Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia

Instabilità spinale ed algoritmi decisionali

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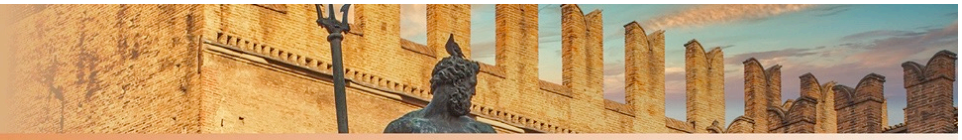
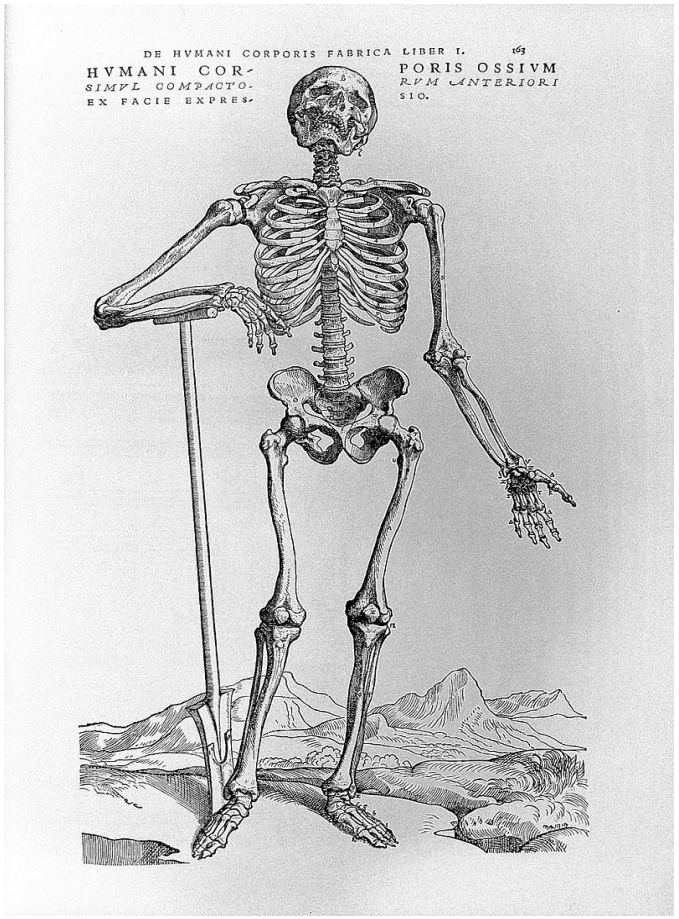


DICHIARAZIONE

Relatore: Donato Pezzulla

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Consulenza ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazione ad Advisory Board (**NIENTE DA DICHIARARE**)
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (**NIENTE DA DICHIARARE**)



Metastases are the most frequent cause of bone tumors and the spine represents the most frequent site of skeletal metastases.

Pain is the presenting complaint in the majority of cases.

Pain syndromes associated with spinal tumors:

- tumor-related pain
- radiculopathy
- mechanical pain due to spinal instability

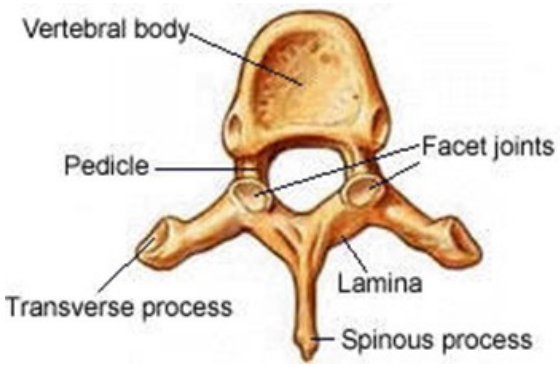
Spinal Stability and Instability

"The ability of the spine under physiologic loads to limit patterns of displacement so as not to damage or irritate the spinal cord and nerve roots and, in addition, to prevent incapacitating deformity or pain due to structural changes.

"Instability is defined as excessive displacement of the spine that would result in neurologic deficit, deformity, or pain."

Panjabi et al 1980
Pope et al 1983

Spinal Stability:



- Disc
- Ligaments
- Rib cage
- Vertebrae
- Spinal muscles

→ Clinical and Strumental Evalutaion

Panjabi et al 1980

The «Three Column Spine» Bio-mechanical Model

Denis et al 1983

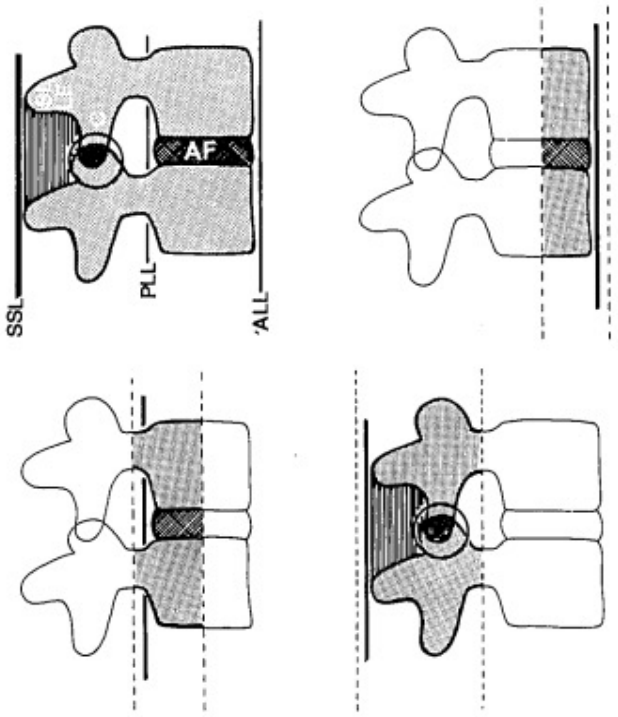


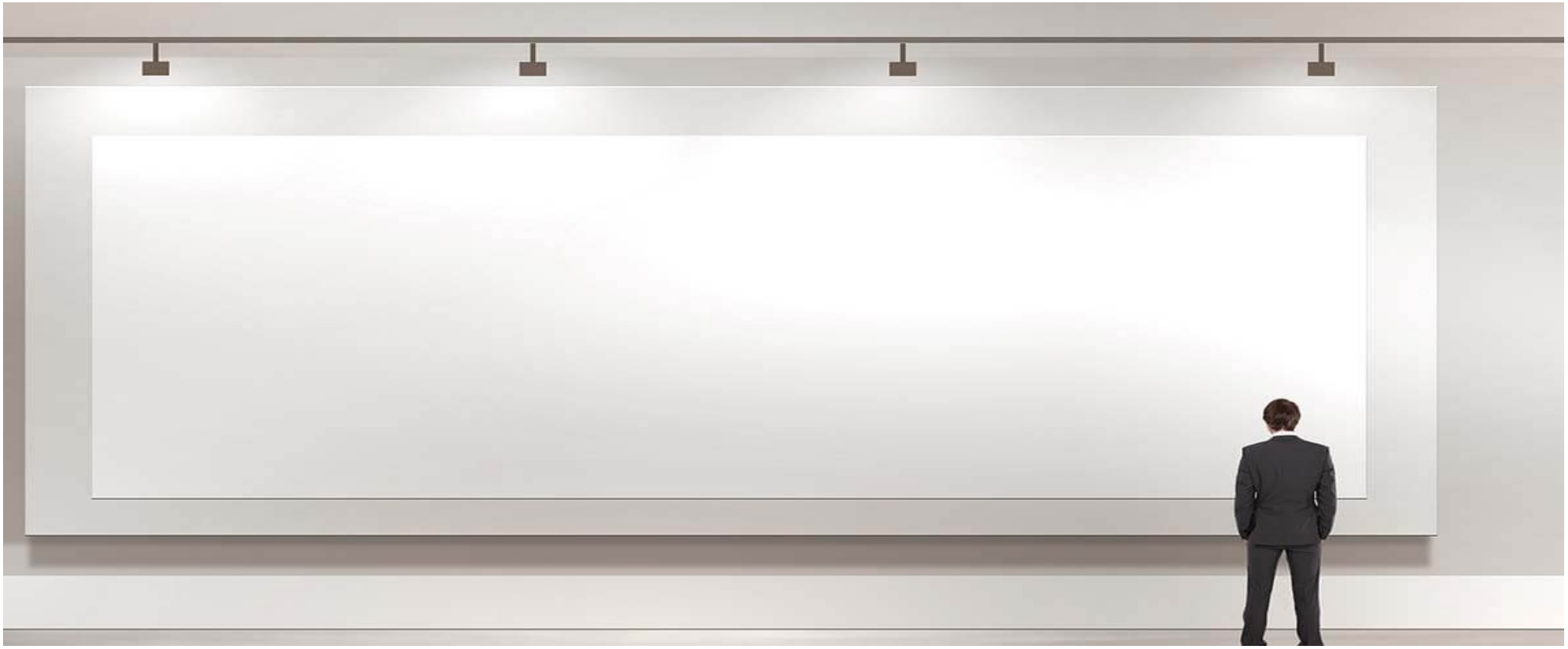
Fig 1. The anterior, middle, and posterior column are illustrated.

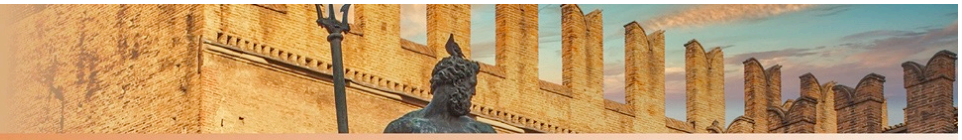
Anterior column: anterior longitudinal legament, anterior portion of the annulus fibrosus, anterior portion of the vertebral body.
Middle column: posterior longitudinal legament, posterior portion of the annulus fibrosus, aposterior portion of the vertebral body.
Posterior column: posterior bony sand legamnet vertebral complexes

Limit of the Model

- Originally developed for use in trauma (not for neoplastic setting).
- Different bone and soft tissue disruption pattern in neoplastic lesions and traumatic injuries.
- Ligaments and disks are rarely affected in neoplastic setting.
- Poor healing potential and bony quality in cancer patients.
- Not useful in predicting risk of pathologic fracture, since impending instability, with the potential for subsequent collapse, is a concept that specifically applies to neoplastic disease

Instability models for metastatic vertebral lesion?





Risk Factors?

Vertebral body collapse

Taneichi et al. 1997

- in the thoracic region (T1- T10): tumor size and costovertebral joint destruction;
- In the thoracolumbar and lumbar spine (T10-L5): tumor size and posterior elements destruction

Initiation Of Burst Fracture

Whyne et al. 2003

tumor size, magnitude of spinal loading, and bone density.

Intervertebral Instability

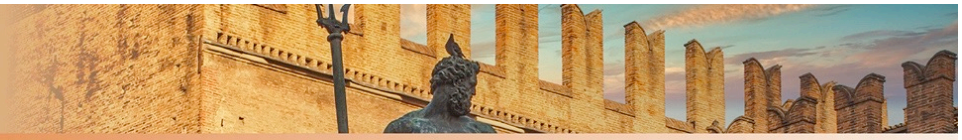
Dimar et al 1998: decreased bone density
Windhagen et al 1997: increased axial rigidity
Taneichi et al 1997: tumor size, destruction of the costovertebral joint (for thoracic tract)
Whyne et al 2003: tumor size, decreased bone density, increased force of spinal loading
Tschirhart et al 2004: dorsal location of the metastasis within the vertebral body
Tschirhart et al 2006: increased force of spinal loading
Tschirhart et al 2007: upper thoracic locations

Risk Factors

- Variables studied in isolation or independently
- Interactive and/or cumulative effect?

How classify Spinal Instability?

- A validated and reliable classification system could lead to standardized therapeutic approach for treatment of metastatic intervertebral instability.
- No accepted evidence-based guidelines for the classification of metastatic intervertebral instability were accepted before 2010.



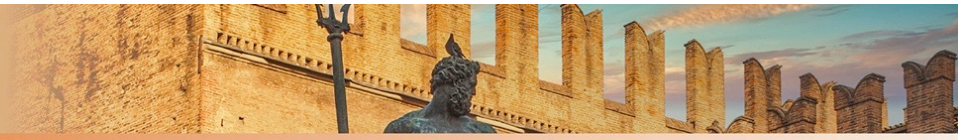
Time Classification

Acute
(e.g. fracture/dislocation)

- Limited
- Overt

Chronic
(e.g. spondylolisthesys)

- Associated with disfuctional motor segment
- Glacial (progressive deformity)



Conceptual Classification

Overt

Excessive motion that is readily documented by radiographic studies and results in pain, deformity, or neurologic deficit

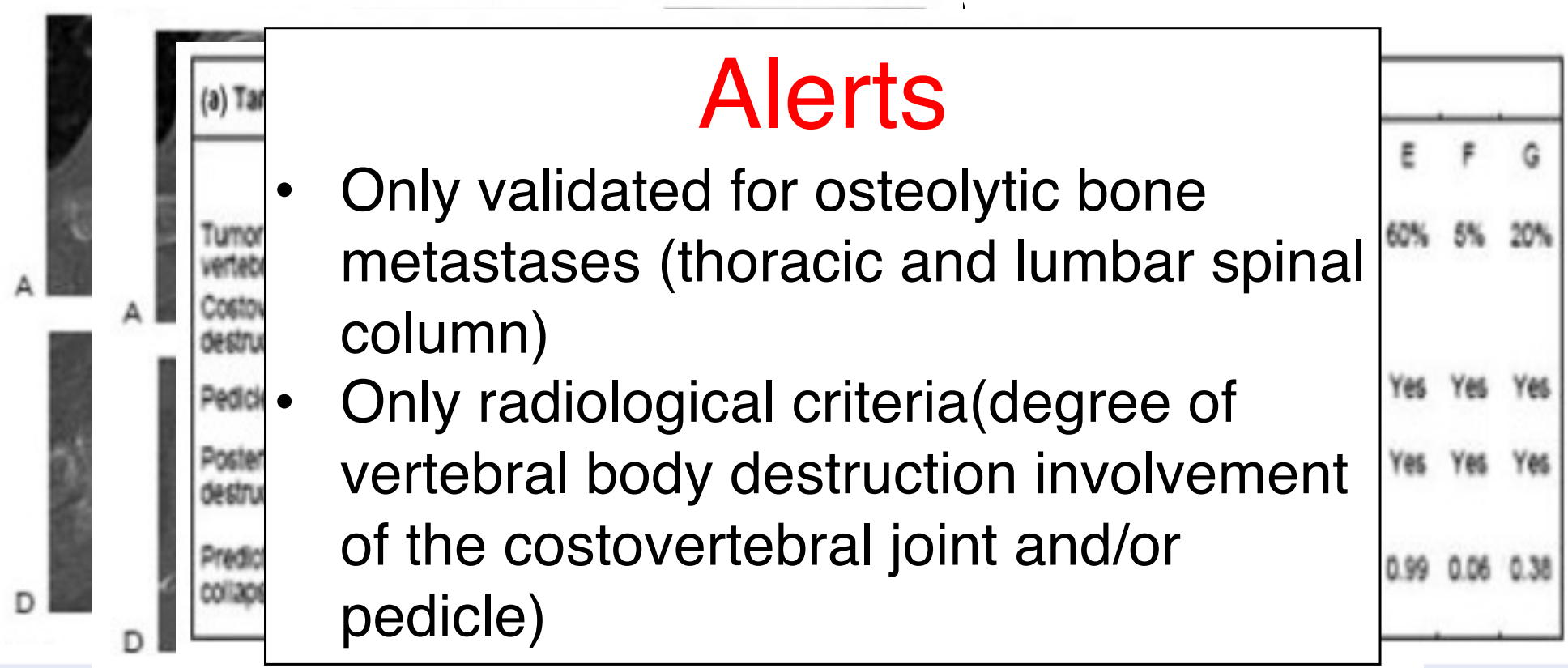
Anticipated

Instability produced by a surgical procedure that is required for proper decompression of neural elements or resection of an offending lesion.

Covert

Excessive motion cannot be grossly demonstrated but is presumed to exist based on the combination of clinical and radiographic findings

Radiological classification



Alerts

- Only validated for osteolytic bone metastases (thoracic and lumbar spinal column)
- Only radiological criteria(degree of vertebral body destruction involvement of the costovertebral joint and/or pedicle)

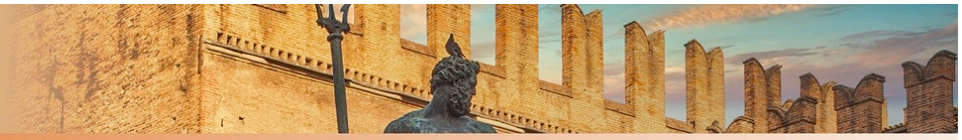
Radiomic Classification?

Diffusion-weighted MRI radiomics of spine bone tumors: feature stability and machine learning-based classification performance

Gitto et al 2022

- 101 patients with spine bone tumor (22 benign; 38 primary malignant; 41 metastatic).
- All tumor volumes were manually segmented on morphologic T2-weighted sequences.
- A total of 1702 radiomic features was considered.

The radiomic model with the best performance and the lowest number of features for classifying tumor types included 8 features. The metrics were 78% sensitivity, 68% specifcity, 76% accuracy and AUC 0.78



A Novel Classification System for Spinal Instability in Neoplastic Disease

An Evidence-Based Approach and Expert Consensus From the Spine Oncology Study Group

Fisher et al 2010

-Stable (0-6)

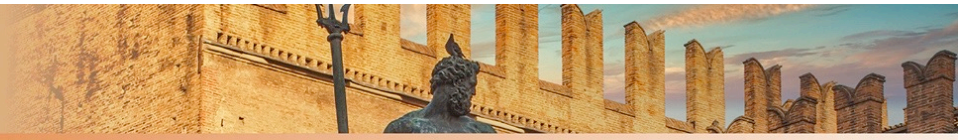
-Potentially Unstable (7-12)

-Unstable (>13)

Sensitivity: 95,7%

Specificity: 79,5%

Score	0	1	2	3	4
Instability Pain	No	Occasional pain but not instability pain	-	Yes	-
Bone lesion	Blastic	Mixed	Lytic	-	-
Location	S2-S5	T3-T10	C3-C6, L2-L4	Occiput-C2, C7-T2, T11-L1, L5-S1	-
Radiological alignment	No change	-	Kyphosis/ scoliosis	-	Subluxation/ translation present
Radiological collapse	No	No collapse but >50% vertebral body involved	<50% collapse	>50% collapse	-
Posterior spinal element involvement	No	Unilateral	-	Bilateral	-



Ten Years After SINS: Role of Surgery and Radiotherapy in the Management of Patients With Vertebral Metastases

Serratrice et al 2022

- Homogenization of literature (more than 1500 articles being published on the matter since SINS first appearance)
- SINS is a reliable tool for radiologists to evaluate tumor-related spinal instability.
- Management of spinal metastases warrants a multidisciplinary approach.

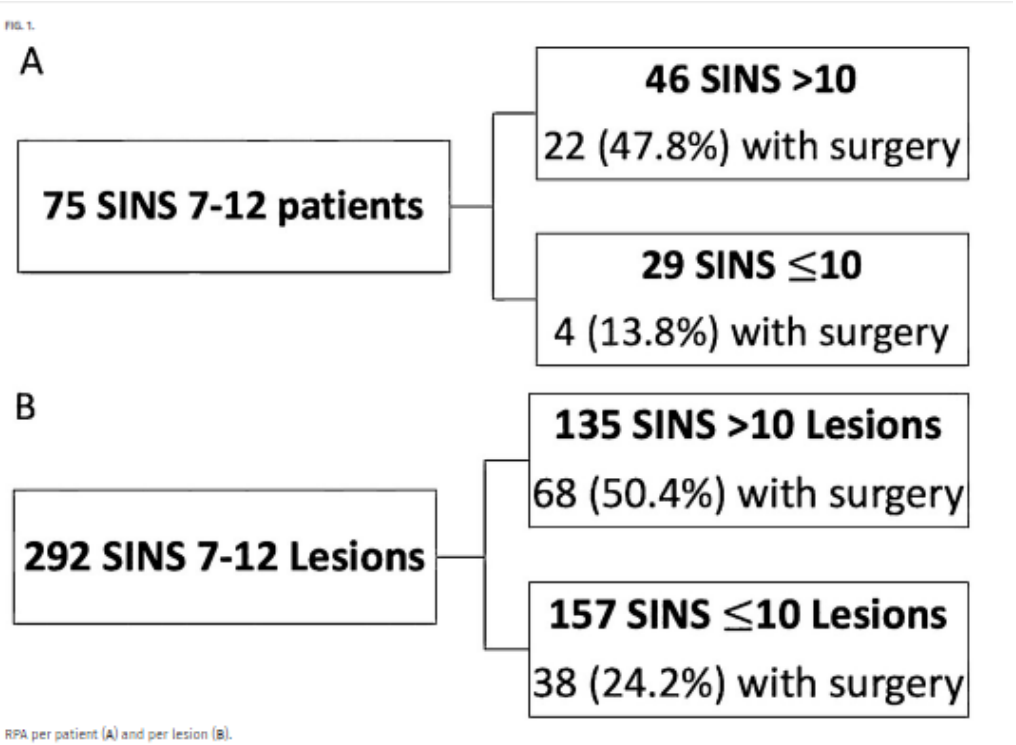
SINS Limitations

- Presence of more than one spinal lesion;
- Risk of instability increases in the junctional regions;
- Pre-existing kyphotic or scoliotic alignment disorders;
- Inaccurate in judgment of the bone matrix quality.
- Majority of patients are generally classified as **undetermined instability**.

An analysis of tumor-related potential spinal column instability (Spine Instability Neoplastic Scores 7–12) eventually requiring surgery with a 1-year follow-up

Vargas et al. 2021

- Examine the proportion of patients in this indeterminate zone who later required surgical stabilization after initial non operative management.
- No difference in age, sex, comorbidities, or lesion location between the groups.
- SINS > 11 (OR 8.09, CI 1.96-33.4, p = 0.004) and KPS) score < 60 (OR 0.94, CI 0.89-0.98, p = 0.008) associated with an increased risk of surgery.



RPA per patient (A) and per lesion (B).

SINS and Radiotherapy

Spinal instability as defined by the Spinal Instability Neoplastic Score (SINS) is associated with radiotherapy failure in metastatic spinal disease

Huisman et al 2014

- Retrospective study: relation between spinal instability (SINS) and response to radiotherapy in patients with spinal metastases.
- 38 patients with spinal metastases who were retreated after initial palliative radiotherapy were matched to 76 control patients who were not retreated.

"….a higher spinal instability score increases the risk of radiotherapy failure in patients with spinal metastases, independent of performance status, primary tumor and symptoms. **These results may support the hypothesis that metastatic spinal bone pain, predominantly caused by mechanical instability**, responds less well to radiotherapy than pain mainly resulting from local tumor activity."

SINS and Radiotherapy

Prospective Evaluation of the Relationship Between Mechanical Stability and Response to Palliative Radiotherapy for Symptomatic Spinal Metastases

Van der Velden et al 2017

- Prospective study investigating the relationship between SINS and response to radiotherapy in patients with symptomatic spinal metastases in a multi-institutional cohort.
- 124 patients: 16 patients experienced a complete response and 65 patients experienced a partial response

"A **lower SINS** is associated with a complete pain response to radiotherapy.This supports the hypothesis that pain resulting from mechanical spinal instability responds less well to radiotherapy compared with pain from local tumor activity…..**No association could be determined between SINS and an overall pain response, which might indicate that this referral tool is not yet optimal for prediction of treatment outcome**."

SINS and Radiotherapy

Spinal instability as defined by the Spinal Instability Neoplastic Score (SINS) is associated with radiotherapy failure in metastatic spinal disease

Bollen et al 2017

- Retrospective cohort study evaluating the predictive value of SINS in a cohort of patients treated with radiotherapy for spinal bone metastases
- 110 patients: 16 patients (15%) experienced an adverse event during follow-up. The cumulative incidence for the occurrence of an adverse event at 6 and 12 months was 11.8% (95%CI 5.1%-24.0%) and 14.5% (95%CI 6.9%-22.2%), respectively.

"..Competing risk analysis showed that the **final SINS classification was not significantly associated with the cumulative incidence of an adverse event** within the studied population."

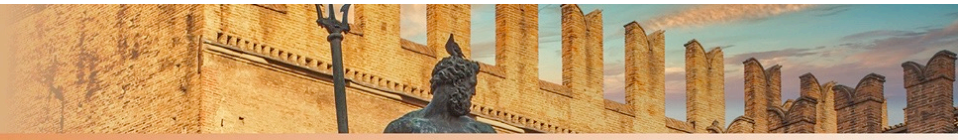


Table 2: Key determinants of the LMNOP system for spinal metastasis

L	Location	Extent of disease at symptomatic level(s): involvement of anterior and/or posterior columns
	Levels	Solitary or multilevel
M	Mechanical stability	Stable (SINS = 0-6)
		Potentially unstable (SINS = 7-12)
		Unstable (SINS = 13-18)
N	Neurology	Symptomatic epidural cord compression
O	Oncology	Highly radiosensitive
		Radiosensitive
		Radioresistant
P	Patient fitness	Medical fitness for surgery
	Prognosis	Mostly dependant on tumor type (O)
	Prior therapy	Previous radiation therapy at symptomatic levels
		Failed multiple systemic treatments

Contemporary Treatment Strategy for Spinal Metastasis: The "LMNOP" System

Gillian R. Paton, Evan Frangou, Daryl R. Fourney

- Epidural spinal cord compression (N) or mechanical instability (M): surgery depending on fitness/prognosis (P) and location/extent of disease (L).
- Mild-moderate instability (M) in absence of spinal cord compression (N): percutaneous vertebral augmentation (patients who are unfit for more extensive surgery (P), estimated survival less than 3-6 months (P) or have multiple levels of disease (L)).
- Highly radiosensitive tumors (O): external beam radiation therapy regardless of the degree of spinal cord compression (N).
- Radioresistant tumors (O) without significant cord compression (N) are offered stereotactic radiosurgery to control local tumor growth.

NEUROLOGY	Points
No deficits or Radicular Pain Complete cord damage > 72 h	0
Compressive Radicular pain without motor impairment	1
Motor radicular impairment or Mechanical radicular pain	3
Complete cord damage < 72 h	4
Incomplete cord damage Cauda Equina Syndrome	5

STABILITY	Points
SINS 0-6 (Stable)	0
SINS 7-12 (Potentially Unstable)	3
SINS 13-18 (Unstable)	5

EPIDURAL COMPRESSION ESCC scale (Bilsky scale)*	Points
Types 0-1a-1b (Bone Only Disease or impingement or deformation of the dural sac, without spinal cord compression)	0
Type 1c (Spinal cord abutment without compression)	1
Type 2 (Spinal cord compression but CSF visible)	3
Type 3 (Spinal cord compression, no CSF visible)	3

ASA	1	2	3
ECOG	0	1	2

N	
S	
E	
Total	

0-2 No surgery
3-4 Grey Zone
>5 Surgery

NSE SCORE

"The Neurology-Stability-Epidural compression assessment: a new score to establish the need for surgery in spinal metastases."
Cofano et al 2020

PALLIATIVE RADIOTHERAPY FOR BONE METASTASES: AN ASTRO EVIDENCE-BASED GUIDELINE

Lutz et al 2011

Palliative Radiotherapy for Bone Metastases: Update of an ASTRO Evidence-Based Guideline

Lutz et al 2017

"The choice of surgical decompression should be made by an interdisciplinary team that includes a neurosurgeon, with the performance status, primary tumor site, extent and distribution of metastases, and expected survival taken into account."

Table 7. Suggested inclusion and exclusion criteria for patients considered for surgical intervention for spinal cord decompression

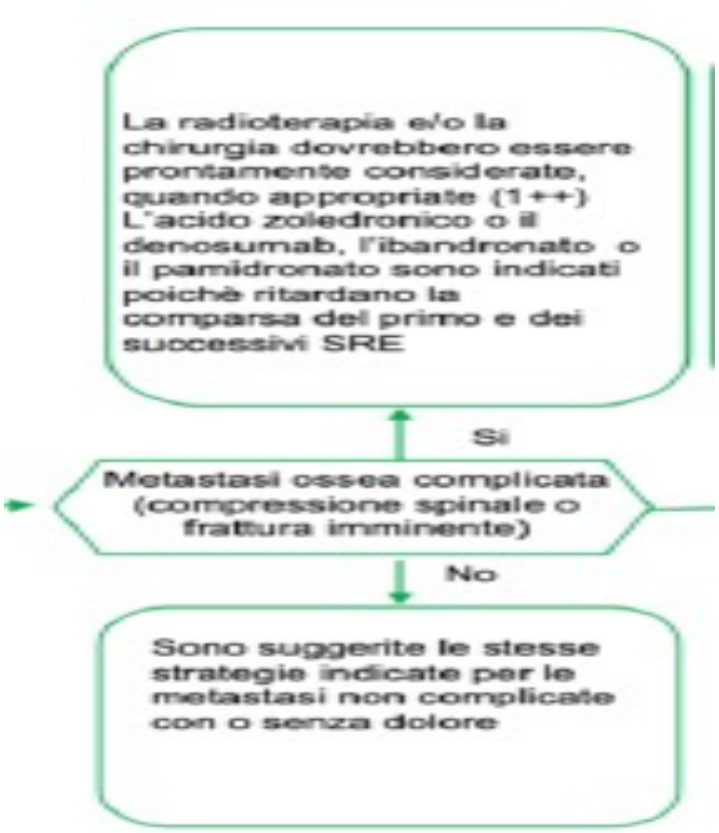
Characteristic	Factors favoring surgical decompression plus postoperative RT
Radiographic	1) Solitary site of tumor progression
	2) Absence of visceral or brain metastases
	3) Spinal instability
Patient	1) Age <65 y
	2) KPS ≥70
	3) Projected survival of >3 mo
	4) Slow progression of neurologic symptoms
	5) Maintained ambulation
	6) Nonambulatory for <48 h
Tumor	1) Relatively radioresistant tumor histologic type (*i.e.*, melanoma)
	2) Site of origin suggesting relatively indolent course (*i.e.*, prostate, breast, kidney)
Treatment	1) Previous EBRT failed

METASTASI OSSEE E SALUTE DELL'OSSO

LINEE GUIDA 2021

8.6.1. Quali sono i parametri da considerare nella scelta terapeutica del paziente con Lesioni Metastatiche al Rachide?

- le condizioni generali del paziente;
- la sensibilità dell'istotipo ai trattamenti adiuvanti;
- l'entità del danno neurologico;
- l'instabilità del rachide e il rischio di frattura patologica;
- la diffusione scheletrica e viscerale della malattia [6, 50].



Bone health in cancer: ESMO Clinical Practice Guidelines†

Coleman et al 2020

"Instability of the vertebral body may cause intractable pain and progress to neurological impairment. The Spinal Instability Neoplastic Score (SINS) uses six features of the metastasis to give a score (SINS 0e18), with higher scores indicating the more unstable lesion and need for intervention."

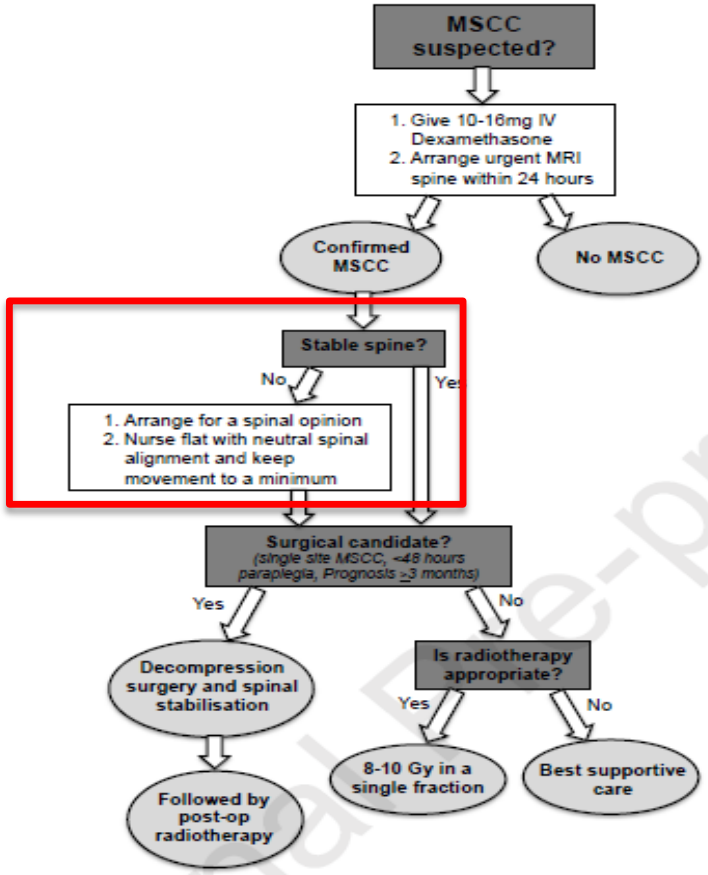
ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases

Oldenburger 2022

"To help assessment for surgery, radiotherapy or systemic therapy…"

Box 3. Key recommendations: Pathological fracture

- An increase in pain, deformity or loss of weight bearing is an indication for urgent imaging to identify pathological fracture
- Imaging includes plain x-ray but more detail is obtained with CT or MRI
- 30mm axial cortical involvement should be used for clinical evaluation of fracture risk as an alternative to Mirels
- Spinal instability should be assessed using the SINS score



Conclusions

- Spinal Instability evaluation is fundamental for the therapeutic process
- SINS score is an useful instrument in the instability evaluation
- Multidisciplinarity


Grazie per l’attenzione