DEcompressive CRAniectomy

DECRA Trial

SCCS 2010  Jeddah, Saudi Arabia

Prof Jamie Cooper
Melbourne, Australia

Supported by:
Victorian Trauma Foundation
ANZIC Foundation
WA Institute of Medical Research
NHMRC

Endorsed by ANZICS-CTG; Formally supported by NSA
Conflicts of Interest

• None

Primary injury

Inflammatory cascade

Cerebral oedema

Secondary injury

Outcome
**Background**

With current TBI management; neuro outcome 6 months...

<table>
<thead>
<tr>
<th>Severe TBI</th>
<th>50% unfavourable (GOSE 1-4)</th>
<th>Not independent living</th>
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<tbody>
<tr>
<td>Severe TBI</td>
<td>75% unfavourable (GOSE 1-4)</td>
<td>(only 25% independent long term)</td>
</tr>
<tr>
<td>+ CT grade III</td>
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Australia: *J Trauma* 2008 23:387
Alfred TBI database 1999-2001

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**Idea of pressure reduction is not new**
Hieronymous Bosch 1475-1480
**Early Decompressive Craniectomy**

**Hypothesis**  
DC: ↓ ICP  ↓ secondary injury

**CASE SERIES 1**

- 20 years case series; 57 pts
- No controls
- Wide frontotemporoparietal craniectomy
- Dura opening and dura patch
- **58% favourable outcomes**

*Perform before irreversible ischaemic brain injury*

Kleist-Welch Guerra  
*J Neurosurg 1999. 90:187-96*
Case Series 2. Cambridge UK

• 26 patients
• No controls
• Bifrontal craniectomy
• 69% favourable outcomes

* Suggest: DC for selected patients


ANIMAL STUDY

• Induced trauma to mice (control + craniectomy)
• Craniectomy mice
  – ↓ contusion volume
  – ICP controlled
  – improved motor function, compared to control

Zweckberger J.Neurotrauma 2003; 20: 1307-1314
CASE CONTROL STUDY  USA

- n= 35; 9 years
- Control population from TCDB
- Large bifrontal craniectomy + duraplasty
- Favourable outcomes:
  - Craniectomy 37%
  - Medical 16%  P=0.01
  - Age < 40 & < 48 hrs; 60% vs 18%;  P=0.0001
- Supports early surgery

Polin et al Virginia Neurosurg 1997; 41:84

Surgical technique -
Open the dura is best

- DC 50% ↓ ICP
- Opening dura - further 35% ↓ ICP

YOO et al  J Neurosurg 1999; 91:953-9
Pilot randomised trial
Children, Melbourne, Australia

- RCH Melbourne, Australia
- Taylor Butt Rosenfeld et al
- n=27; 7 years
- Children (>12 mths)
- First 24 hours, refractory ICP
  – (ICP > 20 for 30 mins)
- p=0.046
- Results suggest improved outcome with early DC in children

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<tr>
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<th>Favourable outcome</th>
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<tr>
<td>DC</td>
<td>54%</td>
</tr>
<tr>
<td>Medical</td>
<td>14%</td>
</tr>
</tbody>
</table>

(Child's Nerv Syst 2001 17:154-162)

However......

- Other case series found no benefit
  
  and

- Decompressive craniectomy might increase severe disability survivors
Many calls for a Randomised Trial

“decompressive craniectomy…a randomised controlled trial of the procedure is warranted”
Whitfield 2001; Brit J Neurosurg 15:500

“Prospective randomised trials are on the way to further clarify the role of decompressive craniectomy in victims of head trauma”
Piek J 2002 Curr Opinion Crit Care; 8:134

“to define the role of secondary decompressive craniectomy in the management of high ICP in patients in whom conventional measures have failed, a randomised trial is clearly needed”

International Randomised trials

• **DECRA**
  – Aust, NZ, Canada, US, Saudi Arabia

• **RESCUE ICP**
  – UK, Europe
DECRA
A randomized trial of early decompressive craniectomy in patients with severe diffuse traumatic brain injury

- ICU patients
- Diffuse brain injury, not pen. or mass lesions
- Early refractory ICP

DECRA Trial

**Chief Investigators:**
- Prof D Jamie Cooper (Intensive Care)
- Prof Jeffrey V Rosenfeld (Neurosurgery)

**Project Manager:**
- Lynne Murray

**Coordinating centre:**
- NTRI, Alfred Hospital, Melbourne, Australia

**Methods Centre:**
- School Public Health & Preventive Medicine, Monash University, Melbourne Australia
DECRA Inclusion Criteria

- Age 15-60 yrs
- < 72 hrs post injury
- ICP monitor in situ (prefer EVD)
- Severe diffuse brain injury
- Early Refractory ICP, despite best conventional management

CT brain scan - Marshall score grade 3
Compressed basal cisterns
DECRA Exclusions

- Mass lesion
- Penetrating neurotrauma
- Spinal cord injury
- Neurosurgery contraindicated
- No chance of survival

DECRA Pilot Study

2003: The Alfred
- Feasibility
- Refined protocol

Severe TBI screened
n=61

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<tr>
<td>Mass lesions</td>
<td>33%</td>
</tr>
<tr>
<td>ICP controlled</td>
<td>33%</td>
</tr>
<tr>
<td>Other</td>
<td>22%</td>
</tr>
<tr>
<td>Eligible</td>
<td>12% (7)</td>
</tr>
<tr>
<td>Randomised</td>
<td>5</td>
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Cooper DJ  J Crit Care 2008; 23:387
DECRA Trial Design

• Prospective, multi-centre RCT
• concealed allocation
• Stratified by site & presence of EVD
• Outcome:
  – Neurological function (GOSE) at 6 (& 12) months after injury
  – Trained assessor central site
    • Structured interview (telephone)
    • Assessor Blinded to intervention

TBI management strategy

• Based on Brain Trauma Foundation guidelines
  – ICP monitoring + ventriculostomy
  – Optimise sedation & ventilation
  – Normothermia
  – Osmotherapy as required
  – Barbiturate bolus for emergencies prior to randomisation

• Barbiturate coma only after randomisation

• Temperature not < 35°C
Surgical Technique

- Wide bilateral frontotemporal craniectomy
- Dura opened with cruciate incision
- Bone stored at -70°C or in an abdominal pouch
- Replaced 1-3 mths post craniectomy
Analysis (1)

• **Primary outcome**
  – neurological outcome at 6 mths
  – median GOSE (Mann-Whitney test)
  – (Glasgow Outcomes Score)
Analysis (2)

Secondary outcomes

• Proportion of **favourable** neurological outcomes at 6mths
  – proportion of good outcomes GOSE 5-8
  – using *sliding dichotomy*

• Mean ICP

• **Mortality** 6mths, 12 mths
King Fahad, National Guard Hospital,
King Abdulaziz Medical City
Riyadh, KSA

- Dr Yaseen Arabi
- 19 /155 patients = 13% of total
- 2008 largest recruiting site in DECRA!!
- 2009 second largest recruiting site!
Interim analysis Jan 2007
Baseline Demographics; n=80

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<tr>
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<th>Group 1 (n=42)</th>
<th>Group 2 (n=38)</th>
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<tbody>
<tr>
<td>Age (mean SD)</td>
<td>27 ± 10</td>
<td>26 ± 9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>74</td>
<td>79</td>
</tr>
<tr>
<td>Motor vehicle accident(%)</td>
<td>55</td>
<td>47</td>
</tr>
<tr>
<td>GCS (median)</td>
<td>5</td>
<td>5.5</td>
</tr>
<tr>
<td>CT Brain Grade III Marshall (%)</td>
<td>64</td>
<td>63</td>
</tr>
<tr>
<td>Max Head AIS (median)</td>
<td>4.5</td>
<td>4.5</td>
</tr>
<tr>
<td>ISS (mean SD)</td>
<td>34 ± 11</td>
<td>32 ± 11</td>
</tr>
<tr>
<td>TRISS (mean SD)</td>
<td>65 ± 24</td>
<td>67 ± 27</td>
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</tbody>
</table>

Interim Analysis

- Eligible patients randomized = 92%
- 6 month loss to follow up = 0%
- Surgical complications <10% (all categories)
- Neither group exceeded
  - Efficacy p<0.005
  - Harm p<0.05

Stopping rules
Independent DSMC
Report & Recommendations

March 2007; Chair: Prof. Paul Myles
– No ethical issues
– No safety issues
– No grounds for terminating the trial
– Continue to completion

April 2010 Recruitment complete!!

= 155
Some patients do remarkably well after enrolment in DECRA
Some patients do remarkably well after enrolment in DECRA

The answer is very close.... recruitment is complete, ....end 2010

DECRA Trial
Supported by

Australian Government
National Health and Medical Research Council

TRANSPORT ACCIDENT COMMISSION

Intensive Care FOUNDATION
making miracles happen

Western Australian Institute for Medical Research (WAIMR)
Thank you