Validity of the Contrast Reagent Concentration versus Signal Intensity Relationship in Brain Perfusion Imaging

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SYNOPSIS
This study tested the hypothetical direct linear relationship between contrast reagent concentration and gradient-echo signal intensity that is frequently used in the quantitative evaluation of brain contrast reagent passage perfusion studies. Hospitalized stroke patients underwent two perfusion studies in which different amounts of contrast reagent were administered. The results indicate that the hypothetical relationship is not valid and suggest an alternative.

INTRODUCTION
The usual assumption used in the quantitative analysis of contrast reagent (CR) passage perfusion imaging is
\[ R_2^* = R_2^*0 + KC \]  
(1)
where \( R_2^* \) is the relaxation rate measured in the presence of CR, \( R_2^*0 \) is the intrinsic relaxation rate in the absence CR, \( K \) is a scaling constant, and \( C \) is the CR concentration. Previous studies have universally assumed a direct linear relationship (i.e. \( y = 1 \)) in eqn 1, despite reservations discussed by Boxerman et al (1995). Eqn 1 leads to the estimation of the instantaneous CR concentration from the signal intensity measured with an \( R_2^* \)-weighted imaging technique:
\[ C = - \left( \frac{\ln(S/S_0)}{KTE} \right) \]  
(2)
where \( S \) and \( S_0 \) are the signal intensities measured in the presence and absence of CR and \( TE \) is the time to gradient echo.

In the present study the validity of eqns 1 and 2 was tested by performing two CR passage perfusion studies in close succession using total CR doses of 0.1 mmol/kg (low dose) and 0.2 mmol/kg (high dose). Assuming no physiological changes in perfusion or cardiac output over the short time interval between the two studies, each image voxel should experience a two-fold greater amount of CR passage in the high dose study compared to the low dose study. Therefore the time integral of the CR passage calculated using eqn 2 for the high dose study should be twice that observed for the low dose study. This hypothesis was tested.

SUBJECTS & METHODS
Patients hospitalized for a recent stroke (< 96 hr from symptom onset) were examined because such patients are expected to exhibit a spectrum of regionally unique perfusion characteristics (i.e. normal tissue, ischemic penumbra and infarction). Five subjects were successfully examined using a protocol that included two CR passage perfusion studies using Omniscan (gadodiamide) boluses of 0.1 mmol/kg (low dose) and 0.2 mmol/kg (high dose) in succession. The order of the high and low dose studies was randomized. CR passage was detected at 1.5 T using a time series of gradient-echo-echo-planar (TE = 60) image acquisitions (40 time points at 2.0 sec intervals). A power injector was used to inject CR into an antecubital vein at a rate of 5.0 ml per sec. Safety considerations necessitated administering the higher dose at the same (maximal) rate as the low dose so that the duration of the high dose bolus was twice that of the low dose bolus. The instantaneous CR concentration delivered during each bolus was identical.

RESULTS
When the conventional methodology (eqn 2) was employed for quantitating CR concentration, the mean ratio of the high dose CR passage time integral to that observed in the low dose study was 1.32 +/- 0.38. This is significantly less than the expected value of 2.0 suggesting that the conventional methodology embodied in eqns 1 and 2 may not be valid. Evaluation CR passage time curves indicated that the finding was not related to truncation of the high dose CR passage (which was delivered as a longer bolus). The results suggest that a more appropriate value for \( y \) is 0.4 (rather than 1) over the CR concentration ranges encountered in typical perfusion imaging studies.

An unanticipated finding was that the maximal instantaneous CR concentration observed in the high dose study was 1.8 +/- 0.26 times higher than that observed in the low dose study despite that the instantaneous CR concentration delivered by the power injector was the same for the high and low dose studies (the CR bolus delivered by the injector in the high dose study had twice the duration compared to that delivered in the low dose study). This observation emphasizes the significance of CR bolus dispersion between the site of administration and the site of detection.

CONCLUSIONS
This study suggests that a commonly-made assumption used in evaluating CR passage perfusion imaging is not valid. This finding has important implications for quantitative derivation of cerebral blood volume and cerebral blood flow from CR passage data.

REFERENCES

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