SPINAL CORD COOLING CATHETER: NEW CONCEPT IN PARAPLEGIA PREVENTION

John A. Elefteriades, MD, PhD (hon)
William W.L. Glenn Professor of Surgery
Director, Aortic Institute at Yale-New Haven
Yale University School of Medicine
New Haven, Connecticut, USA

Disclosure

Speaker name:

.....John A. Elefteriades, MD, PhD (hon).....

I have the following potential conflicts of interest to report:

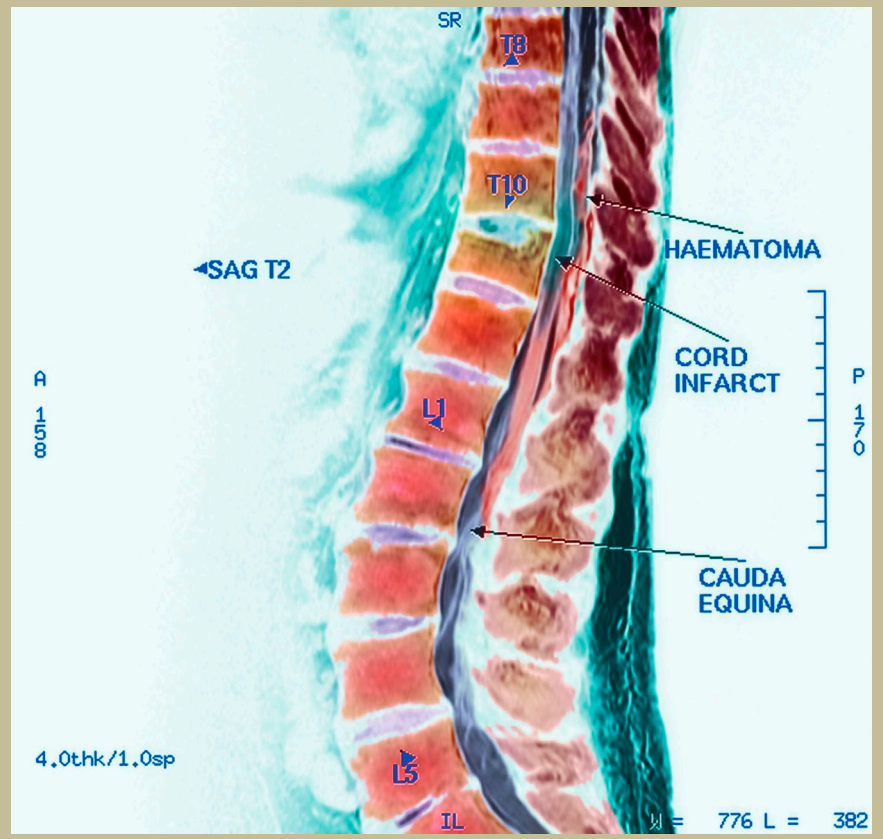
- ■ Consulting, Coolspine, Inc.
- ☐ Employment in industry
- ■ Stockholder of a healthcare company, Coolspine, Inc.
- ☐ Owner of a healthcare company
- ☐ Other(s)

☐ I do not have any potential conflict of interest

50% Early Mortality

Consequences

- **Motor**
- **Sensory**
- **Bowel**
- **Bladder**
- **Sexual function**
- **Skin (decubitus)**



Emotional and physical devastation of PARAPLEGIA

It's just temporary, right?
When will it go away?
How could this happen?

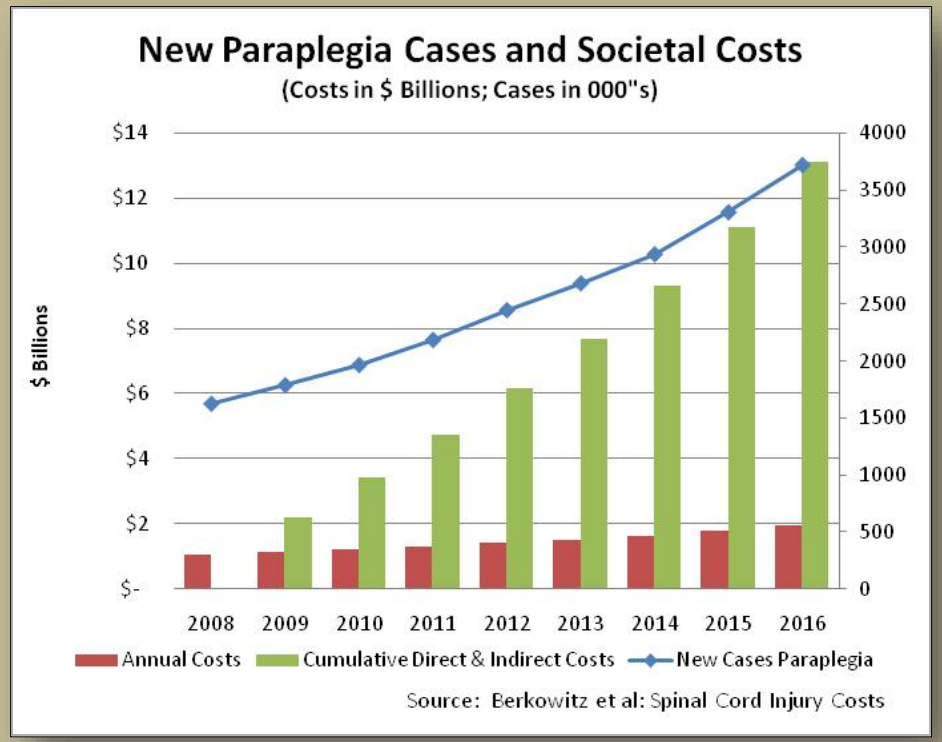
Paraplegia is still a problem!

Author (year)	Institution	No. of Pts.	Incidence of spinal cord injury with permanent dysfunction					Comments
			Descending thoracic	Crawford I	Crawford II	Crawford III	Crawford IV	
Coselli (2007) [1]	Texas, Baylor	2286	Not reported	3.3% (23/706)	6.3% (48/762)	2.6% (10/391)	1.4% (6/427)	
Zoli (2008) [2]	Mount Sinai	609	2.3% (7/304)	2.5% (3/121)	11.5% (7/61)	3.9% (3/77)	2.2% (1/46)	2.3% (20 cases of paraplegia in 858) [3]
Greenberg (2008) [4]	Cleveland	372	1% (1/136)	14% (7/51)	22% (13/59)	10% (6/62)	2% (1/64)	
Conrad (2008) [5]	MGH	471	7% (7/93)	24% (14/58)	20% (13/65)	13% (21/156)	2% (2/99)	
Fehrenbacher (2010) [6]	Indianapolis	343	1.0% (1/98)	4.3% (3/69)	5.4% (6/111)	3.1% (1/32)	0 (0/33)	DTA + Type I 2.4% (4/167)
Kulik (2011) [7]	St Louis	218	Not reported	1.8% (1/57)	5.5% (5/91)	5.7% (4/70)	4.6% (10/70)	5.3%(13/243), 9 paraplegia, 4 paraparesis [8]
Lima (2012) [9]	Cleveland	330	8.3% (9/108)	10.0% (9/90)	10.6% (9/85)	12.2% (5/41)	0 (0/7)	
LeMeire (2012) [10]	Texas	823	Not reported	3.3% (7/209)	5.6% (15/264)	8.9% (14/157)	3.1% (6/193)	Jan 2005-May 2012
Tanaka (2015) [11]	Japan	100	Not reported	0 (0/13)	2.6% (2/76)	0 (0/11)		
Coselli (2015)	Texas, Baylor	3264	Not reported	3.2% (29/907)	8.0% (84/1047)	6.7% (44/652)	2.4% (16/658)	2015 AATS meeting

Paraplegia is still a problem!

- TAA Surgery the most common cause of spinal cord infarction.
- EndoRx paraplegia perisists, ½ that of open: No cross-clamp time.

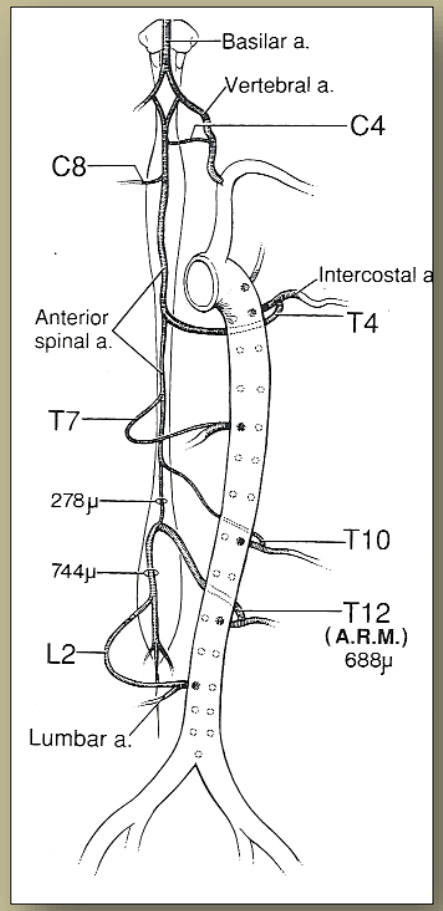
HUGE, ESCALATING SOCIETAL COSTS

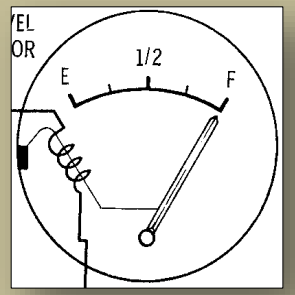


Radiographics.2006;26 Suppl 1:S63-73.
Neurocrit Care. 2008;9(3):344-51

Etiology of Paraplegia is multi-factorial

Artery of Ademkiewicz





"Gas Tank"Model

- Cross-clamp interval (no lower body blood flow)
- Air/particulate emboli ("stroke" of cord)
- Permanent deletion intercostal arteries
- Obliteration of intercostal artery origins by endograft (including upper and lower "landing zones")

Methods of Protection

1. Good hemostasis and hemodynamics
2. Distal perfusion
3. Proximal hypertension
4. Early recruitment of subclavian artery
5. Spinal artery identification
6. Intercostal artery reimplantation
7. Spinal drain
8. DHCA
9. MEP monitoring
10. ~~Neuroprotective drugs~~

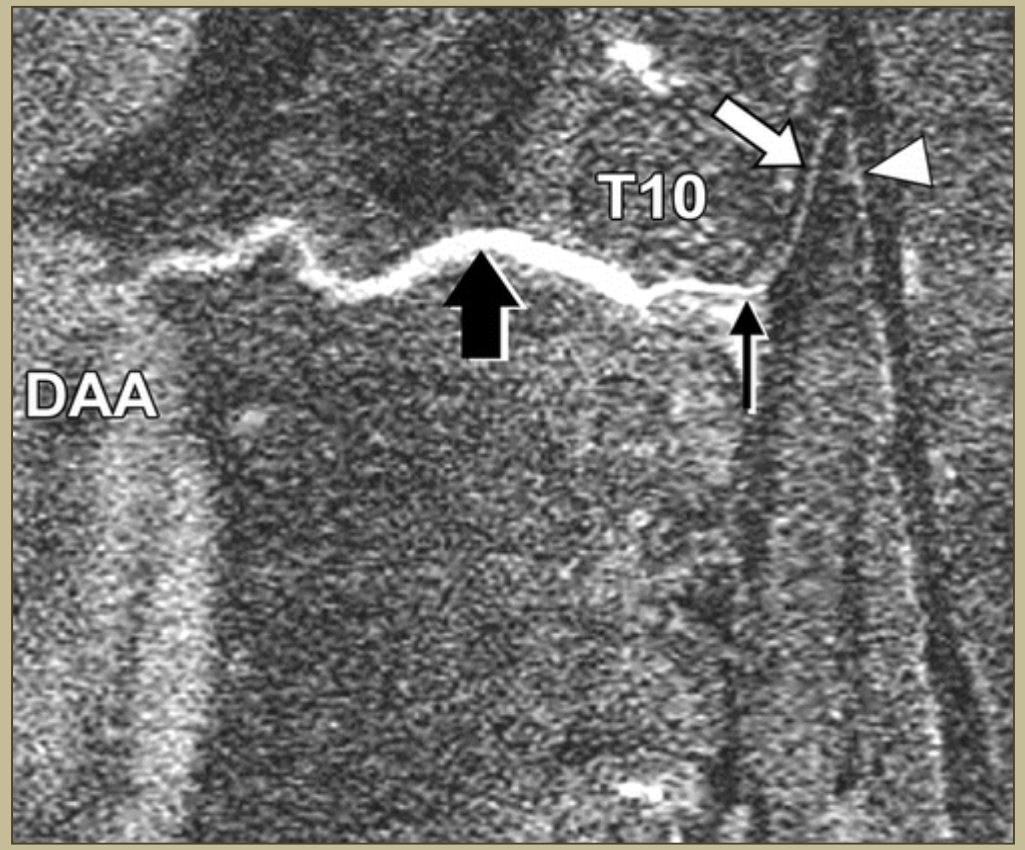
~~Neuroprotective drugs~~

Direct spinal cooling

5. Spinal artery identification

The artery of Adamkewicz **is** **the only vertical artery in the midline.**

We image this successfully in 85% of cases (Dual Energy CT)
We never leave OR without this artery in continuity with the bloodstream.



9. Motor evoked potential(MEP) monitoring

DISEASES OF THE AORTA

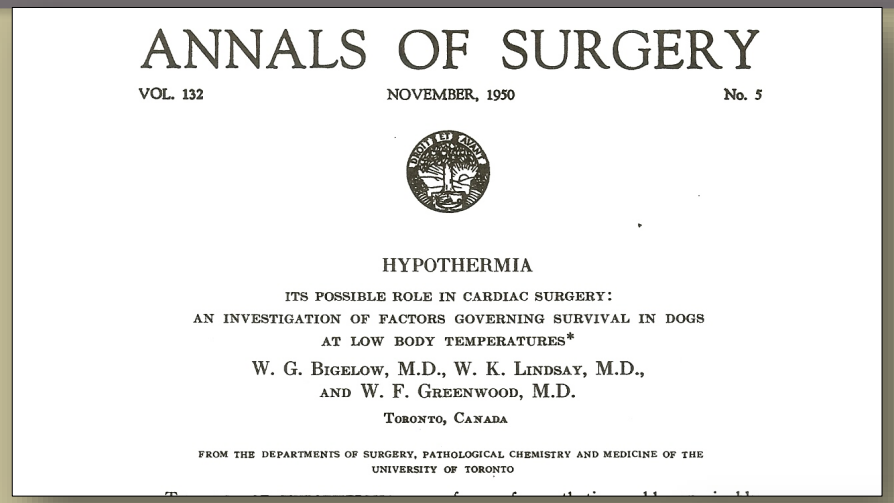
ORIGINAL ARTICLE

Neuromonitoring Using Motor and Somatosensory Evoked Potentials in Aortic Surgery

Lucy Y. Liu, B.A.,* Brooke Callahan, Au.D.,† Sven Peterss, M.D.,*,‡
Julia Dumfarth, M.D.,* Maryann Tranquilli, R.N.,* Bulat A. Ziganshin, M.D.,*,§
and John A. Elefteriades, M.D.*

MEPs preserved throughout—FINE
MEPs lost, then recovered–FINE
MEPs lost, not recovered—20% PARAPLEGIA

History of Hypothermia in Cardiac Surgery



ANNALS OF SURGERY

VOL. 132 NOVEMBER, 1950 No. 5

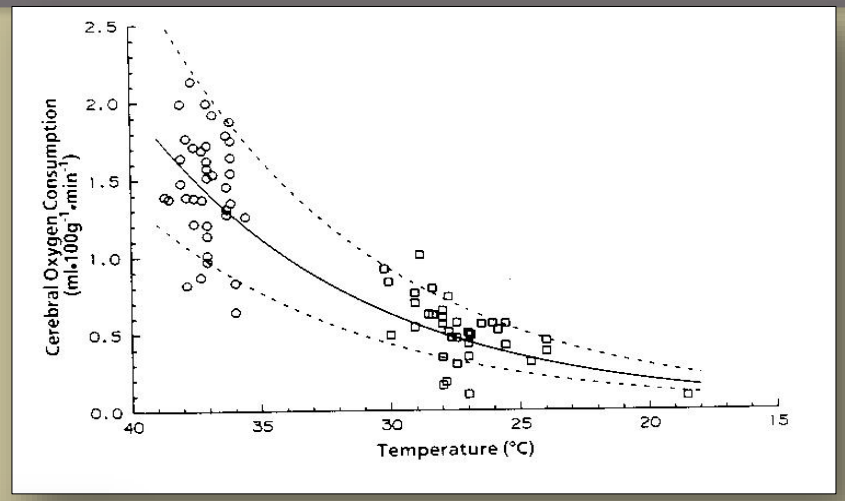
HYPOTHERMIA

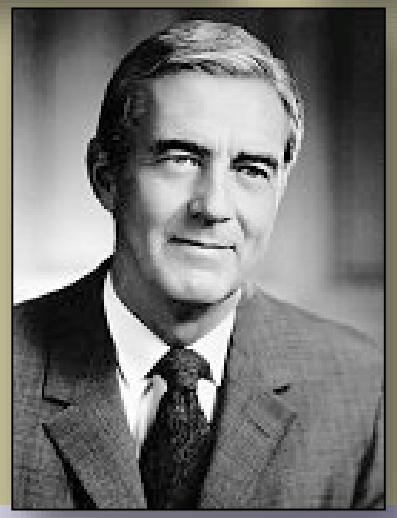
ITS POSSIBLE ROLE IN CARDIAC SURGERY:
AN INVESTIGATION OF FACTORS GOVERNING SURVIVAL IN DOGS
AT LOW BODY TEMPERATURES*

W. G. BIGELOW, M.D., W. K. LINDSAY, M.D.,
AND W. F. GREENWOOD, M.D.

TORONTO, CANADA

FROM THE DEPARTMENTS OF SURGERY, PATHOLOGICAL CHEMISTRY AND MEDICINE OF THE UNIVERSITY OF TORONTO

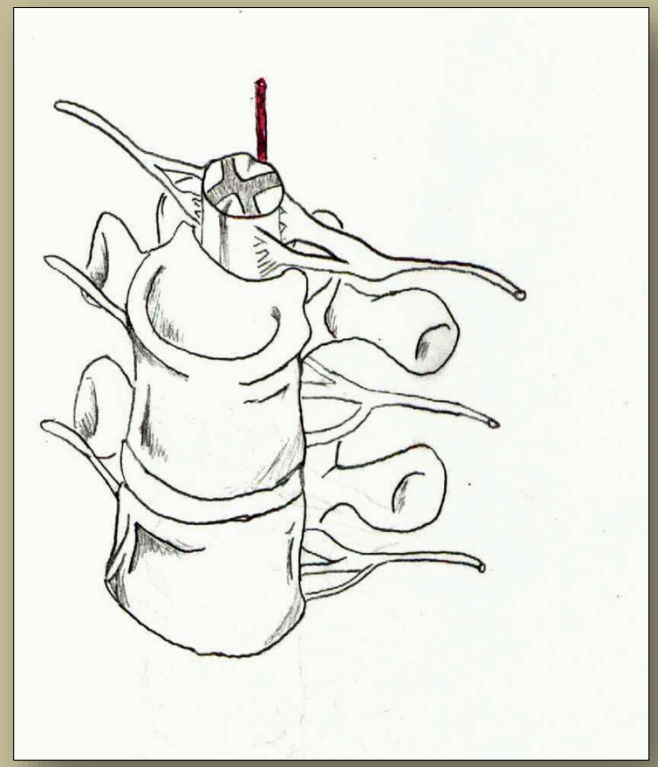




Concept:
Protect the spinal cord by cooling it topically

- Simple design
- User friendly
- Quick placement, <15 min
- Localized spinal hypothermia
- No more effort than conventional spinal drain

NSF SBIR Phase I
NSF SBIR Phase 2
NSR SBIR Supplemental



Introduction to Spinal Cooling Catheter

- **Novel approach**

- Localized hypothermia to the spinal cord via a catheter that lies in the spinal canal.
  - The catheter is placed just like a conventional spinal drain.
  - The catheter recirculates refrigerant fluid, thus substantially cooling the spinal cord.

- The *localized* application of cooling avoids the well-known complications of *systemic* cooling

- Simple, easy-to-use format—essentially “free” cooling for the same effort as a spinal dr

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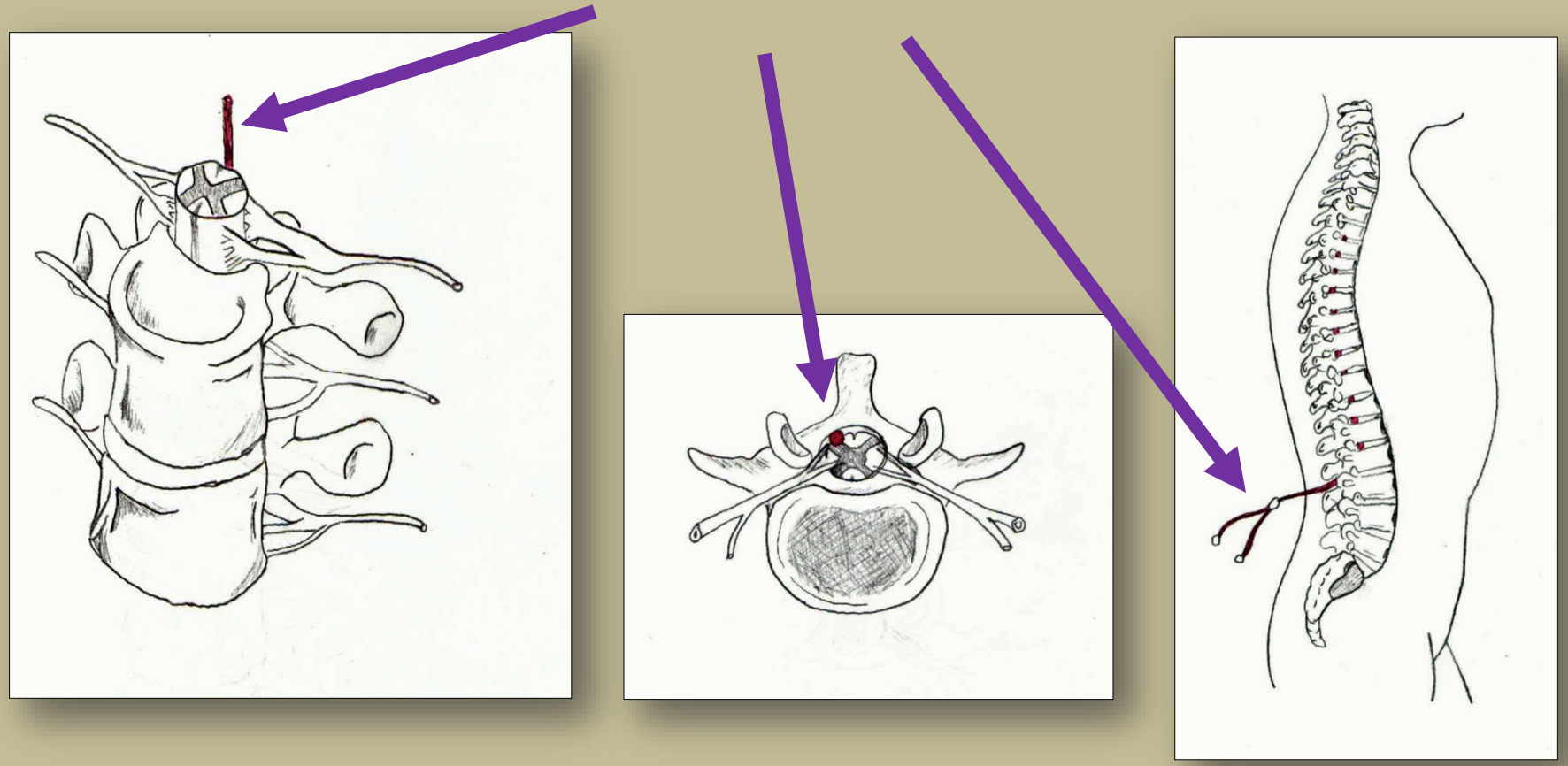
Schematic Placement



Prototype: Spinal Cooling Catheter

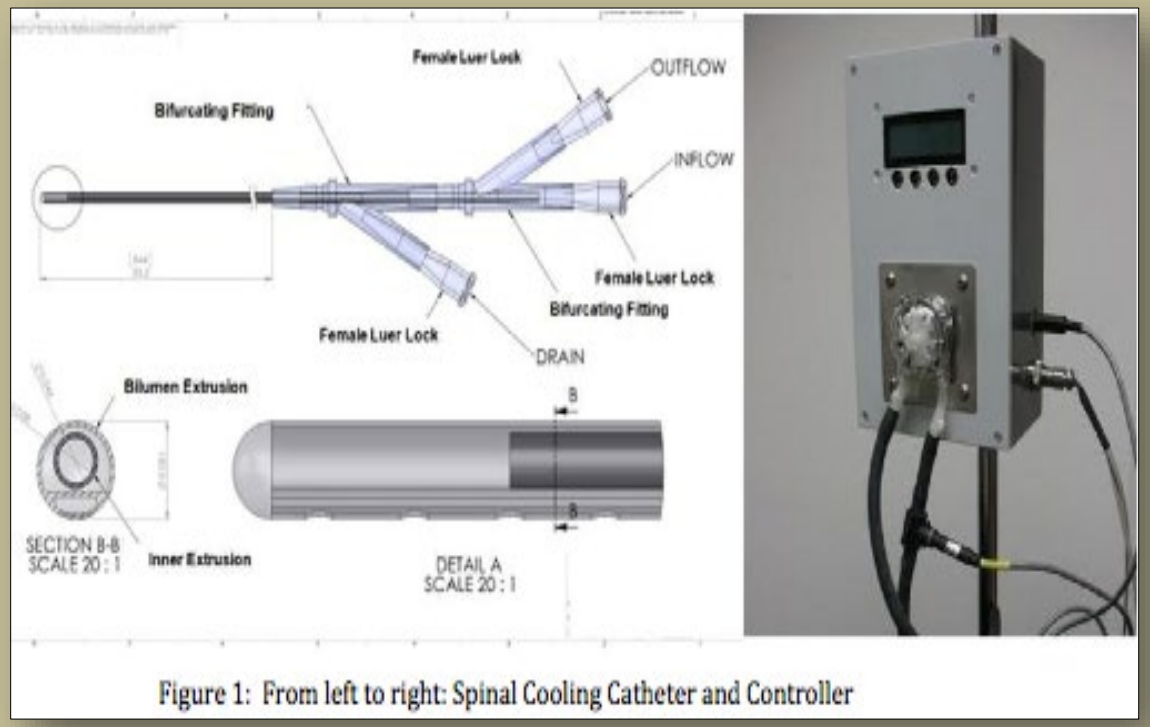
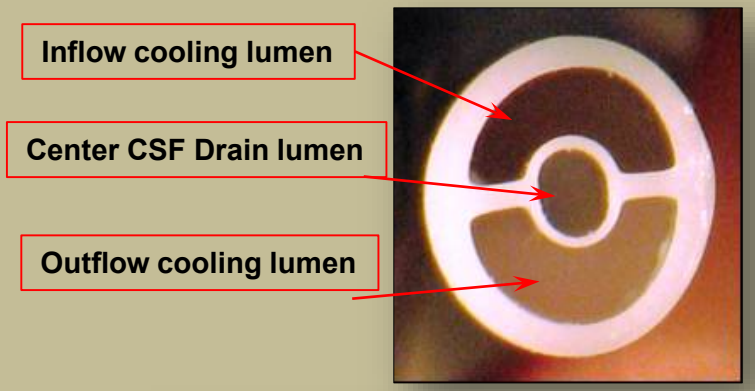
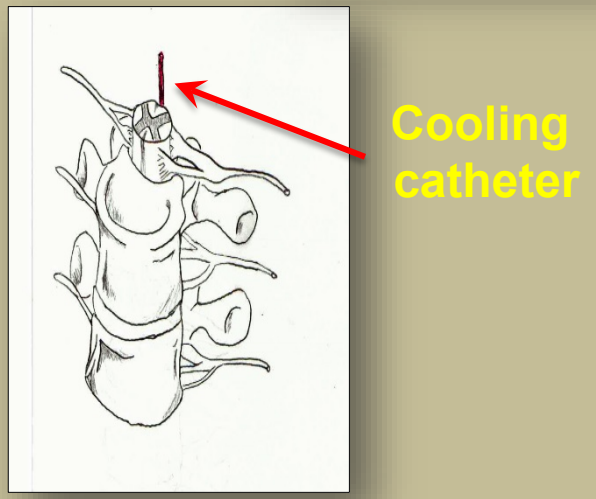
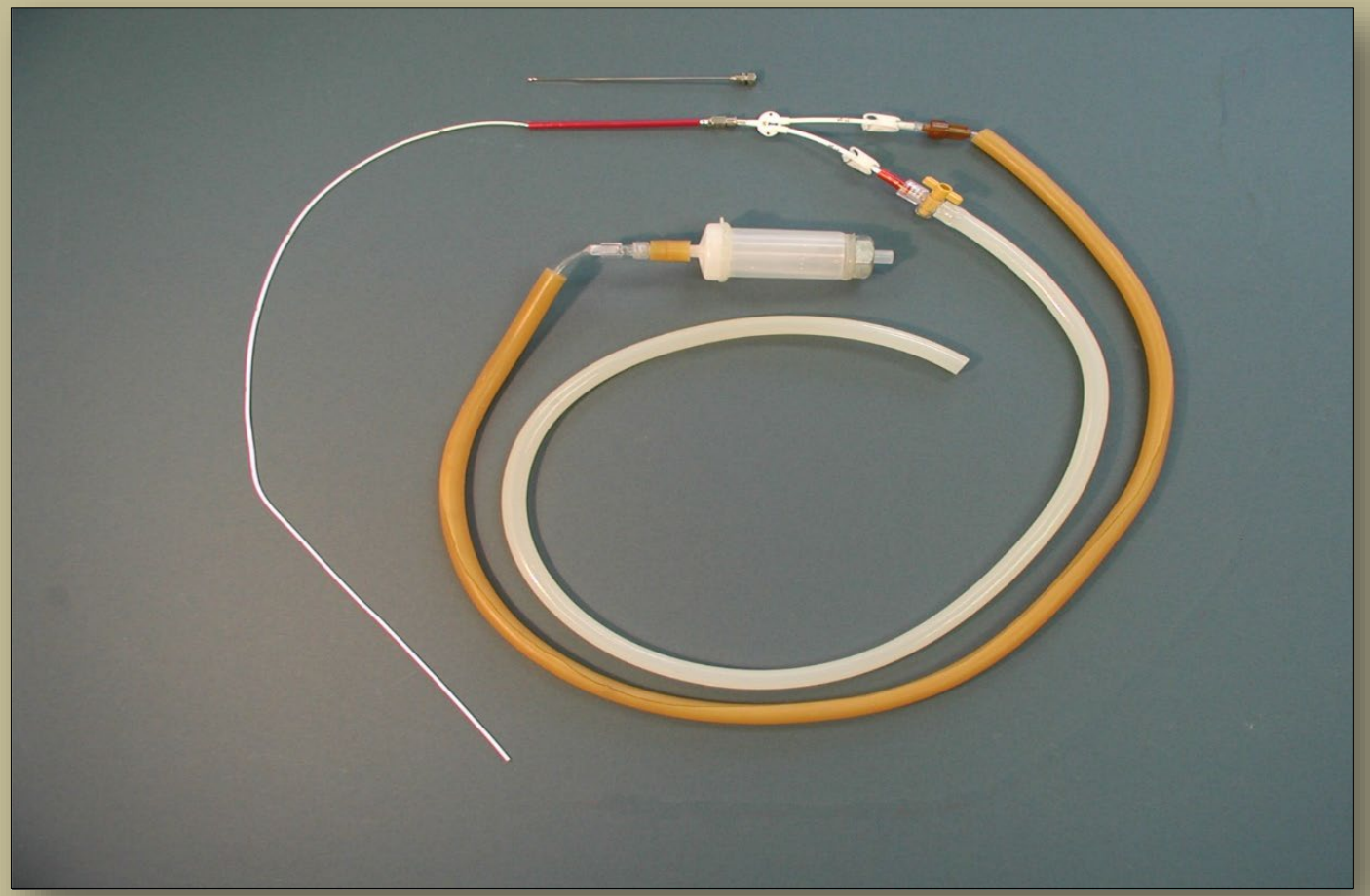


Figure 1: From left to right: Spinal Cooling Catheter and Controller

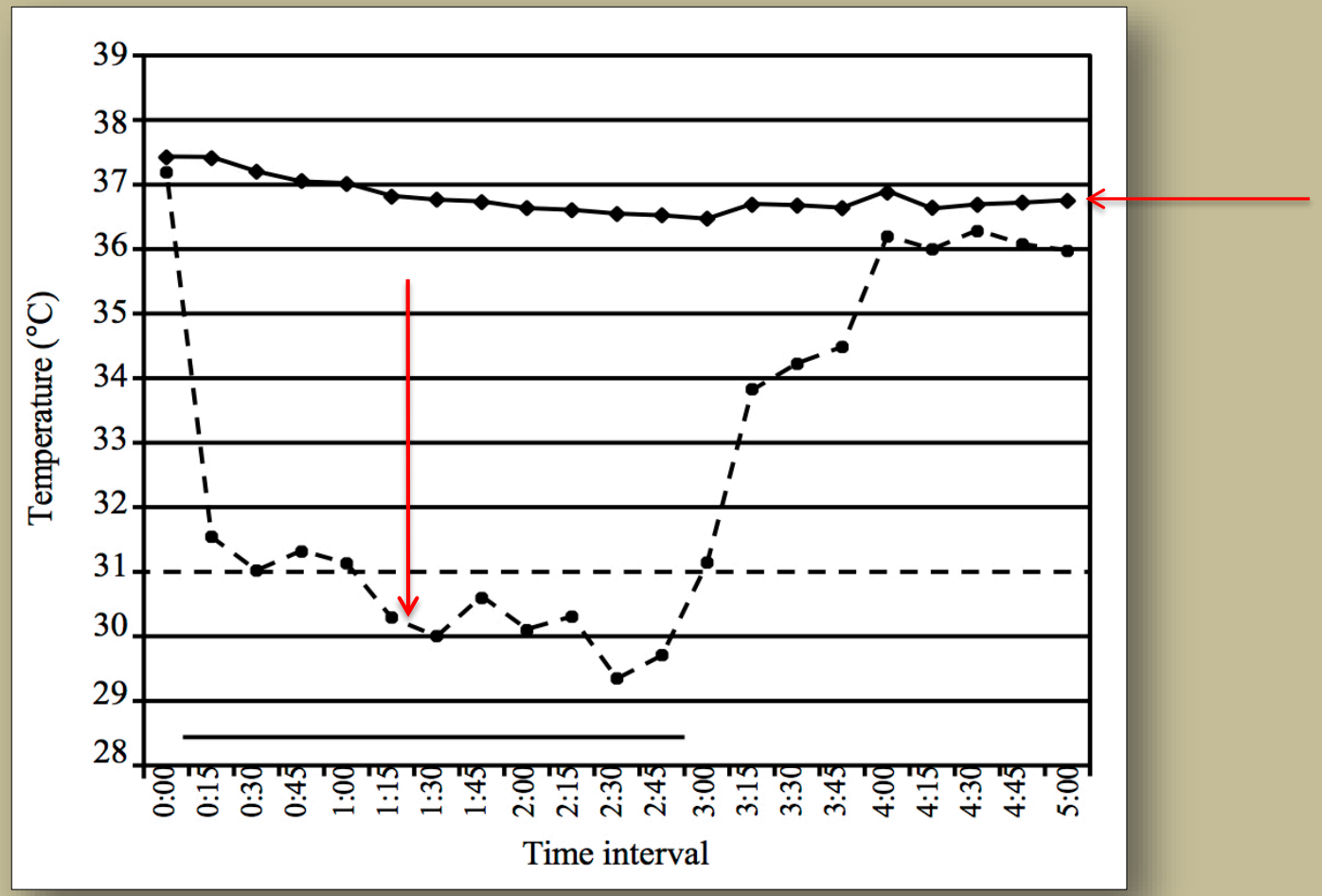




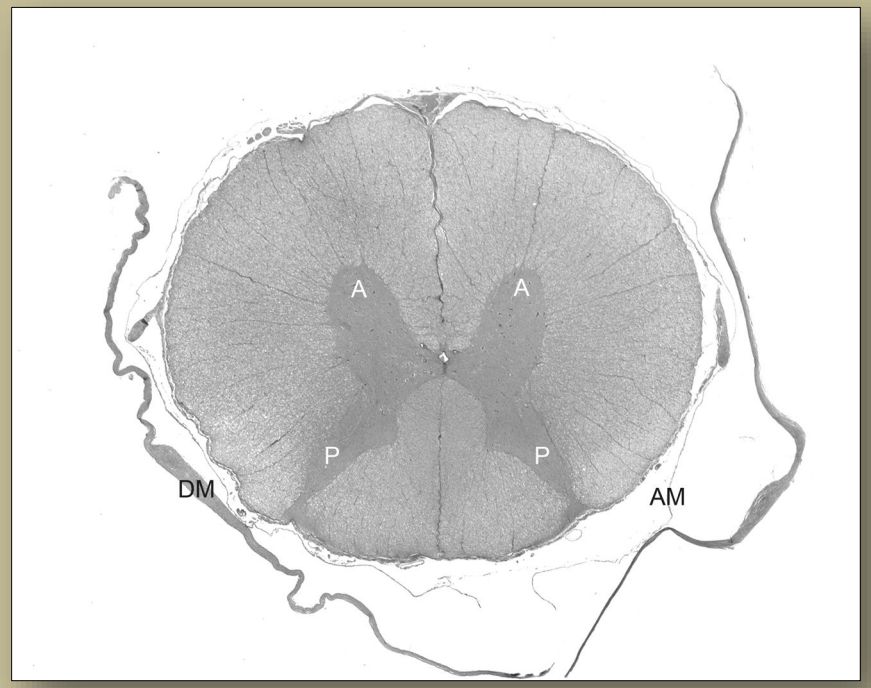
Cooling Catheter (early prototype)



Deep cord cooling @ systemic normothermia – All Four Sheep



Postmortem Examination



- Gross examination:
  - no trauma
  - no hypothermic damage
  - properly placed temperature probes.
- Histologic examination:
  - Unremarkable

Survival Experiments

7 out of 7 long-term survivors fully ambulatory without any neurologic deficit

Publications

J CARDIOVASC SURG 2007;48:103-8

Cooling catheter for spinal cord preservation in thoracic aortic surgery

R. M. A. MOOMIAIE [1], J. RANSDEN [2], J. STEIN [2], J. STRUGAR [3], Q. B. ZHU [4], J. H. KIM [5], J. A. ELEFTERIADES [1]

[1]Section of Cardiothoracic Surgery
Yale University School of Medicine, New Haven, CT, USA
[2]Synectic Engineering, Inc., Milford, CT, USA
[3]Department of Neurosurgery
Yale University School of Medicine, New Haven, CT, USA
[4]Department of Anesthesia
Yale University School of Medicine, New Haven, CT, USA
[5]Department of Pathology (Neuropathology)
Yale University School of Medicine, New Haven, CT, USA

Aim. **Despite advances in spinal cord protection, paraplegia continues to be a serious complication of descending and thoracoabdominal aortic operations. We devised and tested a novel, self-contained catheter designed to cool the spinal cord topically after being threaded into the spinal column.**

Methods. **A cooling catheter for this purpose was specifically designed and produced. The catheter has two lumina, one for ingress and one for egress of fluid. The system is self-contained, so that the fluid does not communicate in any way with the spinal fluid. A console device circulates cold fluid through the catheter. The catheter was tested in 5 adult sheep, with direct monitoring of core body temperature and spinal cord temperature in both active cooling and passive re-warming cycles.**

Results. **In testing in 4 sheep (five attempted implants, with one failure), the catheter worked without problem, producing effective cooling of the spinal cord, from a mean temperature of 36.8 °C (core temperature) to 30.5 °C (spinal temperature) (P<0.0001). In no case did post-mortem examination or histology reveal any evidence of damage to the spinal cord from hypothermia. Temperature rose toward body temperature after cessation of active cooling.**

Conclusion. **Effective topical cooling of the spinal cord can be achieved via a specially designed, self-contained cooling catheter placed into the intra-thecal space. This catheter holds promise for spinal cord protection in aortic surgery. Also, this catheter may be useful as well in mitigating injury to the spinal cord in cases of traumatic spinal column injury.**

KEY WORDS: Aorta - Spinal cord - Paraplegia - Hypothermia.

some 40 years ago. Paraplegia continues to devastate the lives of certain patients undergoing surgery for thoracic aortic aneurysm; in cases of postoperative paraplegia, mortality is high and, even in survivors, quality of life is dramatically impaired.

We report here the initial laboratory experience with a novel catheter that permits direct topical cooling of the spinal cord without need for systemic hypothermia or fluid instillation into the intra-thecal space. The catheter is self-contained, is designed for percutaneous placement, and requires no maintenance during operation. This catheter is intended to reduce incidence and/or severity of paraplegia in aortic surgery, via topical hypothermia in the spinal canal. The present experiment explores the effectiveness of this cooling catheter in decreasing the temperature of the spinal cord in animals at systemic normothermia.

ORIGINAL RESEARCH

Novel intracranial brain cooling catheter to mitigate brain injuries

Remo M Moomiaie,[1] Graham Gould,[2] Daniel Solomon,[1] John Simmons,[3] Jung Kim,[4] Donald Botta,[1] John A Elefteriades[1]

[1]Section of Cardiac Surgery, Yale University School of Medicine, New Haven, Connecticut, USA
[2]Section of Neurosurgery, Yale University School of Medicine, New Haven, Connecticut, USA
[3]Coolspine LLC, Woodbury, CT, USA
[4]Department of Pathology, Yale University School of Medicine, New Haven, Connecticut, USA

Correspondence to
Dr J A Elefteriades, Section of Cardiac Surgery, Yale University School of Medicine, Boardman 2, 333 Cedar Street, New Haven, CT 06510, USA; john.elefteriades@yale.edu

Received 28 November 2010
Revised 24 February 2011
Accepted 4 April 2011
Published Online First
14 June 2011

ABSTRACT

Background The neuroprotective effects of cooling the spinal cord in a sheep model by a self-contained intrathecal catheter was reported recently by the authors. The present study was designed to determine if cooling catheters in the lateral ventricles of the brain can effectively cool the CSF and thereby reduce brain temperature while maintaining systemic normothermia.

Methods The cooling catheter is a self-contained system that circulates a cold fluid and cools the CSF that circulates in the brain. The CSF in turn cools the surrounding brain by conduction. Burr holes were made in the skull and the catheter was placed into the lateral ventricles using the standard method for placement of ventriculostomy catheters. To monitor the cooling effect, four temperature probes were placed in the brain (left and right hemispheres of the brain in anterior and posterior locations to the ventricles).

Results Five experiments were successfully completed. The mean brain temperature for all sheep decreased to 34.5°C (mean) during the 3 h cooling period (9.7% reduction from baseline brain temperature of 38.2°C). Cooling fluid was circulated through the catheter at a rate of 50 ml/min. The lowest achieved brain temperature during cooling was 26.7°C. When cooling was stopped, the brain temperature readings equilibrated with the core temperature promptly. Post mortem examination of the brains showed no morphologic changes under gross or histologic examinations.

Conclusion Localized cooling of the brain to moderate hypothermic levels while maintaining relative systemic normothermia was demonstrated in an animal model with intraventricular cooling catheters.

survive cardiac arrest.[4 5] Also, hypothermic neuronal protection underlies the fascinating and widely applied technique of deep hypothermic circulatory arrest used for decades in surgical procedures on the aortic arch.[6 7]

Despite its clear therapeutic benefit, *systemic* hypothermia is associated with side effects that have limited its use in modern medical practice. Notable side effects of systemic hypothermia include bleeding diathesis, shivering, arrhythmias, suppression of the immune system with increased susceptibility to infection and electrolyte imbalance.[8] As current cooling methods are not ideal, there is much interest in developing a technique that would provide the neuroprotective benefit without the significant side effects of global, systemic hypothermia.[9]

We set out to investigate the efficacy of cooling the brain *topically*, using a self-contained cooling catheter that is inserted into a lateral ventricle of the brain. In a previous study, our group demonstrated effective localized cooling of the spinal cord by inserting a similar catheter into the intrathecal space and cooling the CSF surrounding the spinal cord.[10] Building on the successes of the spinal cord experiments—in which average spinal cord temperatures were reduced by 6.3°C (−17.1% from baseline)—the current investigation aims to apply topical intracranial cooling to the brain (via cooling the intracranial CSF). We believe this technique would offer an alternative method of providing hypothermic protection from ischemic neuronal injury without the deleterious effects of inducing systemic hypothermia.

14.5.2. Recommendations for Spinal Cord Protection During Descending Aortic Open Surgical and Endovascular Repairs

CLASS I

1. Cerebrospinal fluid drainage is recommended as a spinal cord protective strategy in open and endovascular thoracic aortic repair for patients at high risk of spinal cord ischemic injury. (522,523,713) (*Level of Evidence: B*)

CLASS IIa

1. Spinal cord perfusion pressure optimization using techniques, such as proximal aortic pressure maintenance and distal aortic perfusion, is reasonable as an integral part of the surgical, anesthetic, and perfusion strategy in open and endovascular thoracic aortic repair patients at high risk of spinal cord ischemic injury. Institutional experience is an important factor in selecting these techniques. (380,382,714,715) (*Level of Evidence: B*)
2. Moderate systemic hypothermia is reasonable for protection of the spinal cord during open repairs of the descending thoracic aorta. (525) (*Level of Evidence: B*)

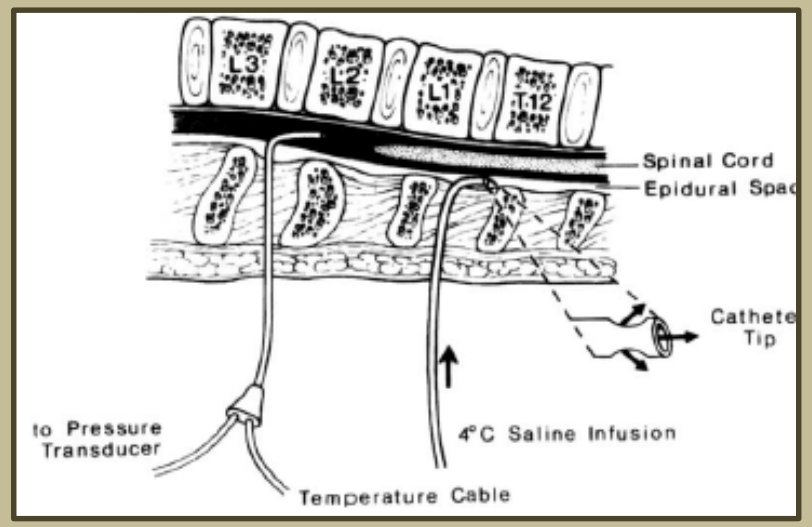
CLASS IIb

1. Adjunctive techniques to increase the tolerance of the spinal cord to impaired perfusion may be considered during open and endovascular thoracic aortic repair for patients at high risk of spinal cord injury. These include distal perfusion, epidural irrigation with hypothermic solutions, high-dose systemic glucocorticoids, osmotic diuresis with mannitol, intrathecal papaverine, and cellular metabolic suppression with anesthetic agents. (520,715–717) (*Level of Evidence: B*)
2. Neurophysiological monitoring of the spinal cord (somatosensory evoked potentials or motor evoked potentials) may be considered as a strategy to detect spinal cord ischemia and to guide reimplantation of intercostal arteries and/or hemodynamic optimization to prevent or treat spinal cord ischemia. (483,634,718,719) (*Level of Evidence: B*)

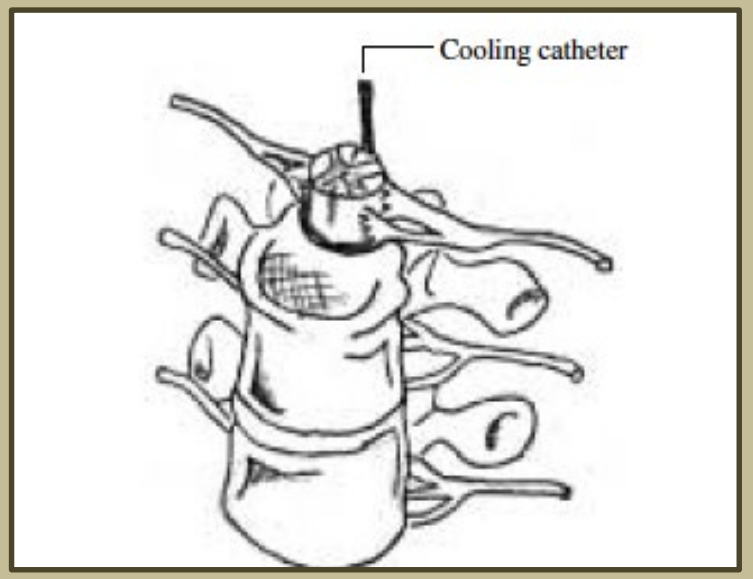
"Adjunctive techniques to increase the tolerance of the spinal cord to impaired perfusion may be considered…including epidural irrigation with hypothermic solutions…."

2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease

Epidural infusion of cooled saline may be used to induce regional hypothermia. Although this technique was associated with substantial increases in CSF pressure, a significant reduction in postoperative neurologic deficits was noted (520,716).



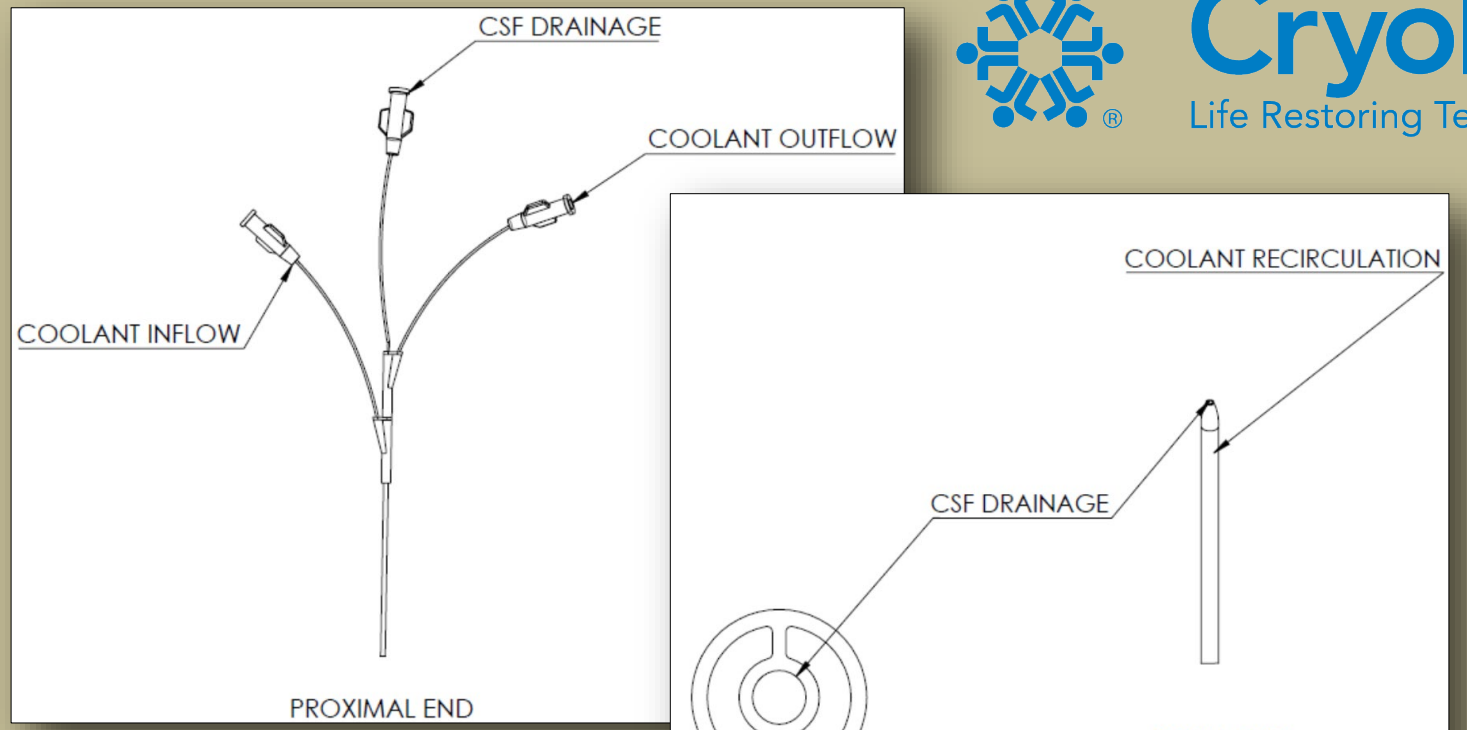
A new, self-contained catheter for topical cooling of the spinal cord without infusion into the CSF or CSF pressure rise has been shown in the laboratory to provide topical spinal cord hypothermia, while systemic normothermia is maintained; clinical trials are being organized (752).



2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the Diagnosis and Management of Patients With Thoracic Aortic Disease

Product Development to Commercial Stage

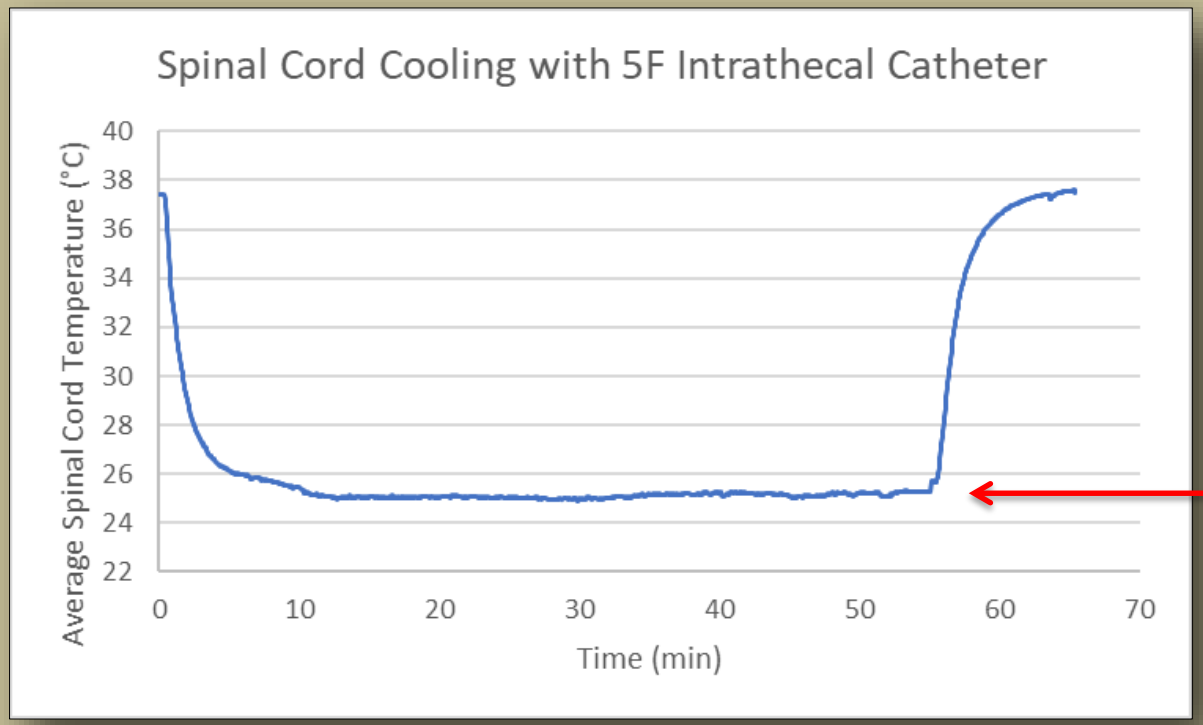
CryoLife Inc. commercializing 5F catheter and cooling and drainage console



CryoLife®
Life Restoring Technologies®

Product Development to Commercial Stage

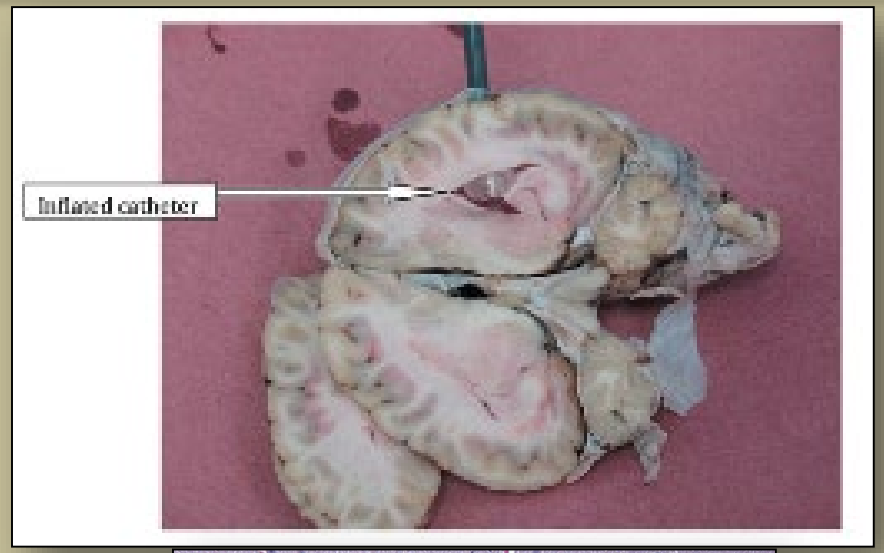
Successful pre-clinical animal study in an un-altered porcine model shows cooling 12°C below body temp.

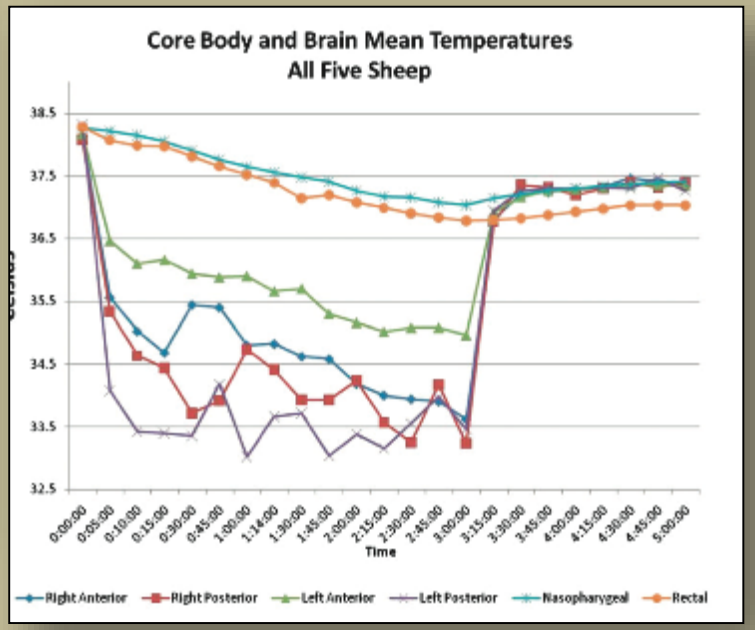


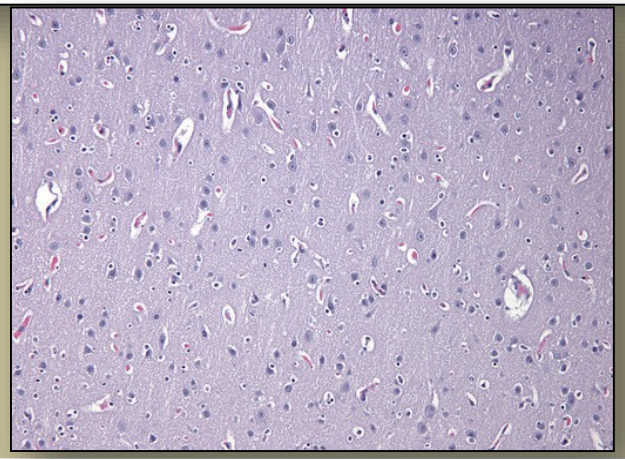
25°C sustained cooling

Catheter inserted 30 cm from L6/S1
Four spinal cord thermocouple probes along length of catheter

Brain Cooling Catheter



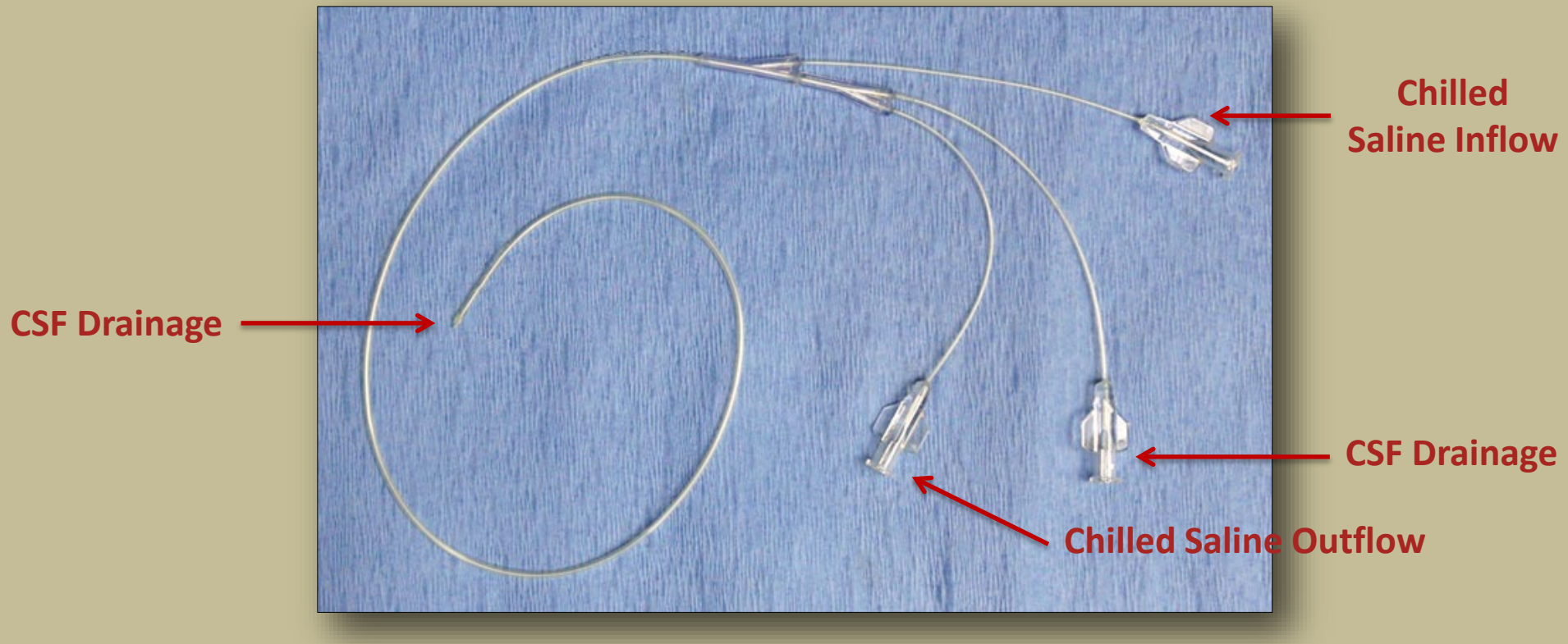


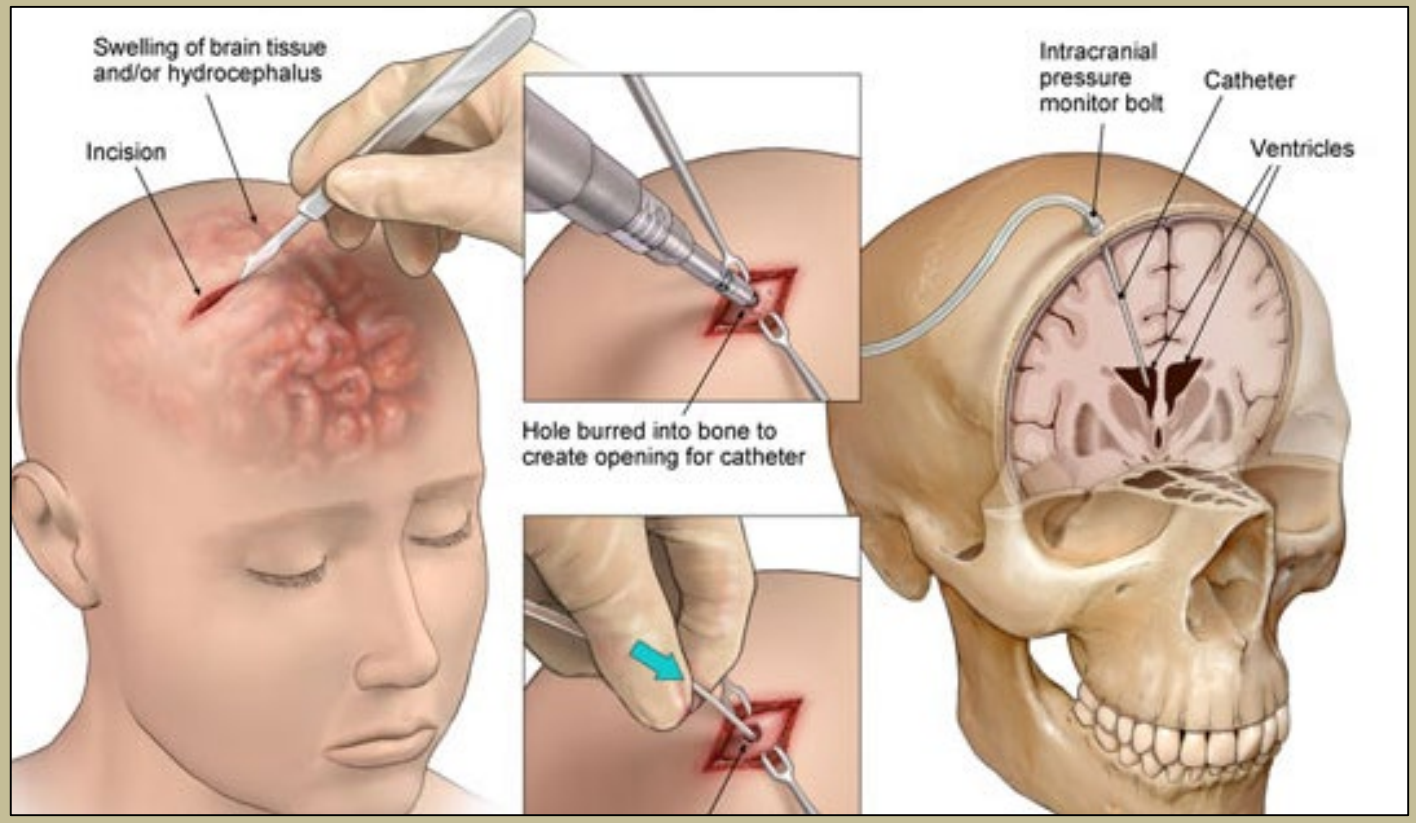


Cerebral Tissue shows no sign of hypothermic damage

Product Development to Commercial Stage

- Successful pre-clinical animal study in an un-altered porcine model shows gravity driven CSF drainage up to 24 mL/hr





Ventriculostomy is a common, safe bedside procedure (since 1744).
It was performed for Abraham Lincoln's bullet wound of the brain
It is often employed in trauma cases anyway (as well as hemorrhagic stroke), as part of standard care for relief of increased intracranial pressure.
Our Brain Cooling Catheter provides "free" hypothermia with no additional effort beyond that required to relieve pressure.

Brain Cooling Wave by MRI

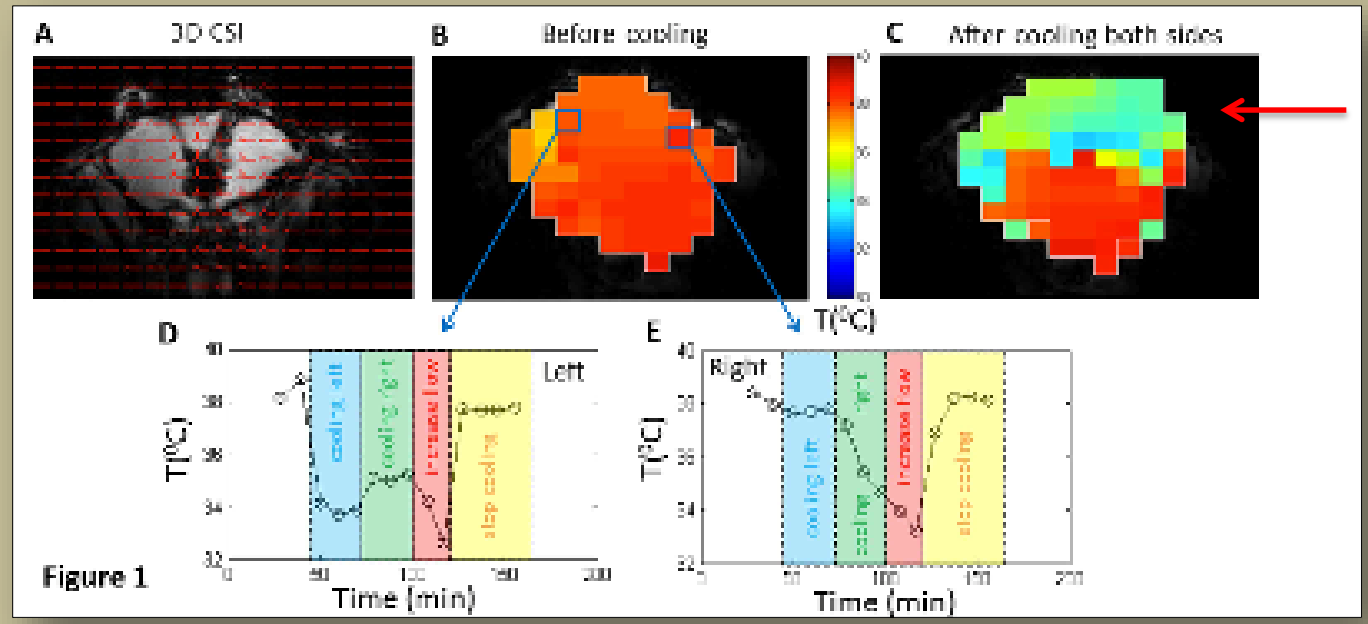


Figure 1