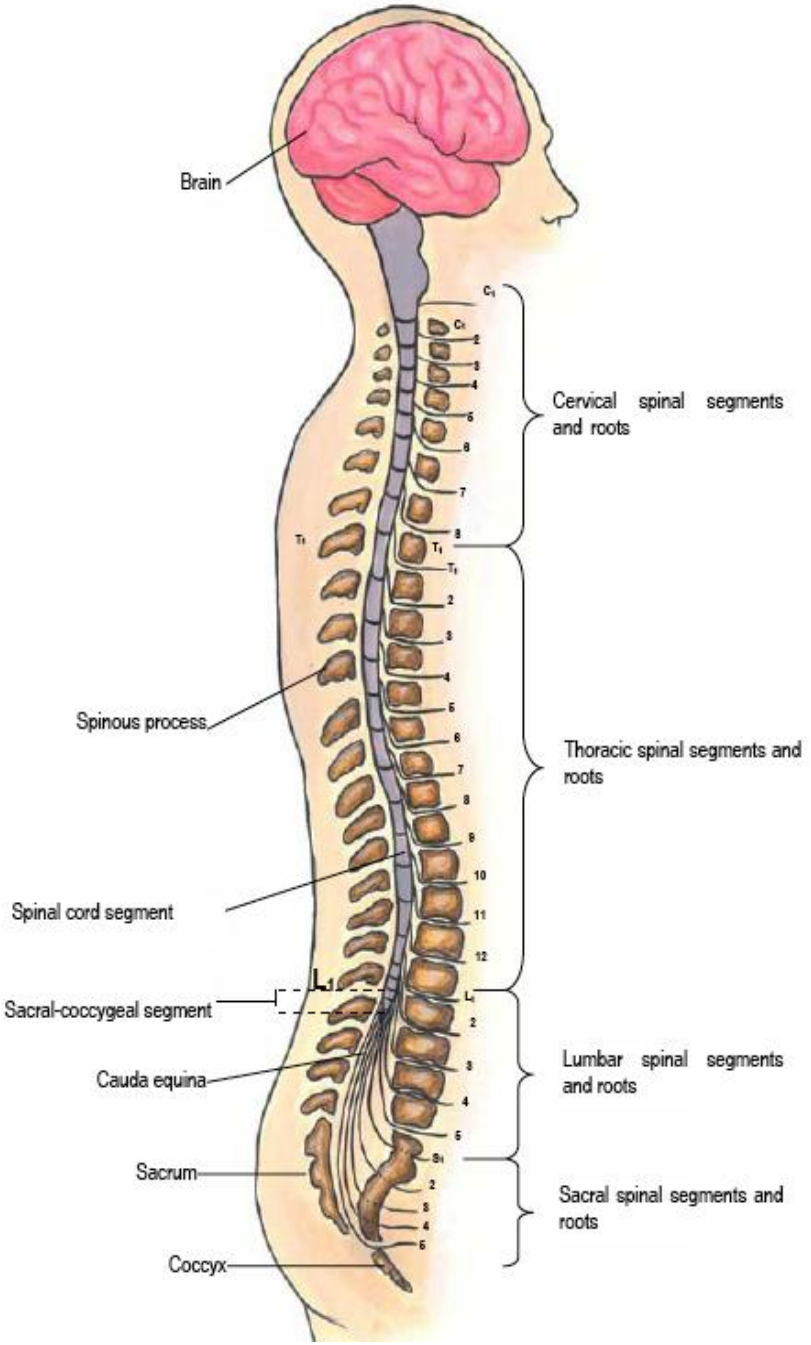
Spinal Repair

Rick Acland

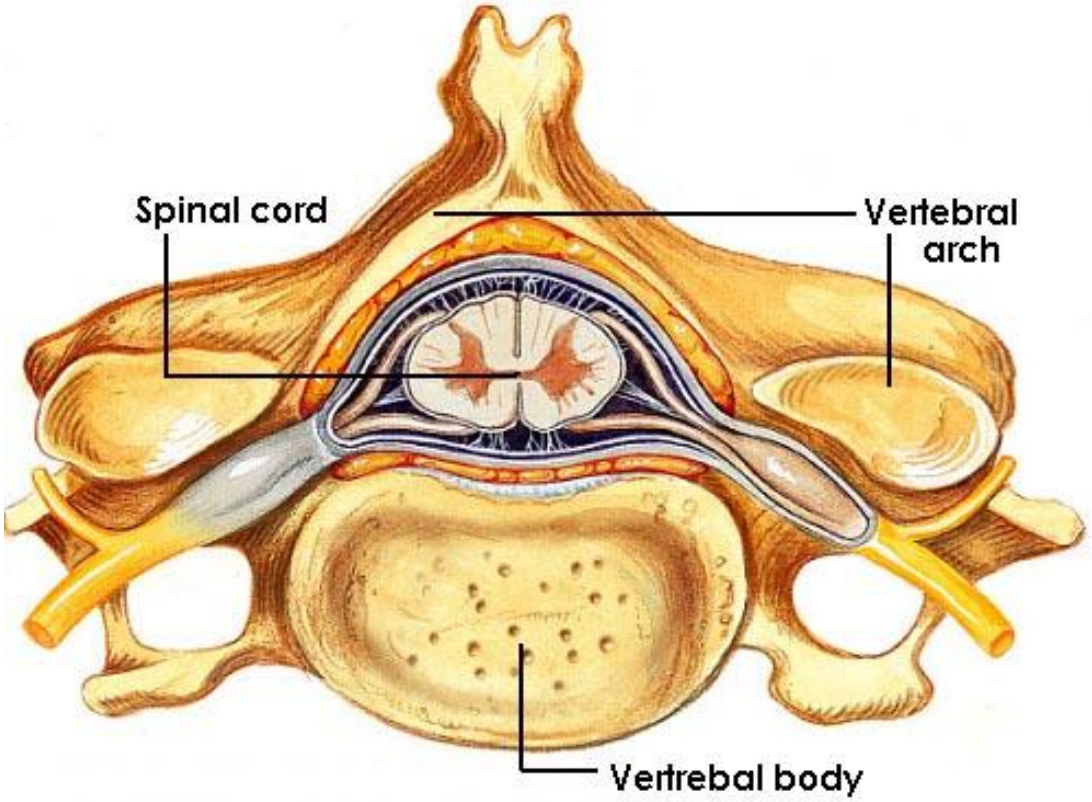
‘REPAIR’

- Spinal function
- Spinal first aid/protection
- Spinal advice
- Spinal manoeuvres
- Spinal radiology
- Spinal degeneration
- Spinal pain
- Spinal units
- Spinal implants
- Spinal stem cells


Brain
Spinous process
Spinal cord segment
Sacral-coccygeal segment
Cauda equina
Sacrum
Coccyx
Cervical spinal segments and roots
Thoracic spinal segments and roots
Lumbar spinal segments and roots
Sacral spinal segments and roots

Spinal Column

- Protects the spinal cord



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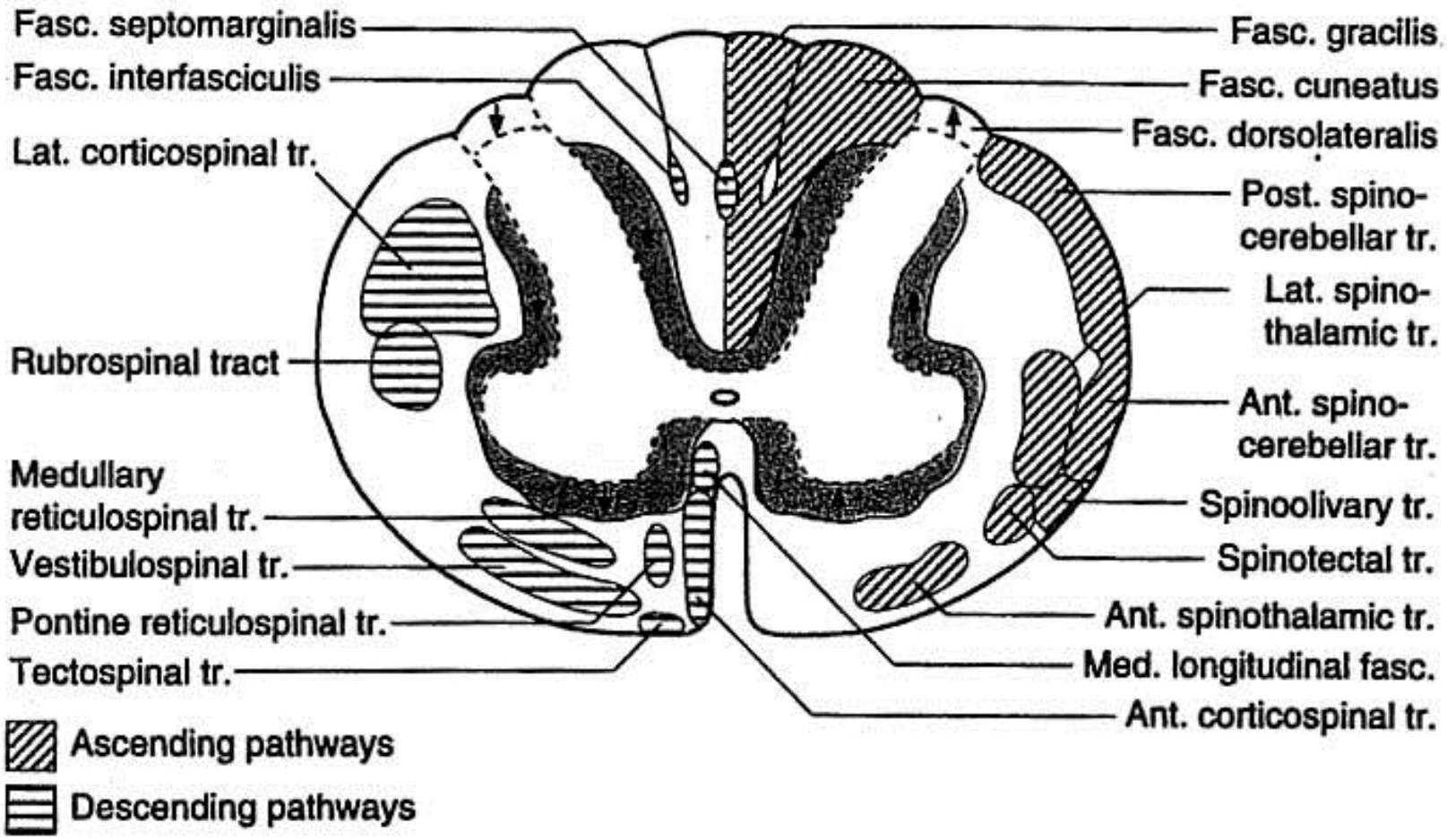
ST. JUDE MEDICAL
MORE CONTROL. LESS RISK.
OBEX


Fasc. septomarginalis
Fasc. interfasciculis
Lat. corticospinal tr.
Rubrospinal tract
Medullary reticulospinal tr.
Vestibulospinal tr.
Pontine reticulospinal tr.
Tectospinal tr.
Fasc. gracilis
Fasc. cuneatus
Fasc. dorsolateralis
Post. spino-cerebellar tr.
Lat. spino-thalamic tr.
Ant. spino-cerebellar tr.
Spinoolivary tr.
Spinotectal tr.
Ant. spinothalamic tr.
Med. longitudinal fasc.
Ant. corticospinal tr.
Ascending pathways
Descending pathways

SPINAL CORD SIGNALLING

- Dermatome dogma
- The Reflex Arc
- Upper and lower motor neuron deficit disorders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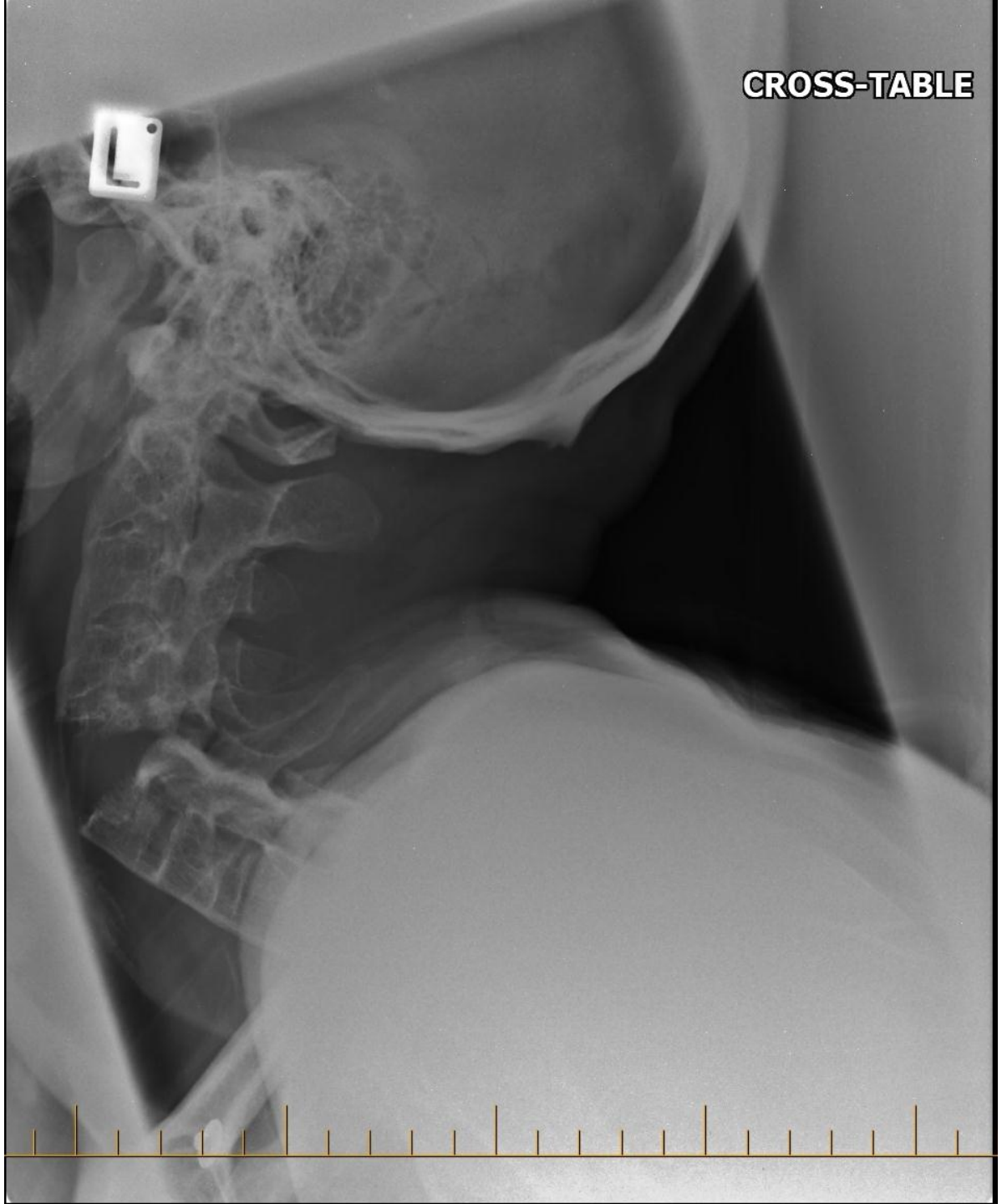

CROSS-TABLE


S
I

FIRST AID
IN
SPINAL CORD INJURY

RECOVERY

‘Complete’: 2% walk

Pin prick preserved: 80% walk

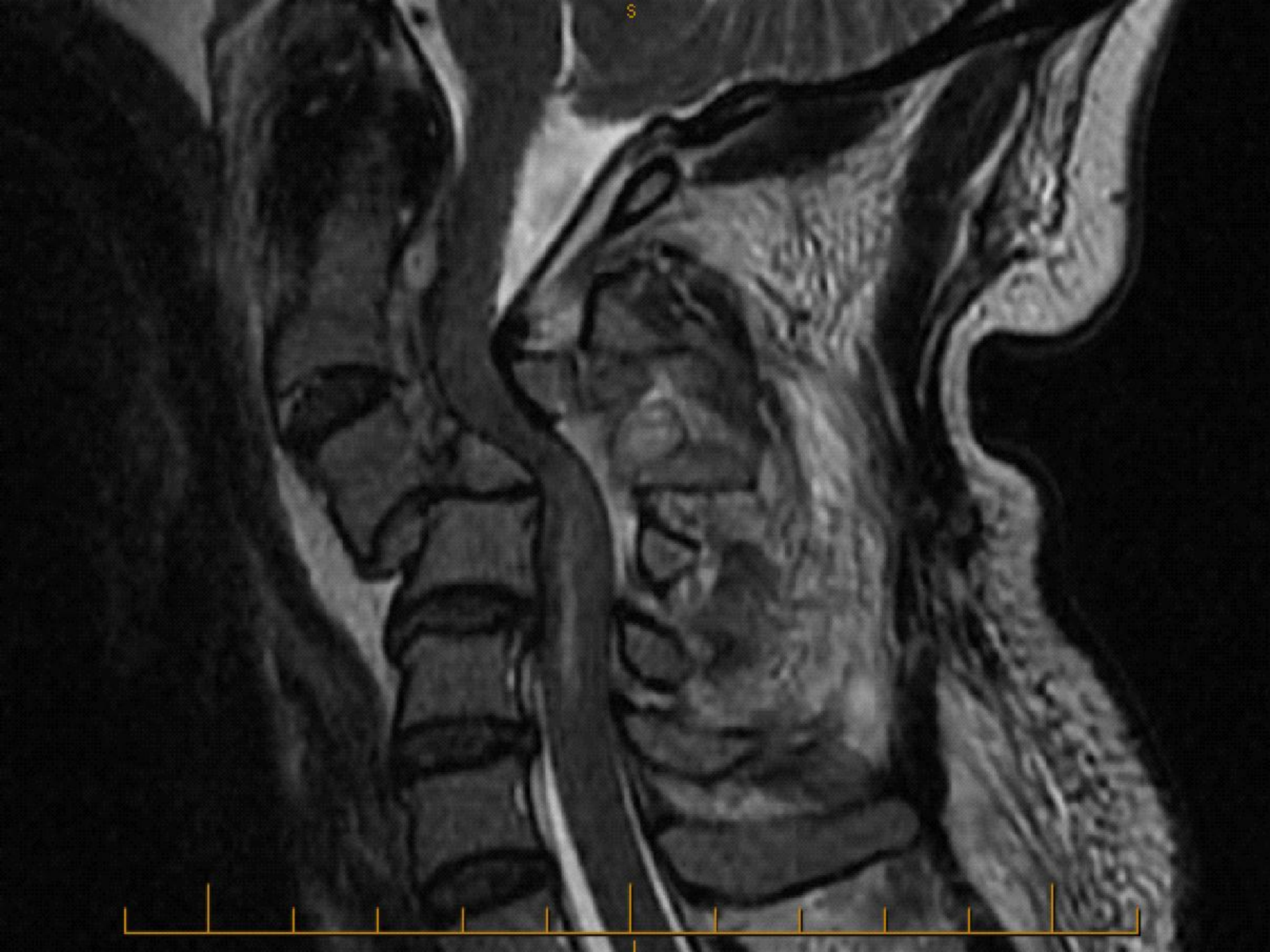
Light touch preserved: 20% walk

WHY DO WE NEED SPINAL UNITS?

CORD DYSFUNCTION ISSUES

- MOTOR
- SENSORY
- RESPIRATORY
- CARDIOVASCULAR
- BLADDER
- BOWEL
- SKIN
- SEXUAL FUNCTION/FERTILITY
- PSYCHOSOCIAL


PRESSURE SORE


S


BEDSIDE
Intra-op

BRAIN EXPLOSION

Are horrific sporting injuries sheer, rotten bad luck or accidents waiting to happen? **Mark Reason** investigates.

THE WALLABIES last night wore black armbands in memory of Dalley Appleby, the 21-year-old who died from brain and spinal injuries suffered in a tackle last weekend. Any death from sporting injury is a tragic waste of life, but was this just "sheer, rotten bad luck", as articulated by a Queensland spokesman, or was it a tragic accident waiting to happen?

Last term at Christchurch Boys' High School, one of the most famous rugby academies in New Zealand, the under-14 boys suffered seven broken arms, five concussions and a broken leg. Such a spate of injuries is clearly more than just sheer, rotten bad luck.

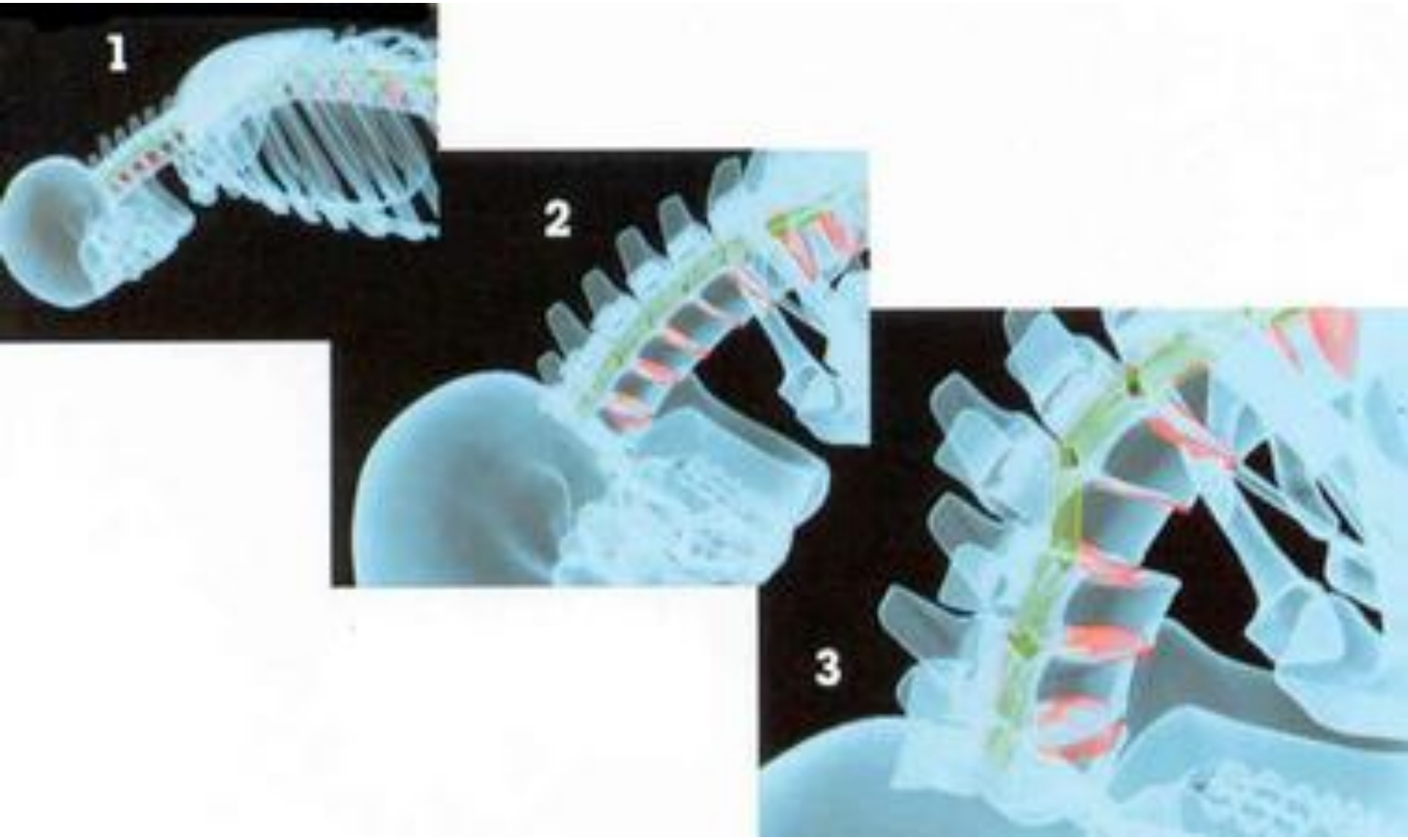
At the time I remarked to the school's director of rugby that in 20 years from now there would be more New Zealand kids playing football than rugby. "Make that 10," he replied.

According to research done by Ken Quarrie, the NZRU's senior scientist for injury prevention and performance, the amount of tackles per game has risen by more than 50% in the previous 40 years. At the same time the average weight of the All Blacks has increased by 10kg. In other words, there are vastly more tackles with a far greater level of impact.

THE BIG question is how do we manage risk so that we can keep it at a level that parents find acceptable? Graham Henry, who talked to me before Appleby's tragic accident, says: "Going forward there needs to be research on how we can decrease the physicality of the game. There's more and more guys getting injured, we need to know why."

> Tackling at the hip and below might be a very good solution. It is a good thing


6
8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Is it an injury?

‘The Degenerative Spine’

Diagnostic Imaging for LBP

What are the indications?

‘Ordering an image may be viewed as more expedient than explaining to a patient why imaging is not necessary’

LUMBAR XRAYS

- Clinically unsuspected findings occur in 1 of every 2500 patients, 20-50 yrs of age.
- Affect management in only 1 or 2%
- Average radiation exposure is 75 times higher than for CXR
- More pain and worse overall health status than those not having XRays
- In USA, 40% of family practitioners and 13% of physicians reported ordering LXRs for acute back pain

DIAGNOSTIC IMAGING FOR LOW BACK PAIN.

RISK FACTOR ASSESSMENT:

- ? cancer
- ? spinal infection
- Evidence of cauda equina or progressive neurological deficit
- Failed trial of therapy

Advanced Spinal Imaging

- Alarming rise in use of CT and MRI's
- In USA, more than 30% of physicians order MRI's for uncomplicated acute low back pain if a patient insisted on it, even if clinically unnecessary
- High radiation exposure with CT's leads to higher incidence of cancer
- Should be reserved for situations in which findings are more likely to affect clinical decision making: major trauma, severe neurological compromise or infection

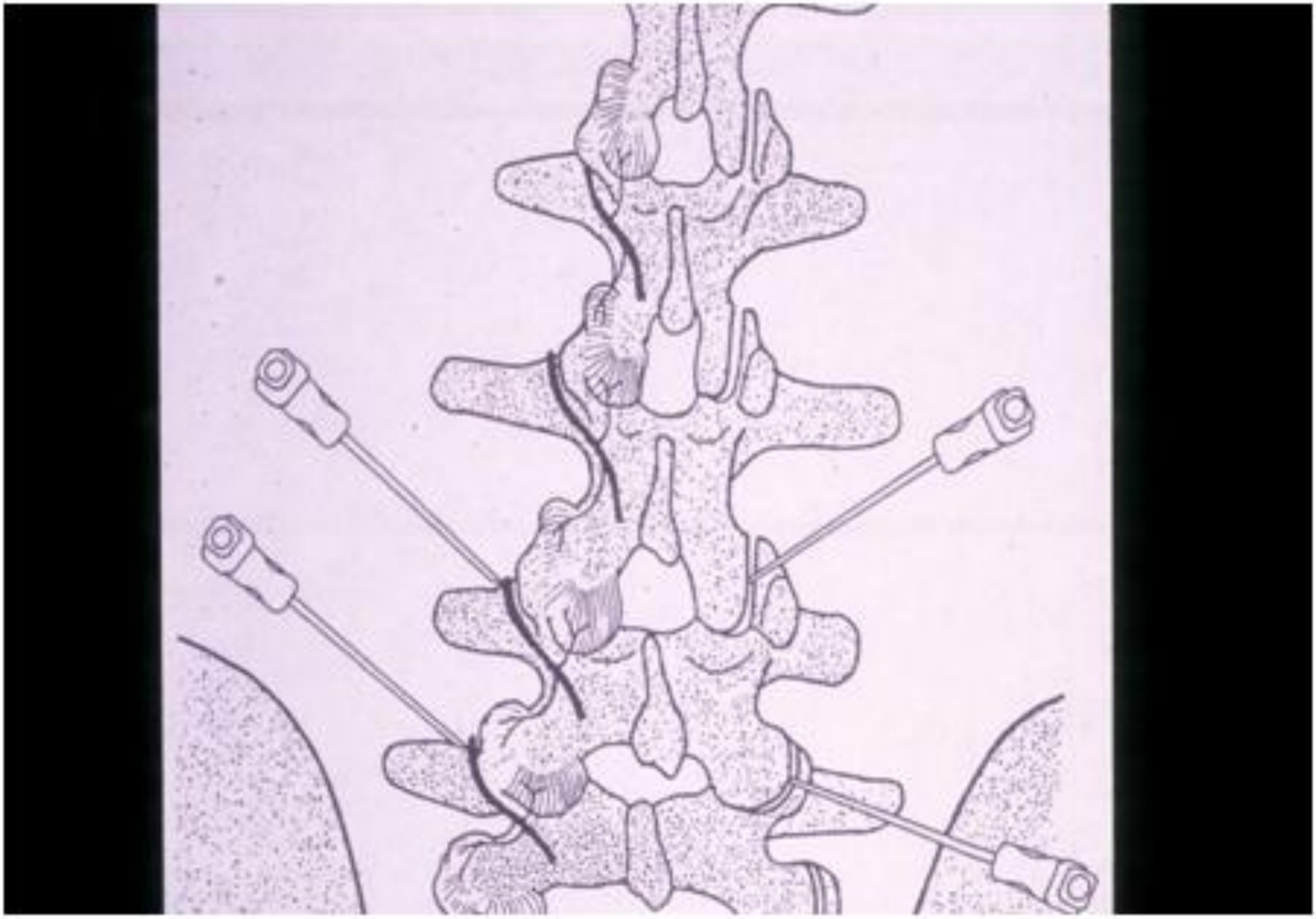
Who owns the spine?!


H.R.OWEN
TRADITION OF EXCELLENCE
CUSTOMER
PARKING ONLY
UNAUTHORISED VEHICLES
WILL BE CLAMPED
H.R.OWEN


IMPERIAL
WAR MUSEUM
HEN·VIII·REGE·FVNDATVM·CIVIVM·LARGITAS·PERFECIT.

FAILED BACK SURGERY SYNDROME

- What is it?
- Incidence?
- Management?



Can we stick it back together?

SCI DAMAGE

- PRIMARY- mechanical
- SECONDARY-vascular dysregulation, increased cellular calcium, free radical production and excitotoxic amino acid release

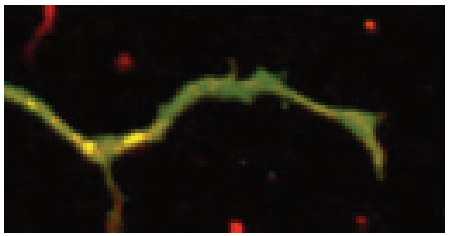
REPAIR

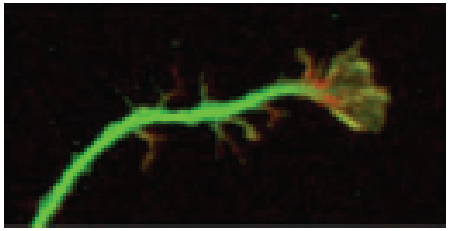
- NEUROPLASTICTY-harnessing inherent plasticity to reset neurons
- NEUROMODULATION-altering the signalling within the CNS by use of electricity or medications

(Dunlop, NRP Talk, June 21 2011)

Cethrin® (BA-210), Phase I/IIa trial (Non-randomised, open-label)

Basic science	**Rho inhibitor, prevents growth cone collapse**
Sponsor	Alseres Pharmaceuticals, Inc (Sites: 9 in USA and Canada)
Patients	Acute <7 days ; **AIS A** (motor & sensory complete) @ 12h before surgery
Delivery	Epidural; Accommodate 2mL thrombin/fibrin sealant (carrier) Scheduled to undergo decompression/other surgery (e.g. fixation)
Groups	Cervical C4 - T1; Thoracic T2-T12 0.3, 1, 3, 6, 9 mg
N	48
Status	Completed: Fehlings et al., J Neurotrauma 2011
Outcomes	1º: Safety & tolerability **YES**
	2º: Efficacy, AIS motor scores **YES**



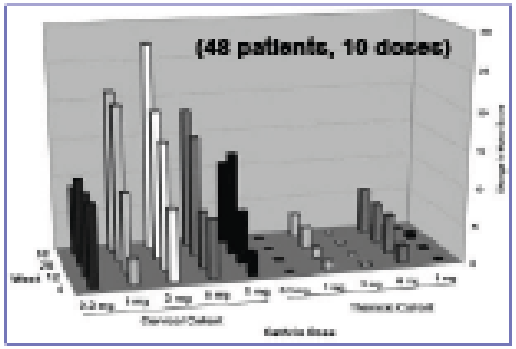


(Shi et al., 2007 PNAS)

(Dunlop, NWP Talk, June 21 2011)

Cethrin® (BA-210), Phase I/IIa trial (AIS A patients)

ASIA motor score change



Cethrin *(Fehlings et al., 2011)*	
All doses	Thoracic: 1.8 ± 5.1
	Cervical: 18.6 ± 19.3
Largest change: 3mg cohort	Cervical: 27.3 ± 13.3
Spontaneous *(Fawcett et al, 2007, ICCP)*	
	~10 over 2 years

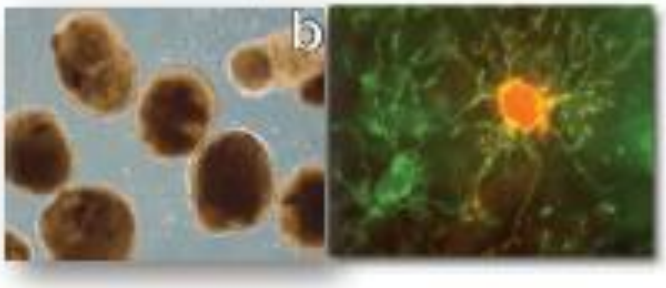
AIS Conversions

Cethrin (A to C/D) *(Fehlings et al., 2011)*	
All doses	Thoracic: 6%
	Cervical : 31%
3mg	Cervical: 66%
Spontaneous *(Fawcett et al, 2007, ICCP)*	
AIS A – AIS A	~80% (78-82%)
AIS A – AIS B	~12% (7-17%)
AIS A – AIS C	~8% (5-10%)

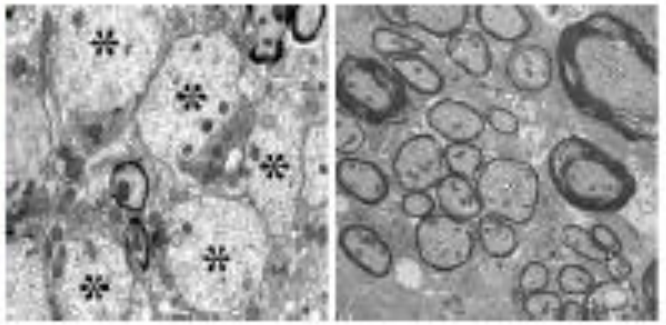
(Dunlop, NRP Talk, June 21 2011)

Geron, Phase I trial; GRNOPC1 (non-randomised, open-label)

Basic science	**Human embryonic stem cell derived oligodendrocyte precursor cells**
Sponsor	Geron
Patients	Acute, 7-14 days; T3-T10, AIS A (complete)
Delivery	Transplantation, 1 injection of 2million GRNOPC1 cells
Groups	-
N	10
Status	Jan 2009: FDA approval; August 2009: halted; July 2010: restarted Oct 2010: 1 patient recruited; planned for 1 per month
Outcomes	1°: Safety. 2°: sensory & motor function (None as yet)



(Kierstead et al 2005); Berglee et al., 2005 Nature)



(Dunlop, NWP Talk, June 21 2011)

Minocycline, Phase I/II trial (randomised; double-blind)

Basic science	Synthetic tetracycline broad spectrum antimicrobial; metalloproteinase inhibitor anti-apoptotic, anti-inflammatory, anti-oxidant, blocks microglial activation, wide range of animal models including stroke, ALS, Huntington's, Alzheimer', Parkinson's
Sponsor	University of Calgary, PVA
Patients	Acute, < 12 hours; C0-T11 motor complete or incomplete
Delivery	Intravenous 2x daily for 7 days
Groups	200mg 2x daily (n = 5); pharmodynamic profiling and changed to: 800 mg loading + 400 mg 2x daily (n = 22) Placebo control (n = 25)
N	52 (Spinal cord perfusion pressure augmentation iv fluids for MAP <75mm Hg)
Status	Completed 2010
Outcomes	1°: Safety & Protocol compliance YES
	2°: AIS Motor recovery @ 1 year Thoracic complete, no difference Cervical complete +8.7 (p=0.269); Cervical incomplete +20.1 (p=0.024)

Future: issues with compromise of positive aspects of innate immune response

(Casha et al., 2009 NeuroSurgery Abstract)

(Dunlop, NRP Talk, June 21 2011)

STASCIS: Surgical Treatment of Acute Spinal Cord Injury Phase II, non-randomised, prospective

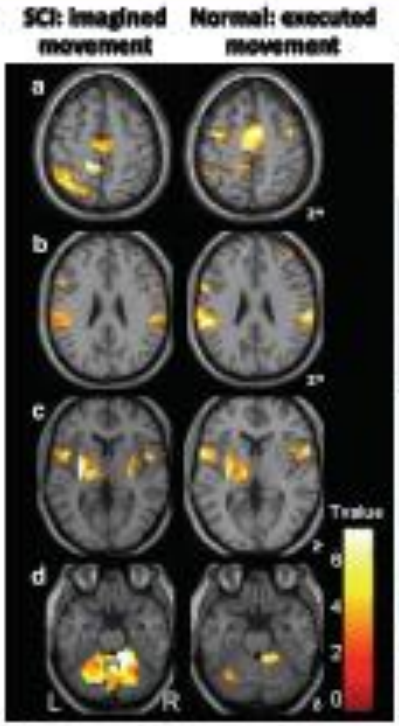
Patients	Acute < 24/>24h; C3-T1; Complete or incomplete (A, B, C, D)
Delivery	Surgical decompression
Groups	Early (< 24h) versus delayed (> 24h)
N	~450
Status	Completed, submitted for publication NEJM (not on ClinicalTrials.gov)
Outcomes	1º: Efficacy. AIS YES
	Early <24h: 24% show 2 or more grade improvement **Late >24h: 4%** **"One in 5 more people walking away"**
	2º: sensory scores and other functional measures

Spontaneous *(Fawcett et al, 2007, ICCP)*					
A - A	~78%				
A - B	~10%	B - B	~28%		
A - C	~8%	B - C	~30%	C - C	~14%
A - D	~4%	B - D	~30%	C - D	~73%
A - E	0%	B - E	~2%	C - E	~5%

(Fehlings et al., NEJM submitted)

(Dunlop, NRP Talk, June 21 2011)

Neuromodulation: Mind over mind



Chronic SCI patients

- Motor cortex activation during attempted or imagined foot movement
- Same networks recruited as healthy subjects who executed foot movement
- Use attempted & imagined movement in rehabilitation

C4, AIS A

Braingate, Phase 1 open label	
Patient	SCI, stroke, MD, ALS High dependency
N	15 by 2015
Device	Intracortical implant

(Hotz-Boendermaker et al., 2008 Neuroimage 39, 383-394; Cramer et al., 2005 Brain 128, 2941-2950; Hochberg et al 2006 Nature 442, 164-171)

(Dunlop, NRP Talk, June 21 2011)

Epidural stimulation

Cats:

Complete SCI, only learn to step with treadmill training, epidural stimulation

Humans:

Treadmill training improves stepping in motor incomplete, not motor complete

Motor complete: Epidural stimulation can induce rhythmic activity when supine

Circuitry exists but cannot work without some crucial level excitability from supraspinal centres

Harkema et al., The Lancet, May 2011

Epidural stimulation: "short circuit" & "turn up the amplifier"

(i.e. modified spinal circuitry into a physiological state that enabled sensory input from stepping and standing to serve as a source of neural control to undertake these tasks)

AIS B

2006:108h of locomotor training over 26 months; no change in EMG

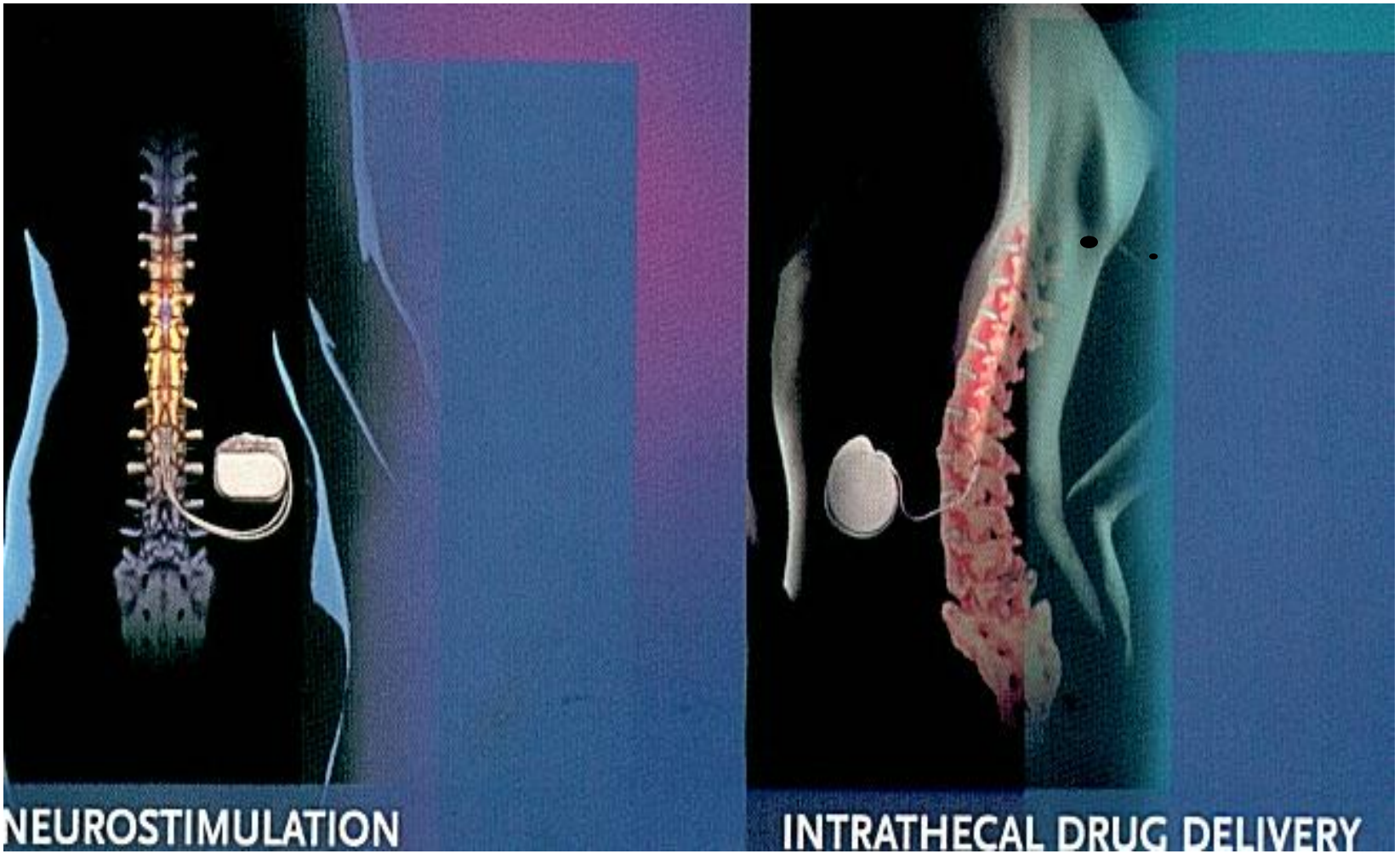
2009: Stimulator implanted

Suitable: 10 – 15% of patients

(Harkema et al., Lancet 2011)

..and what about the Dunedin stem cell trial?

ADVANCED THERAPIES



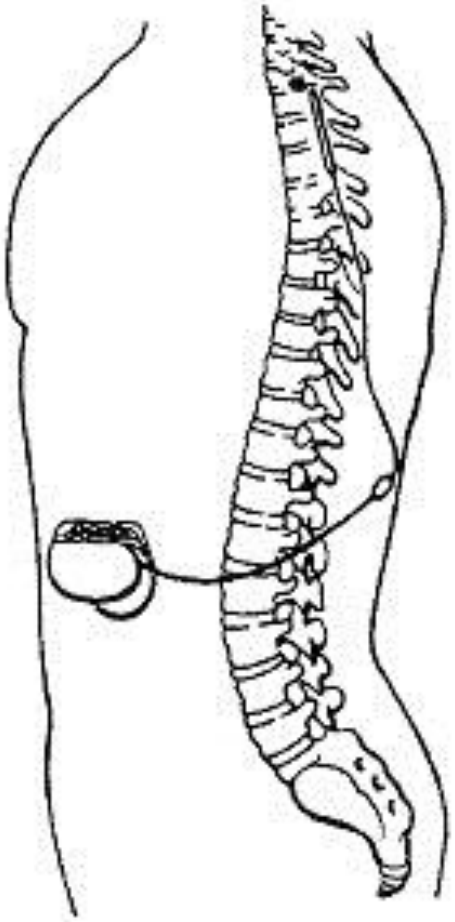
“What is this thing called pain?
This funny thing called pain,
just who can solve its mystery?”

Cole Porter 1926

- “ I’ve come close to killing myself, several times.
- I’ve clutched a fistful of lollies behind my white knuckles- the orange nortriptyline, green temazepam, imovane, neurontin, voltaren and a few others for good measure- then flushed them down the toilet. I can’t sleep, I can’t concentrate, and I’m not a very nice person to be around.
- That’s when my pain is at its worse.
- I’m a T11 complete paraplegic after a road accident 15 years ago.
- I believe my life would be pretty good - except for the pain”

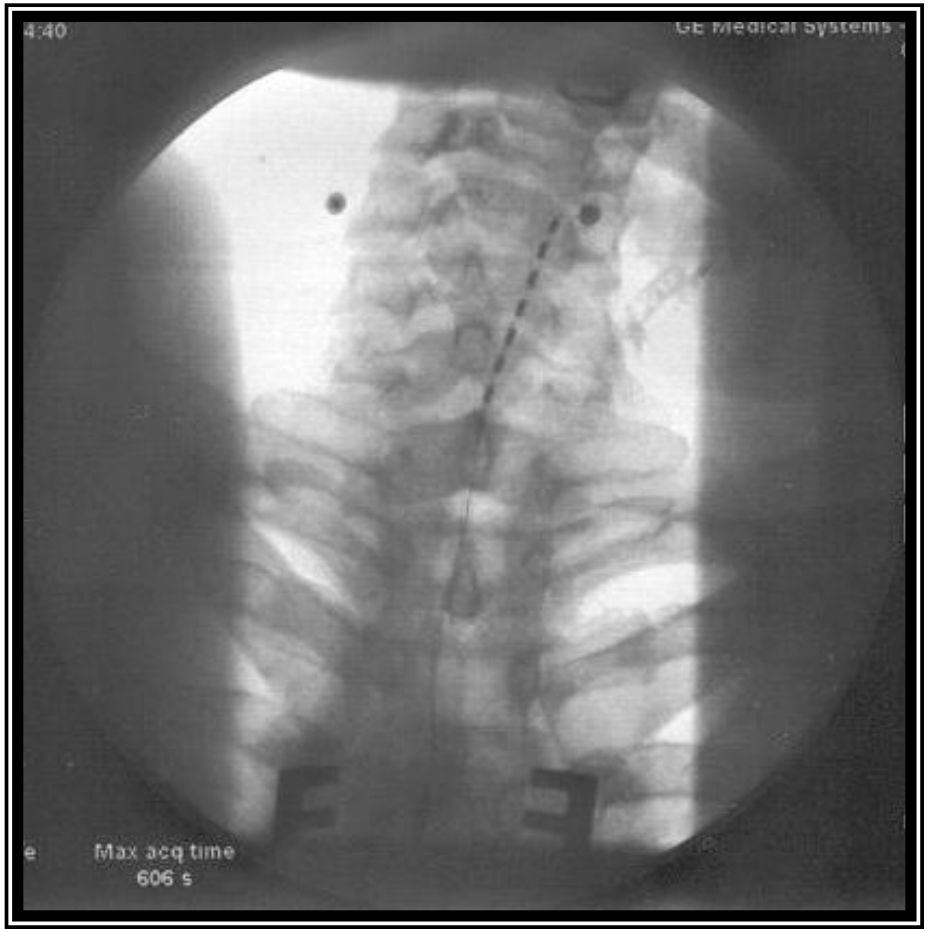
Spinal Cord Stimulators

Spinal Cord Stimulation



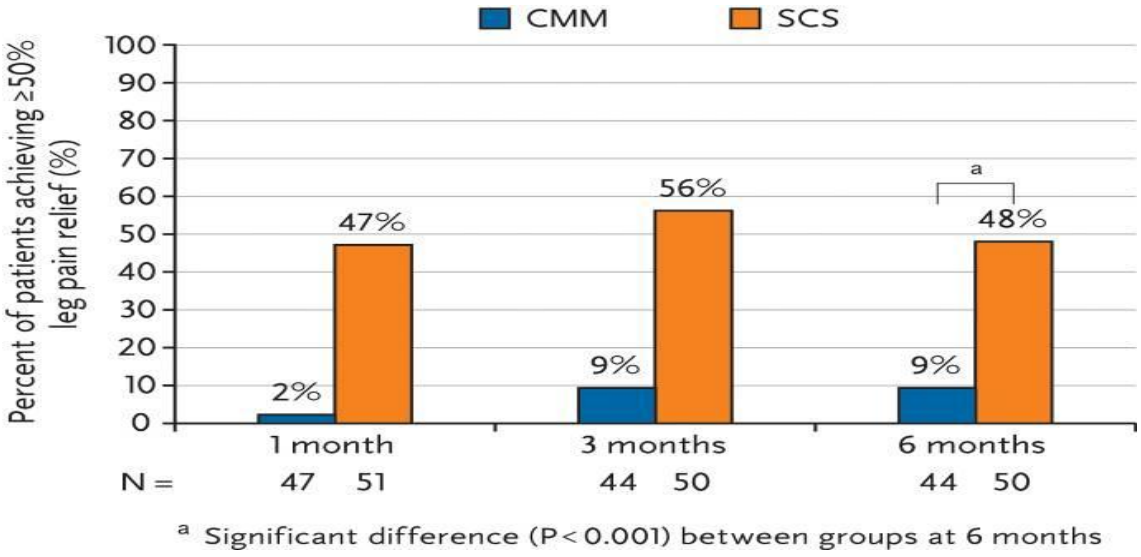
- Angina
- Failed Back Surgery Syndrome
- Phantom pain
- Stump pain
- Brachial plexus injury
- Complex Regional Pain Syndrome (CRPS)
- Visceral pain


Max acq time
606 s


4:40
GE Medical Systems
Max acq time
606 s

PRIMARY OUTCOME AT 6 MONTHS: ≥ 50% LEG PAIN RELIEF

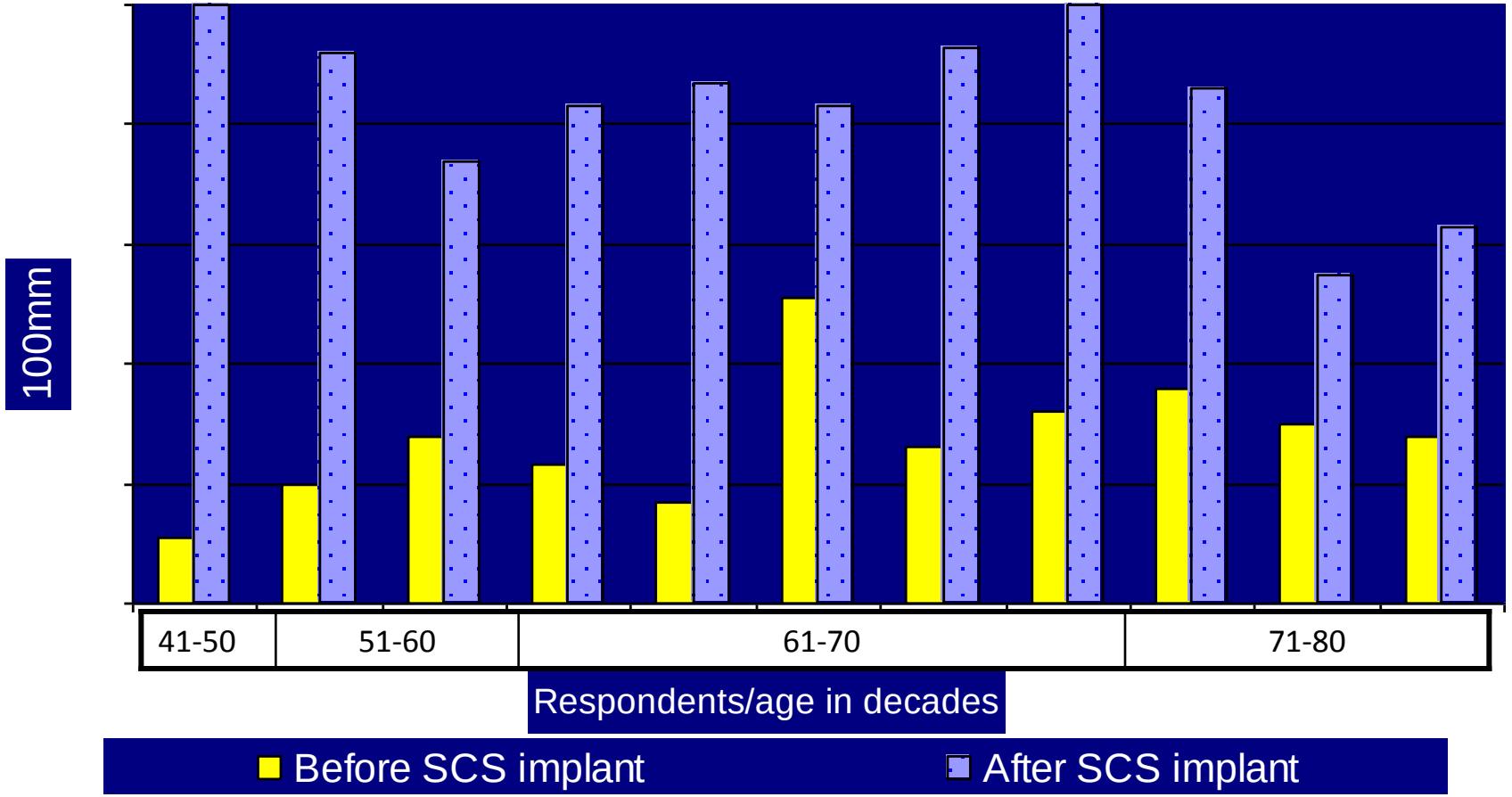
SIGNIFICANTLY MORE SCS PATIENTS (48% vs 9%) achieved the primary outcome



Self-reported QOL before and after SCS

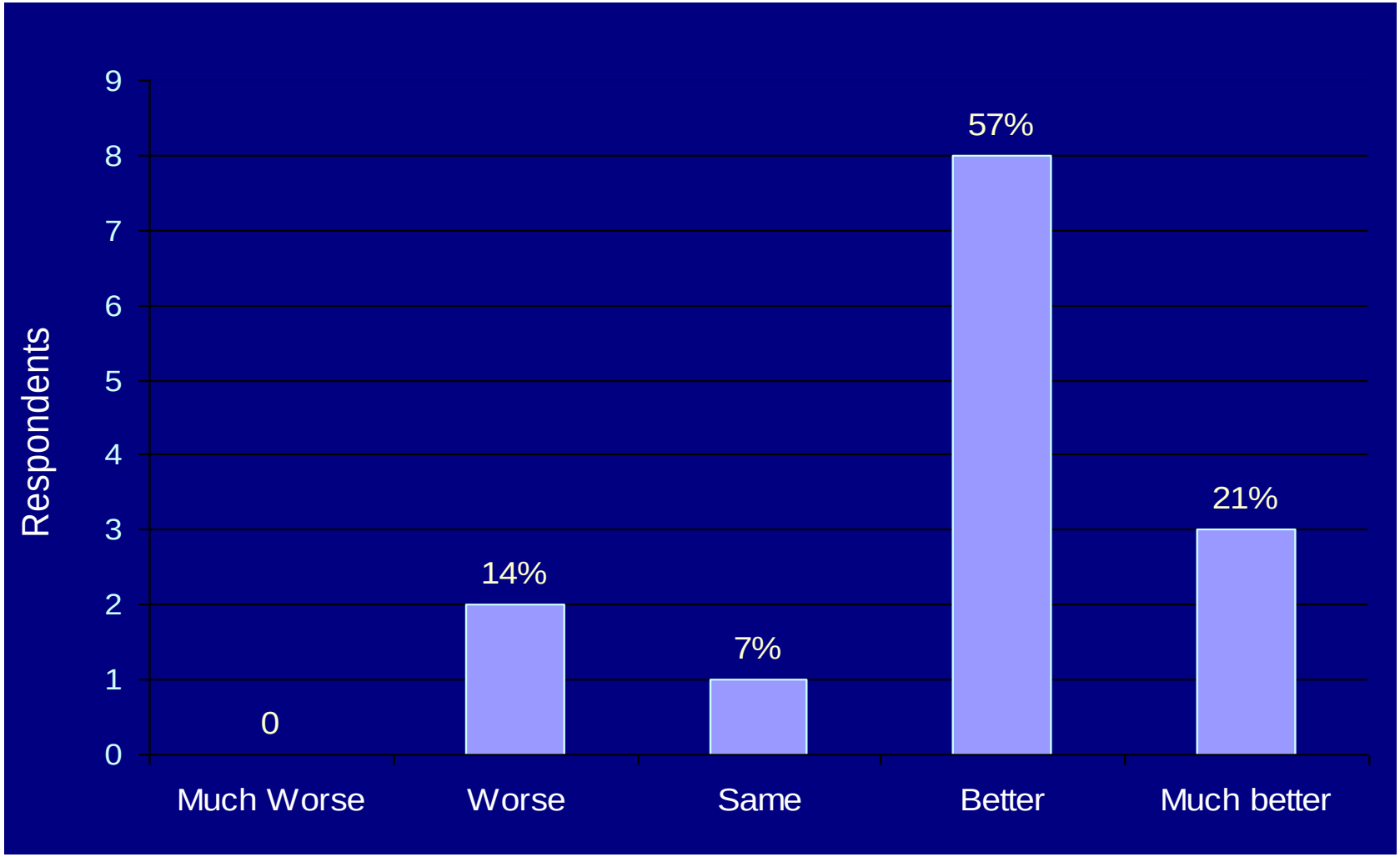
n = 11, mean improvement = 56mm

(Mean before implant = 27mm. Mean after implant = 83mm)



Sandom (2005) Neuromodulation for Angina: Quality of Life Survey; Thesis University of Otago

Control of angina after SCS



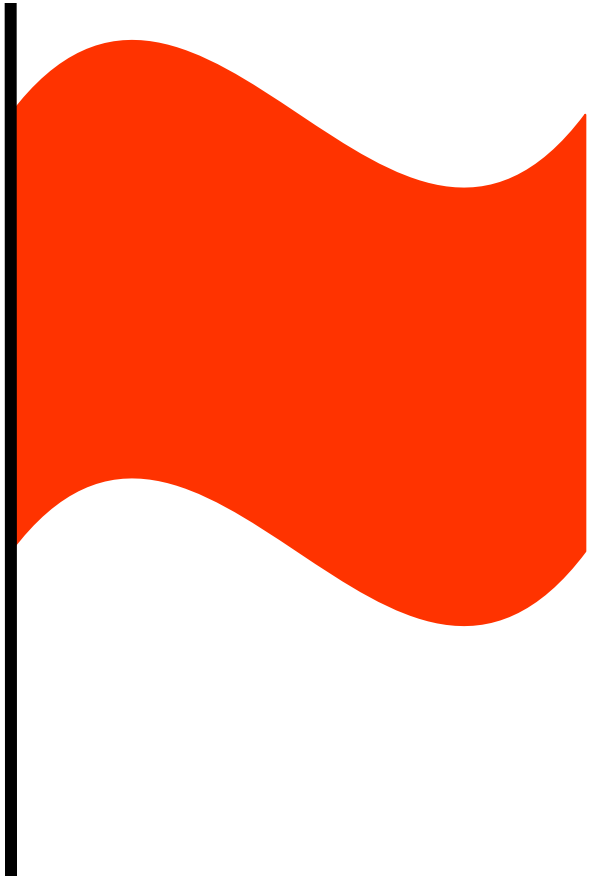
Sandom (2005) Neuromodulation for Angina: Quality of Life Survey; Thesis University of Otago

IMPLANTED INTRATHECAL PUMPS

Assessing Back Pain

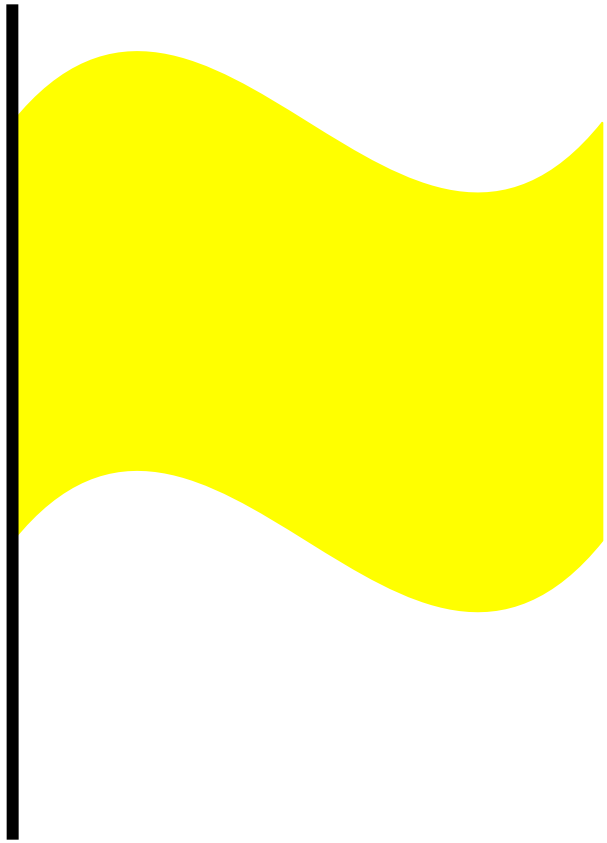
- What is the context?
- Is it ‘mechanical’?
- Are there neurological features?
- Are there other features?
- Are investigations required?
- What do you say to the patient?

Red Flags



- Most clues for ‘red flag’ conditions are found in the patient history
- Pre-test probabilities for major red flag conditions have been suggested:
  - Cancer <0.7%
  - Infection <0.01%
  - Ankylosing spondylitis <0.3%

Yellow Flags



- Psychosocial variables associated with poor prognosis in terms of pain and related disability
- Early identification and management is required

Other Factors to Consider

- Are there other contributors?
  - Psychosocial factors
  - Pain beliefs (fear-avoidance)
  - Patient expectations
- Are investigations required?
  - X-rays
  - CT/MRI scans
  - Surgical consultation

HOPE

- “My hopes are not always realised, but I always hope”. Ovid