



COGITATE: an update

Cambridge seminar

22-08-2017

Marcel Aries

Or....



A **stroopwafel** (Dutch pronunciation: [\[ˈstroːpuːfəl\]](#) ([listen](#)); literally "**syrup waffle**") is a [waffle](#) made from two thin layers of baked dough with a caramel-like [syrup](#) filling in the middle.^{[2][3]} It is popular in the [Netherlands](#), where they were first made in the city of [Gouda](#).

Making of...



A ball of dough is placed on a waffle iron to make the waffle for a *stroopwafel*



A pot of steaming hot syrup is used to fill the *stroopwafels*



A packet of shop-bought *stroopwafels*



Stroopwafels on a saucer



A *stroopwafel* is placed over a hot drink to warm it and soften the syrup

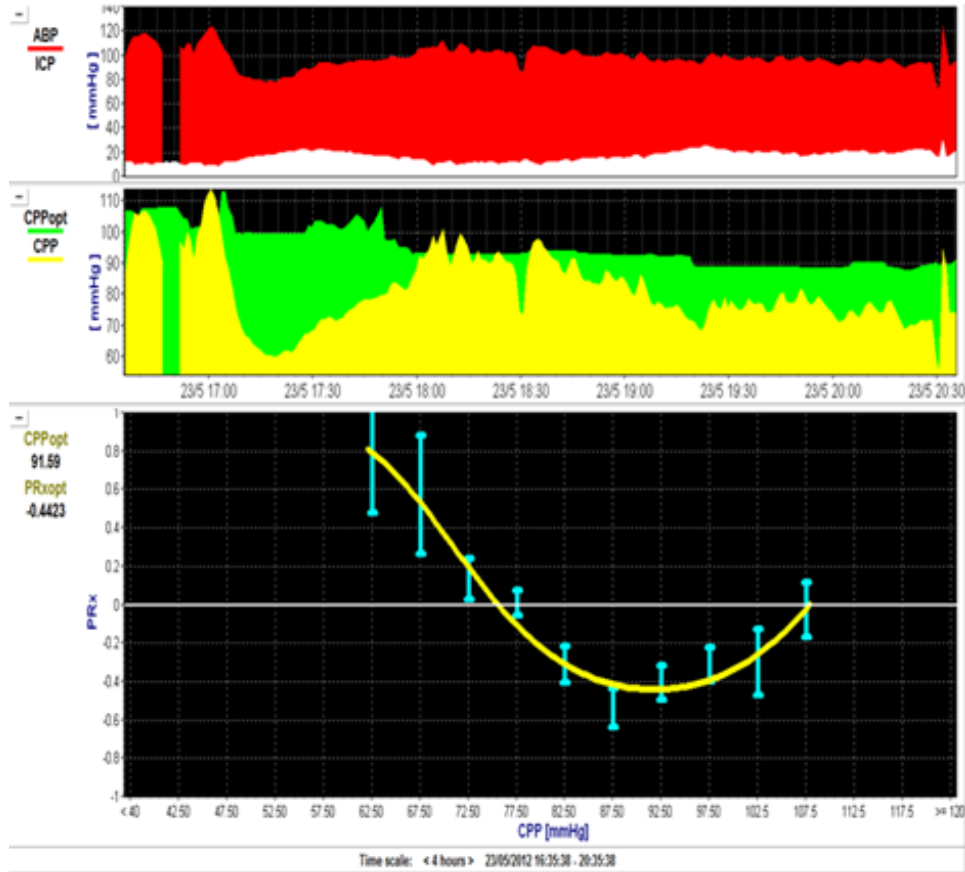


End 2017...



CPPOpt Guided Therapy: Assessment of Target Effectiveness

CPPopt



January 2017

FUTURE: 3 CENTER RANDOMIZED INTERVENTION STUDY

FEASIBILITY AND SAFETY STUDY



Covering 5 days after admission

GOGITATE

COGiTATE
CPPopt Guided Therapy: Assessment of Target Effectiveness

CPP treatment arm	CPPopt treatment arm
<ul style="list-style-type: none">• CPP: 60-70 mmHg• No CA information is displayed	<ul style="list-style-type: none">• Target the CPPopt• CA information is provided• CPP > 50 and < 100
<p>In common</p> <ul style="list-style-type: none">• ICP < 22 protocol• Review every 4 hours (3x review by research team)• Clinicians might decide/choose different CPP targets• Simple CPP treatment protocol	

N = 30

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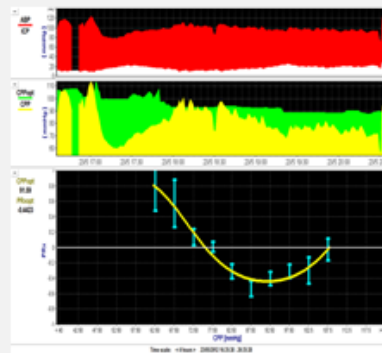
→ 6x

Feasibility and Effectiveness study

Jan 2017

INDIVIDUALISED TREATMENT

OPTIMAL CPP



2002-2017

- 'Preparation phase'
- 'Magic bullet'/ 'Holy grail' ?
- Small and careful steps
 - ICP monitoring
 - Feasibility and safety study
- Offline → online analysis → recommendation
- Software challenge

Opinion?

- Magic Bullet/Holy grail?
- Feasibility and Effectiveness (phase II)?
 - Very broad?
 - Endpoints
- Software + educational challenge
 - Website
 - Study module + simulation



Magic bullet/holy grail

- Why sceptical?
- Physiological point of view?
- Practical point of view?

Feasible and effective?

- When is CPPopt feasible and effective?
- (When is CPPopt safe?)

Chosen Endpoints

OUTCOMES

MAIN PRIMARY (FEASIBLE)

- Percentage of time CPP is within 5 mmHg of CPPopt
- During first 5 days

MAIN SECONDARY (SAFE AND EFFECTIVENESS)

- Average treatment intensity level score (TIL) score (> 3 points)
- Many different secondary outcomes
 - Physiological parameters
 - Organ damage
 - Adherence to monitoring protocol
 - GCS at NCCU discharge
 - Outcome at 6 months

Daily TIL score

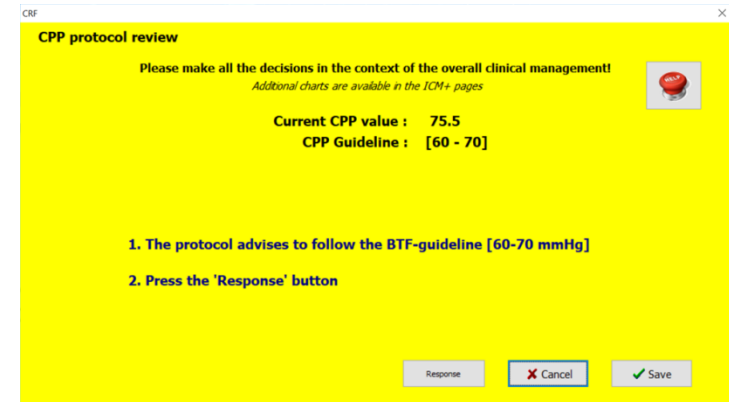
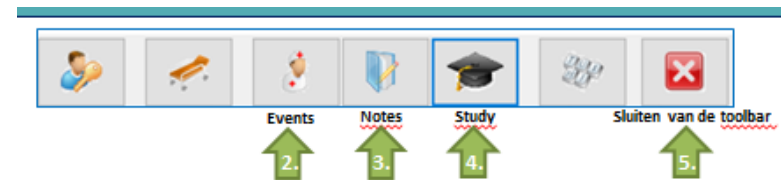
Therapy Intensity Level Scale*

Item	Details	Specifics	Score	Max	Patient
Positioning	Head elevation for ICP control		1	1
	Nursed flat (180°) for CPP management		1		
Sedation and neuromuscular blockade	Low dose sedation (as required for mechanical ventilation)		1	8
	Higher dose sedation for ICP control (but not aiming for burst suppression)		2		
	High dose propofol or barbiturates for ICP control (metabolic suppression)		5		
	Neuromuscular blockade (paralysis)		3		
CSF drainage	CSF drainage–low volume	< 120 mL/day (<5 mL/h)	2	3
	CSF drainage–high volume	> 120 mL/day (>5 mL/h)	3		
CPP management	Fluid loading for maintenance of cerebral perfusion		1	2
	Vasopressor therapy required for management of cerebral perfusion		1		
Ventilatory management	Mild hypocapnia for ICP control, based on arterial CO ₂ in mmHg, >35, <40		1	4
	Moderate hypocapnia for ICP control, >30, <35		2		
	Intensive hypocapnia for ICP control, <30		4		
Hyperosmolar Therapy	Mannitol	< 2g/kg/24h	2	6
	Mannitol	> 2g/kg/24h	3		
	Hypertonic saline	0.3g/kg/24h	2		
	Hypertonic saline	>0.3g/kg/24h	3		
Temperature control	Treatment of fever	(T>38°C or spontaneous T<34.5°C)	1	5
	Cooling for ICP control,	(>35°C)	2		
	Hypothermia	(<35°C)	5		
Surgery for intracranial hypertension	Intracranial operation for progressive mass lesion, NOT scheduled on admission		4	9
	Decompressive craniectomy		5		
Maximum (daily) total possible score				38

*Zuercher P, Groen JL, Aries MJ, Steyerberg EW, Maas AI, Ercole A, Menon DK. Reliability and Validity of the Therapy Intensity Level Scale: Analysis of Clinimetric Properties of a Novel Approach to Assess Management of Intracranial Pressure in Traumatic Brain Injury. J Neurotrauma. 2016;33:1768-1774.

Software + educational challenge

- Software (ICM+)
 - Special research requirements
 - Clinical input (events)
 - Data transport
 - Monitoring based interventions
 - Investigational product (REC)



Education

- Researchers + users (fellows/intensivists)
 - Not too familiar
 - Follow the project protocol
- ‘Autoregulation + CPPopt’ concept
- Work with (unknown) software
- Flexible (jumpy) targets
 - Thresholds
 - No recommendation
 - Some information hidden

Education

- www.cppopt.org
 - Jeanette Tas
- Background module
 - TBI
 - Secondary damage
 - Autoregulation
 - CPPopt
- Study module + simulation (review)

Summary

- We are getting close (and ...still enthusiastic)
- Feasibility and effectiveness
 - Protocol!
- Need lots of ‘stroopwafels’
 - Really get started
 - Inclusions
 - Volunteers
- Marek and Zofia



Thank you

- Cambridge Brain Physics group
- CPPopt group
- Special thanks for Jeanette Tas
- Special thank for Jo Donnelly!