{1-\cos\alpha\cdot\exp\left(-\frac{TR}{T10}\right)} = \exp\left(-TE\cdot r2\cdot Cp(t)\right)\cdot\frac{1-\exp\left(-\frac{TR}{T1}\right)}{1-\cos\alpha\cdot\exp\left(-\frac{TR}{T1}\right)}\Big/\frac{1-\exp\left(-\frac{TR}{T10}\right)}{1-\cos\alpha\cdot\exp\left(-\frac{TR}{T10}\right)}$$

where relaxation property *1/T2*-1/T20 = r2Cp(t)* is utilized. *Cp(t)* is the contrast concentration and r2 is the T2* relaxivity. Our goal is to retrieve arterial input function *Cp(t)* from the above equation. Fortunately we are only interested in contrast agent concentration time curves in arteries or veins. Moreover, the behavior of the concentration time curve in the blood pools has been well studied and several functional forms that incorporate the rapid rising and subsequent decaying part of a typical plasma concentration curve have been used to model the real vascular time curve with success. Here we will use the formula below as our functional form and replace *Cp(t)* with it.

$$Cp(t) = A\cdot(t-t_0)^2\cdot\exp\left(-\frac{t-t_0}{t_1}\right)+\sum_{i=1}^{2}B_i\cdot\exp\left(-\frac{t-t_0}{t_i}\right)$$

when *t > to* and *Cp(0) = 0* otherwise. This functional form replacement dramatically simplifies the nature of our equation. It now turns the *Cp(t)* estimation into a fitting problem. By adjusting the six functional parameters to make the calculated signal best resemble the experiment data; we could efficiently retrieve the plasma concentration curve with T2* effects taken into consideration.

B. Image acquisition

DCE-MRI data were acquired from a glioblastoma patient (recruited by an IRB approved phase 2 AZD2171 investigational study at the Dana-Farber/Harvard Cancer Center[1]) using a 3 Tesla MRI system (TimTrio, Siemens Medical Solutions, Malvern, Pennsylvania). The DCE imaging parameters include TR = 5.7 sec, TE = 2.7 sec and flip angle = 10. 0.1 mMol/kg of Gd-DTPA was injected 52 seconds after the beginning of the acquisition at 5 cc/second. Data to allow computation of a T1 map of the tissue of interest is created using five different flip angles (2, 5, 10, 15, 30 degrees).

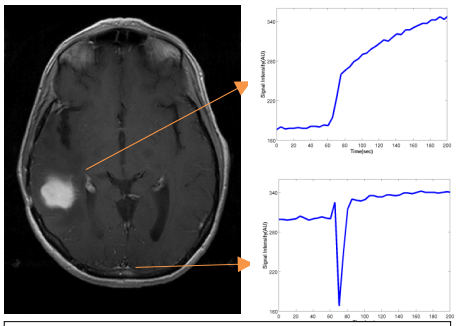

Fig. 1 is the post-contrast T1-weighted image. It shows the signal curves extracted from two different brain regions respectively. The example shows that susceptibility effects are pervasive in blood pools.

Results and Discussions:

Fig. 1 demonstrated examples of two signal time courses taken from regions showing distinct dynamic behavior. They are chosen from tumor tissues and big vessels respectively. The disruption of blood brain barrier, a distinct phenomenon in Glioblastoma, allows Gd-DTPA to leak from blood beds into tumor tissues. Nonetheless, the leaked GD-DTPA concentration in tumors is relatively low compared with that in the blood pool. As a result, the signal curve does not suffer evident T2* effects. On the other hand, the curve from superior sagittal sinus suffers dramatic signal loss during the bolus's first pass. The high GD-DTPA concentration during the period allows complete T2* domination. The result shows T2* effects have to be carefully addressed for AIF estimation. In Fig 2, the blue dots in the upper and bottom panels are MR signal time courses selected from superior sagittal sinus and anterior cerebral artery respectively while the red lines are the fitting results from our model. The fitting curves captured all important kinetic features of the experiment data. The right pandel in Fig. 2 is the comparison between T2* uncorrected and corrected plasma concentration curves retrieved by traditional method neglecting susceptibility effects and our model respectively. In the upper panel, our method restored the plasma time curve from a T2* dominated signal curve that normally has to be discarded by traditional methods otherwise a concentraion curve bears no physical meaning will be obtained. (The contrast agent concentraion drops upon the arrival of tracer as shown in the blue line). The signal curve in the buttom panel possessed very similar kinetic features with those with negligible T2* effects. However, if the susceptibility effect is not accounted in the curve, the converted concentration curve will miss the transient first pass phase; consequently, a false input function with wrong kinetic feature will be retrieved and applied in kinetic modeling. In Fig.3, the ability for our method to retrieve plasma concentration curve signal from data imbedded in T2* effect is demonstrated.

Conclusions:

In summary, it is evident that, in our 3T DCE-MRI data, the susceptibility effect is pervasive in blood pools. The ability for a model to incoporate T2* effects is inevitable in order to retrieve an accurate AIF. It is demonstrated in this work that by adapting a simple functional form as the plasma concentration input, we are able to account the susceptibility effect and accordingly retrieve AIF from T2* corrupted data where the traditional method encounter difficulties. When an accurate unique arterial input function can be obtained for each individual subject, it is expected that the kinetic model could prove better insights for the tumor vasculature; in turn a better predictive biomarker for vascular-targeted therapy.

Reference: V. Kuperman et el. Differentiation Between the Effects of T1 and T2* Shortening in Contrast-Enhanced MRI of the Breast. JMRI 2000:9:172-176

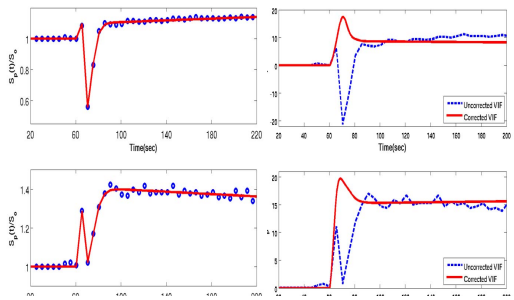

Fig. 2 Performace of T2* effects compensated model. Left: The blue dots are the measured signal intensity time curves. The signal time courses in upper and buttom are chosen respectively from voxels near superior sagittal sinus and anterior cerebral artery. The red lines represent the calculated signal time curve using the retrieved concentraion by our model. This indicated that the retrieved concentraion curve is very close to the "true" one according to the theory. The results demonstrate that the model is able to correct T2* effects and return plasma concentraion accordingly. Right: comparison of retrieved T2* corrected and uncorrected concentraion curve.