On the Time to Peak Factor of Dynamic Susceptibility Contrast of Microbubbles

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Introduction:

Dynamic susceptibility contrast MRI (DSC-MRI) has been widely applied in measuring cerebral blood volume (CBV) and perfusion for years. However, using Gd-DTPA as a contrast agent in DSC-MRI may not be an appropriate option for patients with renal diseases. Recently, microbubbles, originally developed as a contrast agent in ultrasound imaging, were used as a novel MR susceptibility contrast agent because of its susceptibility differences between the gas-liquid interface [1,2]. In this study, we aim to investigate systematically the correlation of rCBV derived from Gd-DTPA and the induced susceptibility effect from microbubbles, trying to find out factors of signal changes in microbubbles-enhanced MRI

Materials and Methods:

In this study, 7 normal male Sprague-Dawley rats (mean weight of 295±30g) were anesthetized with 1.5% Isoflurane and scanned in a 4.7T animal MRI scanner (Bruker Biospec 47/40). For DSC imaging, 500 consecutive gradient echo EPI scans were applied with TE/TR as 30/1000 ms, FOV as 2.9 mm, and matrix size as 96x128. 0.2 ml of custom-made microbubbles(volume fraction=7%, mean diameter=1-2 um) was manually injected into the tail vein at the 120th scan and flushed with 0.5 ml of saline. $\triangle R_2$* maps were calculated on a pixel-by-pixel analysis as the following equation:

$$\Delta R_2^* = \frac{\ln\left(S_{pre}/S_{ave-post}\right)}{TE}$$

where S_{pre} is the average intensity of 50 pre-injection images and $S_{ave\text{-}post}$ is the average intensity of consecutive 50 post-injection images around the timing of maximum susceptibility contrast for microbubbles [2]. For comparison, 0.2 mL Gd-DTPA (Magnevist) was also manually injected with the same scheme to acquire a conventional rCBV map. The time-to-peak information was extracted from the concentration –time curve of whole brain.

Results:

Figure 1 showed the intensity-time curves from two rats. The time-to-peak for rat 1 and rat 2 were 255 s and 38 s, respectively. The $\triangle R_2$* maps from microbubbles and rCBV maps from Gd-DTPA of the two rats were displayed in figure 2. With the correlation coefficient of 0.82, $\triangle R_2$* map from rat 1 which had longer time-to-peak was higher correlated with rCBV map from Gd-DTPA. The relationship between the time-to-peak and the correlation of microbubbles v.s. Gd-DTPA was portrayed in Figure 3. Note the high correlation (r=0.97) between time to peak and the correlation with Gd-DTPA derived CBV maps. Therefore, the time-to-peak has profound effect on microbubble-enhanced DSC-MRI.

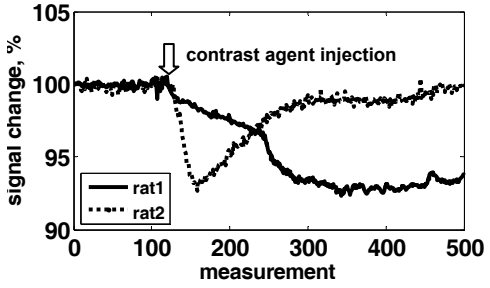

Figure 1
The intensity-time curves from rat 1 and rat 2. The time-to-peak for rat 1 and rat 2 were 255s and 38s, respectively.

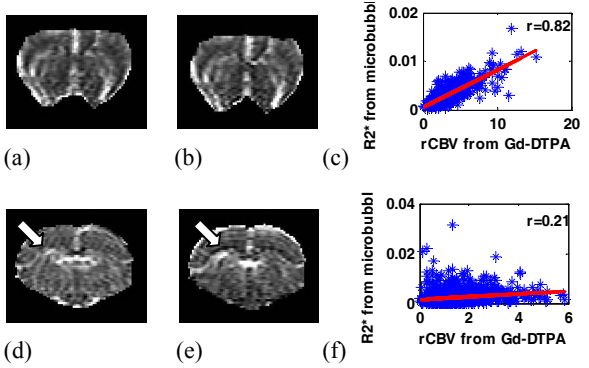

Figure 2
The rCBV map derived from Gd-DTPA-enhanced trial (a) and $\triangle R_2$* map derived from microbubble-enhanced trial (b) of rat 1 showed similar intensity, responding by high correlation coefficient (r=0.82) in (c).
The rCBV map derived from Gd-DTPA-enhanced trial (d) and $\triangle R_2$* map derived from microbubble-enhanced trial (e) of rat 2 showed inconsistence, indicated by arrows. The low correlation of these two maps was evident with low correlation coefficient in (f).

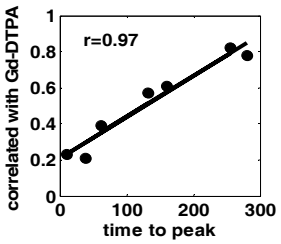

Figure 3
The relationship between the time-to-peak and the correlation for $\triangle R_2$* from microbubbles and rCBV from Gd- DTPA of 7 rats was displayed. The high correlation (r=0.97) shown in Fig. 3 indicated, the time-to-peak may have profound effect on microbubble-enhanced MRI.

Discussion and Conclusions:

Microbubbles have been proposed as a novel contrast agent for MRI imaging. However, comparing to the conventional contrast agent Gd-DTPA, the signal change provided by the susceptibility effect of encapsulated gas is much less. Furthermore, due to the size and chemical characteristics of the surface, the microbubbles may aggregate and be trapped in local tissue vasculature, and present a delayed and dispersed passage in dynamic scanning. Therefore, the analysis method of conventional DSC could not be appropriate for microbubbles. In this study, we showed that an averaged $\triangle R_2$* map of microbubble could be highly correlated to the Gd-DTPA derived CBV maps. In addition, the correlation of these two maps is highly positive related to the factor of time-to-peak derived from microbubble-enhanced trials. In conclusion, trials with longer time-to-peak, delayed and dispersed perfusion of microbubbles were observed, showing substantially enhanced susceptibility effect which might be helpful for perfusion assessment. Thus, it is suggested that the index of time-to-peak might be a prominent factor for future explorations of microbubble-enhanced MRI.

References:

1. Kelvin K. Wong, et al. *Magn Reson Med* 2004; 52: 445-452
2. Jerry S. Cheung, et al. *NeuroImage* 2009; 46: 658-664