**Supplementary Table 5**

**Studies utilizing direct control of the heart alter cardiac output**

*CBF, cerebral blood flow; CI, cardiac index; CMRO2, cerebral metabolic rate for oxygen; CO, cardiac output; CPN, cardiopulmonary bypass; ETCO2, end-tidal carbon dioxide; HR, heart rate; ICA, internal carotid artery; IJV, internal jugular vein; LVEDP, left ventricular end diastolic volume; MAP, mean arterial pressure; PAC, pulmonary artery catheter; PWA, pulse wave analysis; TCD, transcranial Doppler; VA, vertebral artery; Xe, xenon*

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| **Author (Year)**  **[Reference #]** | **N** | **Subjects** | **Method of CBF measurement** | **Method of CO measurement** | **Intervention** | **Change in CO/CI** | **Change in MAP** | **Change in pCO2 (measure)** | **Change in CBF** |
| Govier 1984 [61] | 67 | 67 patients undergoing coronary bypass requiring cardiopulmonary bypass | Intraarterial 133Xe with single transcranial detector over central sulcus | Pump setting | In all patients, random measures were taken comparing CO and CBF.  PaC02 (33-45mmhg), nasopharyngeal temperature 25.6-29.3), and MAP (45-70 mm Hg) were held within ranges. | Natural variation  In 10 patients, pump flow rate was altered between (1.0, 1.3, 1.6, 2.0 L/min/m2). | No data | No data | In random measurement, there was poor correlation between CBF and MAP ( r = -0.13; p = 0.19) (and CBF and CI (r = 0.15; p =0.11).  There was a highly  significant (p < 0.0001) correlation of regional CBF with temperature during CPB (r = 0.54)  There was a significant (p < 0.005) association between  regional CBF and PaC02 r = 0.27).  No significant change in the measured regional CBF while CO was varied between 1-2L/min/m2. However, the PaCO2 and MAP for these pt were held in wide ranges |
| Shapiro 1969 [67] | 5 | 5 patients with complete heart block | IJV sampling for CMRO2. CBF was approximated from CMRO2 | PAC | Increasing HR by cardiac pacemaker to 60, 70, 90, and 100bpm. | CO increased with initiation of pacing, but remained stable with increases in pacing rate  Unpaced (HR 30-40) = 2.8±0.5 L/min/m2  60bpm = 3.6±0.6  70bpm = 3.4±0.6  90bpm = 3.4±0.5  100bpm = 3.6±0.7 | MAP remained stable with initiation and increasing rates of ventricular pacing  Unpaced = 105±13mmHg  60bpm = 109±17  70bpm = 112±16  90bpm = 110±12  100bpm = 111±7 | PCO2 remained stable with initiation and increasing rates of ventricular pacing  Unpaced = 38±3mmHg  60bpm = 41±1  70bpm = 40±2  90bpm = 41±2  100bpm = 39±2 | CBF increased with initiation of pacing, but remained stable with increases in pacing rate  Unpaced = 100%  60bpm = 118±6%  70bpm = 118±12  90bpm = 118±11  100bpm = 124±16 |
| Schwartz (1995) [62] | 7 | 7 baboons were placed on Cardiopulmonary bypass and cooled to 28°C | 133Xe washout | Pump flow | Altering pump flow; and altering MAP by inducing distributive shock with spinal anesthesia and by artificially stenosing the descending aorta | Pump flow was altered from 0.75 L/min/m2 (low flow) to 2.23 L/min/m2 (high flow) | MAP was artificially altered to high (61±2mmHg) and low (24±3) levels | paCO2 (alpha-stat) remained stable (34±2 mmHg on high flow; 36±4 on low flow) | During high BP, CBF remained stable between high and low flow (27.6±9.9 vs 34.0±8.3ml/100g/min)  During low BP, CBF remained stable between high and low flow (16.8±3.7 vs 14.1±3.7ml/100g/min) |
| Soma (1989) [63] | 21 | 21 adults on cardiopulmonary bypass | Argon washout | Pump flow | Altering pump flow | Pump flow was altered to 40, 50, 60, and 70 ml/kg/min, | MAP did not vary considerably with pump flow | Not measured | CBF increased in a rate dependent manner from 25ml/100g/min at a pump flow of 40ml/kg/min to 42ml/100g/min at 70ml/kg/min |
| Ozdemir (2012) [51] | 22 | 22 patients with idiopathic dilated cardiomyopathy | TCD ICA flow and VA flow | Echocardiography | Cardiac resynchoronisation therapy | CO increased after resynchronisation therapy (2.9±0.7 to 3.7±0.6; p<0.001).  LVEDP also decreased (15.6±4.8 to 13.4±3.9; P= 0.01) | MAP did not change significantly with resynchronization therapy (88.8±12.2 to 86.9±10.9; P=0.1) | Not measured | CBF increased from 502.3±80.2 to 702.3±77.4; P=0.001 (statistically significant increases in both ICA and VA flow volume). Resistivity Index (RI) and Pulsatility Index (PI) were not consistently different before and after resynchronization. |