



**Approccio multidisciplinare nel
trattamento delle metastasi vertebrali:**

INQUADRAMENTO CLINICO

Ernesto Maranzano

**Dipartimento di Oncologia,
S.C. di Radioterapia Oncologica
Azienda Ospedaliera, Terni**

Genova, 19-22 novembre 2011

Epidemiology

- Metastases to **lung** and **liver** are the most frequent, followed by mets to the **bones**, of which the spinal column is the most common site
- It is estimated that roughly **10%** of all cancer patients develop symptomatic **vertebral metastases**
- In a high % of cases, vertebral mets are complicated by a metastatic spinal cord compression (**MSCC**)

Incidence

- by **sex**: similar
- by **age**: ↑ midlife (40-65 yrs)
- by **primary tumor**:
 - prostate & lung (men)
 - breast & lung (women)
- by **vertebral site**:
 - thoracic spine (~ 70%)
 - lumbar spine (~ 20%)
 - Cervical spine & sacrum (~ 10%)

Pathways of spread

➤ *HEMATOGENOUS SPREAD*

Venous routes (e.g., Batson's plexus)

Arterial routes (vertebrae are well perfused)

➤ *DIRECT EXTENTION*

Primary tumors located in paravertebral soft tissues (e.g., lung, prostate, bladder and colon cancers)

➤ *CEREBRAL FLUID SPREAD*

Brain metastases

Back pain syndromes

– *(a) local pain, with pain at rest*

resulting from periosteal stretching from tumour growth and/
or local inflammatory processes

– *(b) mechanical pain, with pain on movement and improved by rest*

because of instability

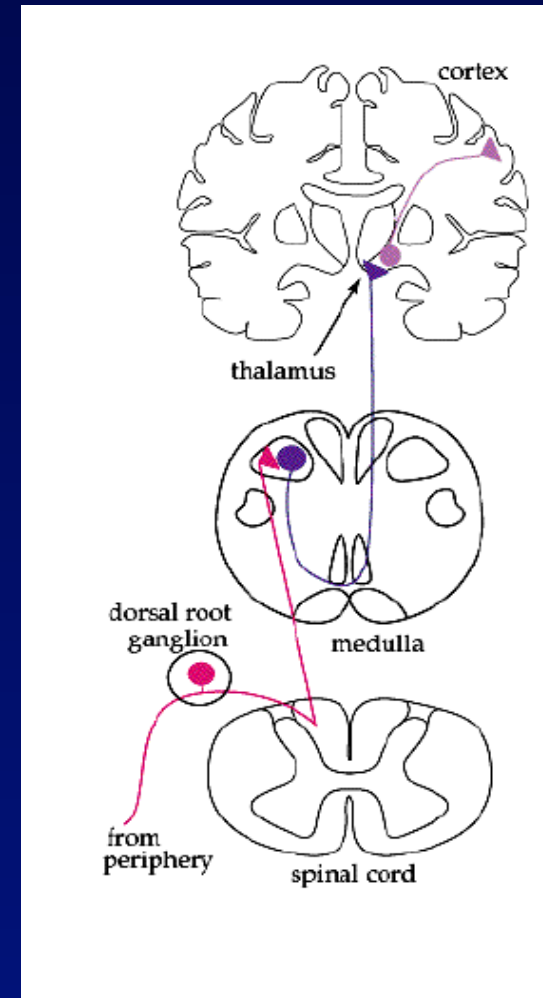
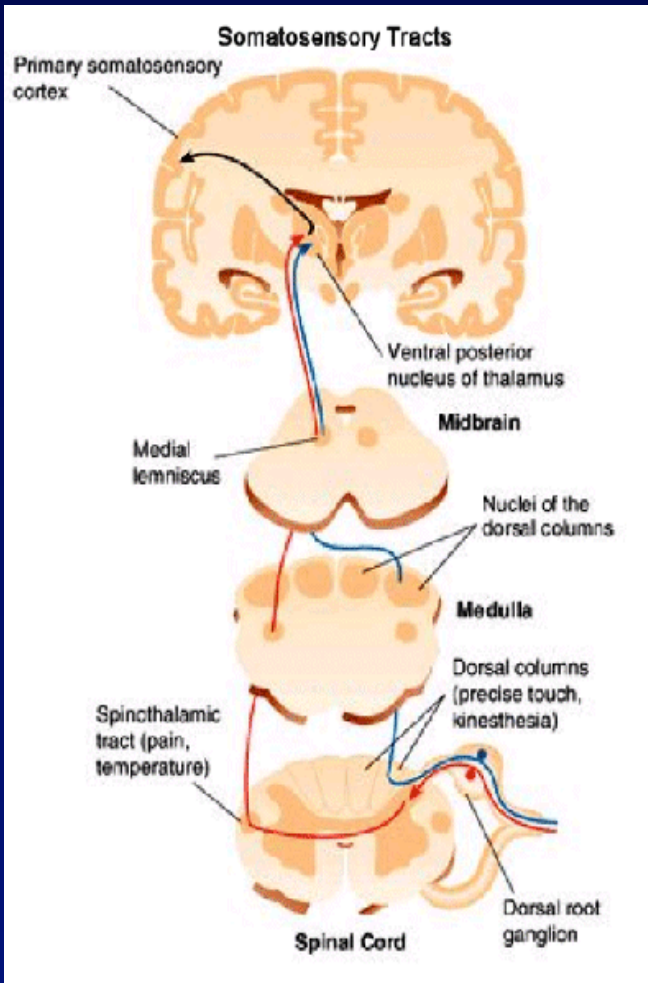
– *(c) radicular pain*

because of irritation of a nerve roots →

MSCC!

Neuropathic pain

Pain arising as a direct consequence of a lesion in regions (*e.g., vertebral body*) that are innervated by dermatomes of the somatosensory system



Neuropathic pain

superficial burning, searing, shooting, stabbing or electric shock-like sensation

plus

parasthesia, allodynia and hyperalgesia (*'hypersensitive' symptoms*)

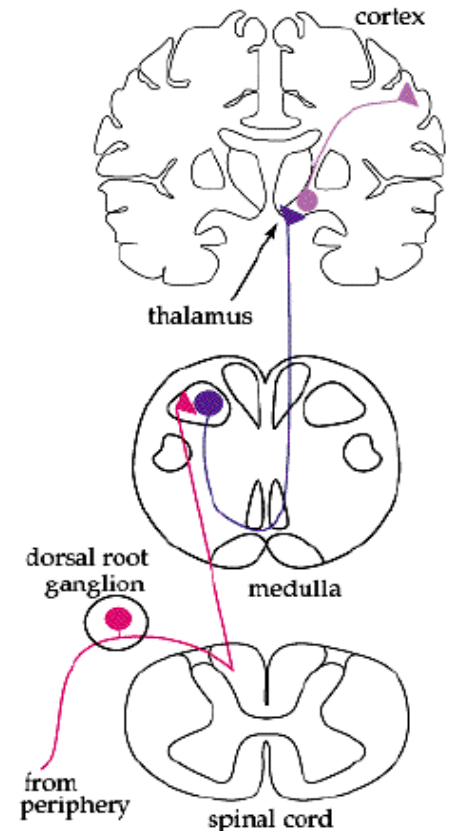
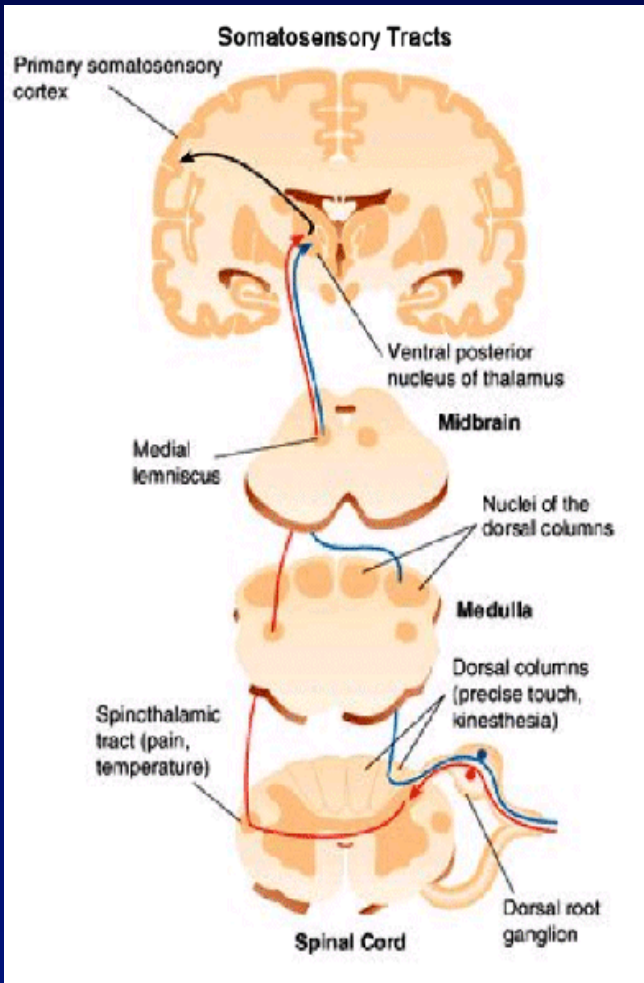
or

decreased perception for mechanical, vibratory, thermal and noxious stimuli (*'hyposensitive' symptoms*)

Neuropathic pain

Pain arising as a direct consequence of a lesion in regions (e.g., *vertebral body*) that are innervated by dermatomes of the somatosensory system

This pain is often resistant to analgesics, opioids too



**A PHASE II RANDOMISED PALLIATIVE RADIOTHERAPY TRIAL OF
30GY IN 10 FRACTIONS VS EITHER 8GY IN 1 FRACTION OR
20GY IN 5 FRACTIONS FOR THE RELIEF OF
NEUROPATHIC PAIN CAUSED BY BONE METASTASES (NeBo2)**

PRINCIPAL INVESTIGATORS

Edward Chow

Daniel Roos

Kristopher Dennis

Carlo De Angelis

Department of Radiation Oncology
Odette Cancer Centre, Sunnybrook Health Sciences Centre
University of Toronto
Toronto, Ontario, CANADA

Vertebral metastases classification

Uncomplicated painful
vertebral metastases

Complicated painful
vertebral metastases

Impending vertebral collapse

Spine instability

Metastatic spinal cord compression

Vertebral metastases classification

Uncomplicated painful
vertebral metastases

Complicated painful
vertebral metastases

Impending vertebral collapse

Spine instability

Metastatic spinal cord compression

Diagnosis and management of vertebral metastases

GUIDELINES

Metastatic spinal cord compression:

Diagnosis and management of patients **at risk of or with** metastatic spinal cord compression

NICE Guideline

National Collaborative Centre for Cancer

Full Guideline

November 2008

Developed for NICE by the National Collaborating Centre for Cancer

Metastatic spinal cord compression:

Diagnosis and management of patients at risk of or with metastatic spinal cord compression

*...new onset back pain in a patient with known cancer must be considered **vertebral metastatic disease** until proven otherwise*

*...early diagnosis and prompt therapy are the most important prognostic factors in **Metastatic Spinal Cord Compression** patients*

Instrumental diagnosis: choice of imaging modality

MRI is the investigation of choice

Although modern **multi-slice CT** scanning is quick and has the ability to image the whole spine, it is less sensitive than MRI. CT may be needed to provide additional information on bone integrity and stability and to help plan surgery

Radioisotope bone scanning does not show the soft tissue extension and the level of cord compression.

There is no evidence that **PET-CT** provides additional clinically relevant information to MRI

Magnetic Resonance Imaging - MRI

MRI is the investigation of choice

➤ MRI has a high sensitivity for identifying metastatic disease within vertebra (sagittal T1 and/or STIR - Short T1 Inversion Recovery):

sensitivity 93%

specificity 97%

diagnostic accuracy 95%

➤ MRI can discriminate between metastatic disease and other pathologies (98% capability to differentiate between benign spondylodiscitis and MSCC).

➤ MRI is an excellent method to detect soft tissue component of the mass and multiple sites of spine mets.

*Marc C. Chamberlain, Andrew Sloan,
and Frank Vrionis*

Metastatic Spinal Cord Compression (MSCC) INSTRUMENTAL DIAGNOSIS

- ✓ **MRI** is the best tool for MSCC diagnosis
- ✓ MRI of the **intere spine** is necessary because approximately 1/3 of pts have asymptomatic but radiographically evident MSCC disease distant from the symptomatic site.
- ✓ These **distant sites warrant treatment** similar to that of the symptomatic site.

International Survey on Patterns of Practice for Treatment of Metastatic Spinal Cord Compression (MSCC)

***T. Holt, S. Schild, E. Maranzano, P. Hoskin,
A. Sahgal, J. Yamada, D. Rades, S. Ryu,***

Demographics of Respondents

Australia/NZ	61	22.6%
Italy	49	18.2%
Canada	34	12.6%
UK	30	11.2%
USA	22	8.2%
Germany	19	7.1%
Netherlands	18	6.7%
Other European	12	4.5%
Other Non European	24	8.9%
Total	269	100%

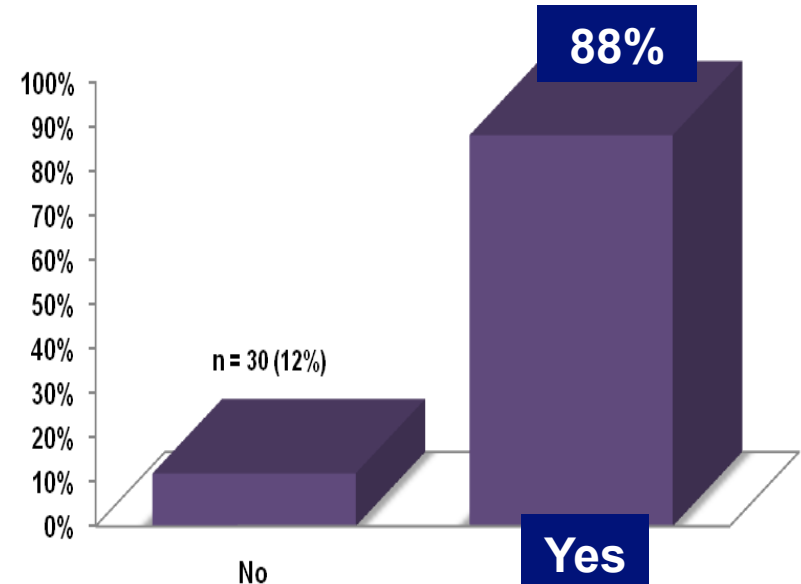
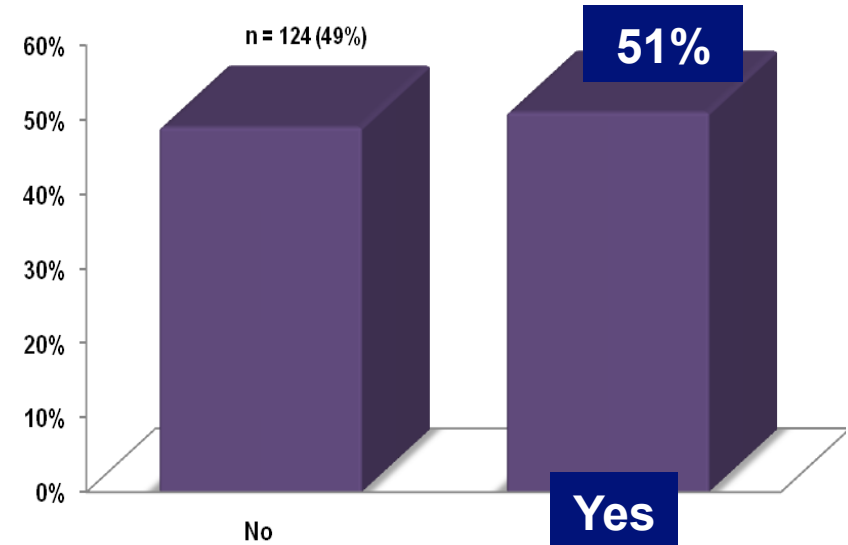
Early Detection of MSCC

			country of practice					Total
			USA	Canada	Australia/ New Zealand	Europe	Other countries	
Do you routinely give written or verbal spinal cord compression education material to your patients with known vertebral metastases	No	Count	12	16	33	70	13	144
		% within country of practice	54.5%	47.1%	55.9%	59.8%	65.0%	57.1%
	Yes	Count	10	18	26	47	7	108
		% within country of practice	45.5%	52.9%	44.1%	40.2%	35.0%	42.9%
Total		Count	22	34	59	117	20	252
		% within country of practice	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

*missing = 17

Early Detection of MSCC

1. Is **MRI** being used as a screening tool to detect occult MSCC in patients with **known vertebral metastases**
2. Is **MRI** routinely performed in patients neurologically intact but with a suspicious pain history i.e. **radiculopathy**



Survey Summary

- **MRI** is commonly used for early detection of MSCC
- incidence of using **MRI for screening** in asymptomatic patients is higher than expected (51%)

Short Report

Frequency of **Screening Magnetic Resonance Imaging** to Detect Occult Spinal Cord Compromise and to Prevent Neurological Deficit in Metastatic Castration-resistant Prostate Cancer

R. Venkitaraman*, S.A. Sohaib †, Y. Barbachano ‡, C.C. Parker §, R.A. Huddart §, A. Horwich §, D. Dearnaley §

* Department of Oncology, Ipswich Hospital NHS Trust, Ipswich, UK

Clinical Oncology 22 (2010) 147–152



Scenarios

➤ patients with castration-resistant prostate cancer and vertebral metastases

Results

➤ serial MRI spine can be used to detect occult spinal cord compromise and to prevent neurological deficits

UK

*Institute of Cancer Research,
Clinical Trials & Statistics Unit*

PROMPTS Trial Schema Full CTAAC Application

ICR
The Institute
of Cancer Research
ICR-CTSU

A **P**rospective **R**andomised Study of **O**bservation versus **S**creening
MRI And **P**re-**E**mptive **T**reatment in Prostate Cancer Patients with **S**pinal **M**etastasis

PROMPTS is a multi-centre trial to evaluate the role of screening MRI in patients with castrate resistant prostate cancer with known spinal metastases.

Eligible patient group:

Castrate resistant prostate cancer patients with spinal metastasis.
No bony back pain
No neurologic deficit
No previous Spinal Cord Compression (SCC)
Able to have MRI scan

RANDOMISE

Control Group
Observation

Experimental arm
Baseline screening MRI spine

*Prognostic factors conditioning
therapeutic choice*

Tokuhashi scoring system: A revised scoring system for preoperative evaluation of metastatic spine tumor prognosis
Spine 2005, 30 (19), 2186–2191

Table 2 Evaluation System for the Prognosis of Metastatic Spine Tumors

Characteristic	Score
General condition (performance status)	
Poor (PS 10–40%)	0
Moderate (PS 50–70%)	1
Good (PS 80–100%)	2
Number of extraspinal bone metastases foci	
≥3	0
1-2	1
0	2
Number of metastases in the vertebral body	
≥3	0
2	1
1	2
Metastases to the major internal organs	
Unremovable	0
Removable	1
No metastases	2
Primary site of the cancer	
Lung, osteosarcoma, stomach, bladder, esophagus, pancreas	0
Liver, gall bladder, unidentified	1
Others	2
Kidney, uterus	3
Rectum	4
Thyroid, breast, prostate, carcinoid tumor	5
Palsy	
Complete (Frankel A, B)	0
Incomplete (Frankel C, D)	1
None (Frankel E)	2

PS

N. extraspinal bone mets

N. mets in vertebral body

Mets to major internal organs

Primary site of cancer

Palsy

Pain relief

and

QoL

UPDATE OF THE INTERNATIONAL CONSENSUS ON PALLIATIVE RADIOTHERAPY ENDPOINTS FOR FUTURE CLINICAL TRIALS IN BONE METASTASES

Edward Chow et al.

THE INTERNATIONAL BONE METASTASES CONSENSUS WORKING PARTY

a) Net pain relief should be assessed along with pain scores and medications

Canadian-led International Development of a European Organization for Research and Treatment of Cancer Quality of Life Module for Malignant Spinal Cord Compression: Results of Phase I



Gunita Mitera¹, Andrew Loblaw¹, Arjun Sahgal¹, Brita Danielson²



¹Sunnybrook Odette Cancer Centre, Toronto, ON, Canada, ²Cross Cancer Institute, Edmonton, AB, Canada

Objective

- To develop a relevant set of items assessing quality of life (QOL) issues in patients with malignant spinal cord compression (MSCC), not sufficiently covered by the European Organization for Research and Treatment of Cancer (EORTC) C15-PAL core questionnaire.

San Diego 2010

Table 1: Top 10 QOL issues ranked by patients (n=35)

Patients' Rank	QOL Issues	Freq (%)	HCPs' Rank
1	Have you had difficulty performing self-care (i.e. bathing, dressing)?	48.6	4
2	Did you have trouble controlling your bladder?	42.3	3
3	Did you have lower back pain?	42.3	7
4	Have you had difficulty in carrying out usual daily tasks (i.e. grocery shopping, housework)?	40.0	N/A
5	Have you worried about becoming dependent on others because of your illness?	40.0	6
6	Have you worried about becoming bed-bound because of your illness?	31.4	10
7	Did you have upper back pain?	28.6	N/A
8	Did you have to modify your daily activities because of your illness?	28.6	9
9	Have you worried about loss of mobility because of your illness?	28.6	7
10	Did you hope treatment would reduce pain as much as possible?	28.6	N/A

1 = Top priority issue for patients

Items included within the red box are items ranked by both groups to be in the top 10

San Diego 2010

Table 2: Top 10 QOL issues ranked by health care providers (n=62)

HCPs' Rank	QOL Issues	Freq (%)	Patients' Rank
1	Were you able to walk without assistance?	49.3	N/A
2	Did you have weakness of both legs?	47.9	N/A
3	Did you have trouble controlling your bladder?	45.2	2
4	Have you had difficulty performing self-care (i.e. bathing, dressing)?	39.7	1
5	Did you experience leakage of bowels?	35.6	N/A
6	Have you worried about becoming dependent on others because of your illness?	28.8	5
7	Have you worried about loss of mobility because of your illness?	28.8	9
8	Did you have lower back pain?	27.4	3
9	Have you had to modify your daily activities because of your illness?	27.4	8
10	Have you worried about becoming bed-bound because of your illness?	27.4	6

1 = Top priority issue for health care providers

Items included within the red box are items ranked by both groups to be in the top 10

Patients suggestions for questions to add:

- ❖ Do you have family support?
- ❖ Do you worry about your ability to drive in the future?
- ❖ Were you able to understand your procedures, treatments, & medications?

Health care provider suggestions for questions to add:

- ❖ Have you experienced weakened relationships with family or friends?
- ❖ Do you feel like a burden to family/friends?
- ❖ Does MSCC have an effect on sexual function?
- ❖ Do you have control of your bowel or bladder?
- ❖ Are you worried of becoming dependant on others now?
- ❖ Are you more concerned about bodily pain or weakness/paralysis in the arms and/or legs?

EORTC Quality of Life Module

Canadian-led International Development of a European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Module for Malignant Spinal Cord Compression

~RESEARCH PROTOCOL~

ODETTE CANCER CENTRE, CANADA

Gunita MITERA

Andrew LOBLAW

Arjun SAHGAL

CROSS CANCER INSTITUTE, CANADA

Brita DANIELSON

Alysa FAIRCHID

Fundación Instituto Valenciano de Oncología, Spain

Estanislao ARANA

LUMC, LEIDEN, NETHERLANDS

Yvette van der LINDEN

TATA MEDICAL CENTER, KOLKATA, INDIA

Indranil MALLICK

TATA MEMORIAL CENTRE, MUMBAI, INDIA

Ashwini Budrukkar

AUSTRALIA & NEW ZEALAND

To be determined at April meeting

GERMANY

Dirk RADES

ITALY

Ernesto MARANZANO

CONCLUSIONS

- Early diagnosis is the most important prognostic factor for patients with complicated vertebral metastases (e.g., MSCC)
- The importance of patient information and MRI for early detection of MSCC
- Pain relief and QoL assessment

CONCLUSIONS

... As survival rates for many cancers improve:

- prevalence of vertebral metastases is likely to increase,
- unexpected long term survivals do occur,
- late iatrogenic toxicity can increase overall if accuracy of delivered radiotherapy is suboptimal.

Commentary

A personal philosophy of a radiation oncologist ☆

Herman Suit *

Department of Radiation Oncology, Harvard Medical School, Boston, USA

Radiother & Oncol 100 (2011) 10-14

A case of incorrect palliative RT

... A patient who are predicted to have a **short life span** received **AP-PA** treatment fields covering cervical and upper thoracic spine.

... Most regrettably, shortly after treatment, he developed complete and permanent **quadriplegia**.

... This could have been avoided by use of a tolerated spinal cord dose and a more complex treatment plan.