



Endovascular Selective Cerebral Hypothermia — First-in-Human Experience

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Introduction

Major limitations in acute ischemic stroke (AIS) therapies

- Time limitation for lytics excludes most patients
- Mech revascularization limited by small number of trained physicians
- Recanalization limited by reperfusion injury* — **need neuroprotection**

Therapeutic hypothermia (TH) — the most potent neuroprotectant in the laboratory

- Influences a variety of cell death mechanisms — “combinational protective strategy”

Failures due to cooling techniques employed

- **BUT, a failed therapy in AIS** →

*K Fargen et al. J Neurointerv Surg 2013; 5:506-11
J Bai and P Lyden. Int J Stroke 2015; 10:143-152

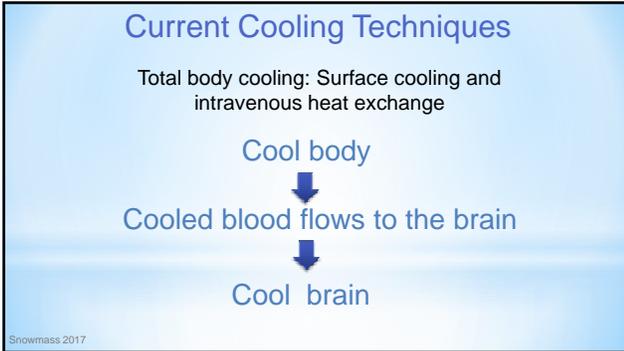
Review of Literature — Stroke

“The efficacy of postischemic hypothermia is critically dependent on the duration and depth of hypothermia...”

D Krieger and M Yenari. Stroke 2004; 35:1482-1489

“Efficacy was highest with cooling to lower temperatures (≤ 31 °C)...”

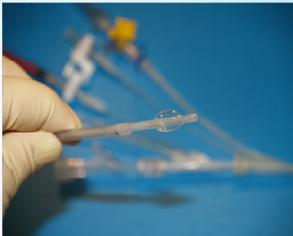
H Van der Worp, et al. Brain 2007; 130:3063-3074



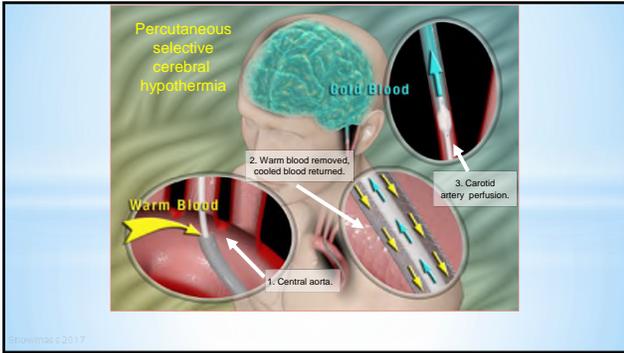
- ### Current Cooling Techniques
- Slow, unpredictable
 - Detrimental systemic effects
 - Pharmacologic paralysis required to suppress shivering
 - Pulmonary infection
 - Electrolyte imbalance
 - Cardiac dysfunction – arrhythmias, arrest
 - limited to $\geq 32^{\circ}\text{C}$
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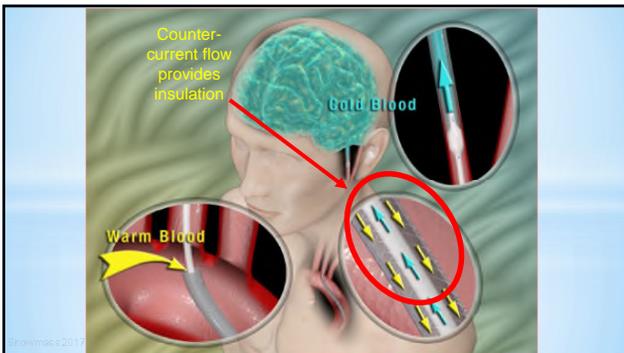
TwinFlo Catheter — Novel endovascular selective cerebral hypothermia device and technique

- Proprietary perfusion catheter
 - Isolates, selectively perfuses CA
 - Single femoral insertion
- Used with std. extracorporeal circuit



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TwinFlo Catheter — Novel endovascular selective cerebral hypothermia device and technique



In addition to providing hypothermia, the design allows selective delivery of drugs (e.g., lytics, Mg) and other devices (e.g., stentrievers and microcatheters), as well as control of perfusion pressure; recanalization be done in a cooled, protected brain to avoid reperfusion injury.

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In Vivo Pig Studies

- Demonstrated cerebral cooling rates up to 2°C/min
- Brain temperatures as low 15°C
- Minimal systemic cooling
- No adverse events
- Normal heart rhythm, systemic arterial blood pressure, arterial blood values
- No rebound *hyper*thermia with passive rewarming

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Porcine stroke model*

- 3 hours of ischemia followed by 3 hours of reperfusion
 - Pigs randomized to selective cooling or normothermia during reperfusion period. Analysis blinded.
- Blood pressure, heart rate, hemoglobin, glucose, and oxygenation levels did not differ between normothermic and hypothermic cohorts
- *Statistically significant reduction in stroke volume by selective cooling with TwinFlo to mean 28°C for 1-3 hrs*

*Mattingly TK, et al. J NeuroIntervent Surg 2016;8:418-422

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Initial Human Experience (1)

Neurosurgical repair of giant aneurysm of MCA in a 59 year-old male; 2-hr occlusion time

- London (Canada) Health Sciences Center
- TwinFlo selectively cooled brain at 26°C with systemic normothermia (≥ 36.9°C)
- Full, rapid recovery with *no neurological deficit*
 - Patient discharged home 4 days post-op

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Initial Human Experience (2)

- Cardiac arrest, non-shockable PVT in a 38 year-old male; no flow >8 minutes*
- No response after 44 min of CPR and 10 hours of 33°C ECMO, so TwinFlo tried as last resort
- TwinFlo selectively cooled brain at 27°C nasal temperature (brain temp. estimated at ~22°C) for 12 hours
- Full recovery with *no neurological deficit*, and patient back at work (urologist) after 2 months

**Wang C-H, et al. BMJ Case Rep 2017. doi:10.1136/bcr-2016-012806*

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Conclusion

This new endovascular system and technique may offer an improved method for neuroprotection in cardiac arrest, acute stroke and other conditions producing cerebral ischemia.

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THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

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Nielsen N, Wetterslev J, Cronberg T, et al. N Engl J Med. 2013; DOI: 10.1056/NEJMoa1310519

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