

• 計畫中文名稱	腦部多重監測系統應用於嚴重腦外傷之跨院研究		
• 計畫英文名稱	Application of Multiple Cerebral Monitoring in Severe Traumatic Brain Injury: A Multi-center		
• 系統編號	PG9805-0247	• 研究性質	應用研究
• 計畫編號	NHRI-EX98-9707PI	• 研究方式	補助(研究/辦理)
• 主管機關	行政院衛生署	• 研究期間	9801 ~ 9812
• 執行機構	台北醫學大學傷害防治學研究所		
• 年度	98 年	• 研究經費	2574 千元
• 研究領域	臨床醫學類, 生物技術, 復健醫學		
• 研究人員	邱文達,林茂榮		
• 中文關鍵字	腦外傷；腦組織氧氣分壓監測；顱內壓；腦灌流壓；壓力自動調節；；；		
• 英文關鍵字	traumatic brain injury；brain tissue oxygen tension；intracranial pressure；cerebral perfusion pressure；pressure autoregulation；；；		
• 中文摘要	本研究團隊有長達 20 年的腦外傷研究經驗，並建置世界上最大的腦外傷資料庫之一（162,734 病例）。藉由該資料庫的研究成果，在 1997 年推動安全帽立法成功，並於 2006 年出版台灣嚴重腦外傷臨床診療指引。在臨床研究的最後階段，研究結果證實顱內壓（Intracranial Pressure, ICP）監測器對治療嚴重腦外傷之重要性。然而，尤其是當病人面臨壓力自動調節功能不良的問題時，關於適當的腦灌流壓（Cerebral Perfusion Pressure, CPP）值仍然有許多爭議。本研究將證明腦組織氧氣分壓監測（Brain Tissue Oxygen Tension, PtO2）、杜卜勒穿顱超音波（Transcranial Doppler, TCD）、維持適當腦灌流壓和顱內壓監測器對於改善嚴重腦外傷病人預後結果之相關性；此將為第一個探討嚴重腦外傷與 PtO2 相關的研究。1995 年起，治療嚴重腦外傷病患需要植入顱內壓監測器已漸形成共識。所以，本團隊將更進一步探究，增加腦組織氧氣分壓監測對於治療嚴重腦外傷與改善病患預後之相關性。本研究目的：(1) 評估多重監測系統應用於嚴重腦外傷之存活效益；(2) 探討實驗組與對照組之間其葛氏預後指數(Glasgow Coma Scale, GOS)、細化型葛氏預後指數(Glasgow Outcome Scale-Extended, GOSE)以及健康相關生活品質(Health Related Quality of Life, HRQL)是否有差異。本計畫為前瞻性、多中心(5 個醫學中心)、隨機分派、具控制組的臨床研究，預計收集五個醫學中心中其昏迷指數 3-8 分之嚴重腦外傷患者，且年齡介於 17-70 歲的病人為研究對象。研究對象將隨機分配到兩組：實驗組(A 組)及對照組(B 組)。A 組使用多重腦監測系統(腦組織氧氣分壓監測、杜卜勒穿顱超音波、腦灌流壓維持及顱內壓監測器植入)；以維持適當腦灌流壓而使腦組織氧氣分壓控制在 25-30 mmHg 之間為治療目標。B 組則只使用顱內壓監測器；以調控 CPP 大於 60mmHg 為治療目標。本研究將每小時記錄病人之顱內壓（ICP）、腦灌流壓（CPP）、平均動脈壓、輸入及輸出量和腦組織氧氣分壓監測(PtO2) 值。以相關係數評估低流速腦灌流壓和平均流速之間的關係，或者以顱內壓作為壓力調節的評估標準。於受傷後第一、第二、第六及第十二個月時，以葛氏預後指數評估病人的預後。結果分為預後良好及預後不良二種，恢復良好及中度失能評為預後良好；重度殘障及植物人則為預後不良。本研究主要評估指標為整體存活率，將以 Kaplan-Meier 方法分別估計實驗組及對照組的整體存活率。並以 stratified log-rank 檢定比較兩組整體存活率是否具顯著差異，有意義水準訂為雙尾 0.05。其他評估指標分別以 Cox's regression model, ANCOVA, 卡方檢定(Chi-square), multiple linear regression 等方法分析，將以 SAS 套裝軟體(9.1 版) 進行統計分析。目前已進行小規模之先驅性研究，共收集六位嚴重腦外傷病患，初步證實腦部多重監測系統(PtO2，TCD，CPP 和 ICP)應用於嚴重腦外傷之預後，與只有植入顱內監測器之病患相比，前者的預後較後者佳。初步研究結果已證明此為可行性研究計畫。更進一步探究評估此兩種監測系統對於病患預後是否有差異之必要性。本計畫預期結果如下：(1) 腦部多重監測系統應用於嚴重腦外傷將降低死亡率並且改善病患慢性期之生活品質；(2) 制定新的治療指引，有助於資歷較淺之醫生訓練課程；(3)嚴重腦外傷病患的預後將因此而提升為預後良好。		
• 英文摘要	With 20-year experience of traumatic brain injury (TBI) studies, our research group has obtained one of the largest data bank of TBI (162,734 cases) in the world. Law-enforced helmet usage law began in 1997 and our first edition of clinical practice guidelines (CPG) for severe TBI (STBI) in Taiwan appeared in 2006. In the last stage of our clinical study, we have proved that there are growing		

evidences about the need of intracranial pressure (ICP) monitoring in the treatment of STBI. However, there are still debates about the optimal cerebral perfusion pressure (CPP), especially in patients with impaired pressure autoregulation. The authors demonstrated that brain tissue oxygen tension (PtO₂) monitors, transcranial Doppler (TCD) monitors, CPP, and ICP monitors were associated with improved STBI outcomes. This was the first time that the results of PtO₂ monitoring were reported for STBI patients. There has been a growing tendency of consensus about the need of ICP monitoring in the treatment of STBI since 1995. We have now decided to explore further whether the addition of PtO₂ monitor in the treatment of STBI will be associated with improved patient outcome. The purposes of this study are (1) to evaluate the survival efficacy of multiple cerebral monitoring; and (2) to investigate the outcome difference with regard to Glasgow outcome scale (GOS), Glasgow outcome scale-Extended (GOSE), and Health Related Quality of Life (HRQL) among patients with different monitoring groups. This prospective, multi-center, randomized-controlled study will deal with TBI patients in 5 medical centers, enrolling STBI patients with Glasgow Coma Scale (GCS) scores 3 to 8, aged 17-70 years. All the subjects will be randomized and divided into two groups: the study group (Gr. A) and the control group (Gr. B). We will use multiple cerebral monitoring systems (ICP, brain tissue oxygen, Pt O₂, and TCD) in Gr. A. The target of Gr. A. is to adjust CPP to maintain PtO₂ around 25-30 mmHg. ICP monitoring only is used in Gr. B. To keep CPP at least at 60 mmHg is the target of Gr. B. The ICP, CPP, mean arterial pressure (MAP) intake, output, PtO₂ will be recorded every hour. We will use correlation coefficients between slow waves in CPP and mean flow velocity (MVF), or between and ICP can be used as a determinant of autoregulation at least daily. In 1, 3, 6, 12 months, we will evaluate the outcome by following up with the GOS, in which 'favorable outcome' is defined as a good recovery or a moderate disability, and 'unfavorable outcome' as a severe disability or a vegetative state. The primary efficacy endpoint is overall survival. The survival function will be estimated using Kaplan-Meier method within each treatment group. Stratified log-rank test will be applied for the comparison between the two treatment groups. The significance level is set at 0.05 (two-sided). The other efficacy endpoints will be analyzed using Cox's regression model, ANCOVA, Chi-square test, and multiple linear regression. SAS package (9.1 version) is used for statistical analysis. A pilot study with multiple cerebral monitoring systems (PtO₂, TCD, CPP and ICP) has been performed in 6 patients with STBI. The preliminary results of Gr.A. have demonstrated a better outcome as compared with Gr. B. in this limited data. Further study is indicated to evaluate the outcome difference in different monitoring groups. We anticipate to show the following results after this study: (1) applying multiple cerebral monitoring in the treatment of STBI will reduce the mortality rate and improve the quality of life in the chronic phase, (2) setting a new guideline helps to train young physicians, and (3) the outcome of STBI patients will be improved with favorable GOS, GOSE, and HRQL.