Noninvasive Techniques for Intracranial Pressure Assessment: A Review from Aerospace Medicine Perspective

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Disclosure Information

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Douglas R. Hamilton

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Will not discuss off-label use and/or investigational use

Learning Objectives

1: To review the existing noninvasive technologies to assess/measure ICP.

2: To learn about the mechanisms of each noninvasive technology for ICP assessment.

3: To discuss advantages and limitations of each technology from aerospace medicine perspective.

Traditional Techniques for ICP

- Lumbar puncture or intraventricular pressure transducer not feasible/practical in microgravity

  Invasive, requires skilled medical provider, logistical concerns in microgravity

- Need an easy-to-use, noninvasive technology

What noninvasive options are currently available?

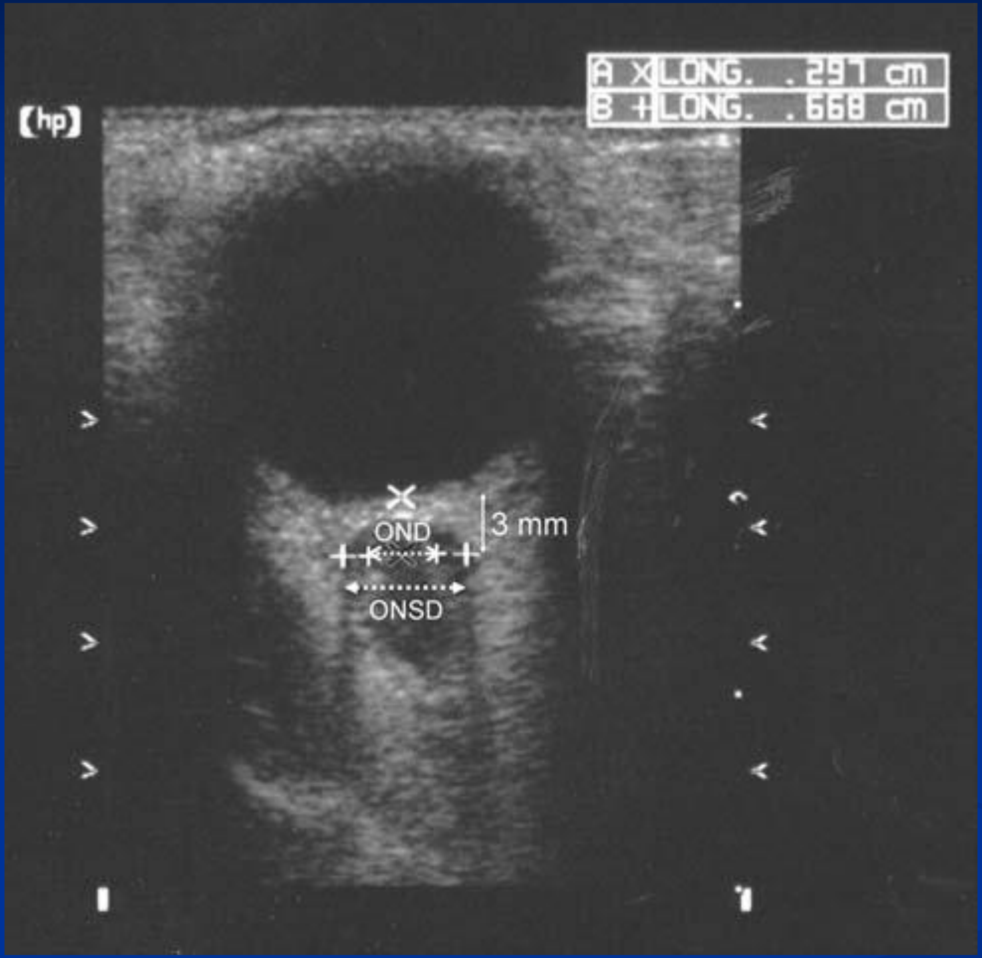
- Ocular Sonography
- Tympanic Membrane Displacement
  - Cerebral Cochlear Fluid Pressure device
- Ophthalmodynamometry
- Transcranial Doppler Imaging
- Pulsed Phase-Lock Loop Ultrasound
- MRI modalities – Not feasible for space flight
- Funduscopic Exam

Ocular Sonography

- Image optic nerve and nerve sheath with ultrasound
- Optic nerve sheath diameter (ONSD) → ICP
- Gives broad sense of increased ICP versus normal
- No reliable linear relationship

Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med 2008;15:201-4.

Optic Nerve Sheath Diameter

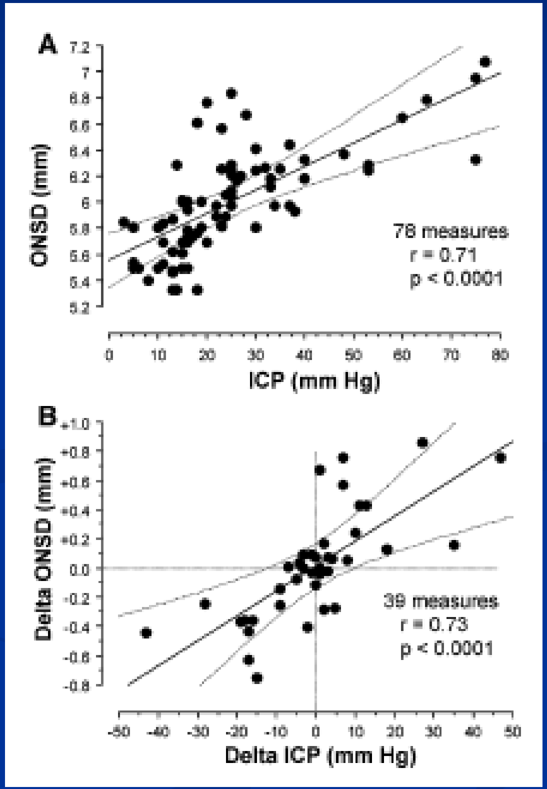


- Generally accepted that ONSD > 5 mm ≈ ICP > 20 cm H_2O

Geeraerts T, Merceron S, Benhamou D, Vigue B, Duranteau J. Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Med 2008;34:2062-7.

Ocular Sonography

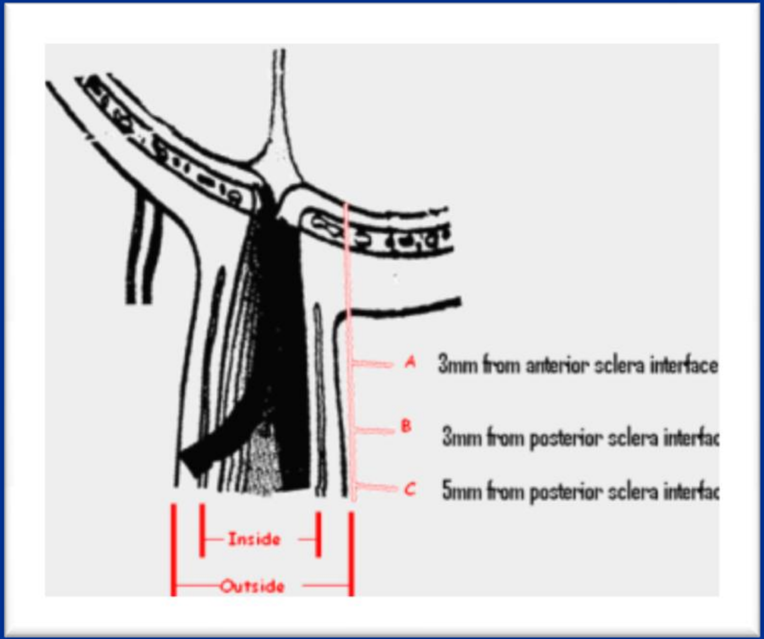
- Benefit
  - Easy to use
  - Available immediately on ISS
- Drawback
  - No linear relationship to ICP →
  - Gives a general sense of ICP
  - No specific ICP value

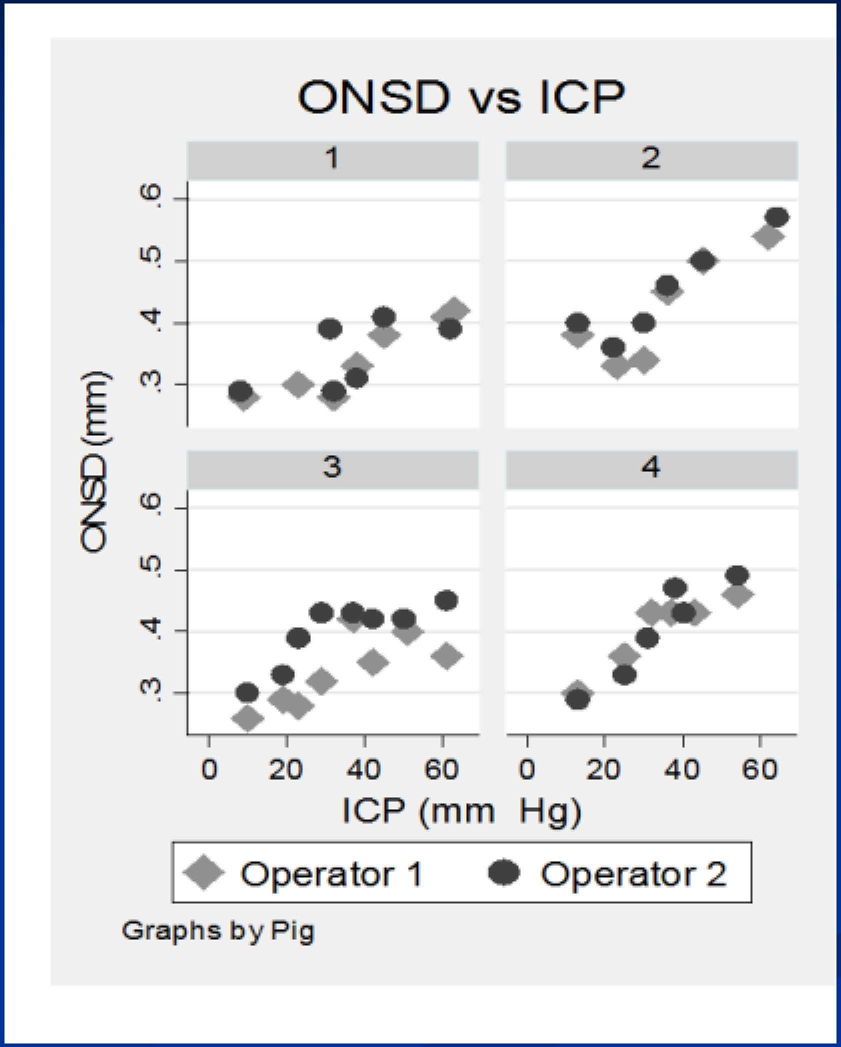


Geeraerts T, Merceron S, Benhamou D, Vigue B, Duranteau J. Noninvasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. Intensive Care Med 2008;34:2062-7.

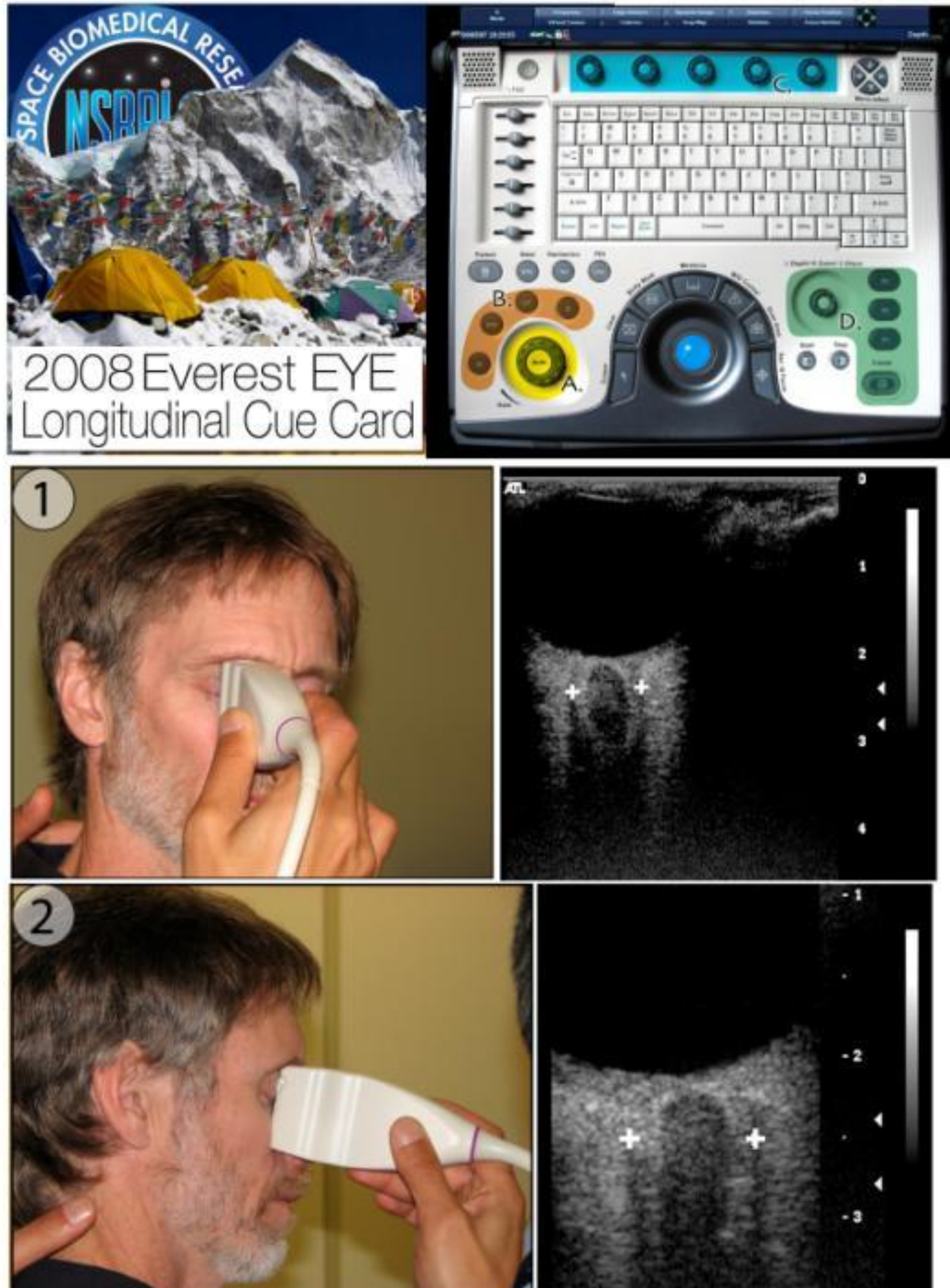
Optic Nerve Sheath Diameter changes with Elevated Intracranial Pressure in a Porcine Model.

Regression analysis of all animals showed ONSD increased by 0.0034 mm per mmHg of ICP





Douglas R. Hamilton et al JUM accepted for publication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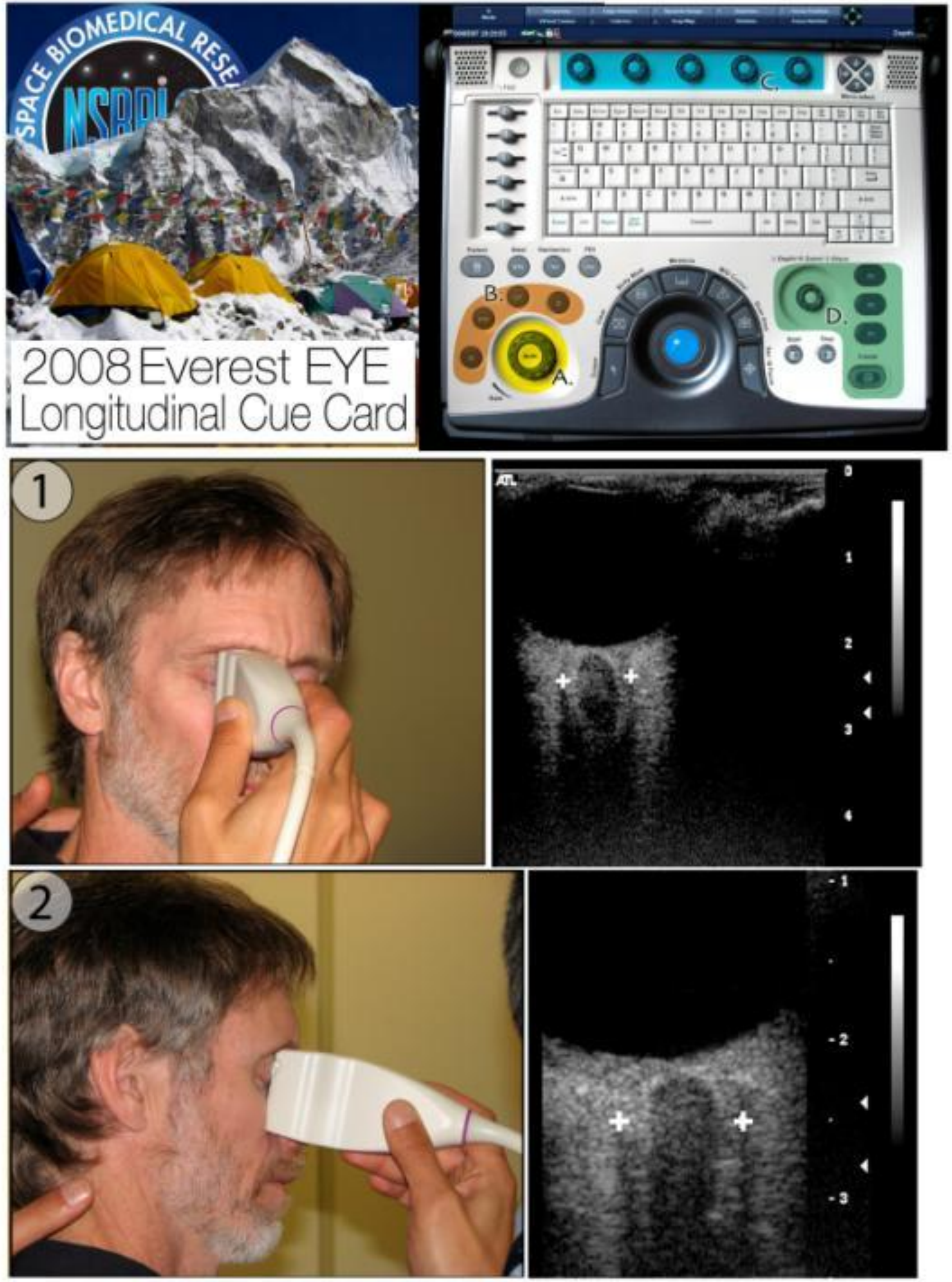
2008 Everest EYE
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ONSD - 1

- Reports published in both MRI and ultrasound literature, however, represent small numbers of “normal” population and offer only few reliable cut-off limits or reference ranges for the “normal” population.
- OND “normal” is relatively consistent at around 2.8-3.2 mm, probably due to a consistent structure comprised of approximately 1.1 million fibers tightly packed within a pressurized conduit, and its small size.
- ONSD “normal” is defined more loosely, due to the lack of systematic studies with methodologies that would allow pooling of data for meta-analysis.

ONSD - 2

- Some ultrasound-based reports are derived from low-resolution imagery and offer grossly underestimated values for ONSD, apparently due to the inability to reliably identify (and include in the measurement) the normal sheath as it blends with the intraconal adipose tissue.
- The danger of such underestimation is obvious, as an “enlarged” ONSD may misdirect the diagnostic and management decisions in complicated cases.
- Normal values measured by MRI in small cohorts are reported without regard to age, gender, and medical or social history of the subjects, thus making it very hard to arrive at a “normal range” for a given population.

ONSD - 3

- Our analysis of literature, and own unpublished data, have led us to favor a *justifiably conservative approach*, whereas the wide "normal range" on ONSD is treated as a range with "indeterminate" risk of elevated ICP.
- We have carefully considered ONSD values that would assure of low risk of ICP elevation, and have found it possible to consider ONSD below 0.59 cm as associated with low risk of ICP elevation.
- This value has been reported by Geeraerts et al (2008) in an 3T MRI-based study as "the best cut-off, corresponding to 92% negative predictive value".
- In the same work, ONSD<0.53 cm is reported as associated with a 100% NPV.

ONSD - 4

- Patients with traumatic brain injury (TBI) had an ONSD of 5.72+-0.71mm, and those with ICP elevation >20 mm H2O – 0.63+-0.05cm.
- It is interesting to note that a substantial number of healthy astronauts and NASA test subjects have higher ONSD than the elevated ICP patients of this study.
- Determining the upper "cut-off" ONSD level is more difficult.
- We have identified ONSDs of 0.75 cm that are easily stretched to >0.82cm after several-minute exposure to 30-degree head down position. Therefore, we temporarily ascribe a high likelihood of ICP elevation to ONSDs >0.75 cm.

ONSD - 5

- Newman et al measured ONSD by US during acute raised intracranial pressure in hydrocephalus.
- This study suggests that the upper limit of normal for optic nerve sheath diameter is 4.5 mm (measured at 3 mm behind the globe) in patients over 1 year of age, and 4.0 mm in children less than 1 year of age.
- Patients with patent ventriculoperitoneal shunts had a mean ONSD of 2.9 (SD 0.5) mm compared to 5.6 (0.6) mm in those with raised intracranial pressure ($p<0.0001$).

Newman WD, Hollman AS, Dutton GN, Carachi R. Measurement of optic nerve sheath diameter by ultrasound: a means of detecting acute raised intracranial pressure in hydrocephalus. Br J Ophthalmol 2002 Oct;86(10):1109-13.

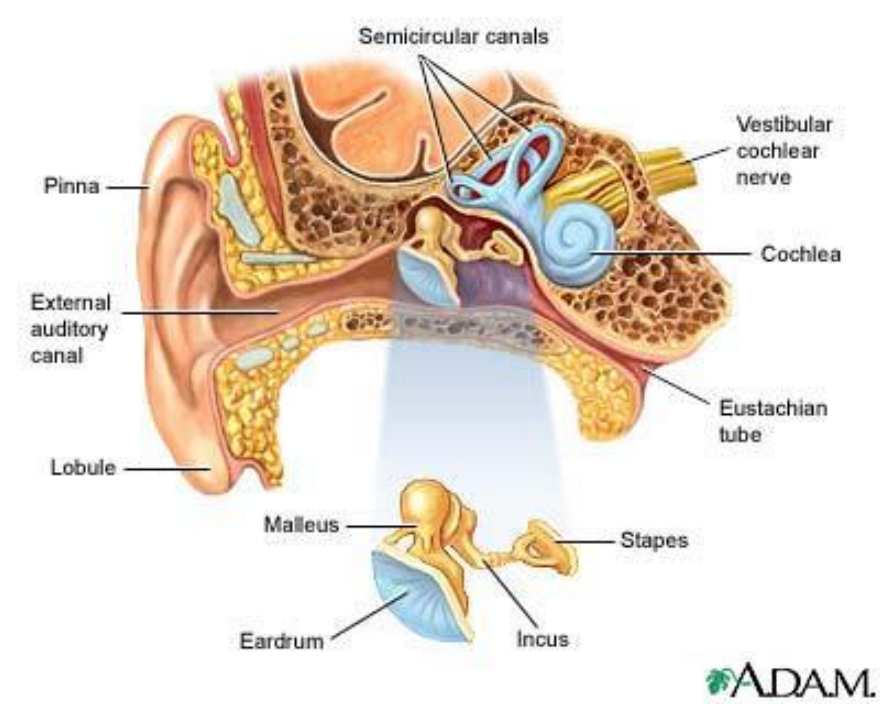
ONSD - 6

- Measurements of the ONSD using bedside US by Kimberly et al and was shown to correlate with clinical and radiologic signs and symptoms of increased intracranial pressure ICP.
- They performed a prospective blinded observational study of adult patients in both the emergency department and the neurologic intensive care unit who had invasive intracranial monitors placed as part of their clinical care.
- The authors concluded that the commonly used threshold of ONSD > 5 mm to detect ICP > 20 cm H2O.

Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. Acad Emerg Med 2008 Feb;15(2):201-4.

Tympanic Membrane Displacement

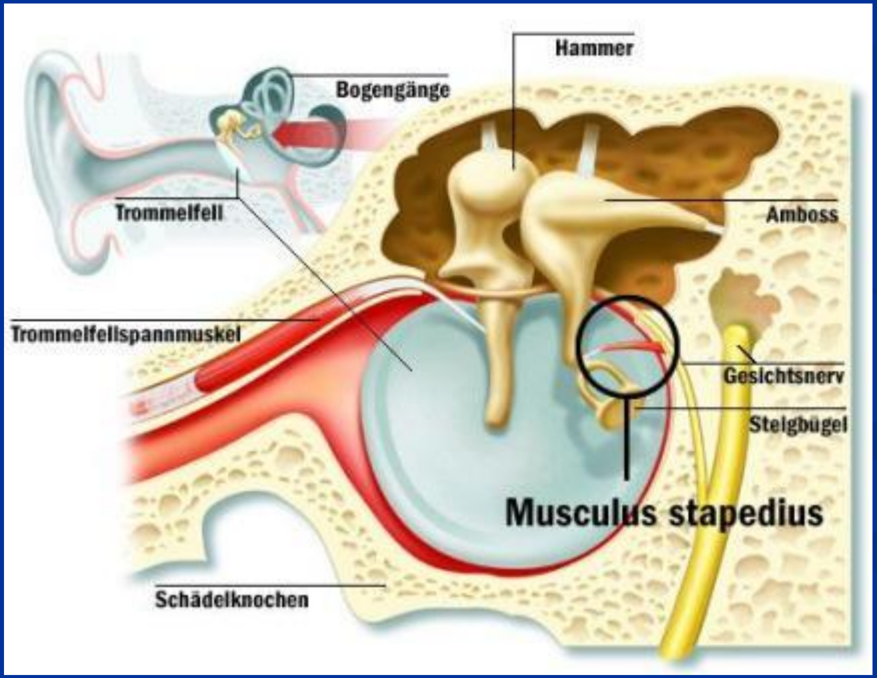
- Cochlear aqueduct – connects perilymphatic space to subarachnoid space
- Pressure from ↑ ICP distributes force to perilymph in cochlea.
- Force affects resting position of stapes via oval window.



Reid A, Marchbanks RJ, Bateman DE, Martin AM, Brightwell AP, Pickard JD. Mean intracranial pressure monitoring by a non-invasive audiological technique: a pilot study. J Neurol Neurosurg Psychiatry 1989;52:610-2.

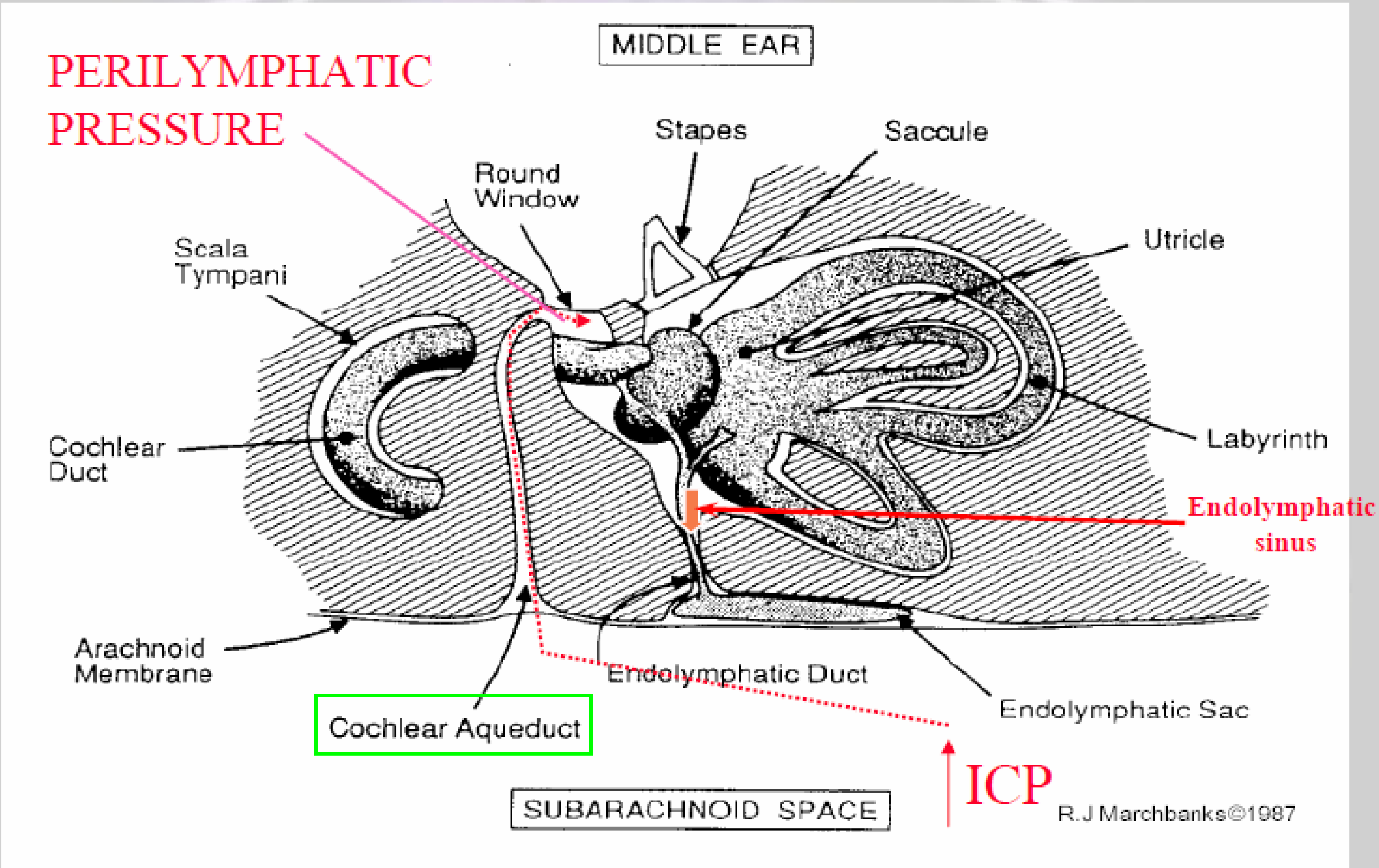
Acoustic Stapedial Reflex

- High-intensity sound (~70-100 dB)
- → Reflex contraction of stapedius and tensor tympani muscles
- Reduction of ~ 20 dB in sound intensity



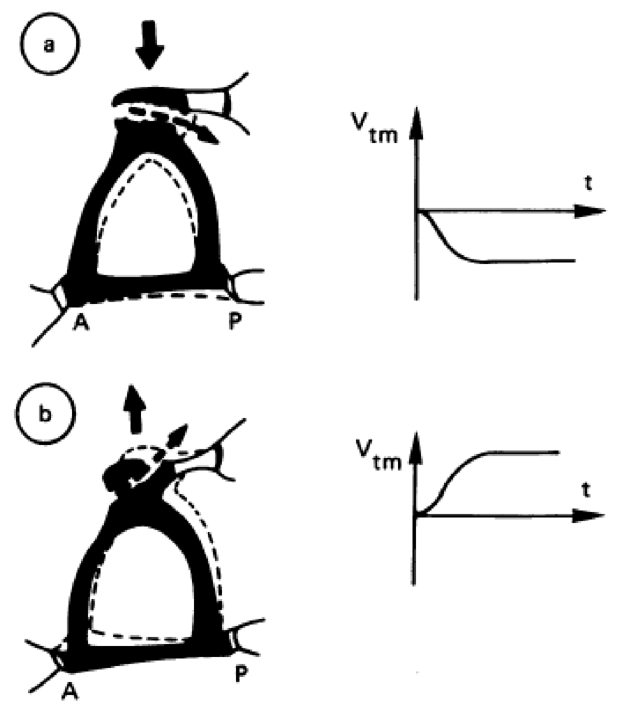
Wright AD, Imray CH, Morrissey MS, Marchbanks RJ, Bradwell AR. Intracranial pressure at high altitude and acute mountain sickness. Clin Sci (Lond) 1995;89:201-4.

Intracranial to Inner Ear Pressure Transfer



Acoustic Reflex and ICP

- Stapes resting position correlates with ICP
- Acoustic reflex changes stapes position
- Measure volume in external canal (nL)
- Inward motion → - ΔV_{tm}
- Outward motion → + ΔV_{tm}



Wright AD, Imray CH, Morrissey MS, Marchbanks RJ, Bradwell AR. Intracranial pressure at high altitude and acute mountain sickness. Clin Sci (Lond) 1995;89:201-4.

Tympanic Membrane Displacement

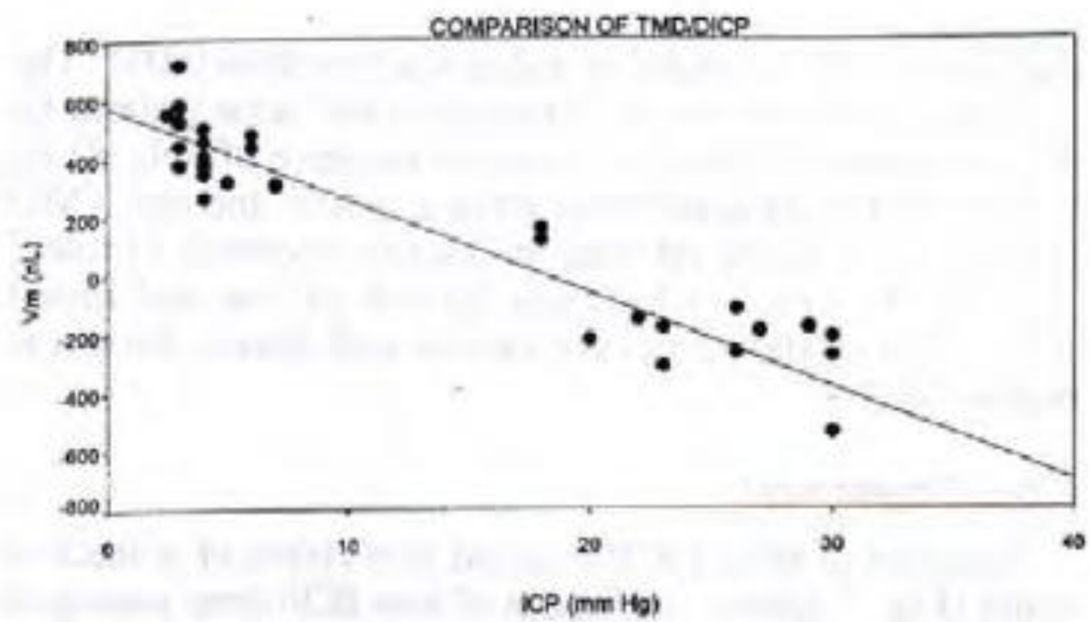


FIG. 8. Scattergram demonstrating Vm values and direct ICP measurements. Correlation coefficient is 0.94, r = 9242, r. = 0.96627, κ = 0.72, and $p < 0.001$ (CI 0.9–0.94).

Samuel M, Burge DM, Marchbanks RJ. Tympanic membrane displacement testing in regular assessment of intracranial pressure in eight children with shunted hydrocephalus. J Neurosurg 1998;88:983-95.

Tympanic Membrane Displacement

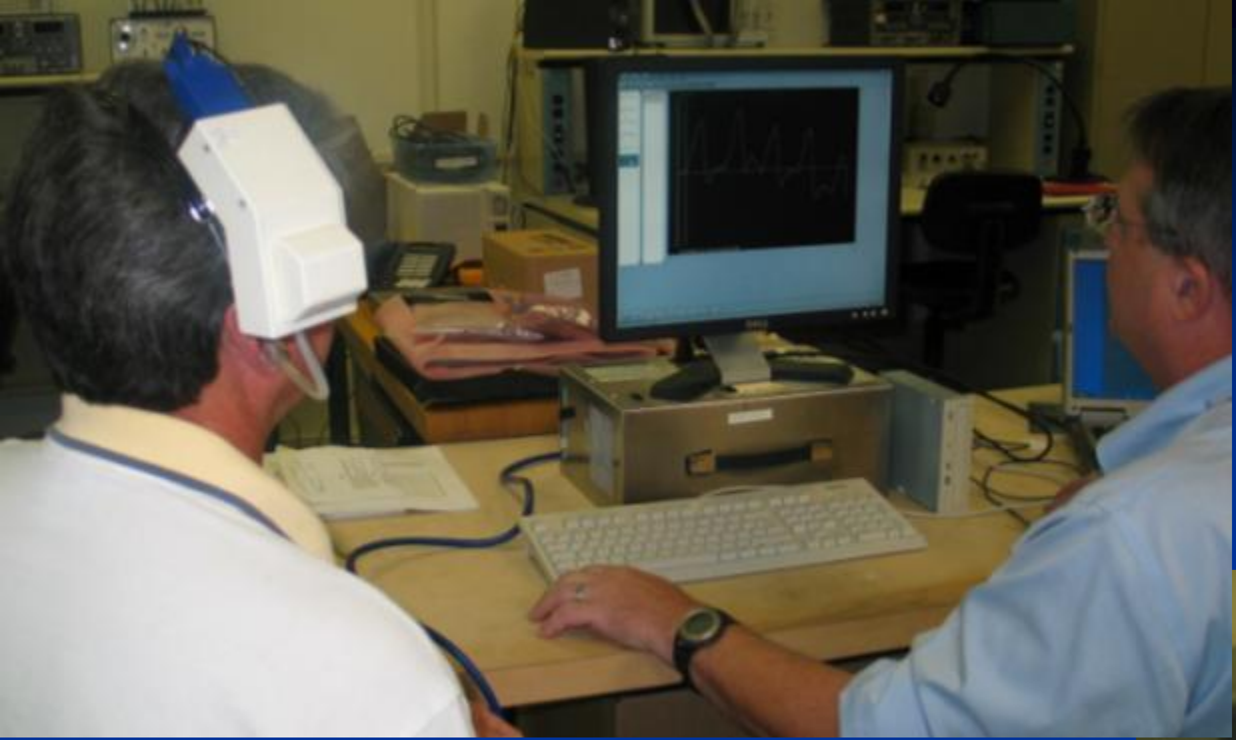
- Advantages
  - Simplicity of use
  - Linear correlation between TMD and ICP
  - CCFP analyzer was flight certified

- Disadvantages
  - Depends on acoustic reflex (ISS background noise)
  - Requires patent cochlear aqueduct (↓ with age)
  - Requires baseline calibration w/ invasive technique

Applications Include

- Adult/paediatric neurology
- Adult/paediatric neurosurgery
- Otolaryngology – ENT
- Ophthalmology
- Anaesthesiology
- Traumatic brain injury clinics

The CCFP measurements impact upon some of the largest areas of healthcare.

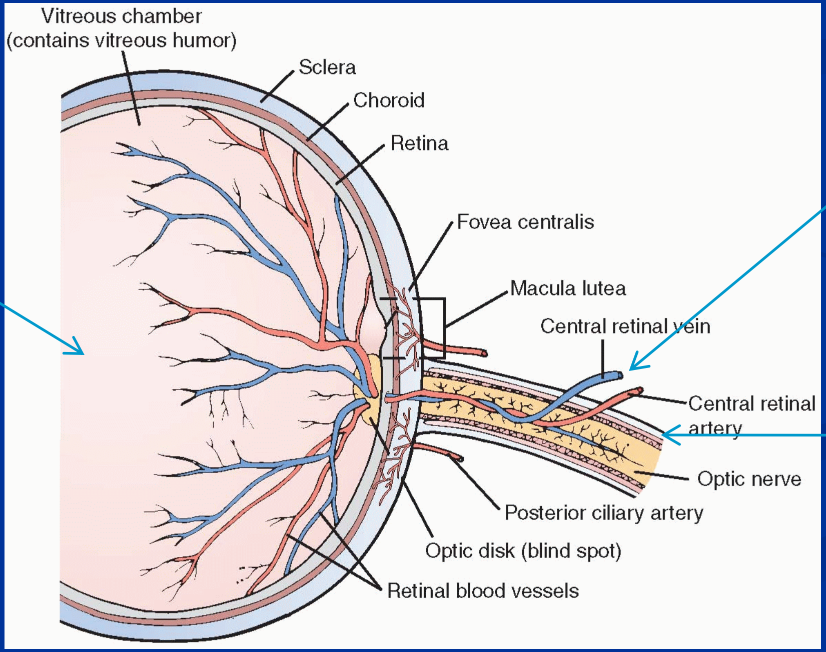


Prototype

Ophthalmodynamometry

- Central retinal vein – Courses from inner eye through optic nerve sheath
- Direct connection between intraocular and intracranial spaces

Intraocular pressure



Venous outflow pressure (VOP)

Intracranial pressure (ICP)

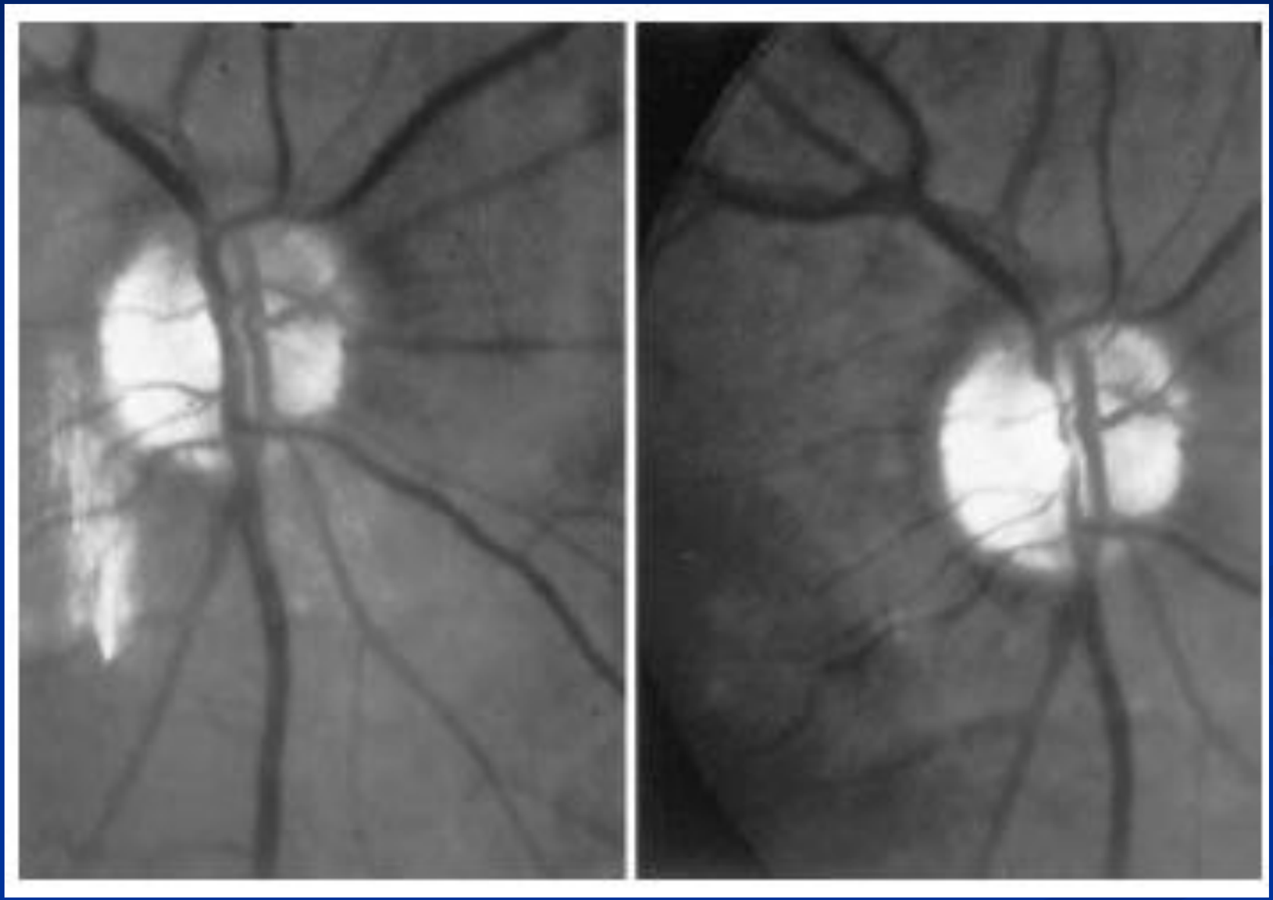
Firsching R, Schutze M, Motschmann M, Behrens-Baumann W. Venous opthalmodynamometry: a noninvasive method for assessment of intracranial pressure. J Neurosurg 2000;93:33-6.

How it works

- Venous Outflow Pressure (VOP) must be > ICP for venous patency
- VOP is also > IOP
- ↑ IOP by direct pressure on eye until central retinal vein collapse by fundoscopy
- → This gives exact value for VOP
- VOP has linear relationship with ICP

Motschmann M, Muller C, Walter S, et al. [Ophthalmodynamometry. A reliable procedure for noninvasive determination of intracranial pressure]. Ophthalmologe 2000;97:860-2.

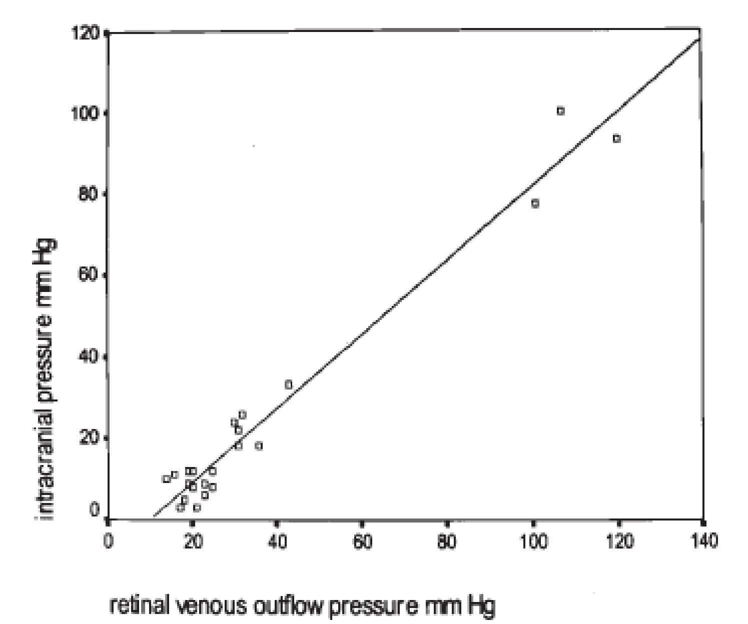
Fundoscopic Exam

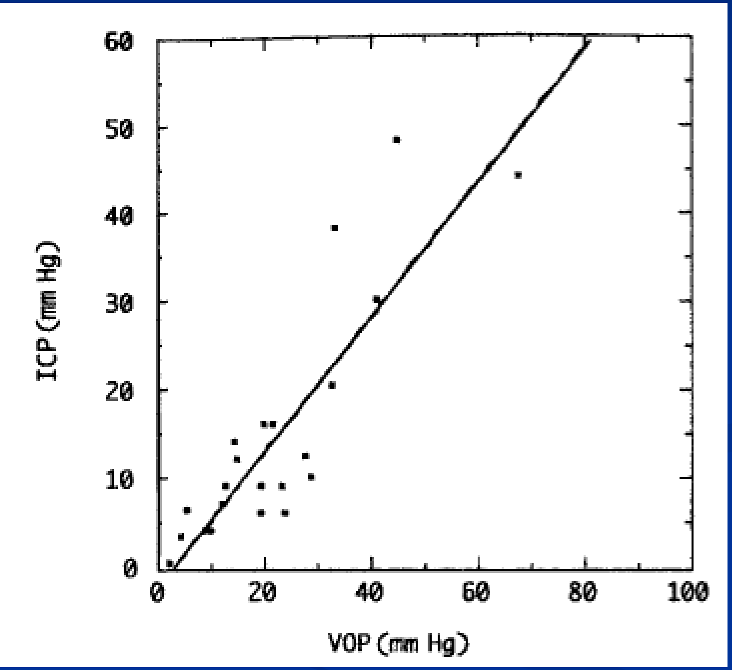


Patent CRV　　　　　　　　Collapsed CRV

Firsching R, Schutze M, Motschmann M, Behrens-Baumann W. Venous opthalmodynamometry: a noninvasive method for assessment of intracranial pressure. J Neurosurg 2000;93:33-6

Relationship of ICP and VOP





ICP = 0.903 x VOP – 8.87
($r = 0.983$, $p < 0.001$)
Firsching et al

Eqn not published
($r = 0.87$, $p < 0.001$)
Querfurth et al

Classic Concept

- Bailliart et al – 1917
  - Described new technique of ophthalmodynamometry
- Baurmann et al – 1925
  - Proposed possible relationship between retinal vein and ICP.
  - Based on his keen observations
- Concept laid dormant until 2000
  - Firsching et al

Ophthalmodynamometry

- Advantages
  - Fairly easy to perform
  - Quick test
  - Small payload
- Drawbacks
  - Requires anesthesia to eye o/w uncomfortable
  - Requires baseline calibration to astronaut population w/ invasive testing
  - ICP/VOP relationship may vary amongst populations
  - Papilledema – Method falls apart

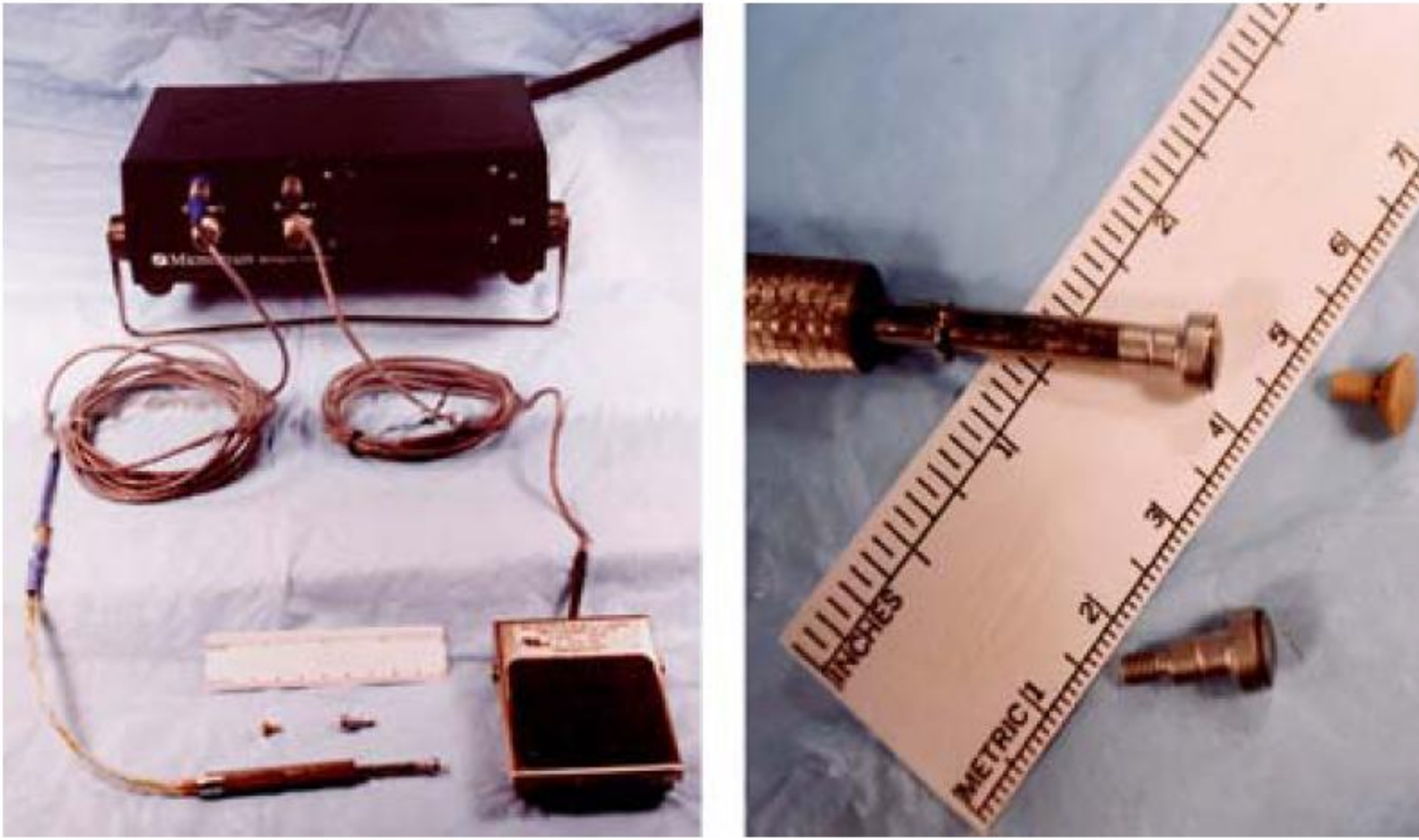


Fig. 1. Venous ophthalmodynamometer. **(A)** Hand-held inductive plunger and foot-activated freeze-go switch are shown with inputs into the signal conditioning box and liquid crystal display. **(B)** Detail of detachable scleral pressure plates.

Transcranial Doppler Imaging

- Core concept: ICP = CPP – ABP
- Arterial blood pressure can be measured
- CPP related to middle cerebral artery flow volume (FV)
- Doppler imaging determines MCA FV
- Data mining approach

Schmidt B, Klingelhofer J, Schwarze JJ, Sander D, Wittich I. Noninvasive prediction of intracranial pressure curves using transcranial Doppler ultrasonography and blood pressure curves. Stroke 1997;28:2465-72.

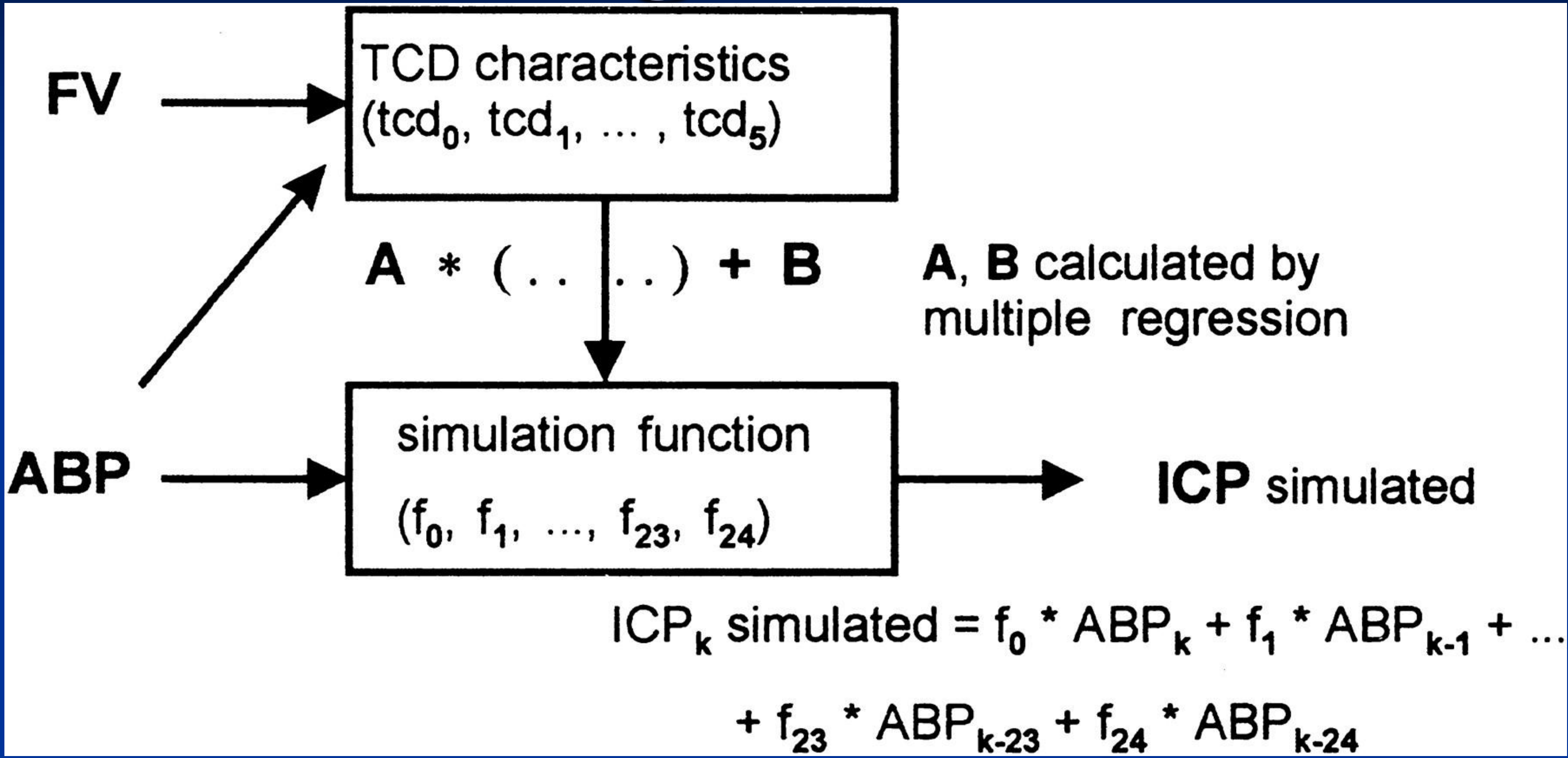
Algorithm Creation

- Schmidt et al – 11 ICU pts
- Looked at MCA FV, ICP (via invasive), and ABP (via art line) in each pt
- For each pt:
  - Used FV, ICP, and ABP data from other 10 to create a linear regression to predict ICP
- Algorithm repeated for larger patient population
  - 113 TBI patients.

Schmidt B, Klingelhofer J, Schwarze JJ, Sander D, Wittich I. Noninvasive prediction of intracranial pressure curves using transcranial Doppler ultrasonography and blood pressure curves. Stroke 1997;28:2465-72.

Schmidt B, Czosnyka M, Raabe A, et al. Adaptive noninvasive assessment of intracranial pressure and cerebral autoregulation. Stroke 2003;34:84-9.

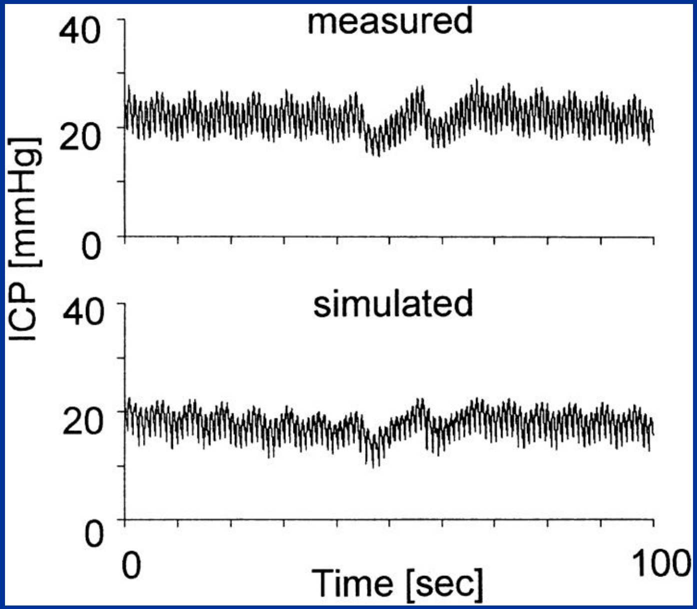
Algorithm

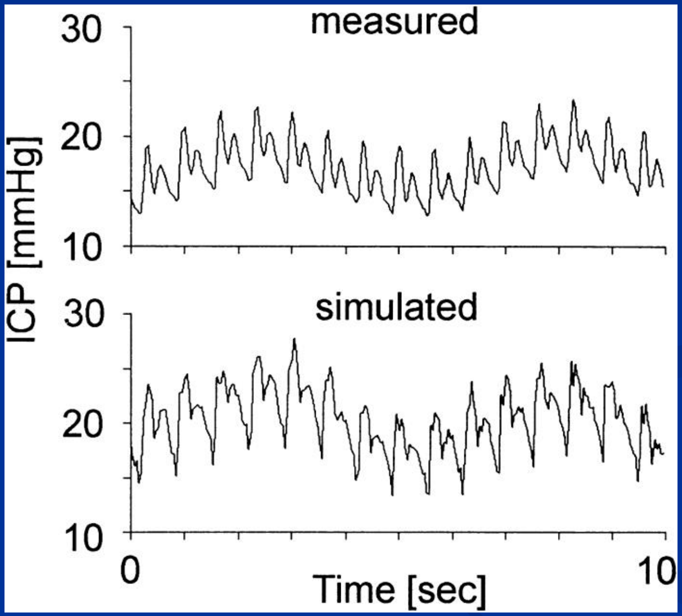


Flow diagram of the ICP simulation. While FV and ABP curves are recorded, the TCD characteristics are computed. Multiplying the TCD characteristics by matrix **A** and adding vector **B,** where **A** and **B** were calculated by a multiple regression analysis, results in the simulation function, which transforms the ABP curve into the ICP curve by means of the given formula.

Schmidt B, Klingelhofer J, Schwarze JJ, Sander D, Wittich I. Noninvasive prediction of intracranial pressure curves using transcranial Doppler ultrasonography and blood pressure curves. Stroke 1997;28:2465-72.

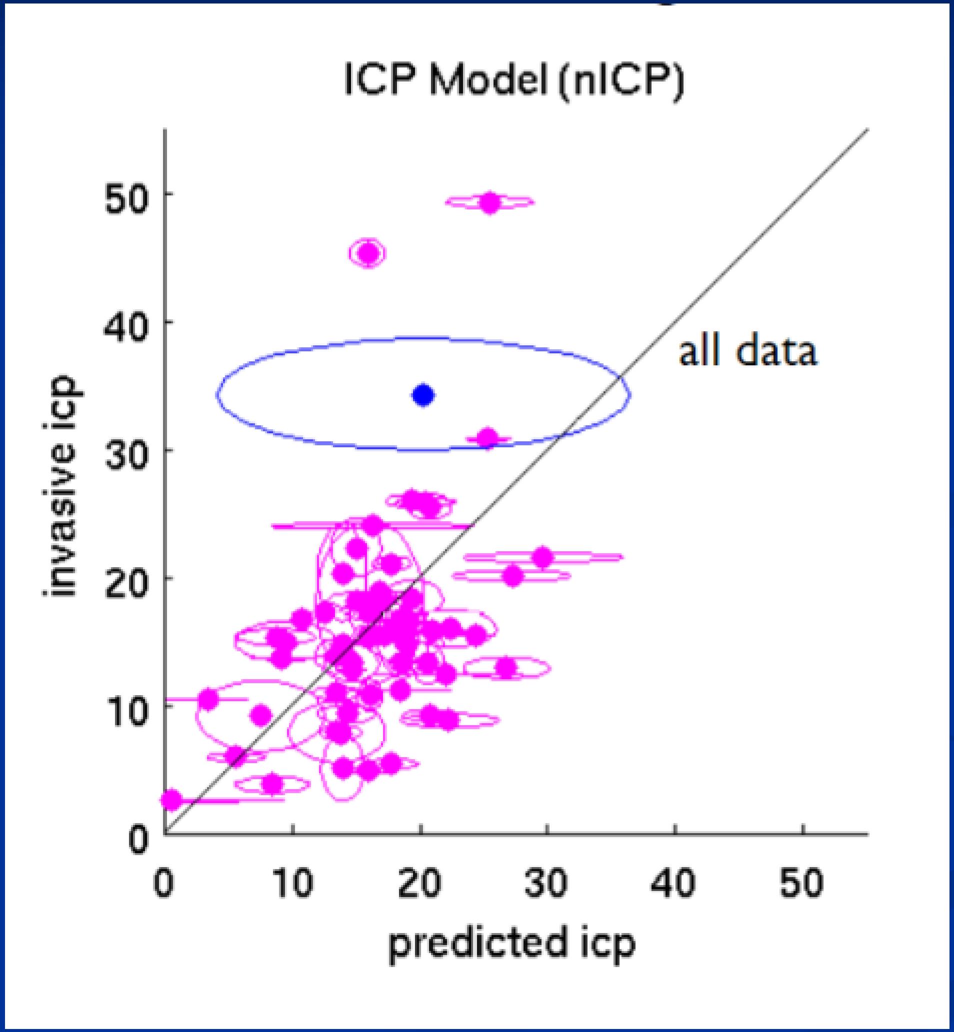
TCD Pressure Curve Examples





Schmidt B, Klingelhofer J, Schwarze JJ, Sander D, Wittich I. Noninvasive prediction of intracranial pressure curves using transcranial Doppler ultrasonography and blood pressure curves. Stroke 1997;28:2465-72.

TCD Results



Mourad P, Kliot M, Harlow B. Towards predicting intracranial pressure and cerebral perfusion pressure. Presentation. 2010

Transcranial Doppler

- Advantages
  - Quick and easy
  - Compact
  - Can provide a pressure curve
- Disadvantages
  - Algorithm requires large astronaut data set of invasive & noninvasive ICP measurements w/ minimal error
    - Includes multiple ICP measurements via transducer or LP
  - All algorithms thus far based on TBI patients – cannot apply to astronauts w/o risk of systematic error
  - Not tested with cuffed BP measurement (only art lines)

Combination of Ophthalmodynamometry and Transcranial Doppler

- Querfurth et al
- Traditional ODM w/ ophthalmic and central retinal artery pulsatility indices
- Modified linear regression

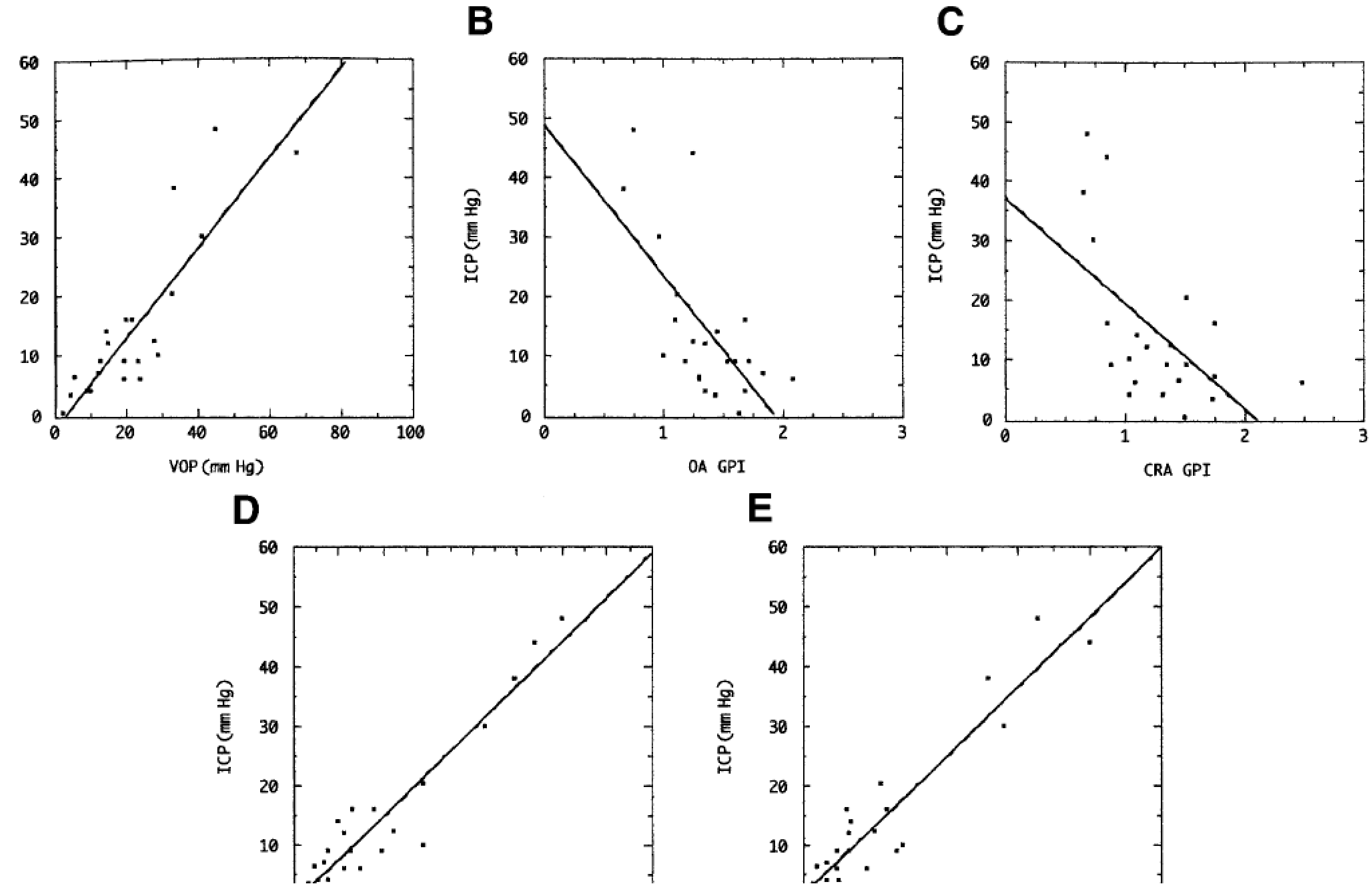


Fig. 3. Simultaneous recordings of ICP and retinal venous, arterial, and composite venous-arterial hemodynamic variables. **(A)** Central retinal vein; direct association between intracranial pressure (ICP) and VOP (venous occlusion pressure). Both continuous variables are given in mmHg. r = 0.87, *n* = 22 independently collected data samples in neurosurgical patients with intraventricular fluid coupled pressure transducers. **(B)** Ophthalmic artery (OA); inverse association of Gosling's arterial pulsatility index (GPI, *see* Methods) with ICP. Arterial velocities were recorded concurrently with venous data in **(A)**, r = 0.66. **(C)** Central retinal artery (CRA); same as in **(B)**, r = 0.58. **(D)** OA; composite index VOP/GPI is plotted against ICP, r = 0.95. **(E)** CRA; as in **(D)**, r = 0.94. ICP prediction using OA or CRA bipartite composite indices is significantly improved over either VOP or corresponding artery GPI used singly ($p < 0.05$).

Querfurth HW, Arms SW, Lichy CM, Irwin WT, Steiner T. Prediction of intracranial pressure from noninvasive transocular venous and arterial hemodynamic measurements: a pilot study. Neurocrit Care 2004;1:183-94.

New Equations, Same Caveats

- $ICP = 0.294 + 0.735\ [VOP/\ GPI_{OA}]$
  ($r = 0.95$ vs 0.87, $p < 0.02$)

- $ICP = 1.734 + 0.582\ [VOP/GPI_{CRA}]$
  ($r = 0.94$ vs. 0.87, $p < 0.05$)

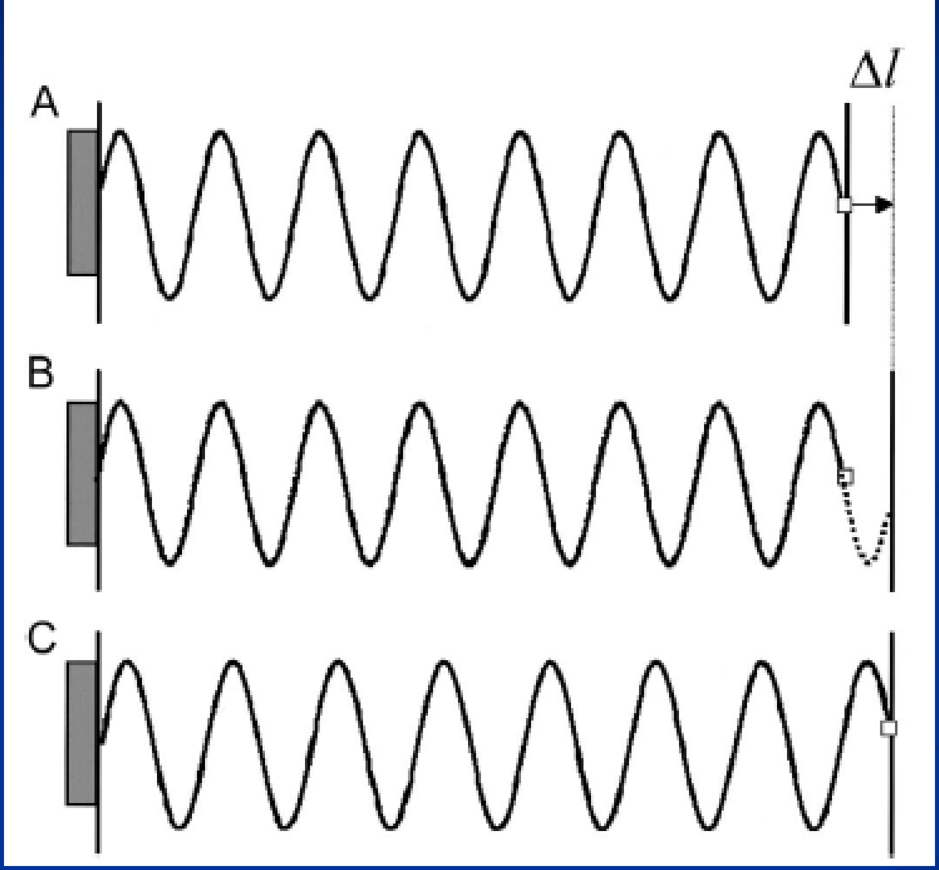
Improvement in linear relationship but would now require more calibration amongst astronauts.

Querfurth HW, Arms SW, Lichy CM, Irwin WT, Steiner T. Prediction of intracranial pressure from noninvasive transocular venous and arterial hemodynamic measurements: a pilot study. Neurocrit Care 2004;1:183-94.

Pulsed Phase-Lock Loop

- Technique based on relationship of skull diameter and ICP
- Place 500 kHz US probe on temple
- Reflected wave is “phase-locked” to skull size
- Detects changes on the order of microns (CSF pulsations)

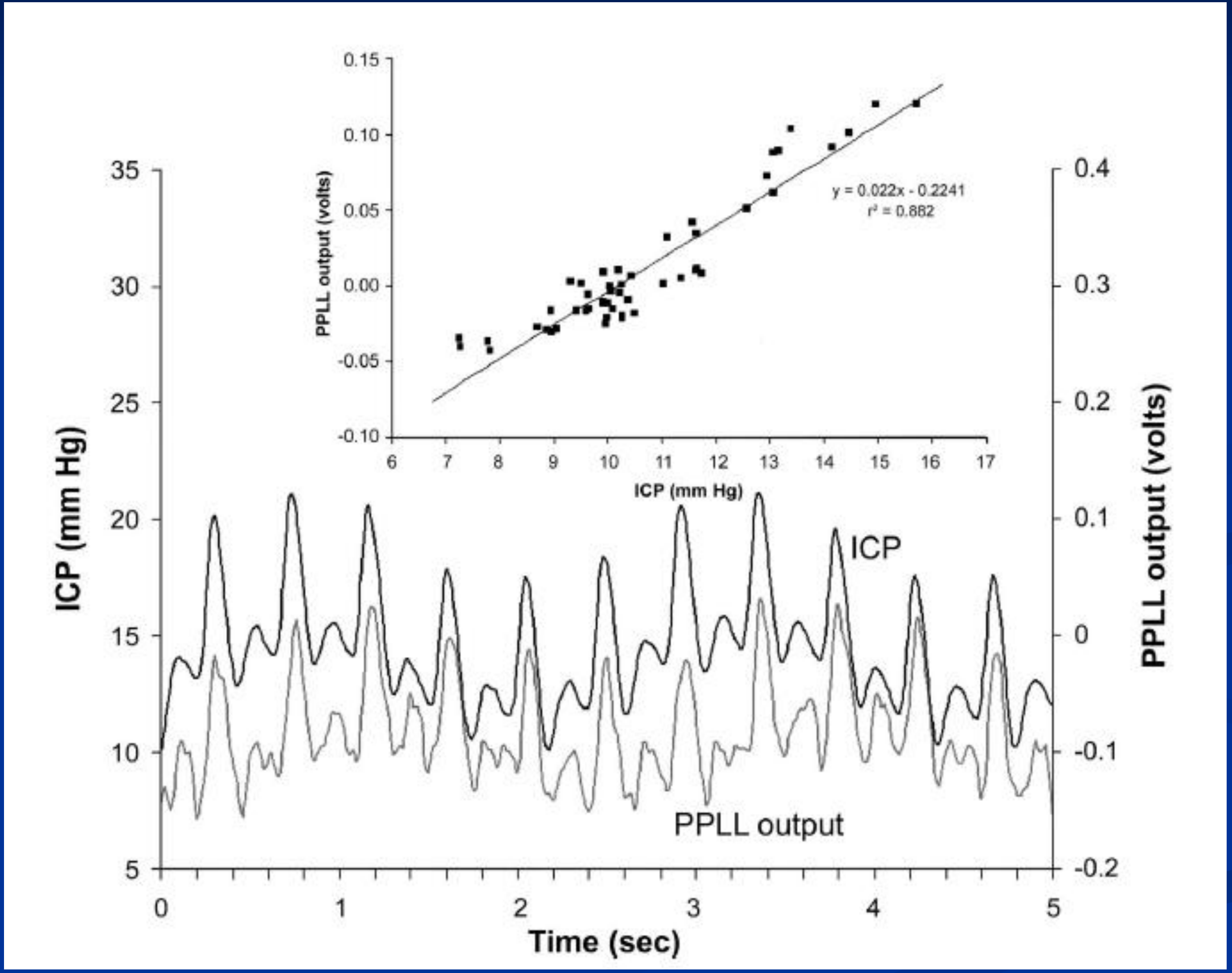
How it Works



$$\Delta f/f = -\Delta l/l$$

Ueno T, Macias BR, Yost WT, Hargens AR. Noninvasive assessment of intracranial pressure waveforms by using pulsed phase lock loop technology. Technical note. J Neurosurg 2005;103:361-7.

What it Provides



Ueno T, Macias BR, Yost WT, Hargens AR. Noninvasive assessment of intracranial pressure waveforms by using pulsed phase lock loop technology. Technical note. J Neurosurg 2005;103:361-7.

Pulsed Phase-Lock Loop

- Advantages
  - Real -time monitoring provides CSF pressure curve
  - Easy to use
- Drawbacks
  - CSF changes may not be only reason for skull diameter changes
  - Intra-use reliability depends on probe placement
  - Bulky equipment
  - Requires preflight calibration for each astronaut

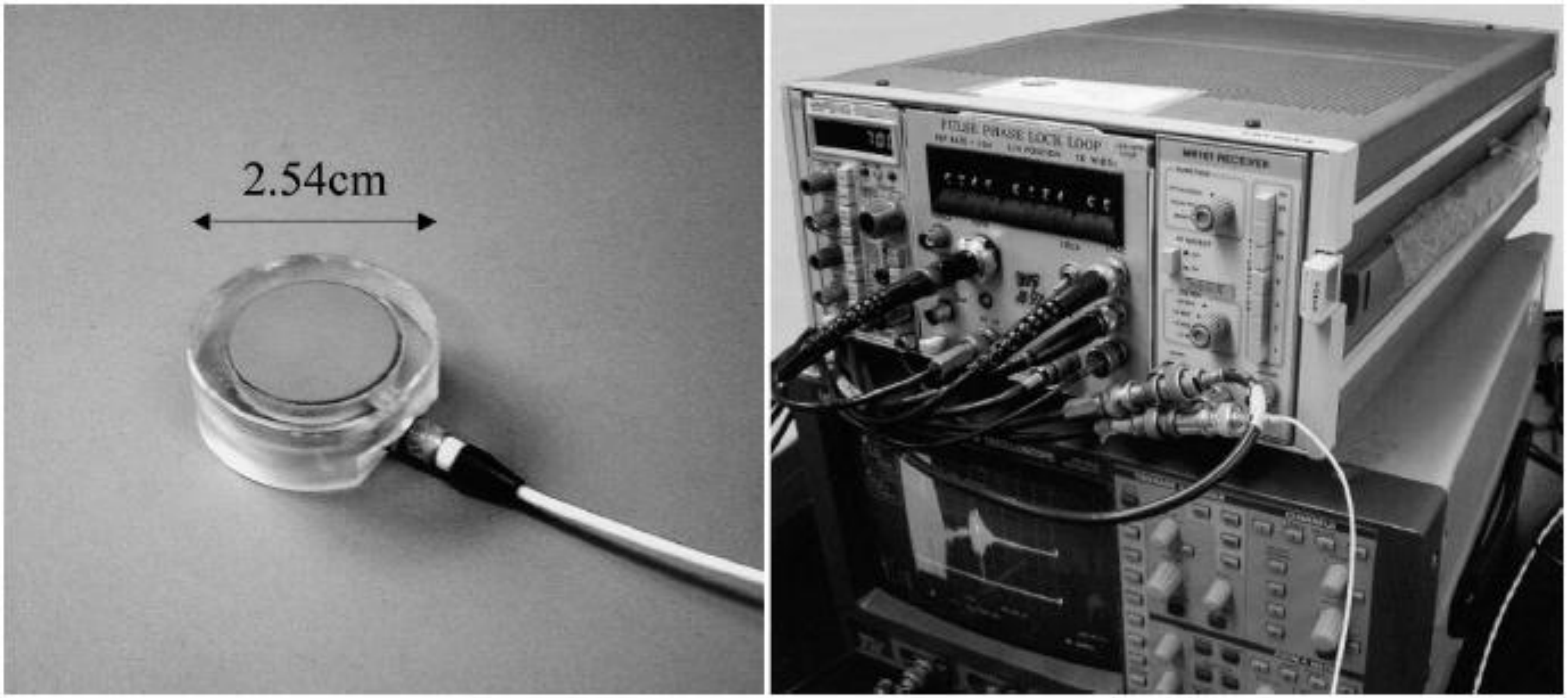


FIG. 1. Photographs showing the PPLL transducer *(left)* and device *(right)* with a digital oscilloscope. An ultrasonic reflection is displayed on the oscilloscope screen.

Ueno T, Macias BR, Yost WT, Hargens AR. Noninvasive assessment of intracranial pressure waveforms by using pulsed phase lock loop technology. Technical note. J Neurosurg 2005;103:361-7.

Summary

- Many techniques available
- None perfect
- Each has different "personality" of advantages and disadvantages
- Any method will require at least one invasive study per astronaut on earth.
- For absolute errors of ± 5 mmHg, will likely need combination