Animal Models for Intracranial Pressure Monitoring in Traumatic Brain Injury

Submitted for Master of Surgery

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Animal Models for Intracranial Pressure Monitoring in Traumatic Brain Injury

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DECLARATION

I certify that, to the best of my knowledge, the material presented in this thesis is my own original work except where due acknowledgement is made. This thesis or any material contained within it has not been previously published for the award of any degree in any university.

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PUBLICATION AND PRESENTATIONS

DP AMATO. *Intracranial Pressure and Brain Tissue Oxygenation Monitoring in a Sheep Model of Traumatic Brain Injury* Presented at the Annual Scientific Meeting of the Neurosurgical Society of Australasia, Alice Springs, Australia, September 17th -19th, 2009.

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LIST OF ABBREVIATIONS

AAMI	Association for the Advancement of Medical Instrumentation
AANS	American Association of Neurological Surgeons
AEC	Animal Ethics Committee
AIHW	Australian Institute of Health and Welfare
ANOVA	Analysis Of Variance
ARDS	Adult Respiratory Distress Syndrome
ASDH	Acute Subdural Haemorrhage
atm	Atmospheres
BBB	Blood-Brain Barrier
BTF	Brain Trauma Foundation
CBF	Cerebral Blood Flow
CDC	Centers for Disease Control
CI	Confidence Interval
$CMRO_2$	Cerebral Metabolic Rate of Oxygen
CO	Cardiac Output
CO_2	Carbon Dioxide
CPP	Cerebral Perfusion Pressure
CSF	Cerebrospinal Fluid
CT	Computed Tomography

DAI	Diffuse Axonal Injury
GCS	Glasgow Coma Scale
ICP	Intracranial Pressure
IM	Intramuscular
IMVS	Institute of Medical and Veterinary Sciences
IP	Intraperitoneal
IV	Intravenous
LFP	Lateral Fluid Percussion
LN	Notch Length
MAP	Mean Arterial Blood Pressure
mg	milligrams
µg	micrograms
msec	milliseconds
mmHg	millimetres of mercury
MRI	Magnetic Resonance Imaging
MVA	Motor Vehicle Accident
NAT	N-Acetyl Tryptophan
O_2	Oxygen
$P_{bt}O_2$	Brain Tissue Oxygen Tension (partial pressure of oxygen in brain tissue)
PCA	Posterior Cerebral Artery

SaO_2	Arterial oxygen saturation (as measured by arterial blood gas analysis)
S/C	Subcutaneous
SpO_2	Oxygen saturation (as measured by pulse oximetry)
TBI	Traumatic Brain Injury
TPR	Total Peripheral Resistance
WHO	World Health Organization

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF EQUATIONS

LIST OF APPENDICES

ABSTRACT

The aim of this study was to identify appropriate animal models of raised intracranial pressure (ICP) and brain tissue oxygenation ($P_{bt}O_2$) following traumatic brain injury (TBI) that would be suitable for the development of novel therapies for secondary brain injury.

Monitoring of ICP and $P_{bt}O_2$ are important for understanding the effects of altered cerebral perfusion pressure (CPP). Tissue oxygenation is determined by the interaction of these variables and is important in the prevention of secondary injury following TBI. Unfortunately, few animal models reproduce the ICP and $P_{bt}O_2$ response that has been observed in the human condition. Previous studies at the University of Adelaide have used an ovine model of TBI in which the neuropathological response in these animals accurately mimics human TBI. However functional studies using sheep, at present, are problematic. Development of an alternative small animal model with scope for functional studies would assist with development of clinical therapies.

Aside from rats, which do not exhibit profound increases in ICP without the presence of a significant mass lesion, guinea pigs have been successfully used previously in studies of TBI. We therefore compared the ICP and $P_{bt}O_2$ response in guinea pigs with those of sheep. Compared to sheep, the guinea pig proved unsuitable for the study of ICP. Their labile response to inhalational anaesthesia, which included significant hypotension and bradycardia, was a confounding factor. With careful review and alteration to the anaesthetic regime, this problem was reduced, albeit that reproducible increases in ICP were never shown after TBI.

Although the reasons for a lack of ICP response in guinea pigs and rats are unknown, we note that sheep have a higher tentorial index than both species, and that the presence of an intact tentorium may restrict increases in pressure to a single compartment, thus increasing ICP. We propose that species with higher tentorial indexes may prove to be a more suitable than rodents for the study of ICP and functional outcome after TBI.

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