Recognition of Cranio-Cervical Instability in the Complex Chiari patient

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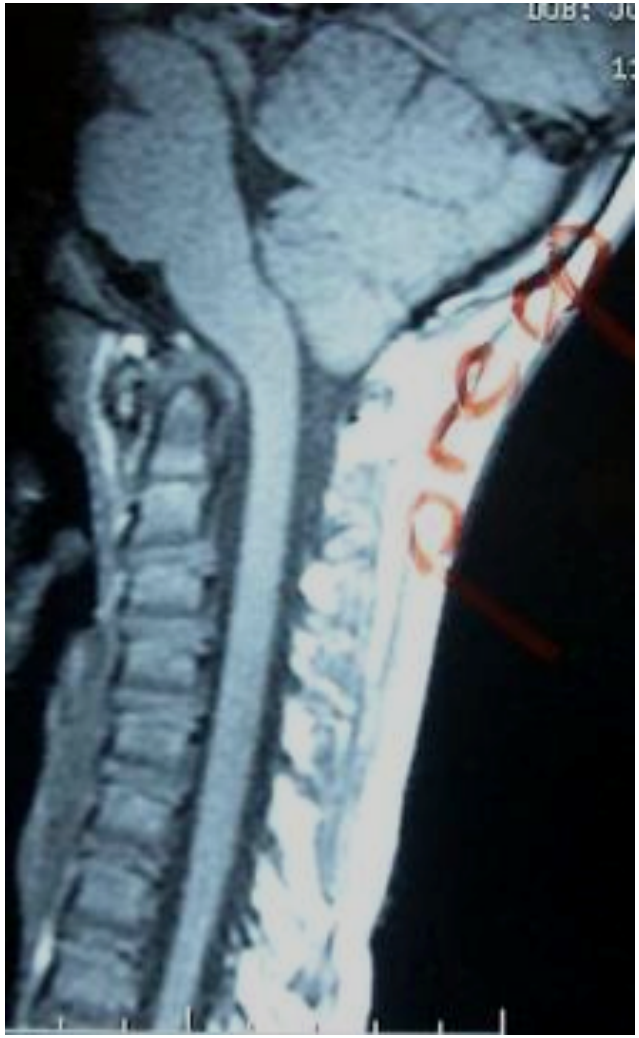
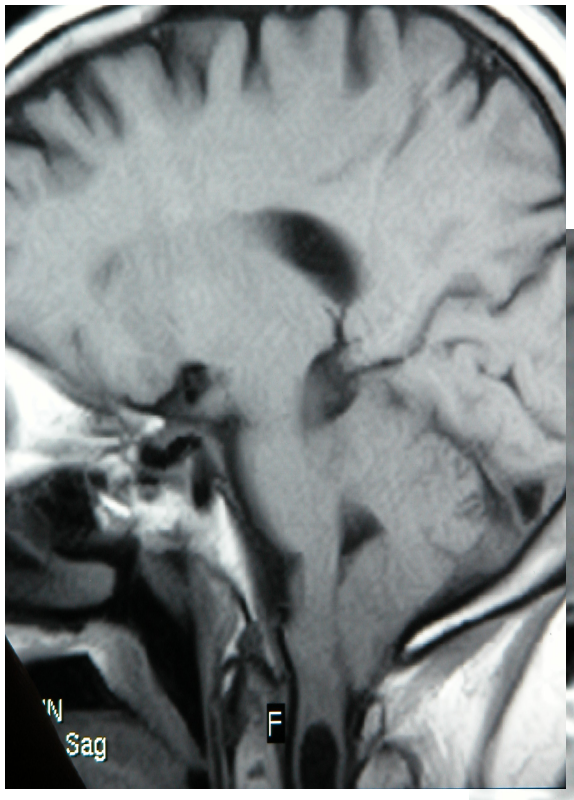
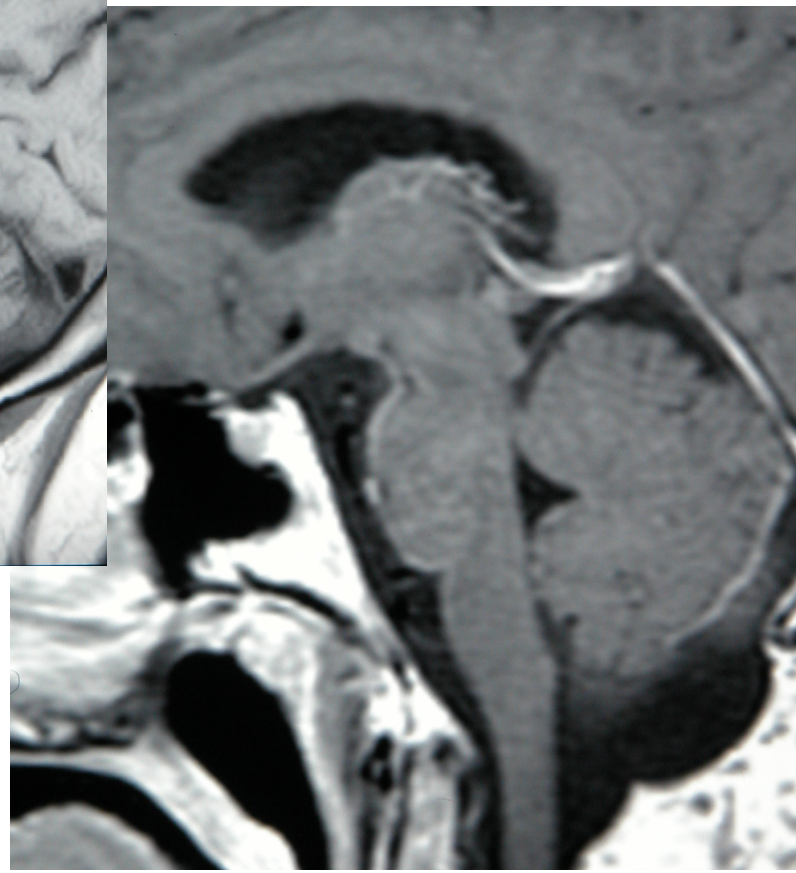


Cervico medullary syndrome in Chiari Malformation

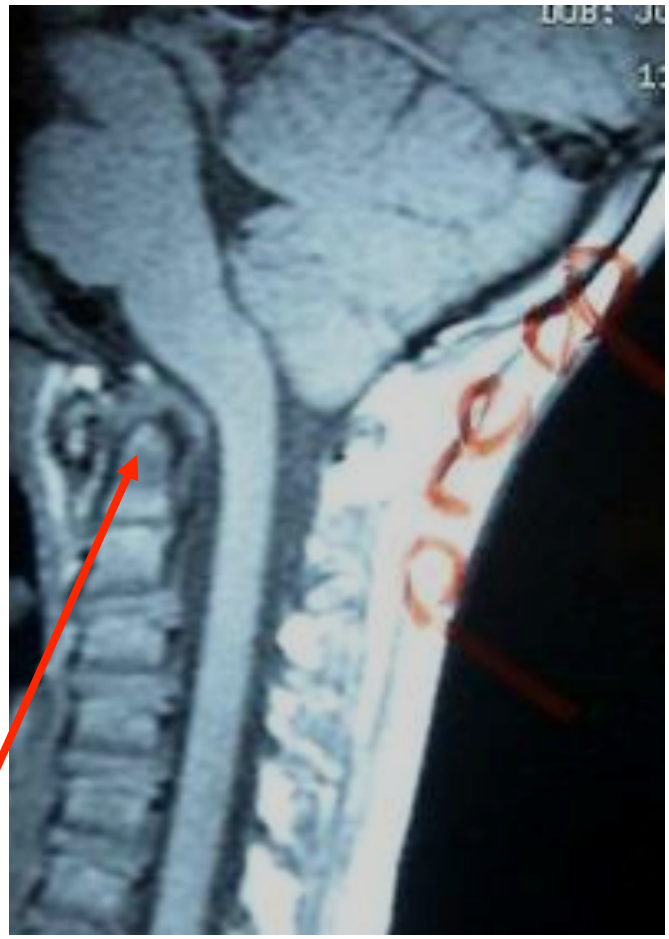
Henderson, J Surg Neurol Int , 2010

- Double vision
- Memory loss
- Speech difficulties
- Dizziness
- Vertigo, Tinnitus
- Difficulty swallowing
- Disorder of breathing
- Choking
- Dysautonomia
- Numbness,Weakness
- Rapid fatigue
- Unsteady gait
- Urinary frequency
- Irritable bowel disease





40% of Chiari decompressions fail



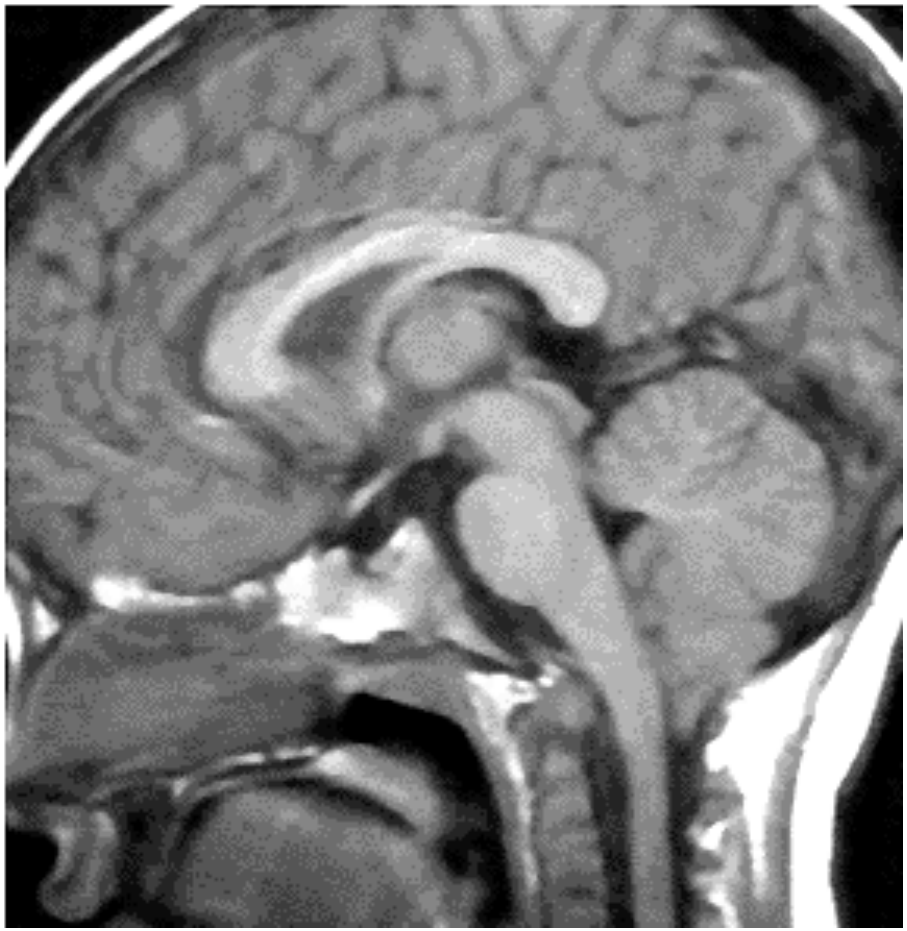
- A significant number of patients worsened after suboccipital decompression
  Dyst ,1988; Bindal ,1995; Dauser, 1988
- 50% pediatric group have "Ventral Brainstem Flattening"
  Grabb,1999
- 40% have basilar impression
  Cahan L, J NSGY,1982
- Angulation over the odontoid process
  Menezes,1988

The Complex Chiari

Doug Brockmeyer Neurol Sci 32 (S345-347) 2011
Robert Bollo J NSGY Ped 10(2): 134-141, 2012

Brainstem herniation (Chiari 1.5)
Medullary kink / retroflexed odontoid
Abnormal clivoaxial angle/ basilar invagination

to treat the deformative stress imparted by these anomalies,
56% required occipito-cervical fusion
22% transoral odontoidectomy



Goals

- Discuss How deformative stress affects the nervous system
- Identify established metrics of anatomic and dynamic deformative stress

What is Deformative stress ?

Stress results from strain ε

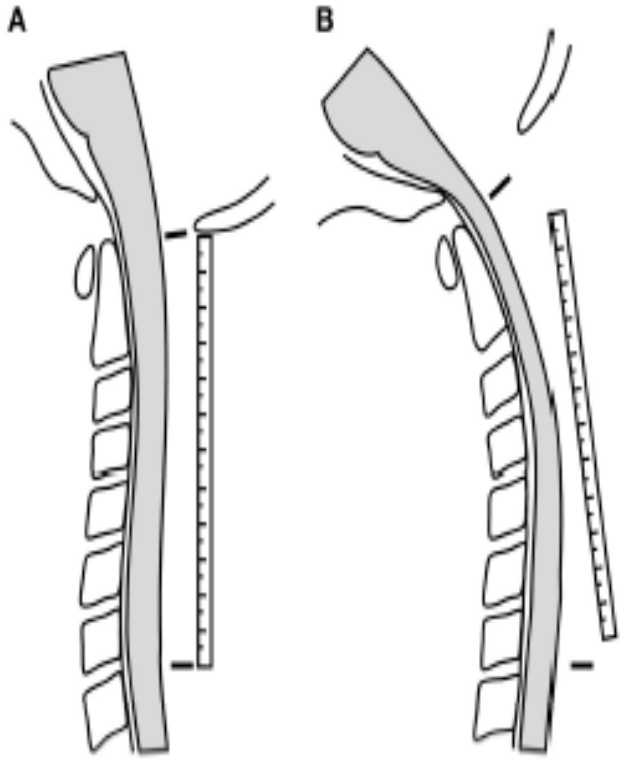
ε = d L / Lo

Normal human neuraxis develops a strain

ε = **.17** on full flexion

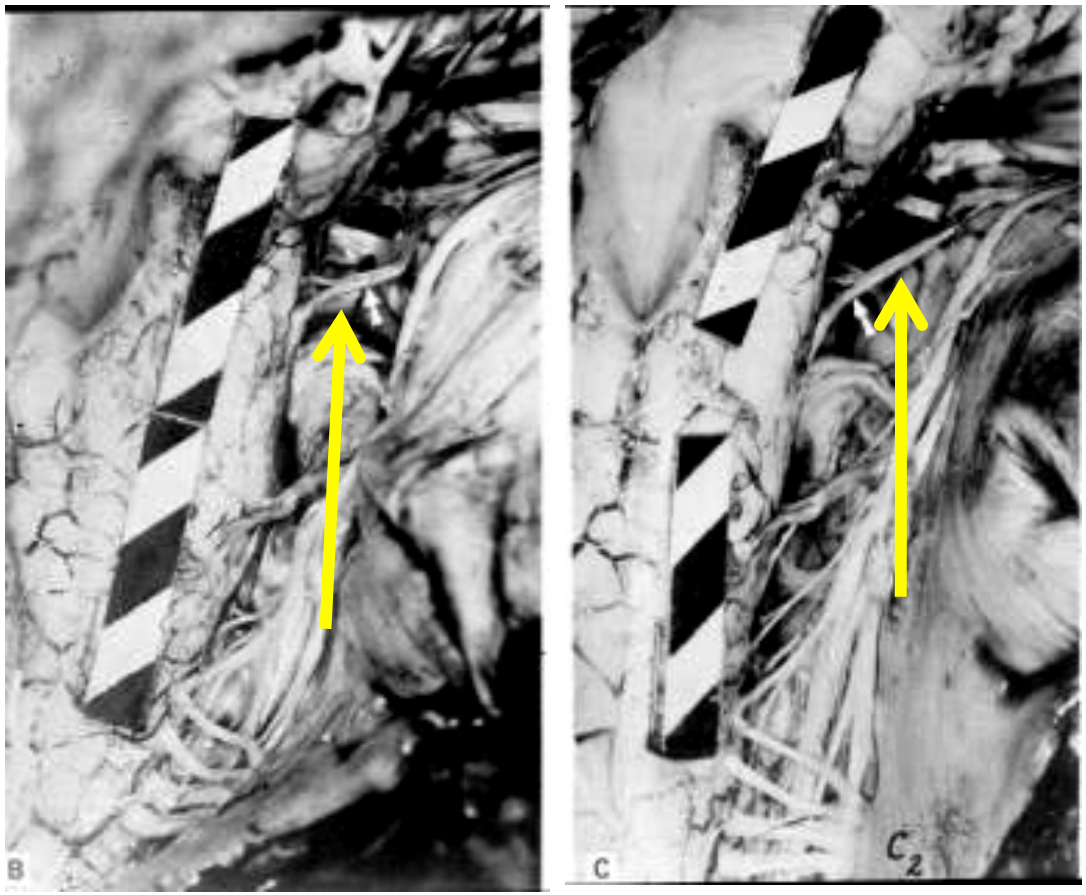
Giant squid axon loses function at

ε = .2



During normal motion, large axial strains are produced in the spinal cord and lower cranial nerves are stretched

- Kitihara, Neurol Med Chir (Tokyo)1995
- Margolies, IRCOB Conference, 1992
- Tunturi, J Neurosurg,1978
- Breig A: Overstretching of the spinal cord--a basic cause of symptoms in cord disorders. J Biomech 3:7-9, 1970

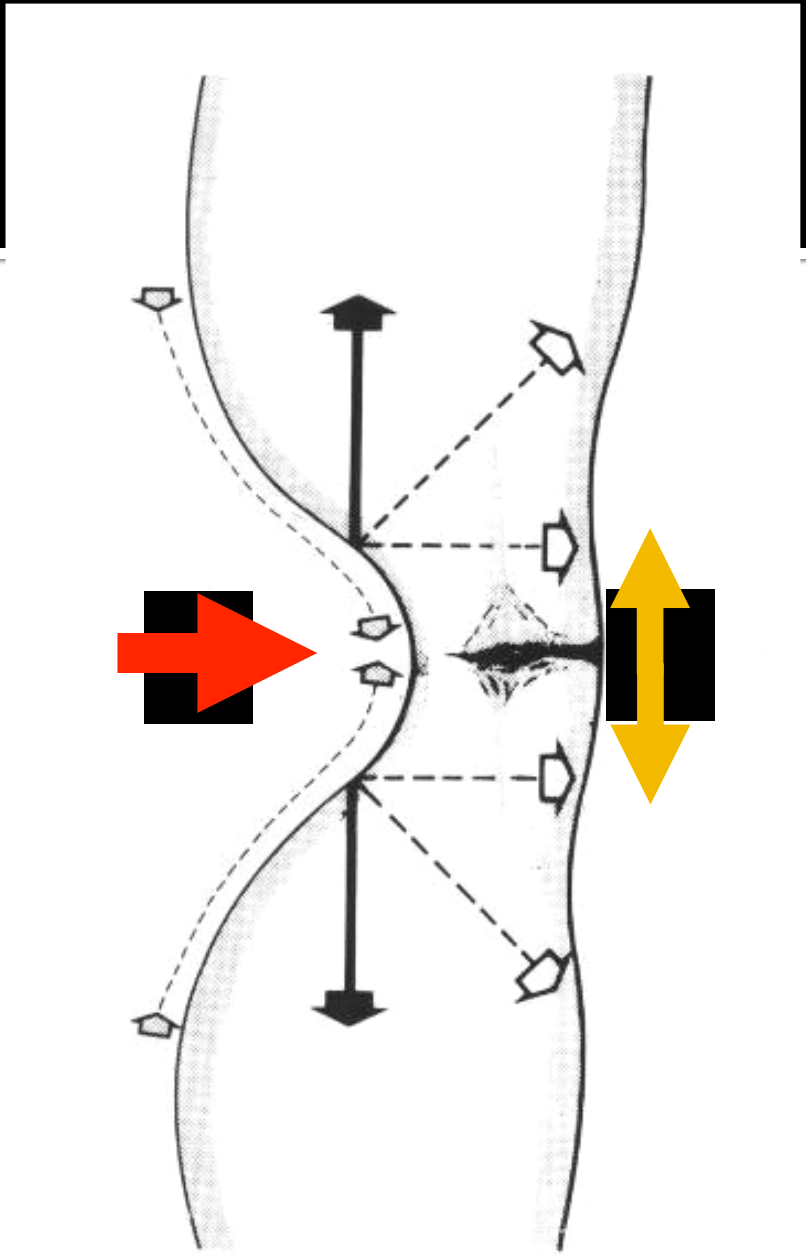


neutral

flexion

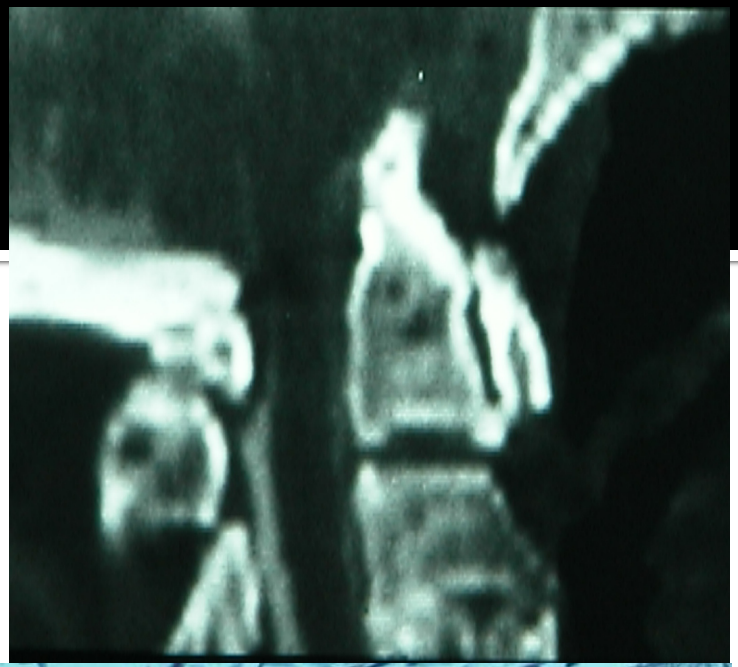
Deformative Stress

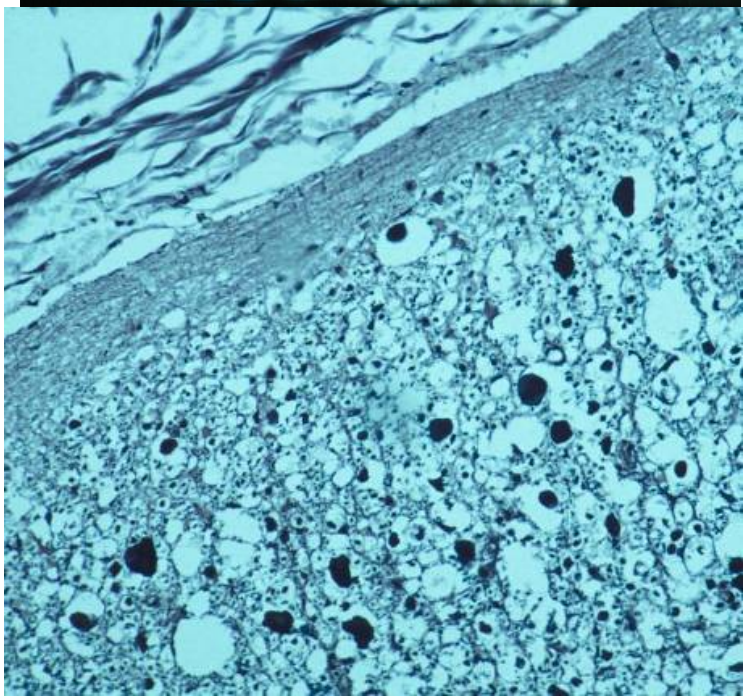
- = "out of plane" loading from a retroflexed odontoid
- Causes local histo-pathological changes and also increases tensile stress



Breig, "Adverse Mechanical Tension in the CNS", 1978

What is the pathological substrate of deformative stress?





EXTENDED REPORTS

Neuropathology of the brainstem and spinal cord in end stage rheumatoid arthritis: implications for treatment

Fraser C Henderson, Jennian F Geddes, H Alan Crockard

Abstract

***Objective*—To study the detailed histopathological changes in the brainstem and spinal cord in nine patients with severe end stage rheumatoid arthritis, all with clinical myelopathy and craniocervical compression.**

***Methods*—At necropsy the sites of bony pathology were related exactly to cord segments and histological changes, and correlated with clinical and radiological findings.**

***Results*—Cranial nerve and brainstem pathology was rare. In addition to the obvious craniocervical compression, there were widespread subaxial changes in the spinal cord. Pathology was localised primarily to the dorsal white matter and there was no evidence of vasculitis or ischaemic changes.**

***Conclusions*—Myelopathy in rheumatoid arthritis is probably caused by the effects of compression, stretch, and movement, not ischaemia. The additional subaxial compression may be an important component in the clinical picture, and may explain why craniocervical decompression alone may not alleviate neurological signs.**

(*Ann Rheum Dis* 1993; **52:** 629–637)

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Accepted for publication
20 May 1993

Rheumatoid arthritis is a systemic disease affecting the cervical spine in 16–88% of patients.[1–6] Progressive subluxation is common,[7–9] associated with increasing compression of the spinal cord and brain stem,[5 10–15] and may cause clinical myelopathy and even sudden death.[3 16 17] Despite these clinical effects, the pathophysiology and histopathology of cord and brain stem injury due to this type of compression are poorly understood, and there are only two studies available in which changes in the cord are described in any detail.[4 18] As part of our wider study of cervical myelopathy in over 250 patients with rheumatoid arthritis we performed a detailed histopathological study of the spinal cord and brain stem in nine patients, and compared the findings with clinical and radiological features.

Methods

This study includes nine patients with seropositive rheumatoid arthritis (eight women, one man) from our ongoing prospective study, who underwent necropsy at the National Hospitals for Neurology and Neurosurgery between 1987 and 1991. All patients were evaluated by rheumatologists, a neurosurgeon (HAC), two neuroradiologists, a physiotherapist, and a research nurse. The clinical assessment included a full neurological examination and a detailed questionnaire about neurological symptoms. In addition, all patients were graded according to Ranawat *et al*[19] and Steinbrocker *et al.*[20] The radiological assessment included plain lateral films of the cervical spine and high definition computed myelotomography with multiplanar reformatting.[21] All operations were carried out by or under the direction of the same surgeon (HAC). Necropsies were performed by or under the supervision of the same neuropathologist (JFG). The necropsy technique used to remove the foramen magnum and cervical spine with the cord and medulla intact has been described previously.[22]

Multiple transverse blocks of the cord were taken, and sections stained with haematoxylin and eosin, luxol fast blue, Woelche, Heidenhain, and modified Bielchowsky stains. Reticulin, Nissl, van Gieson, periodic acid-Schiff, and glial fibrillary acidic protein (Dako; 1:400) stains were performed on selected blocks.

Pre-operative results

CLINICAL FINDINGS

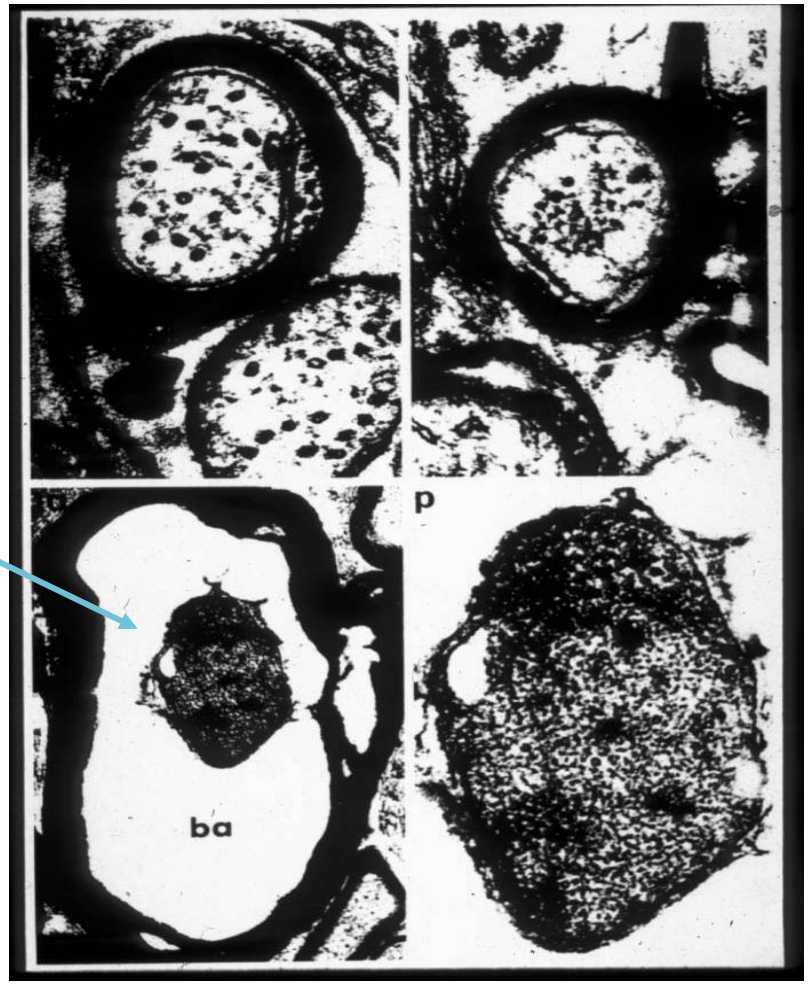
The table gives a summary of the principal clinical details.

The nine patients presented in this study were all white with longstanding seropositive rheumatoid arthritis, aged 47–72 years (average age 60 years, median age 64 years). The only man in the study was the youngest patient.

All patients had been treated with steroids during the course of the disease, three with gold and one with the addition of azathioprine. One other patient had azathioprine without gold.

Stretching Neurons

- Clumping and loss of neurofilaments and microtubules



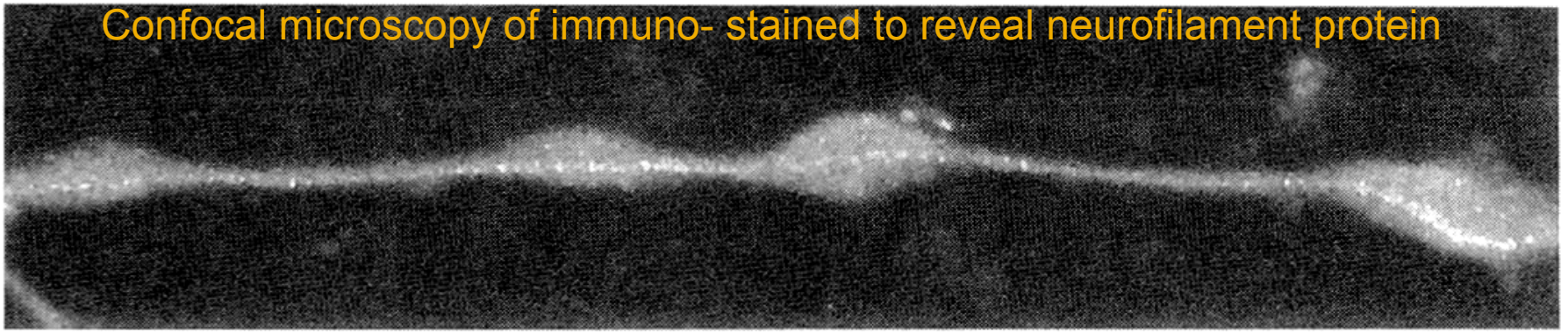
Povlishok, Brain Path,1995

Maxwell, J Neurotrama,2002

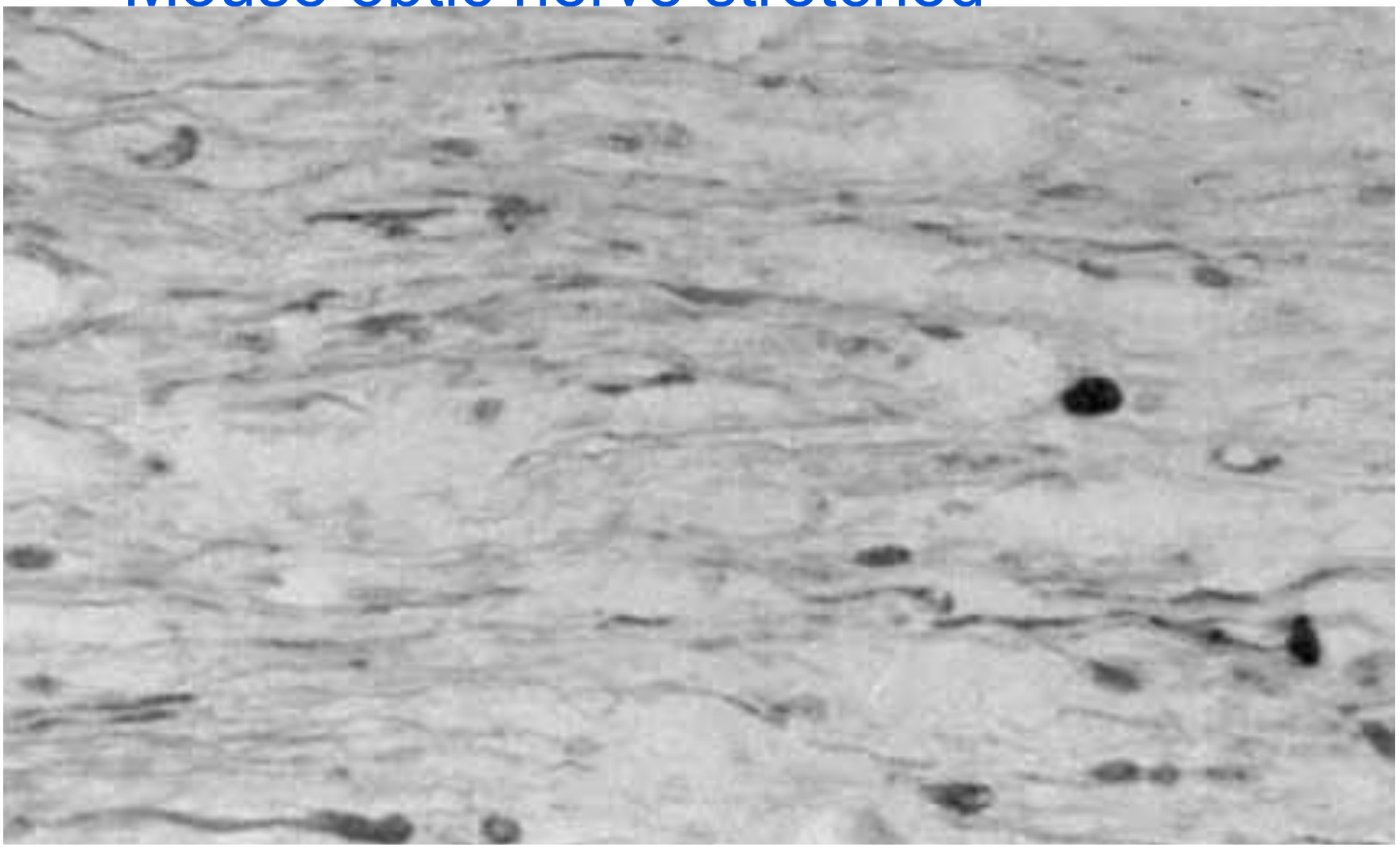
Jafari J Neurocytol,1997

Giant squid axon becomes non functional at $\varepsilon = .2$

Stretch injury → Accumulation of Neurofilament in Axons within 2 hrs.

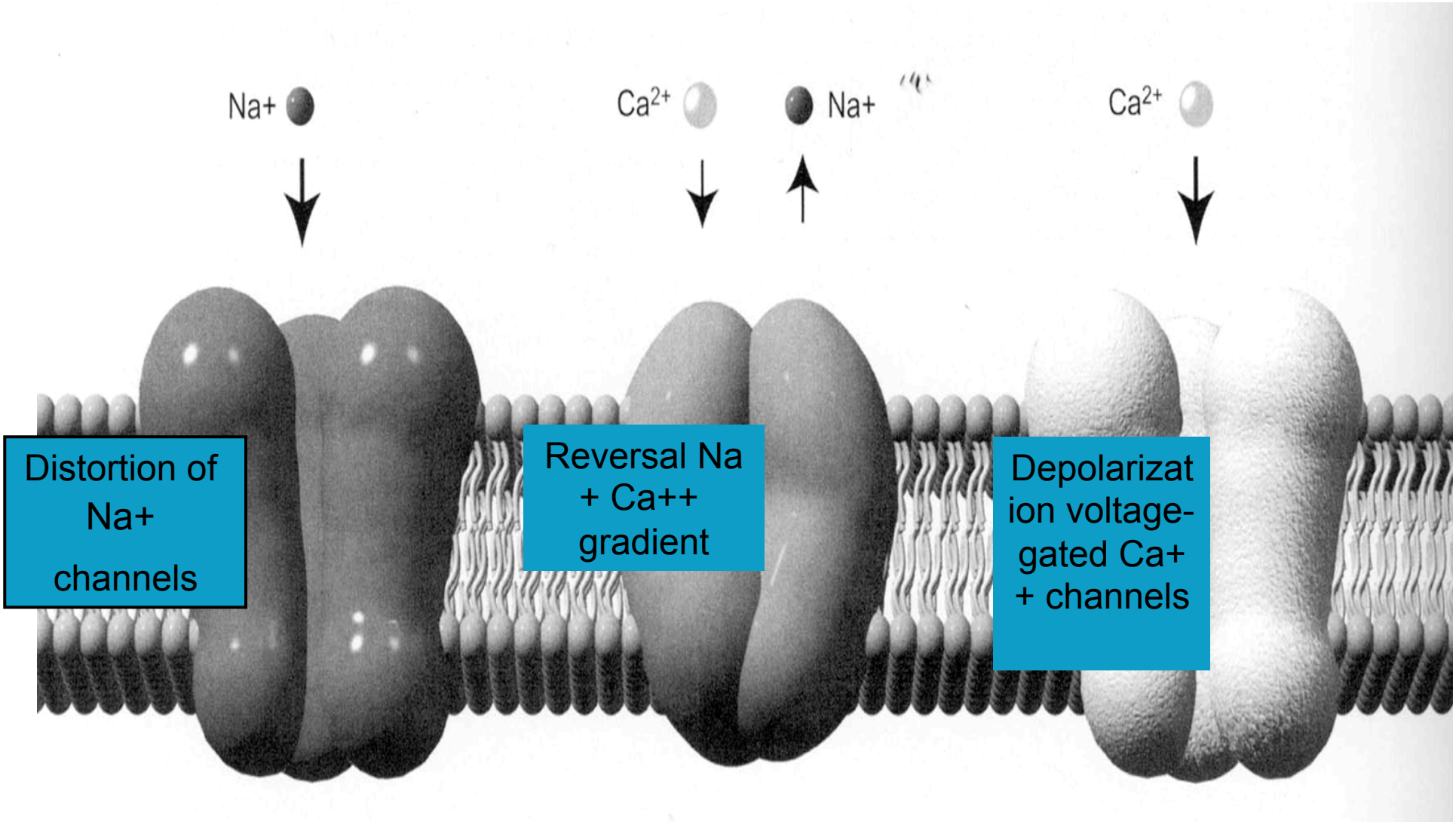


Mouse optic nerve stretched



Saatman KE **J Cereb Blood Flow Metab.** 23(1):34-42, 2003

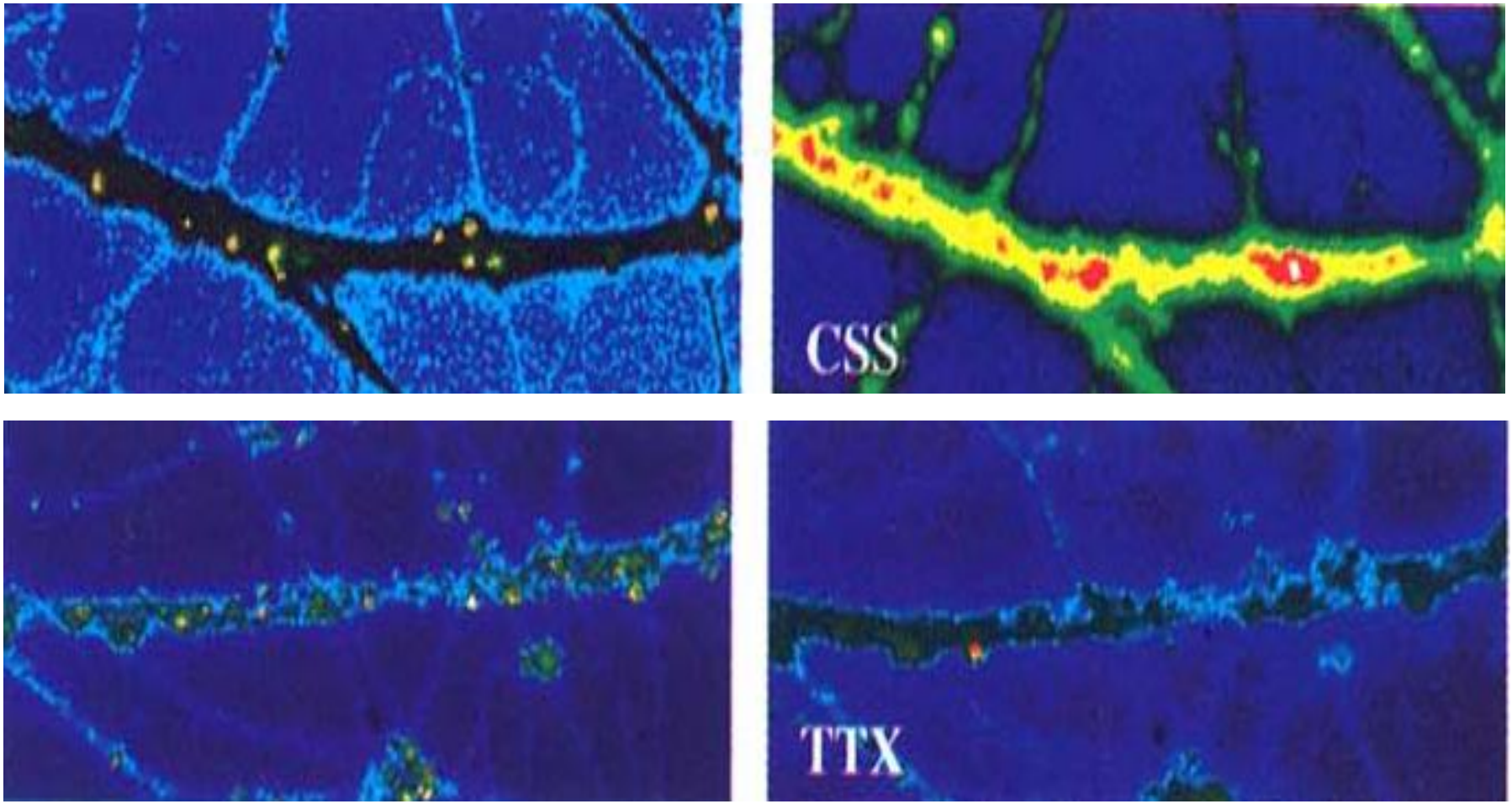
Calcium influx after stretch injury



Wolf et al, J Neurosci 2001

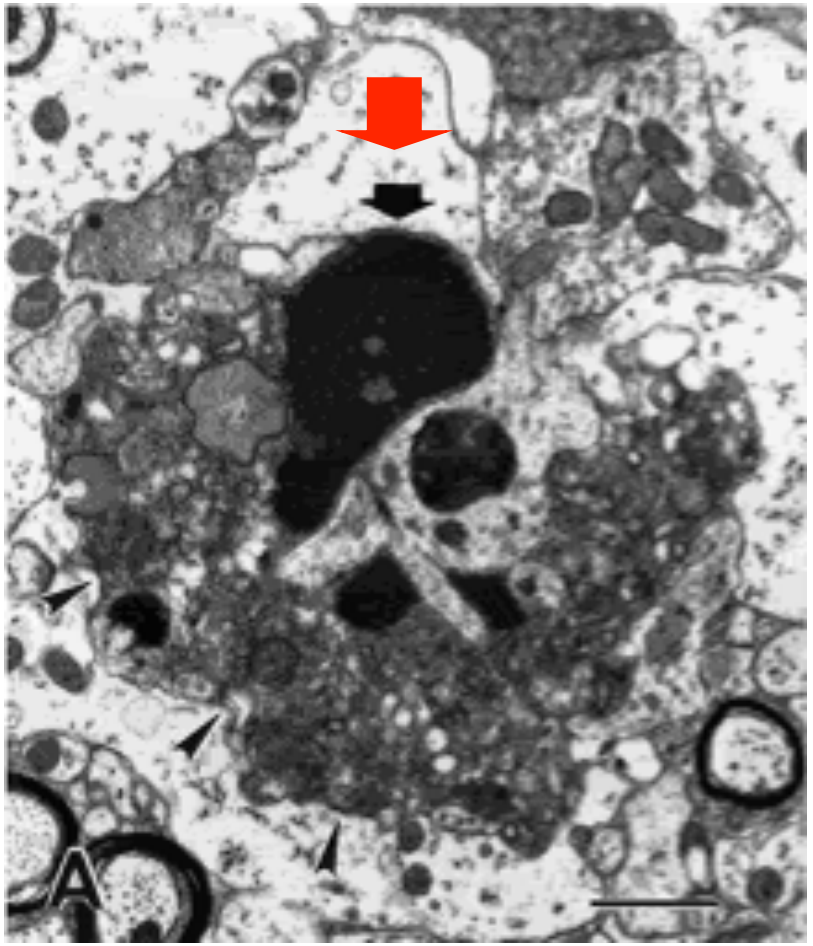
Calcium influx after stretch injury, blocked by TTX

Pre stretch → Post-stretch



Wolf, Sties, Lizard, Smith, J
Neurosci 2001

Stretching Triggers Apoptosis



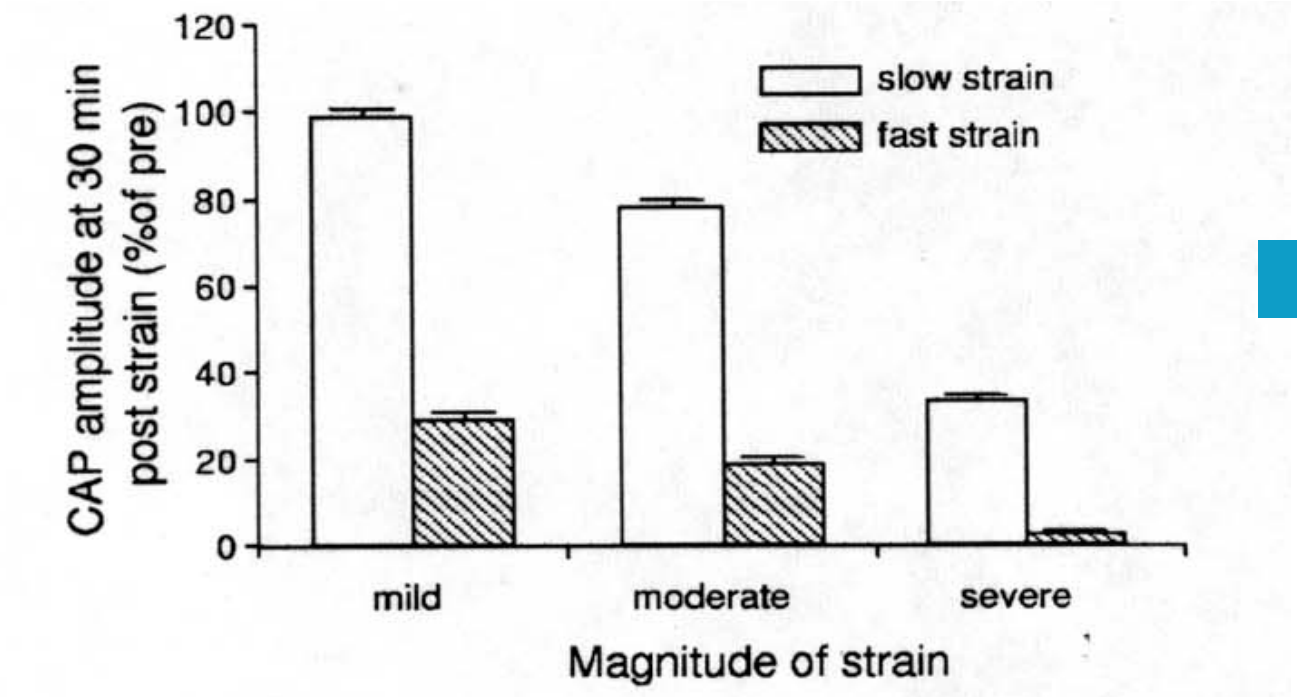
- Secondary injury
- Up-regulation of NMDA receptors
- vulnerability to nitrous oxide and reactive oxygen species
- mitochondrial dysfunction and DNA fragmentation
- Programmed cell death (apoptosis)

(Arundine M et. al. J Neuroscience. 2004, 24(37): 8106-8123)

Biomechanics and cell biochemistry are closely coupled

- Mechanical forces modulate gene expression and biochemical composition of the living system at the molecular level

Effect of strain rate on conduction



P <.01

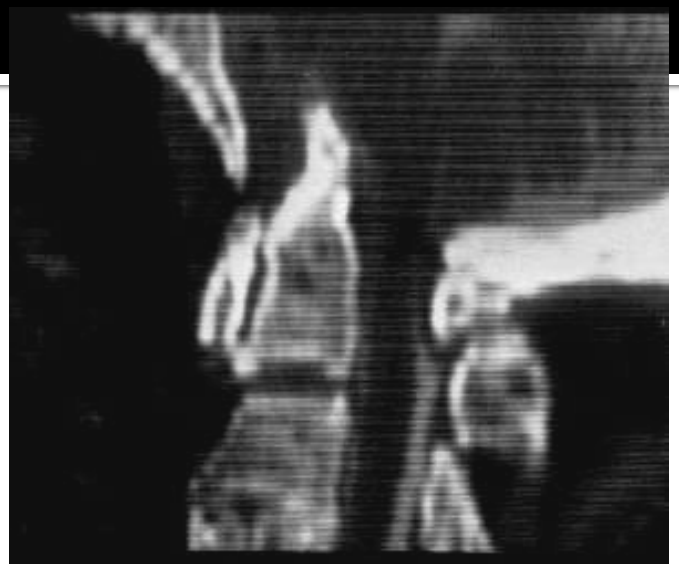
- Amplitude of action potential decreases with strain rate and magnitude of strain

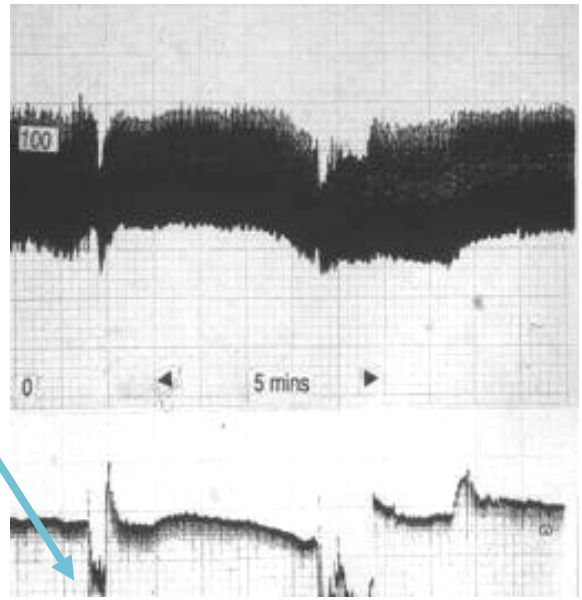
Out of plane loading of the brainstem in pts with basilar invagination results in Sleep apnea

- Compressed arrays of O2 saturation show severe Hypoxia
- Odontoidectomy and stabilization resulted in resolution of sleep apnea

- Howard, **Henderson** et al. Ann Rheum Dis, 1993

  Menezes,J NSGY,1985





Ann Rheum Dis. 1994 February; 53(2): 134–136.
PMCID: PMC1005266

Respiratory abnormalities due to craniovertebral junction compression in rheumatoid disease.

R S Howard, F C Henderson, N P Hirsch, J M Stevens, B E Kendall, and H A Crockard
Harris Unit, National Hospital for Neurology and Neurosurgery, Queen Square, London, United Kingdom.

Abstract

OBJECTIVE--To assess the extent and severity of respiratory insufficiency associated with severe rheumatoid atlantoaxial dislocation and its relation to compression of the neuraxis. METHODS--Twelve patients with severe atlantoaxial dislocation due to rheumatoid disease were studied. Detailed clinical, CT myelography and respiratory assessment including nocturnal oximetry, were performed on all patients

Stretch-Associated Injury in Cervical Spondylotic Myelopathy: New Concept and Review

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THE SIMPLE PATHOANATOMIC concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment, fails to explain the entire spectrum of clinical findings observed in cervical spondylotic myelopathy. A growing body of evidence indicates that spondylotic narrowing of the spinal canal and abnormal or excessive motion of the cervical spine results in increased strain and shear forces that cause localized axonal injury within the spinal cord.

During normal motion, significant axial strains occur in the cervical spinal cord. At the cervicothoracic junction, where flexion is greatest, the spinal cord stretches 24% of its length. This causes local spinal cord strain. In the presence of pathological displacement, strain can exceed the material properties of the spinal cord and cause transient or permanent neurological injury.

Stretch-associated injury is now widely accepted as the principal etiological factor of myelopathy in experimental models of neural injury, tethered cord syndrome, and diffuse axonal injury. Axonal injury reproducibly occurs at sites of maximal tensile loading in a well-defined sequence of intracellular events: myelin stretch injury, altered axolemmal permeability, calcium entry, cytoskeletal collapse, compaction of neurofilaments and microtubules, disruption of anterograde axonal transport, accumulation of organelles, axon retraction bulb formation, and secondary axotomy. Stretch and shear forces generated within the spinal cord seem to be important factors in the pathogenesis of cervical spondylotic myelopathy.

KEY WORDS: Apoptosis, Axon spheroids, Cervical spondylotic myelopathy, Focal axonal injury, Shear, Spinal cord stretch, Strain

Neurosurgery 56:1101–1112, 2005 DOI: 10.1227/01.NEU.0000156518.38370.FC www.neurosurgery-online.com

Cervical spondylotic myelopathy (CSM) is a well-described clinical syndrome that may evolve from a combination of etiological mechanisms. The strong association between a narrowed, spondylotic cervical spinal canal and the development of CSM has previously led to the formulation of a relatively simple pathoanatomic concept that a narrowed spinal canal causes compression of the enclosed cord, leading to local tissue ischemia, injury, and neurological impairment. However, this simple mechanism fails to explain the entire spectrum of clinical findings

ical studies of cervical mobility in patients with CSM, 2) histopathological studies of spinal cord tissue from CSM patients, and 3) biomechanical studies that have led to an improved understanding of the material properties and biomechanical behavior of spinal cord tissue under various physiological and pathological conditions. A growing body of evidence indicates that spondylotic narrowing of the spinal canal results in increased strain and shear forces, and that these pathological forces cause both widespread and localized axonal injury within the spinal cord. The term strain

Neurosurgery: May 2005 - Volume 56 - Issue 5 - pp 1101-1113

The Complex Chiari

- Deformative stress
  - Anatomic
    - basilar invagination due to kyphotic clivo-axial angle
    - congenital anatomic variants
    - syringomyelia
  - Dynamic
    - craniocervical Instability
    - atlanto-axial and sub-axial instability
  - physiological
    - CSF flow
    - hydrocephalus

Instability

"Loss of the ability of the spine under physiological loads to maintain relationships between vertebrae in such a way that there is no damage or subsequent irritation of the spinal cord, (brainstem) or nerve roots, and in addition that there is no development of deformity or incapacitating pain due to structural changes"

White AA Panjabi MM Clin Biomech Spine 1978

Indices of Deformative Stress

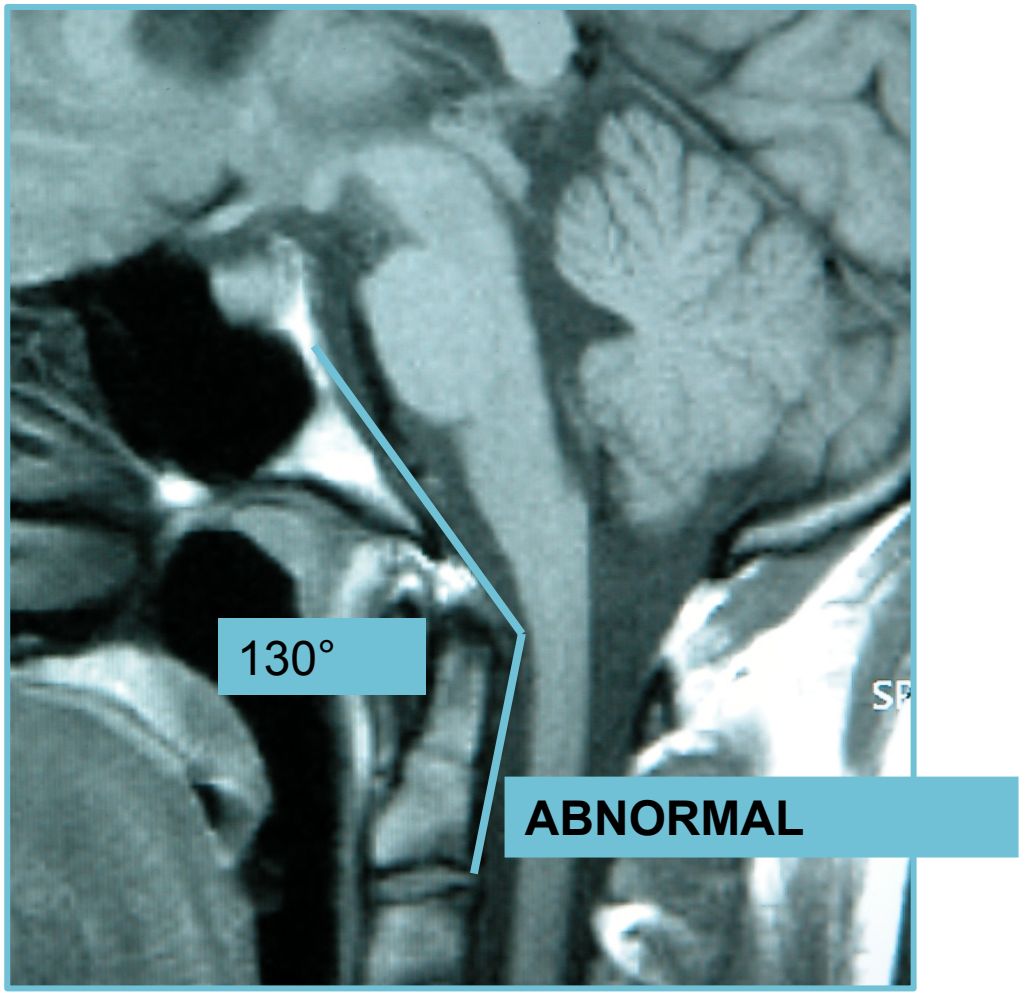
Anatomic
- Basilar invagination

- Clivo-axial angle
- Ventral brainstem compression by Grabb- Oakes method
- Lee's X lines

Dynamic
- Cranio-vertebral instability

- Harris measurements of basion to anterior axial line
- Wholley's Basion- dens interval
- Bull's palato-atlantal angle angle

The Kyphotic Clivo-axial Angle is less obvious



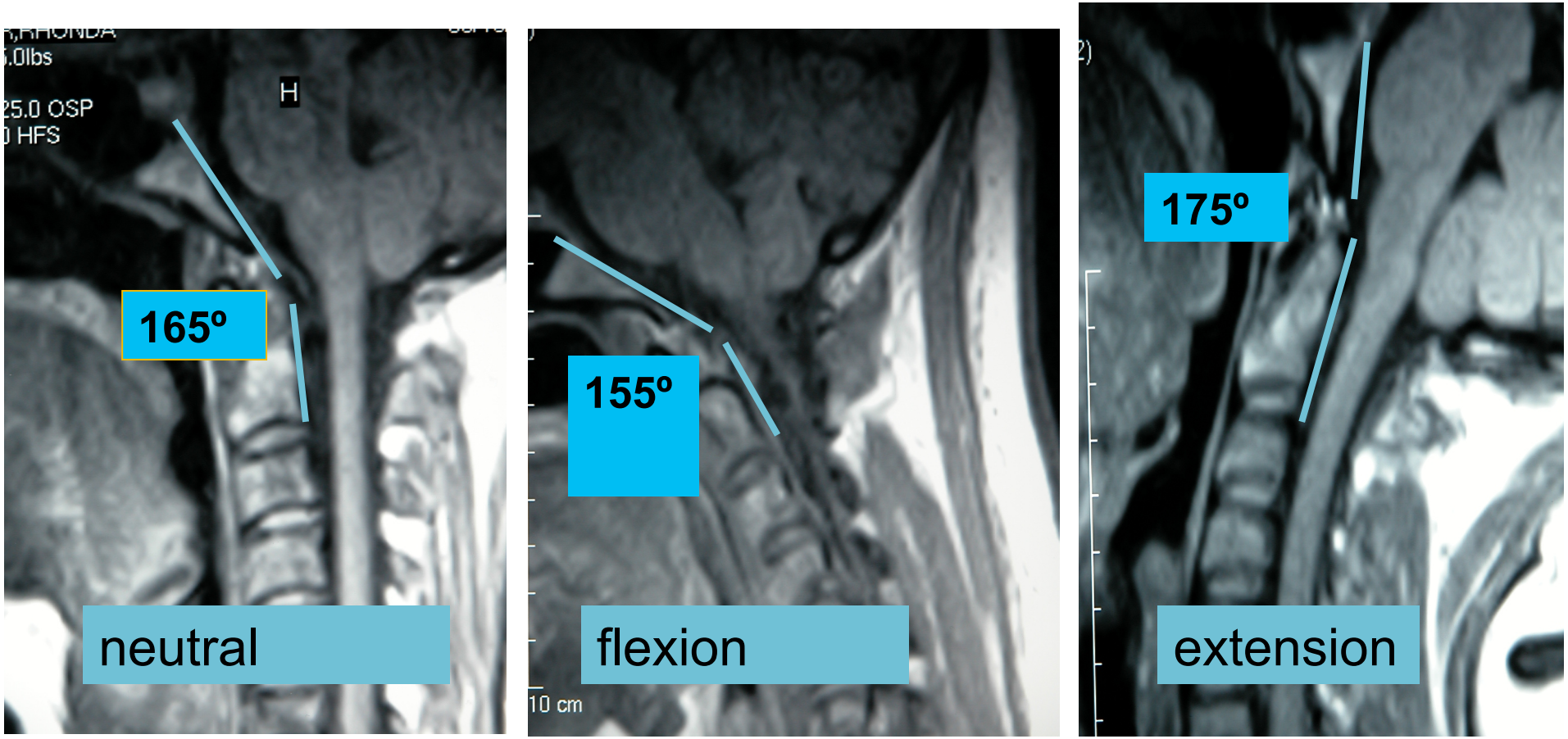
Angulation of the brainstem in basilar invagination causes neurological disability- Scoville,1951

<150ºassociated with deficit. Van Gilder,1984; Smoker 1984Menezes,1988

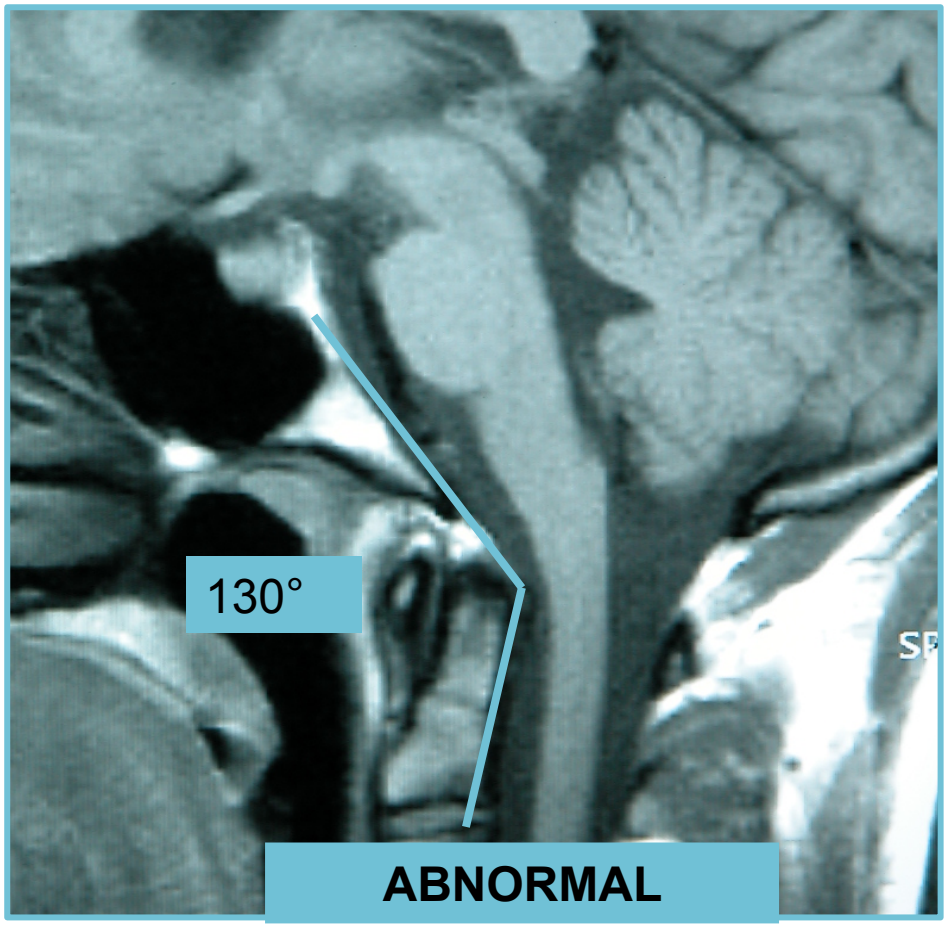
"**fulcrum effect** in basilar invagination applies traction to the caudal brainstem and rostral cervical spinal cord **, producing prominent bulbar dysfunction and myelopathy"** Sawin,Menezes, 1997

Retroflexed odontoid – present in 96/364 Chiari pts Milhorat,1999

The normal Clivo-axial angle



Clivo-axial angle- surrogate measurement of basiilar invagination and cervico-medulllary deformity



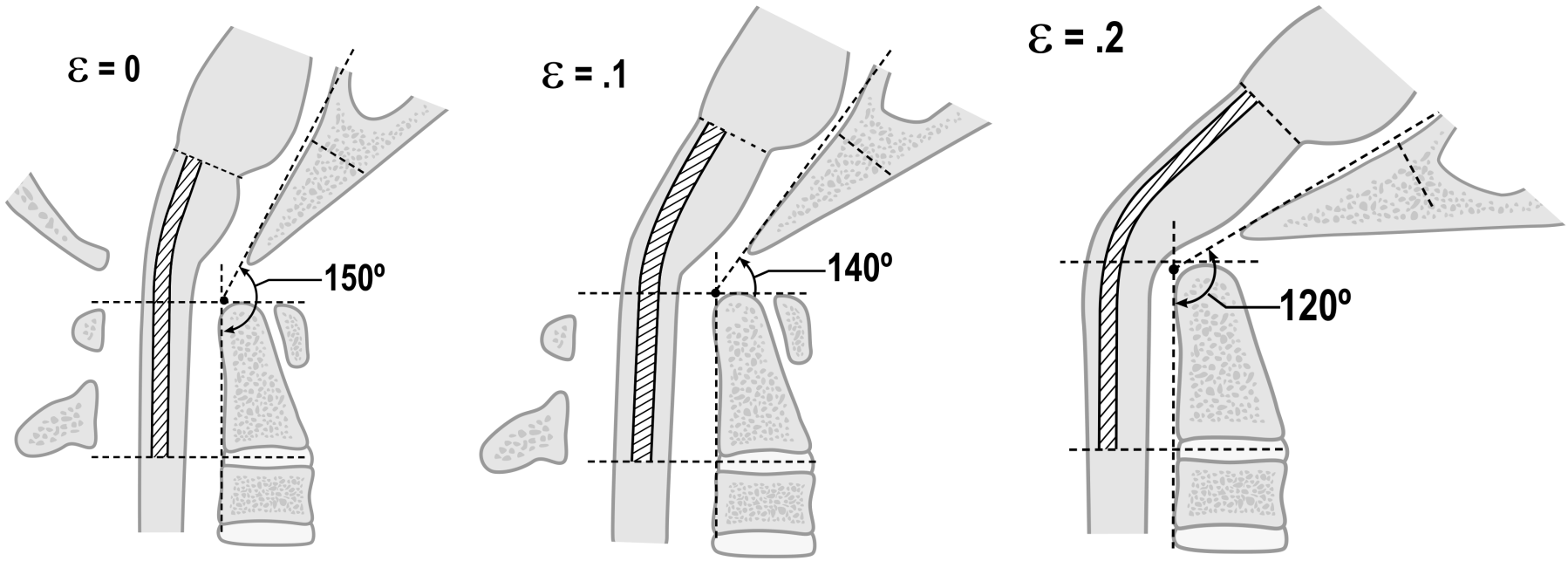
Chiari decompression failed if the CAA < 135º

Kim, Rekate, Klopfenstein, Sonntag 2004

Chiari decompression failed to improve syringomyelia if CAA < 135º KUbota 2004

•

kyphotic clivo-axial angle = deformative stress



Henderson et al, Surg Neurol Internat, 2010

The importance of the Kyphotic Clivo-axial angle

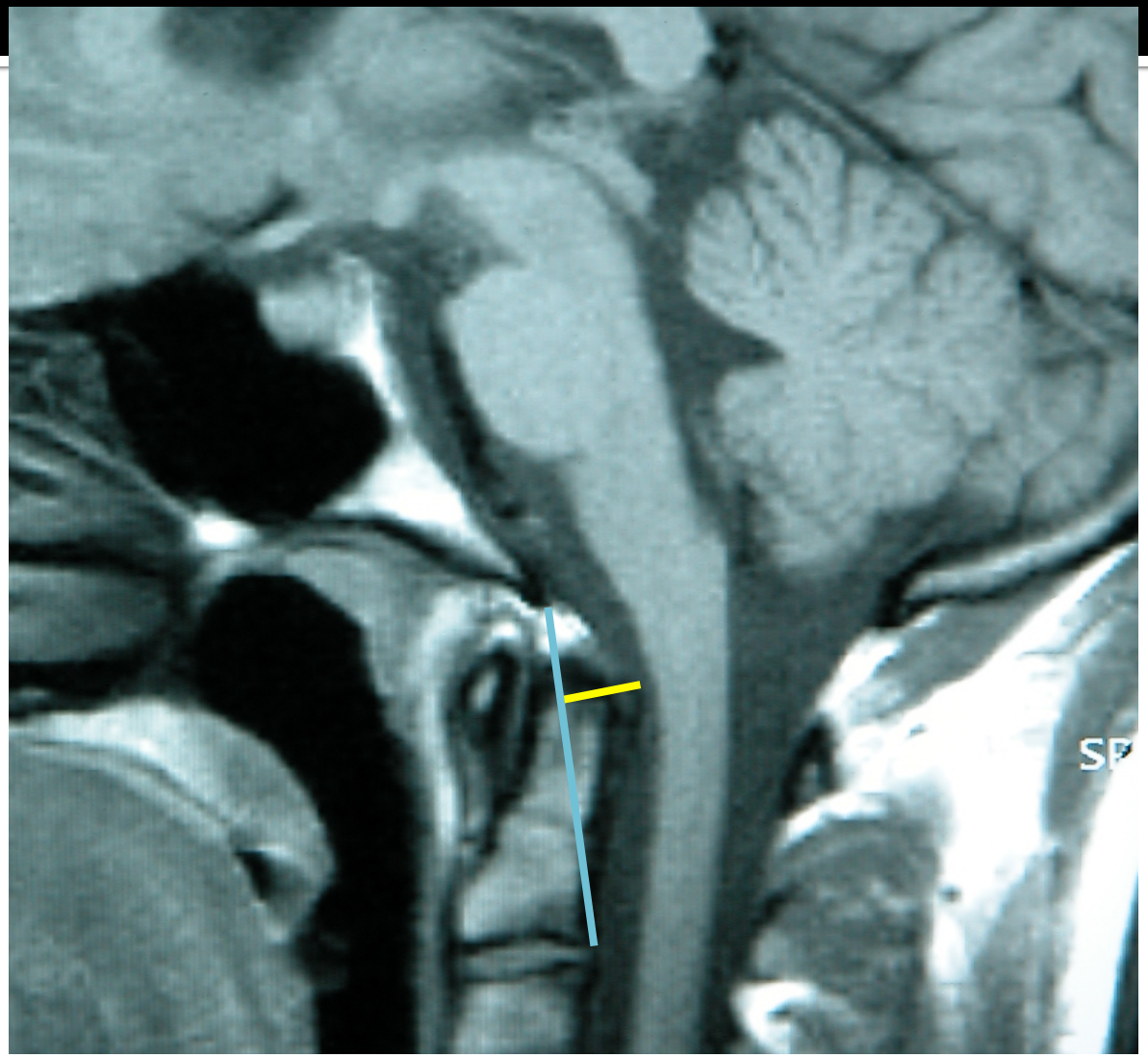
- List 1941
- Van Gilder 1985
- Menezes 1990
- Dickman 1990
- Henderson, Geddes, Crockard 1993
- Grabb, Mapstone and Oakes 1999
- Milhorat 1999
- Kubota 2004
- Goel 1998,2004 Platybasia , retroflexed odontoid and BI associated with medullary kink, alignment craniocervical junction
- Kim, Rekate,Klopfenstein, Sonntag 2004
- Botelho 2007 Traction reduction of Craniocervical kyphosis
- Henderson, Vacarro, Benzel 2004,2010

Ventral Brainstem Compression

B-pC2 Grabb-Oakes line

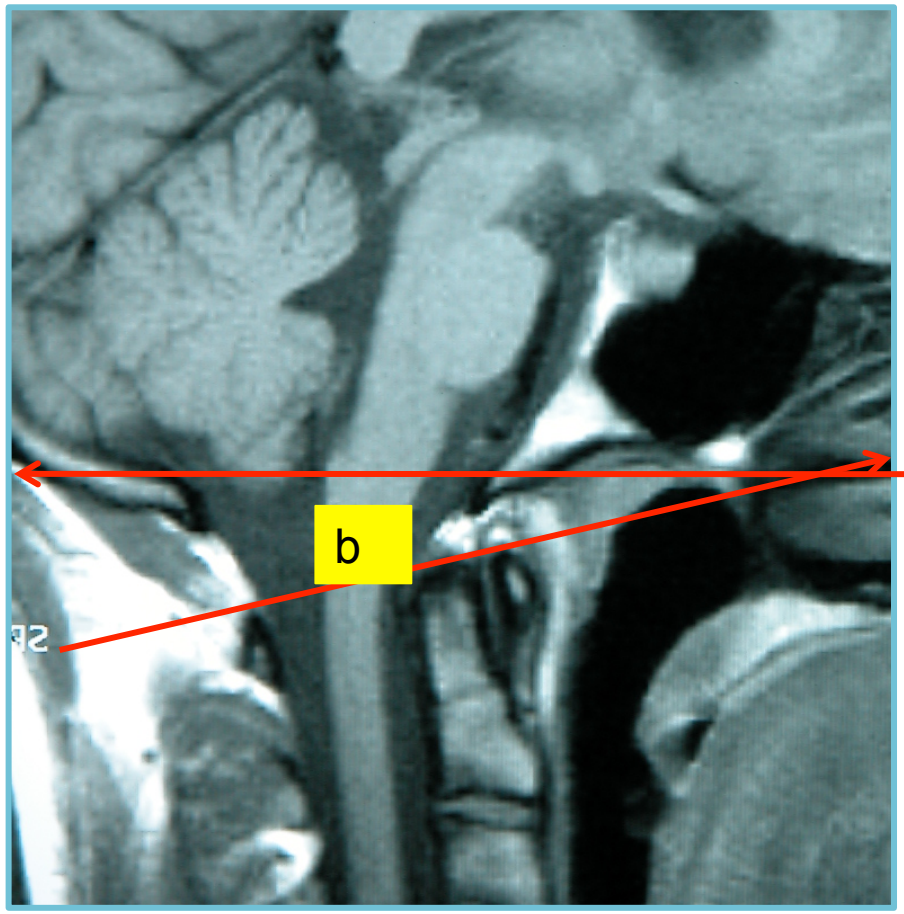
Grabb, Mapstone , Oakes
J NSGY 1999

> 9 mm



Indices of Craniovertebral instability: the palato-atlantal or Bull's Angle

- A line drawn along the hard palate, intersecting a line along the Atlas in the neutral position
  b >13° reflects basilar invagination
- But does not account for variability between flexion extension, nor recognize differential development of face and spine

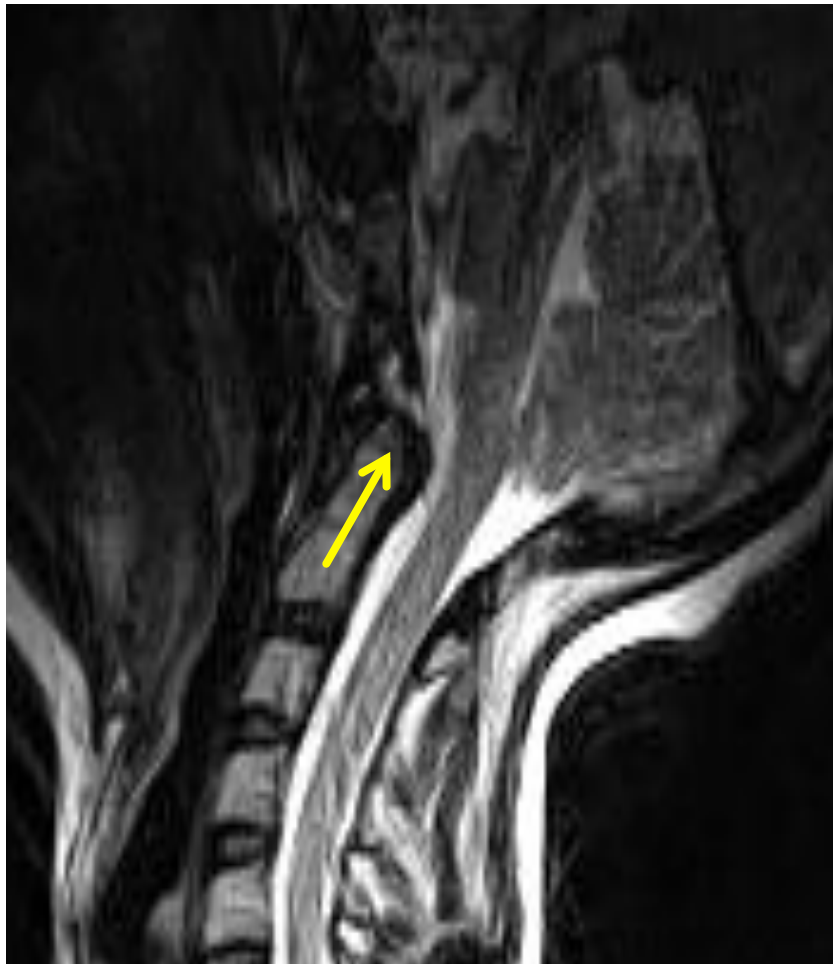


Bull, Nixon and Pratt, Brain 78: 229-247, 1955.The radiological criteria and familial occurrence of primary basilar invagination

Basion dens interval

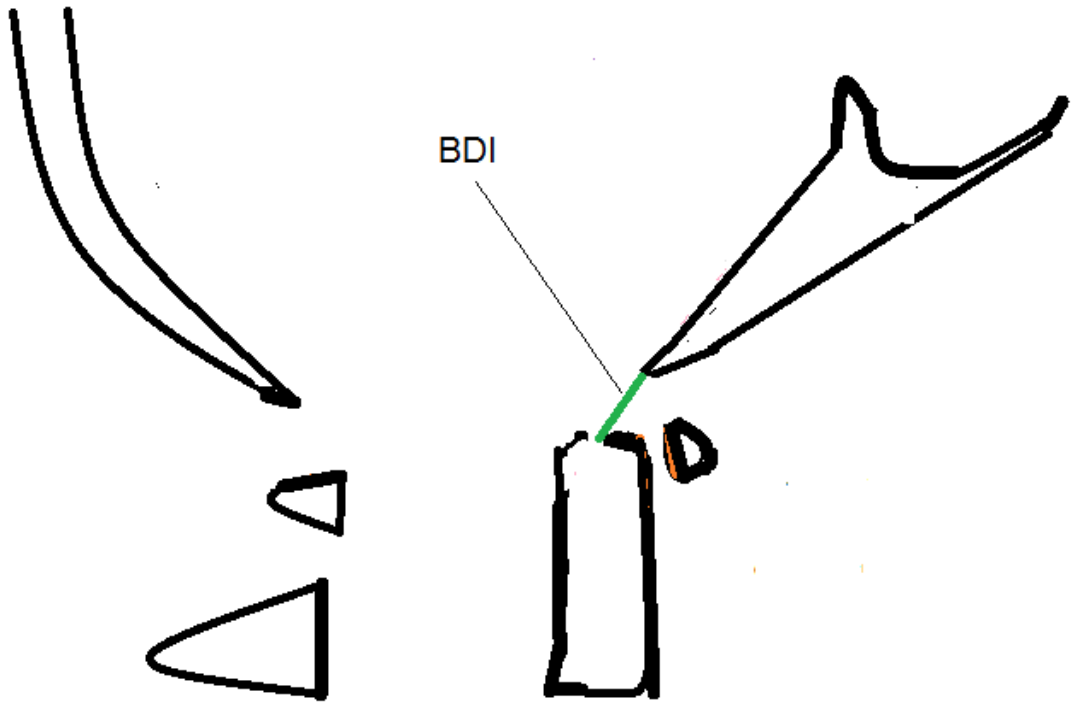
- 600 normal cervical spine x-rays
- basion to dens interval relatively constant

- The middle of the odontoid should lie directly beneath the basion, within 5 mm
- >10mm abnormal



Wholey JH, Bruwer AJ, Baker HLJ The Lateral roentgengram of the neck (with comments on the atlanto-odontoid basion relationship) Radiology 71:350-356, 1958

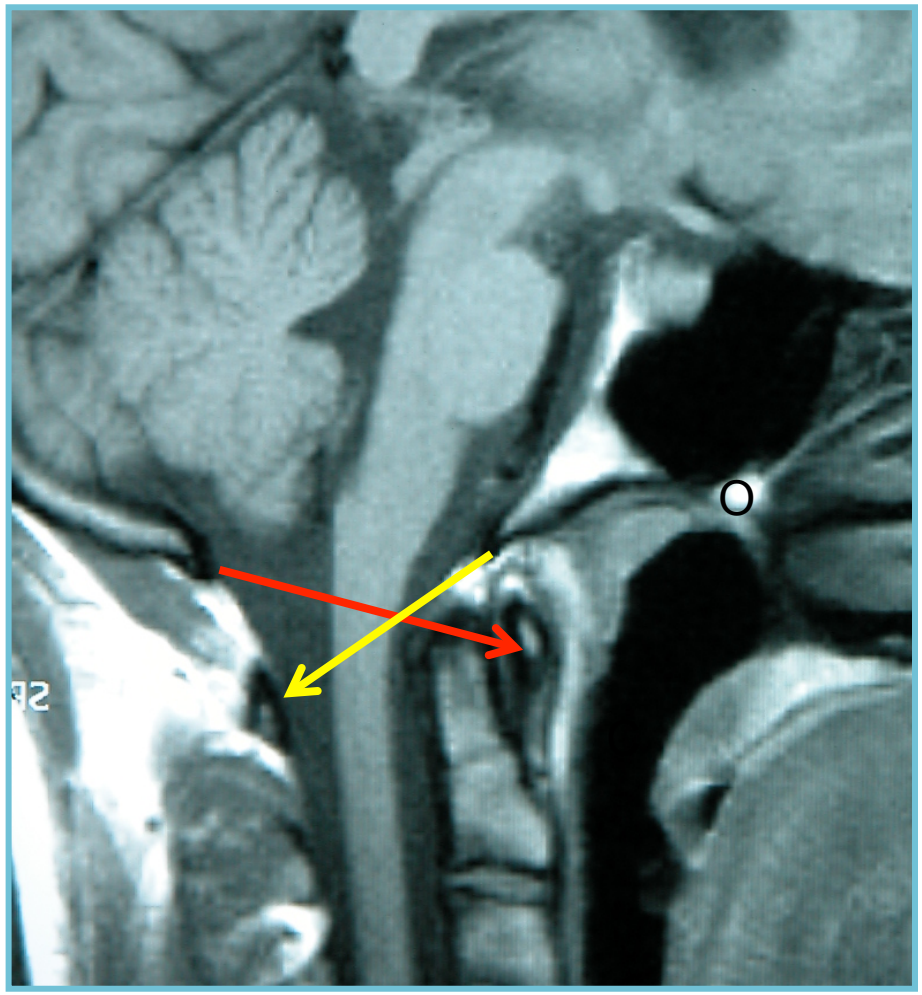
BDI > 10 mm is pathological



Indices of Craniovertebral instability: Power's Ratio

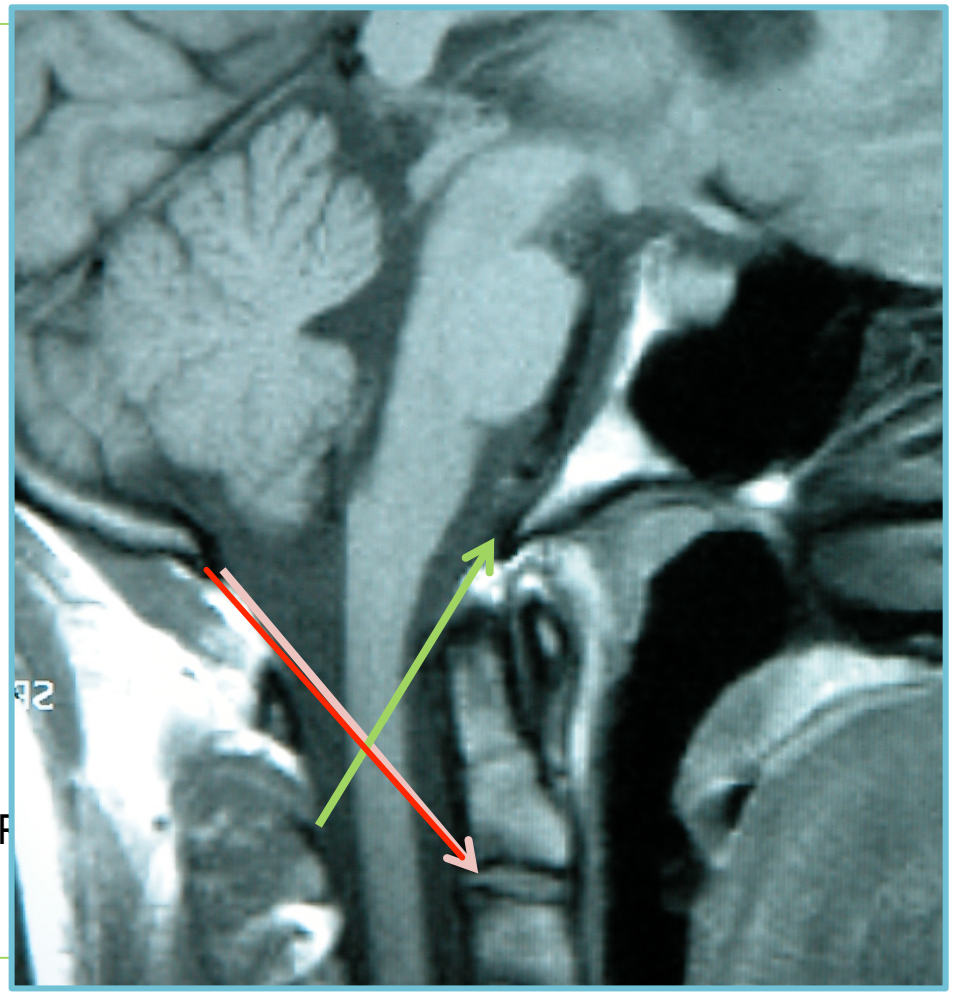
- basio to C1 posterior arch over Opisthion to C1 arch usually BC/OA = .77
- If >1, then occipito-cervical dislocation exists
- May be invalid with atlas fx or congenital anomaly
- Must identify the midpoint of posterior arch of C1

Powers B, Miller md,Kramer RS: Traumatic Anterior Atlanto-Occipital dislocation. Neurosurgery 4:12-17, 1979



Lee's X-lines

- Basion to midpoint spino-laminar line C2 should be tangential to odontoid
- Opisthion to post- inferior C2 should be tangential to C1
- Requires normal C1-C2 relationship

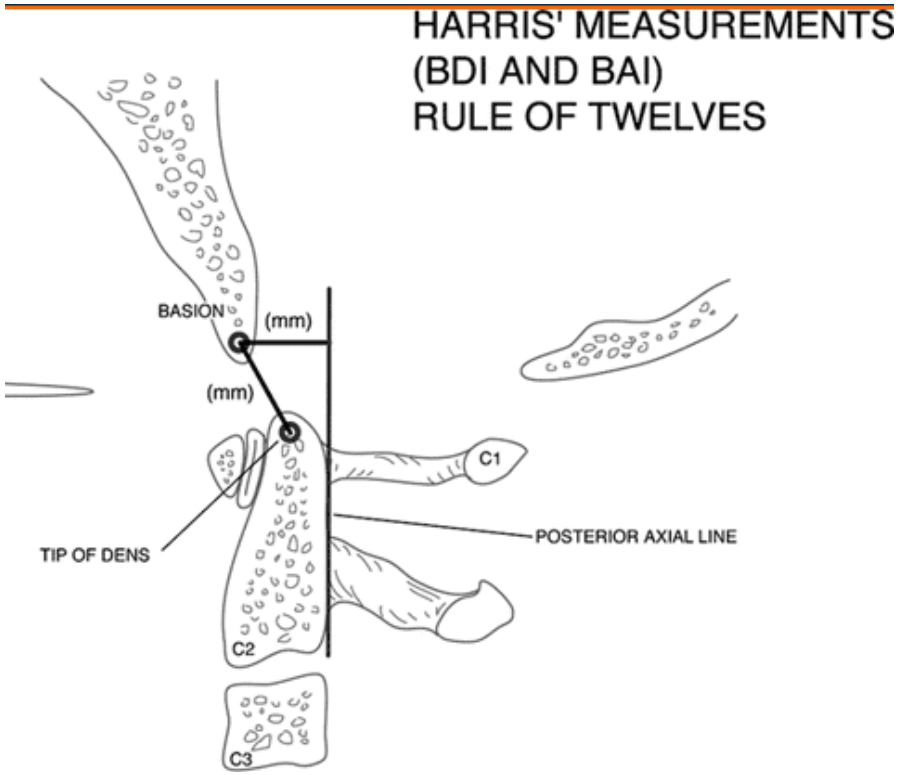


LeeC, Woodring JH, Goldstein SJ: Evaluation of traumatic atlantooccipital dislocations. AJNR 8:19-26

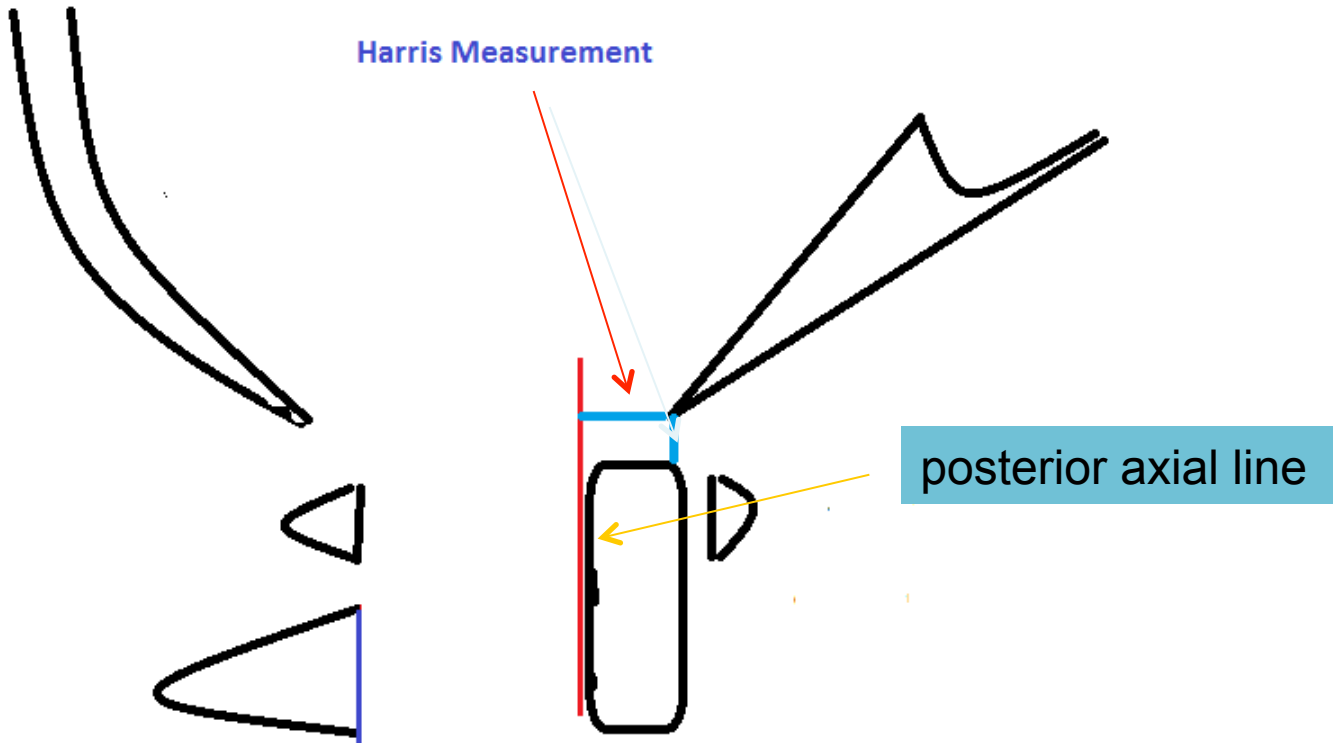
Harris Measurement

- Of 400 normal subjects, none had basion to PAL >12mm
- "In adults, the occipito-vertebral junction can be considered normal when both the basion axial interval and the basion dental interval are 12mm or less"

Harris JH, Carson GC, Wagner LK: Radiological diagnosis of traumatic Occipitovertebr4al Dissociation



Harris measurement >12 mm is pathological
This measurement should not change with flexion and extension



The Harris measurement uniquely measures translation between the basion and odontoid between flexion and extension

- flexion-extension is the only motion at the normal OA jt Fielding JW Cineroentgenography of the normal cervical spine J BJT Surgery 39A1280-1288

- There is no horizontal translation at the OA jt Werne S:Studies in spontaneous atlas dislocation Acta Orthoped ScandSuppl 23,1957

- "The normal range of horizontal translation in flexion/ extension is no more than1 mm . Movement >1mm is clinically significant . Treatment by posterior cranio-cervical fusion has proved successful

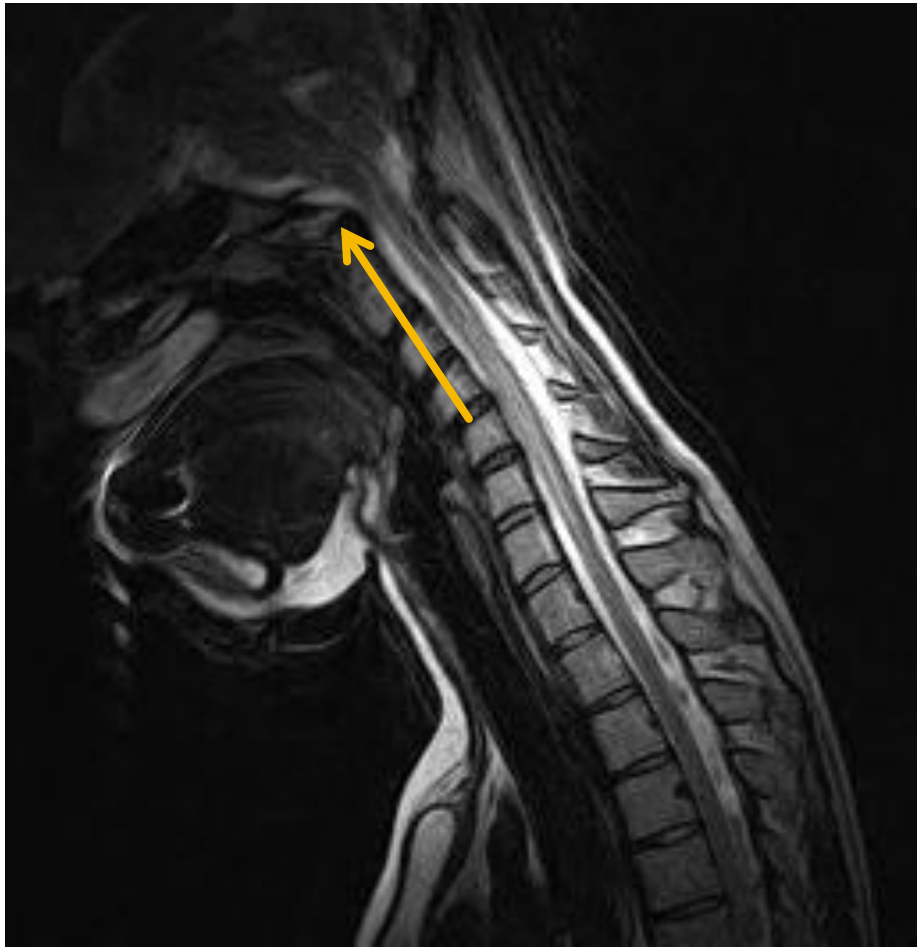
Weisel SW ,Rothman RH: Occipito atlantal Hypermobility .Spine 4:187-191, 1979

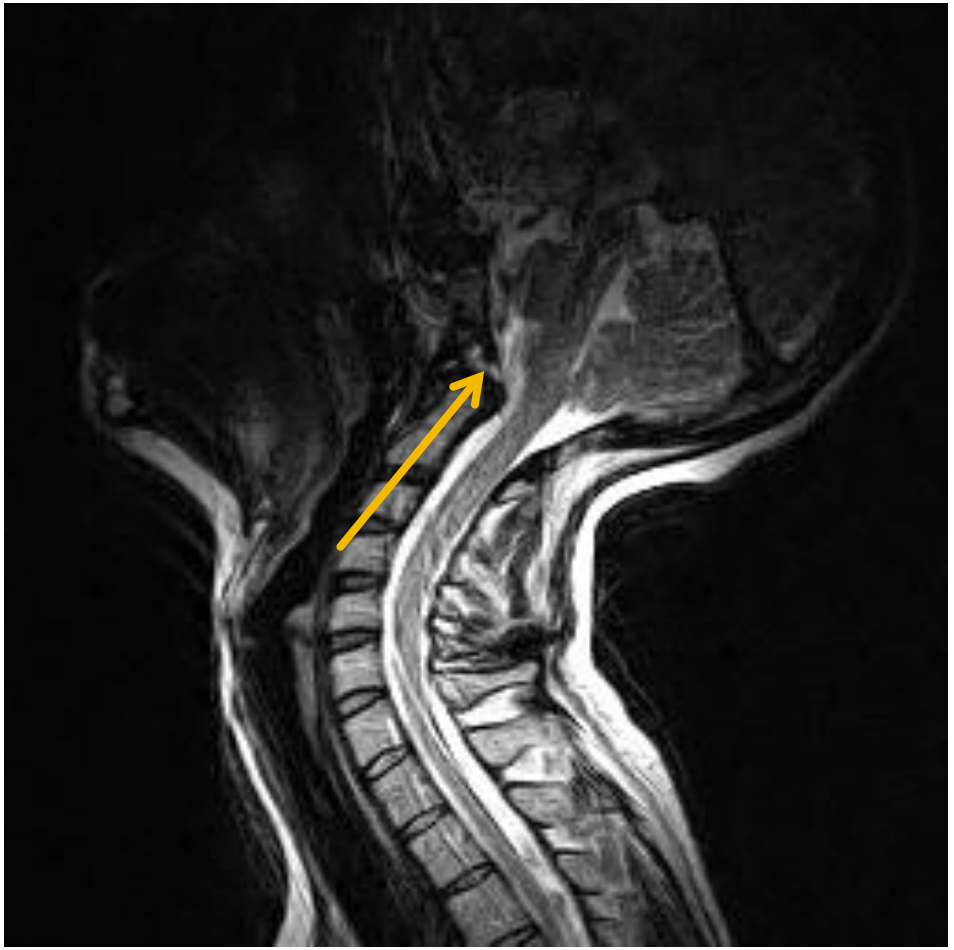
- ">more than 1 mm of translation in flexion /extension is an important and useful criterion. Symptoms of weakness of the limbs and occipital pain are additional indications of instability"

White AA, P unjabi MM Clinical Biomechanics of the Spine :p284-286 ,2ND Edition Lippincott1990

In the normal condition, the basion pivots over the mid odontoid

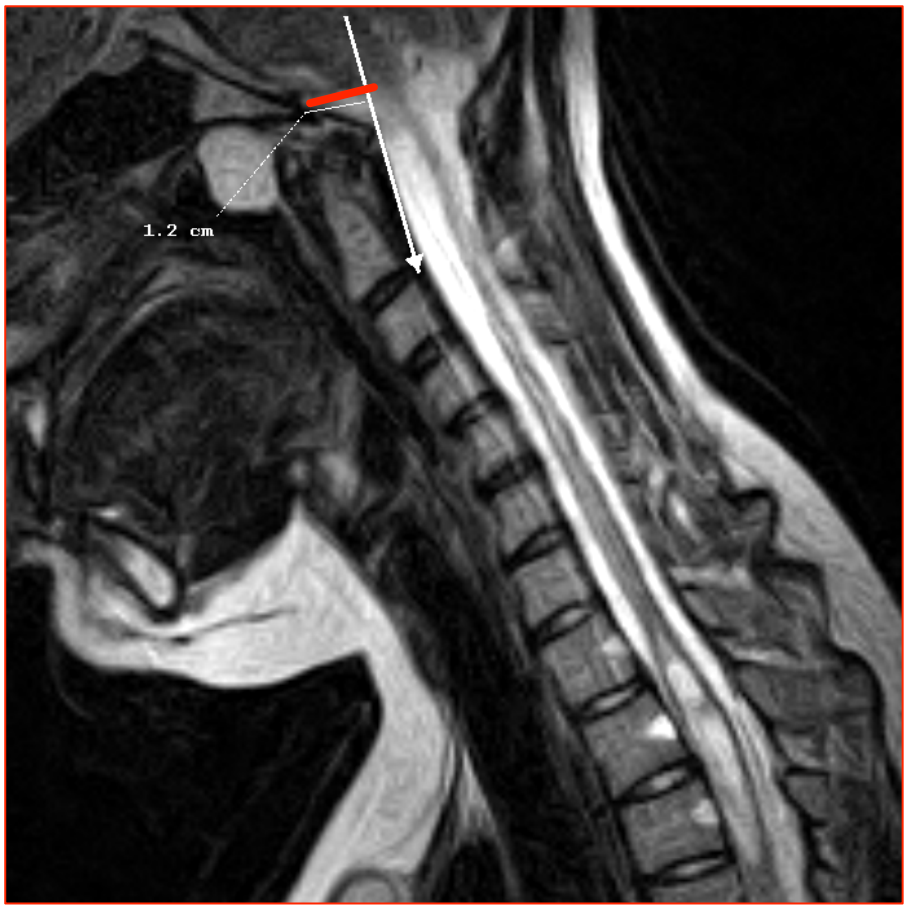
translational movement is < 1 mm



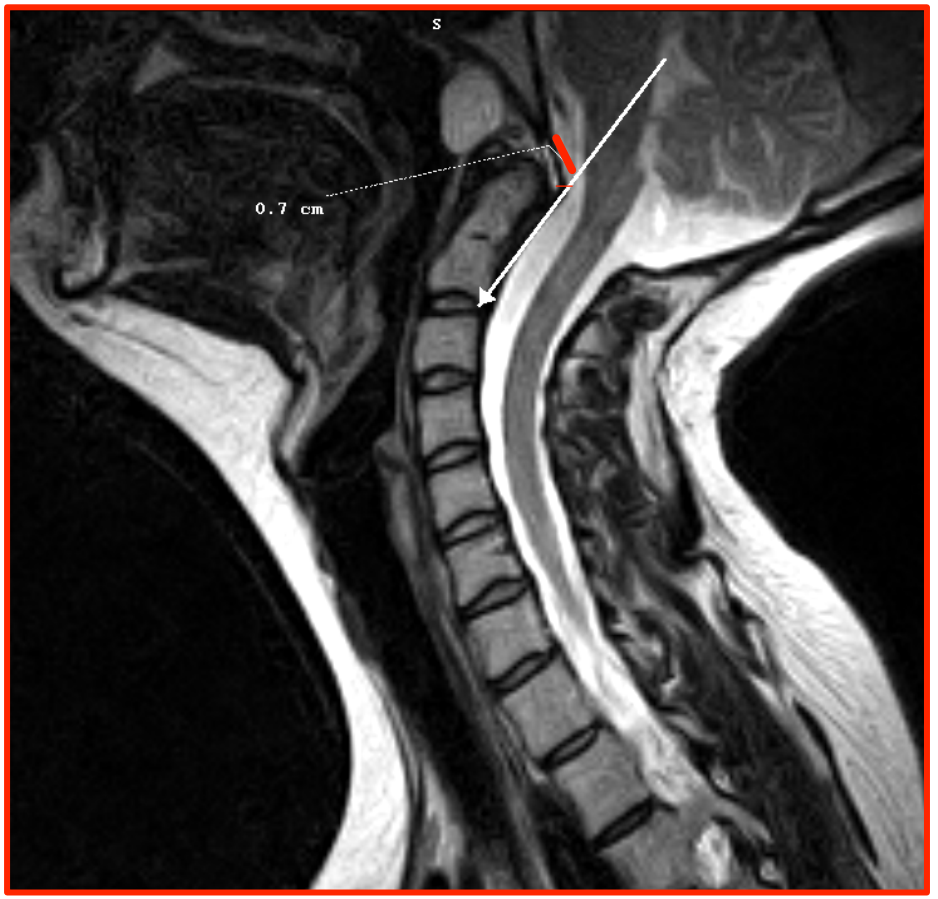


Weisel, Rothman, 1979; White and Punjabi 1980; Menezes, 1990

Pathological occipito-atlantal translation



Harris measurement = 12mm



Harris measurement = 7mm

Many patients with Chiari Malformation have Underlying Cranio-cervical Hypermobility

- At least 12% of Chiari population have EDS Milhorat et al, J Neurosurg Spine 7:601–609, 2007
  - JHS and hypermobility type of EDS are phenotypically indifferentiable
    Grahame 2008
  - Diagnosed by Brighton Criteria
    Leone 2009
  - Hypermobility Syndrome affects 1 % of the population
    Grahame, 2008

biomechanics and cell biochemistry are closely coupled

Mechanical stresses

- modulate gene expression and biochemical composition of the living system at the molecular level
- alter neuronal conduction
- Alter the histology
- Are expressed clinically

Study Paradigm

- prospectively study to compare clinical metrics with neurological deficits in patients with cervico-medullary disorders
- IRB approved
- N =7

Primary outcome measures

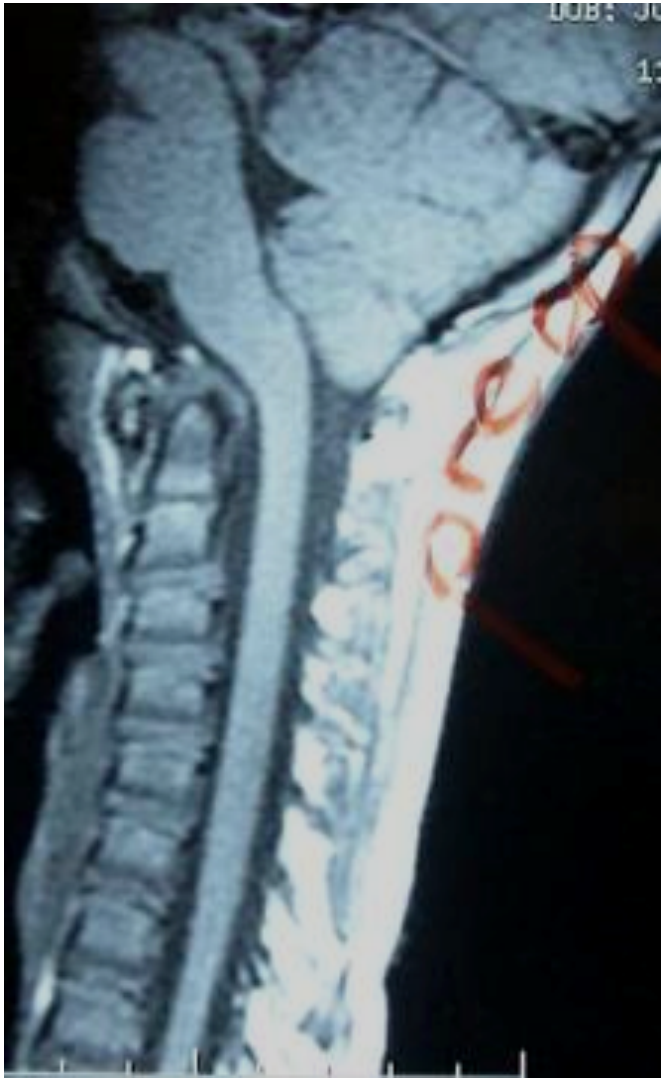
- Neurological assessment
- Sensory motor : ASIA
- Pain : Visual Analog Scale
- Quality of life : SF36
- Function: Karnofsky Index
- Bulbar Dysfunction : Brainstem Disability Index
- FEA computations
- MRI: Clivo axial angle
  b-pC2 (Grabb-Oakes) measurement

Illustrative Case of Complex Chiari

Cervico- medullary syndrome

Chiari, kyphotic clivo-axial angle, ventral brainstem compression

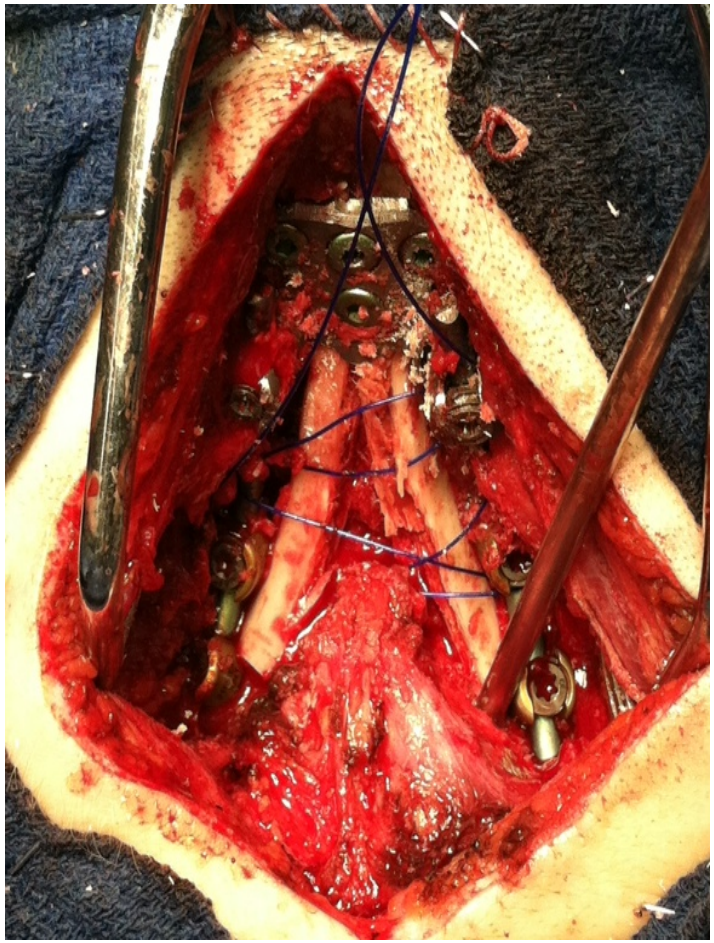
- s/p repeated cardio-respiratory arrests postural orthostatic tachycardia, decreased memory, visual and auditory changes, dysphagia, dizziness, gait change, weakness and sensory loss, bowel and bladder changes
- Babinski, spastic quadriparesis, diffuse sensory deficits
- Clivo-axial angle 115°



Indications for Craniocervical fusion

- Neurological compression and instability at the occiput – C1
- Myelopathy, brainstem dysfunction, lower cranial nerve dysfunction, vertebro-basilar insufficiency
- Neurological deficits = urgent need for decompression and stabilization

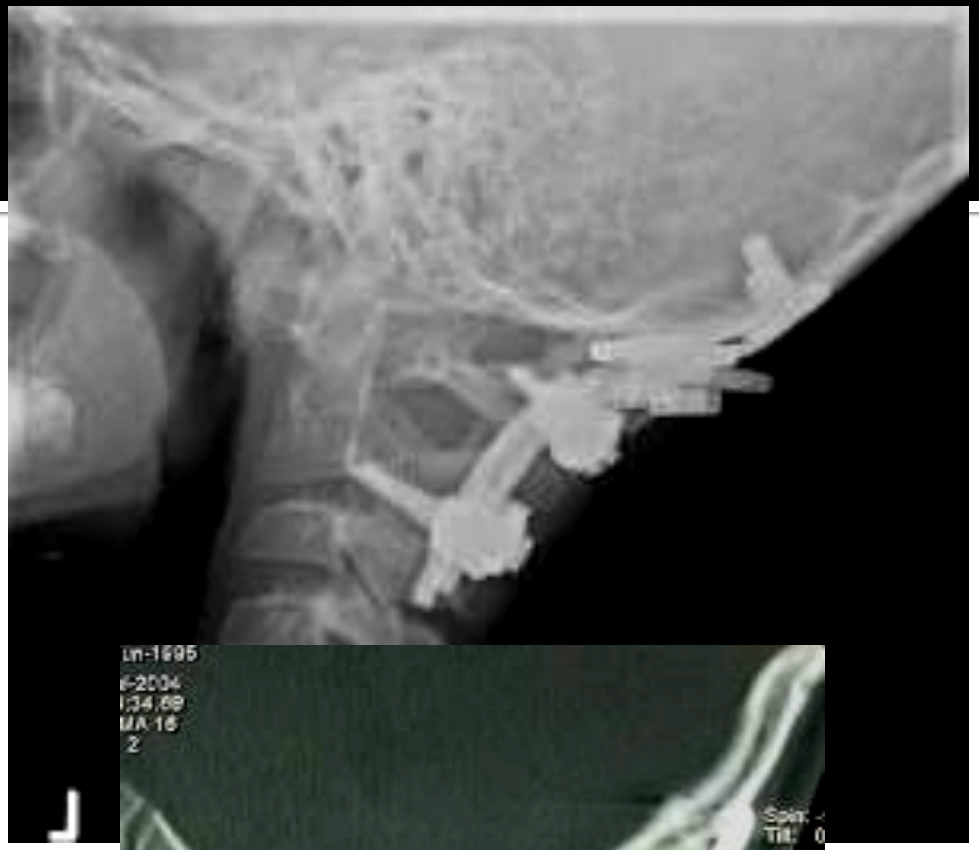
Dickman, Douglas ,Sonntag, BNI Quarterly, 1990

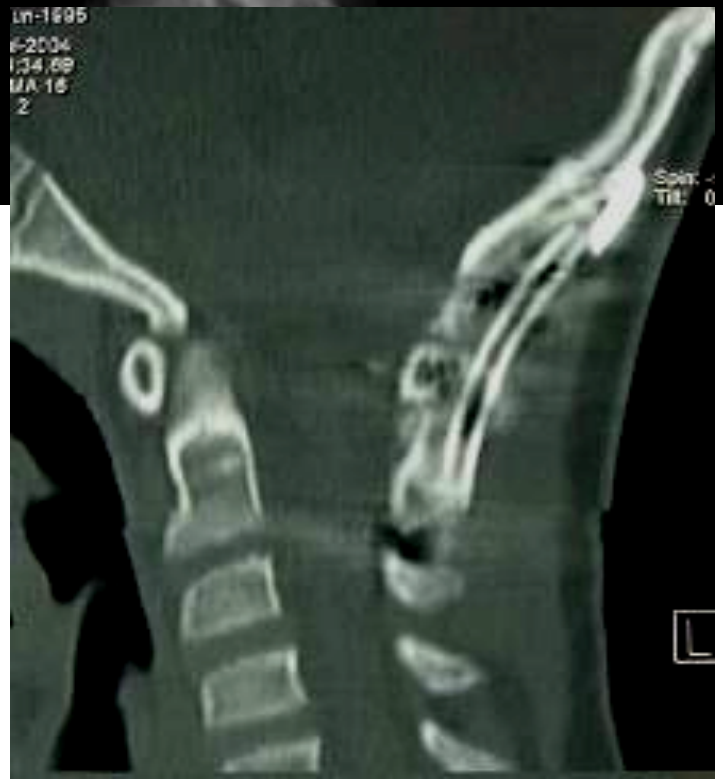


Post-op

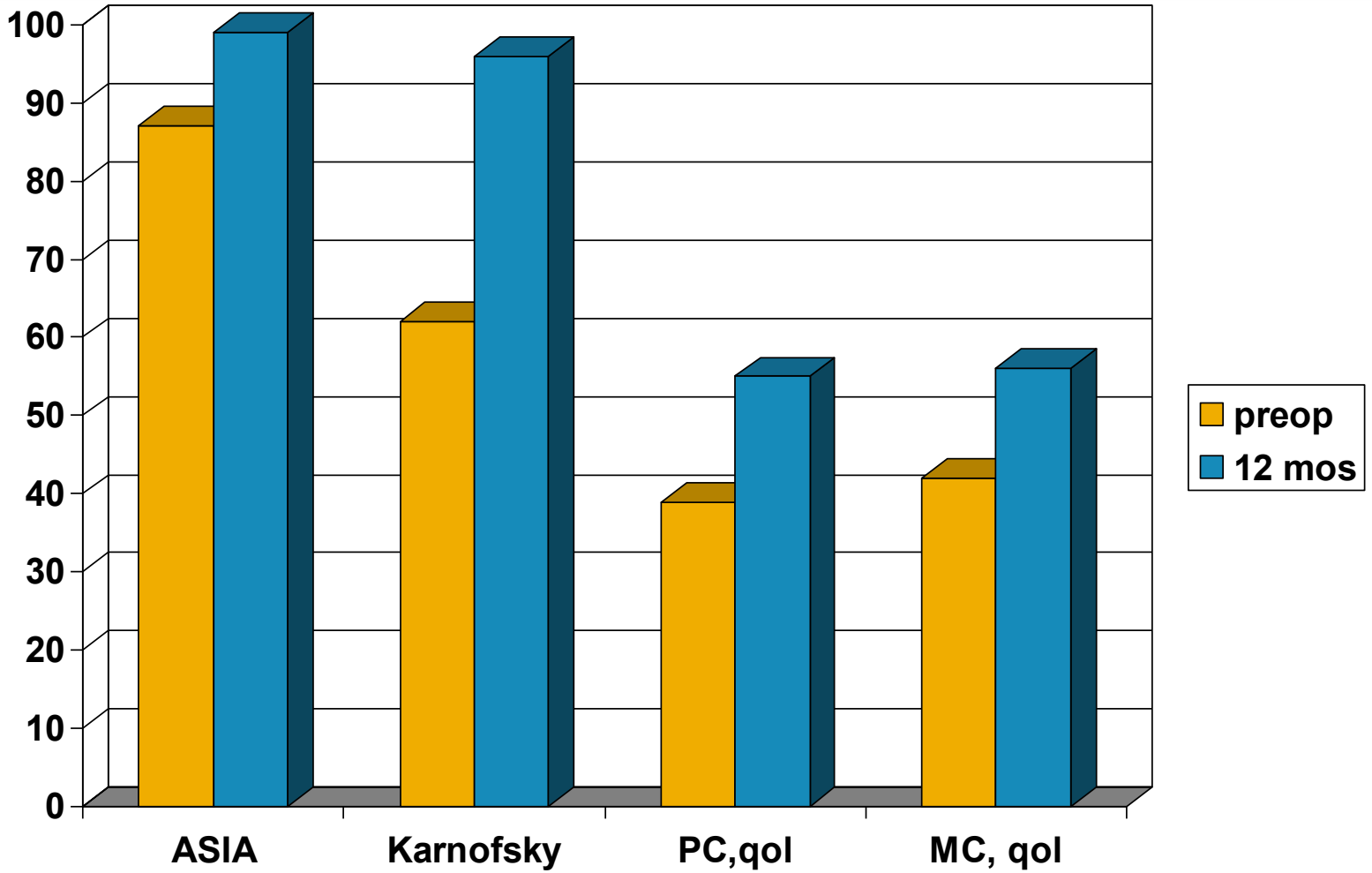
- Clivo-axial angle 145°
- No brainstem symptoms
- Karnofsky index 50 to 100
- Pain level from 4/10 to 1/10
- No breathing problems

- Pt is playing sports, achieving A levels,
- Pilots licence
- accepted to MIT





ASIA, Karnofsky, Quality of Life



Significance n=7

- Pain p .027
- ASIA p .042
- Brainstem Disability p .027
- Karnofsky p .027
- SF 36 Physical component p .026
  Mental component p .12

Wilcoxon signed-ranks test

Surg Neurol Int. 2010; 1: 30.

Published online 2010 July 16. doi: 10.4103/2152-7806.66461.

PMCID: PMC2940090

Deformative stress associated with an abnormal clivo-axial angle: A finite element analysis

Fraser C. Henderson, William A. Wilson,[1] Stephen Mott,[2] Alexander Mark,[3] Kristi Schmidt,[4] Joel K. Berry,[5] Alexander Vaccaro,[6] and Edward Benzel[7]

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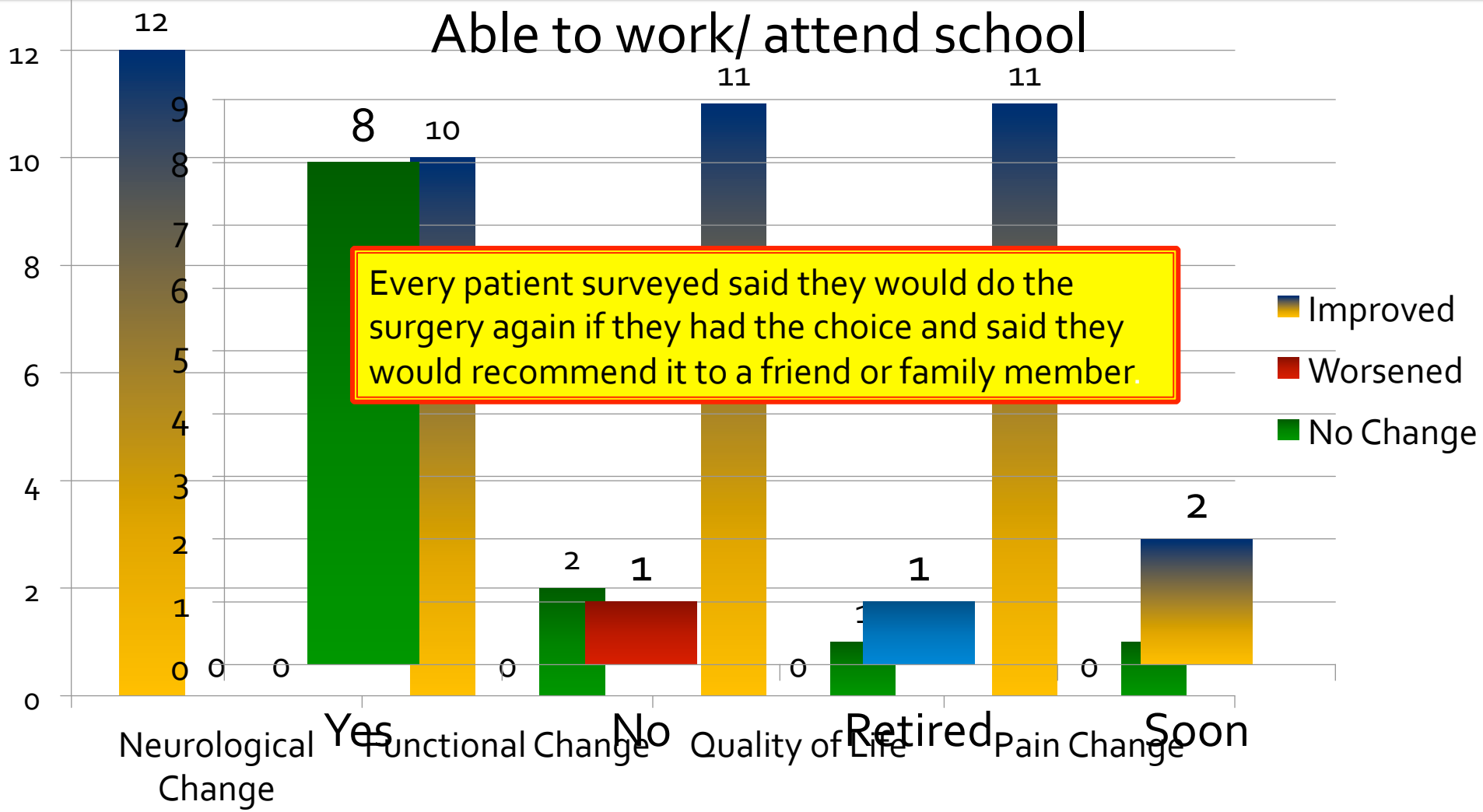
Able to work/ attend school
Every patient surveyed said they would do the surgery again if they had the choice and said they would recommend it to a friend or family member.
Improved
Worsened
No Change
Neurological Change
Functional Change
Quality of Life
Pain Change
Yes
No
Retired
Soon

Conclusions

- Within the population diagnosed with Chiari malformation, there is a subset of patients with "Complex Chiari "
- The designation of Complex Chiari resides in the presence of additional anatomic or dynamic deformative stresses, which may be signaled by:
  - clivo-axial angle <135 ◦
  - Grabb-Oakes >9 mm
  - Harris > 12mm, or translation > 2mm on flexion extension
  - Wholey's BDI > 10mm
  - Bull's palato-atlantal angle > 13◦
  - Transgression of Lee's X lines
- substantial clinical and neurobiological evidence links deformative stress of brainstem and spinal cord to the observed neurophysiological changes
- Complex Chiari should be watched for, and prompt consideration for additional evaluation with dynamic imaging

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- Jessica Adcock MSc,Metropolitan Neurosurgery Grp