

SAFETY OF DIRECT LOCAL COOLING (15° C) OF THE CEREBRAL CORTEX WITH THE CHILLERSTRIP™ DURING FOCAL CEREBRAL ISCHEMIA IN MONKEYS

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1. INTRODUCTION

Systemic hypothermia to 32-33°C has been adopted for cardiopulmonary resuscitation for cardiac arrest from ventricular fibrillation by the American Heart Association¹. Aside from its use in protecting the brain during ischemia on cardiopulmonary bypass, the use of hypothermia has not been proven in stroke or head injury. A recent NIH supported clinical trial failed to show improved outcome with hypothermia induced between eight and twelve hours after traumatic brain injury (TBI)². However, patients who were less than 45 years of age and arrived in the hospital hypothermic (~35C) had better outcome³. One of the problems in the induction of systemic hypothermia is that cooling the entire body mass is difficult and likely to delay cooling. In addition, the induction of systemic hypothermia especially in conscious patients induces a tremendous stress response whereby the body elicits every available mechanism to maintain normothermia which may, itself, detrimentally affect ischemic or traumatic brain injury.

The induction of systemic hypothermia has several limitations. First, cooling the entire body is slow and difficult. Second, cooling of a conscious patient with systemic hypothermia is intolerable and elicits a tremendous stress response causing inappropriate vasoconstriction and metabolic activation.

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Seacoast Technologies, Inc., (Portsmouth, NH) has developed a cooling device (ChillerPad) that can be applied directly onto the dura and the cerebral cortex to cool the brain to 15°C. The aim of this study was to show that the application of hypothermia directly onto the cortical surface using the ChillerStrip™ does not adversely affect the severity of ischemic injury in a monkey model of mild focal cerebral ischemia (FCI) of about 20 min duration followed by spontaneous rewarming beginning five min after reperfusion of the brain.

2. METHODS AND RESULTS

2.1 Study Design

Six male monkeys (M. Mulatta) weighing 6.3-9.6 kg body weight (8.1 ± 1.5 , mean \pm SD) were studied. (Table 1). Two monkeys served as sham controls that did not have the ChillerStrip placed on the cortical surface whereas the others did. The overall study paradigm was:

- 1) Surgical placement of the ChillerStrip™;
- 2) Systemic and cortical cooling five min before FCI;
- 3) Endovascular occlusion of the bifurcation of the internal carotid artery;
- 4) Stable xenon/CT measurement of cerebral blood flow (CBF) during FCI;
- 5) Deflation of the occlusion and reperfusion;
- 6) Stable Xe/CT measurements at 10 and 20 min after reperfusion; and
- 7) Removal of the ChillerStrip,™ closing of the bone flap, and recovery.

The duration of FCI varied from the projected 20 min because in some cases, there were problems in obtaining the CBF measurements within the 20 min time limit. The duration of FCI ranged from 20 to 27.8 min.

Table 1: Study design. Two monkeys served as sham controls. Cortical and rectal temperatures were achieved 5 min prior to induction of FCI. Durations of ischemia varied because some studies had difficulties in initiating the first Xe/CT CBF measurement during ischemia and before the 20 min time limit. Rectal temperature was reduced to 32°C by passive cooling.

Group (N)	ChillerStrip	Cortical Temp (°C)	Rectal Temp (°C)	FCI (min)	Recovery
Contr (2)	No	37	37	20.0/20.0	7 days
Exp 1 (2)	Yes	15	37	27.8/24.0	7 days
Exp 2 (2)	Yes	15	32	22.0/20.0	7 days