# 國科會工程處

# 九十年度多年期計畫

**NSC89-2213-E002-193**

**“磁化率對比微灌流磁振造影對缺血性中風之研究 (2/2)”**

## 成果報告

**計畫主持人：鍾孝文副教授 台大電機系**

**九十年十一月二日**

# 行政院國家科學委員會專題研究計畫成果報告

## 磁化率對比微灌流磁振造影對缺血性中風之研究 (2/2)

## Susceptibility contrast perfusion MRI for the investigation of ischemic stroke (2/2)

計畫編號：NSC89-2213-E002-193
執行期限：89 年 8 月 1 日至 90 年 7 月 31 日
主持人：鍾孝文副教授　　台大電機系
chung@cc.ee.ntu.edu.tw

### 一、中文摘要

本二年期計畫之目的在於發展一系列的影像分析技術，以用於對比劑動態臨床微灌流磁振造影並分析腦部微灌流參數。計畫中以缺血性中風作為評估之一例。在第一會計年度中，有關相對性大腦微灌流參數均已發展完成病最佳化；各項分析軟體亦以成功移植至臨床磁振造影儀之操作平台。在第二會計年度中，對於國際上慣用之標準絕對定量灌流參數的先天缺失，在本計畫執行次年當中有細部的探討。針對此一缺失本研究群提出一新的評量參數: 最大訊號下降量(MSD)，此解決方案更經過臨床實際測試於中風病患，顯示出高度的腦血流相關性。本篇報告，即對於傳統方式絕對定量化微灌流參數之誤差加以分析，並以改進之演算法的臨床分析證明其可行性。

**關鍵詞**：微灌流、磁振、腦缺血、最大訊號下降量、絕對定量灌流參數

### Abstract

The purpose of this two-year project is to develop a series of image analysis methods on clinical perfusion-weighted magnetic resonance imaging (MRI) using the concept of dynamic susceptibility contrast. The specific target of the project is cerebral ischemia. In the first fiscal year we have implemented and optimized conventional analysis methods to estimate the relative parameters. The analysis software has also been successfully transformed into clinical MR system platform. In the second fiscal year, the pitfalls inherent in the absolute quantification of perfusion parameters commonly used as the international standard have been analyzed in detail and a proposed remedy: maximum signal drop (MSD) tested on stroke patients and shown high dependence on CBF. In this report, the estimation errors on the absolute perfusion parameters with the conventional procedure are analyzed and the clinical feasibility of the proposed novel algorithm are shown.

Keywords: perfusion, magnetic resonance, cerebral ischemia, maximum signal drop, absolute quantification of perfusion parameter

### 二、計畫緣由與目的

Dynamic susceptibility-contrast (DSC) perfusion-weighted imaging (PWI) has been used extensively to derive clinically useful parametric maps such as relative cerebral blood volume (rCBV), relative cerebral flow (rCBF), and relative mean transit time (rMTT) for assessing intracranial micro-hemodynamics (1). The absolute

quantification of perfusion parameters from DSC MRI requires the measurement of arterial input function (AIF) to be deconvolved from the tissue concentration time curve. A deconvolution method widely accepted by the scientific society is through the use of singular value decomposition (SVD) (2). However, it was also pointed out that the bolus delay and dispersion were found to introduce significant underestimation of cerebral blood flow (CBF) (3). In the first part of this study, we further demonstrate that significant estimation errors in CBF may arise simply due to difference in tissue MTT, even if bolus delay and dispersion were both absent. A typical AIF was computationally generated as a gamma-variate function to resemble the arterial bolus observed in typical studies (3). The AIF was convolved with residue functions R(t,MTT)=exp(-t/MTT) to yield the tissue time courses, assuming the vascular bed modeled as one single and well-mixed compartment (i.e., the simplest case with true CBF equal to unity) (2). The MTTs were varied from 0.5 to 10 seconds to cover the possible wide range seen in clinical practice. Deconvolution with AIF was then performed on tissue time courses using SVD (2,3), and the initial heights of the resulting residue function were determined as the estimated CBF. The estimation results therefore represented the percentage of the estimated CBF to the true CBF because the initial height of the original residue function was 1. The simulation was repeated with varying time interval of data points (i.e., the image acquisition frame rate) from 0.3 to 5.0 seconds.

Maximum signal drop (MSD) was proposed to provide information similar to CBV maps, but without the need of extensive post-processing (4). However, according to the central volume principle : rCBF=(rCBV/rMTT) which is proportional to the maximum height of concentration-time curve, we deem that rMSD shall be a better indicator of rCBF rather than rCBV. In the second part of this study, we evaluate the correlation between MSD and rCBF compared to that between MSD and rCBV on stroke cases instead of absolute quantification. 14 patients with acute infarction of middle cerebral arterial territories (3 days after onset) were recruited. Multi-slice dynamic susceptibility -contrast echo-planar PWI (TE=44ms, 128x128, 23cm FOV, 5mm slice thickness, 60 frames per slice at one-sec time interval) was performed after intravenous bolus injection of 0.2mmol/Kg Gd-DTPA (Magnevist, Schering, Germany). Images were obtained on a 1.5T system (Siemens Vision+, Erlangen, Germany). Maps of rCBV, rCBF and MSD were derived from concentration-time curves on a pixel-by-pixel basis. For each patient, 2~5 ROIs in the lesion area and one ROI in the normal tissue were drawn manually and applied to each map to compute the lesion to normal ratio (rCBV, rCBF, and rMSD). Correlation coefficients between rCBV and rMSD and that between rCBF and rMSD were examined on stroke groups.

## 三、結果與討論

The estimated CBF (percentages of true CBF) as a function of tissue MTT were plotted in Fig.1. Consistent under-estimation of the CBF was found in all cases, with accuracy decreasing at short MTTs and with increasing inter-frame interval. In particular, with typical MTT values of 2~5 seconds, it is noted that the estimation errors spanned about 20% if one used 1-sec frame rate as typically seen in DSC perfusion studies. Notice that since the errors depend on MTT and that tissue MTT has to be derived from the estimated CBF, the degree of CBF underestimations will not be correctable by, for example, referencing the CBF of healthy white matter or the CBF obtained using other modalities such as PET. One further notices that all estimations shown in Fig.1 were lower than the true CBF by at least 20%. This was due to truncation

of the small singular values during SVD in these noise-free simulations which, nonetheless, is anticipated to have little effects on the MTT-dependent CBF under-estimations investigated above.

Instead of absolute CBF quantification using SVD, implementation of the MSD method as a quick means of relative CBF estimation is feasible. Figure 2 show the correlation between rCBV and rMSD, and that of rCBF and rMSD, respectively, measured from ischemic stroke cases. Since rCBV is the area under the concentration-time curve, it is supposed to be proportional to be the product of rMTT and the maximal height of the concentration-time curve, which is relative to rMSD. Therefore, intuitively, rMSD is a better indicator for rCBF rather than rCBV. In this study, this is proven by the strong correlation between rMSD and rCBF for both tumor and stroke cases. On the other hand, though rMSD is also highly correlated with rCBV for tumor cases, consistent with previous report (4), this relation does not hold as firmly for stroke cases. This could be explained by the relatively uniformed rMTT in the tumor tissue, and thus rCBV behaves similarly to rCBF. Contrarily, in ischemic or infarcted areas, rMTT is usually prolonged. rCBV can not directly represent rCBF by the complication due to rMTT, and consequently does not have as strong correlation with rMSD as rCBF. In conclusion, we suggest that rMSD provides information close to CBF rather than CBV.

## 四、計畫成果自評

Our efforts spent in the second fiscal year of this project have created a massive amount of results substantially greater than that mentioned in this brief report. Overall, the project has generated four conference papers, including two presented in the Annual Meeting of the International Society of Magnetic Resonance in Medicine. Besides, we have published a journal article reporting the discrepancy of ADC evolution between territorial and hemodynamic-induced infarctions on Radiology (5). Furthermore, the achievements from this project have raised the attention of other domestic medical centers, including Taipei and Kaohsiung Veteran General Hospitals who have approached us for mutual cooperation. In short, we have confidence that a successful execution of this project will benefit both the medical centers as well as the patients with ischemic stroke. The future directions include the truly absolute quantification of cerebral blood flow for follow-up examinations and/or inter-subject comparison (2), and a measurement of the cerebrovascular reserve capacity using perfusion-weighted MR imaging before and after the acetazolamide challenging test..

## 五、參考文獻


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## 六、圖表

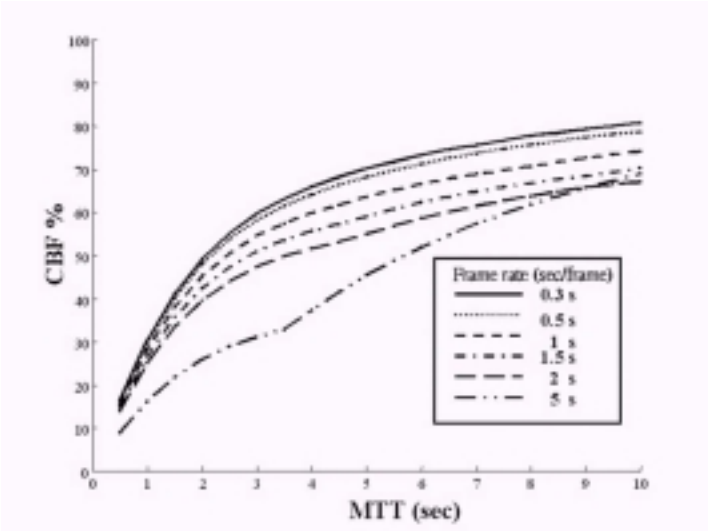


Fig.1. The estimated CBF (represented as percentages of true CBF) as a function of tissue MTT. Note that in addition to the consistent underestimation of the CBF, the estimation accuracy of CBF decreases at short MTTs and with increasing inter-frame interval. With typical MTT values of 2~5 sec, the estimation errors spanned about 20% variations.

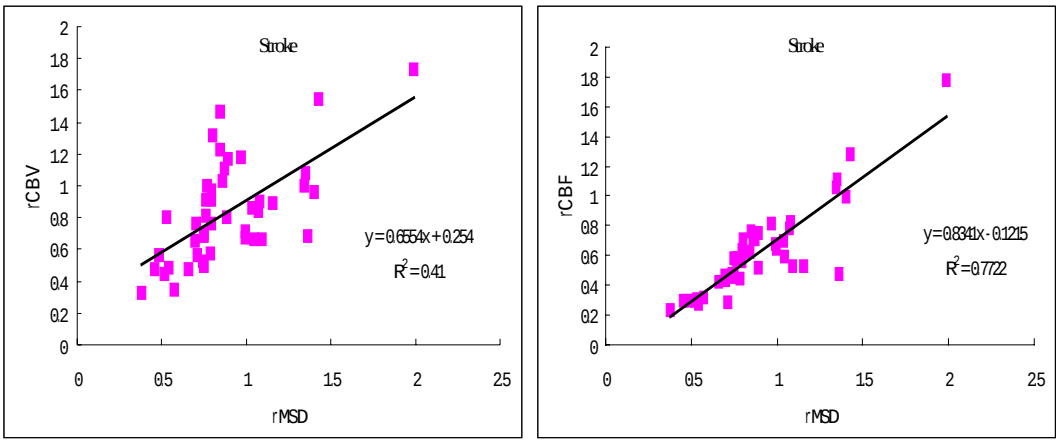


Fig.2 The two plots show the correlation between rCBF and rMSD, rCBV and rMSD, respectively, on stroke group. The vertical axis is lesion to normal ratio of rCBV or rCBF, and the horizontal axis is lesion to normal ratio of rMSD.