



# La gestione del paziente oncologico in fase avanzata.

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# EPIDEMIOLOGIA - cenni (Coleman '01)

(Incidence of Bone Metastases)

Myeloma	(70–95%)
Renal	(20–25%)
Melanoma	(14–45%)
Bladder	(40%)
Thyroid	(60%)
Lung	(30–40%)
Breast	(65–75%)
Prostate	(65–75%)

80%

## TIPOLOGIA

LITICHE

>> eventi avversi (BUNTING '01)

SCLEROTICHE

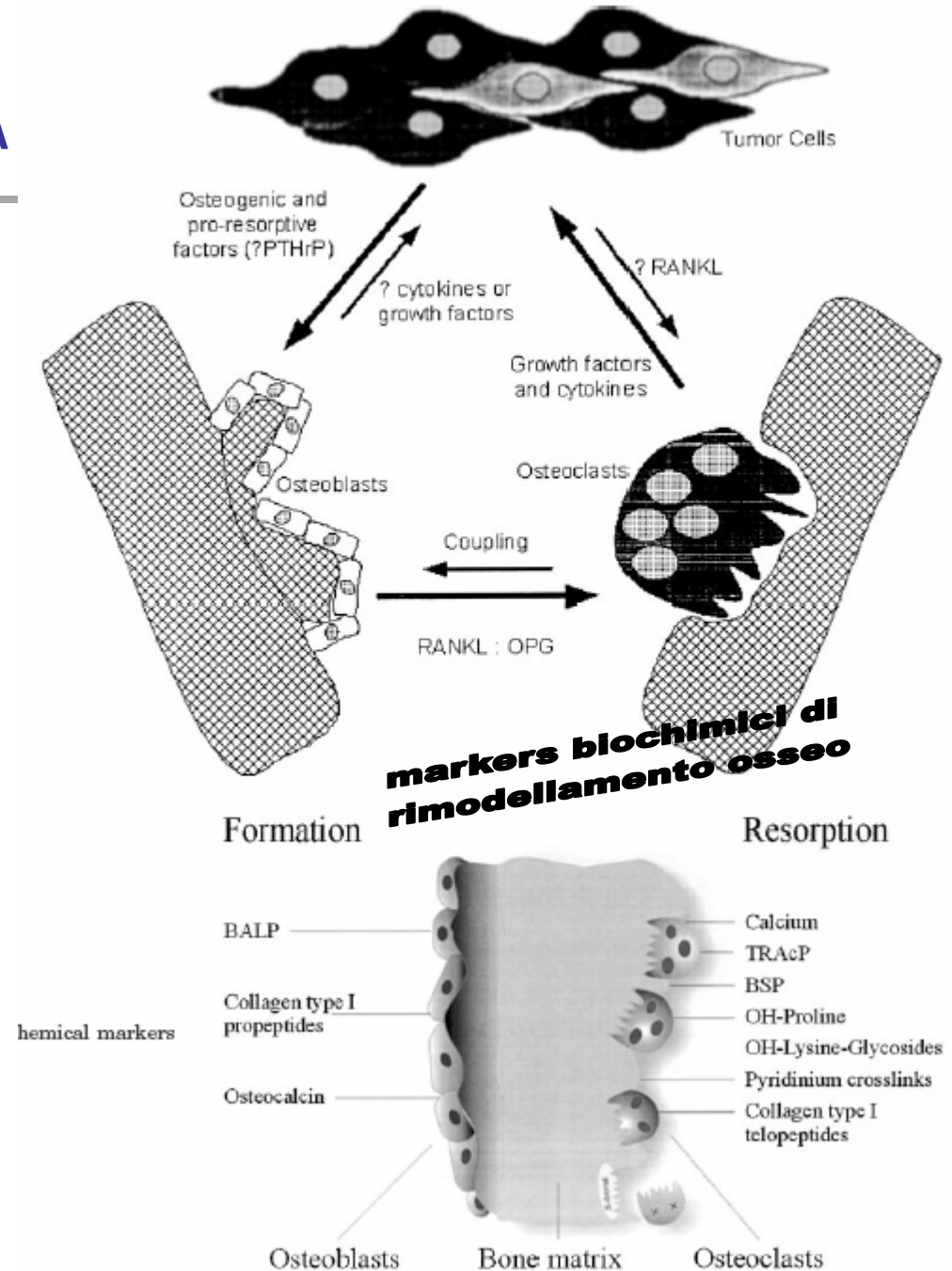
**TABLE I** Incidence, prevalence and prognosis of common solid tumours associated with metastatic bone disease—UK data (52).

Carcinoma	Annual incidence	Prevalence per annum	Deaths per annum	5-year survival (%)
Breast	26 000	105 000	16 000	64
Prostate	14 000	28 000	10 000	46
Lung	42 000	30 000	37 000	<10

# PATOFISIOLOGIA

Fohr '03

- **Caratteristiche del tessuto target**
- **Caratteristiche biologiche del tessuto tumorale**
  - **Ca mammario: PrPTH, + recettori per gli steroidi, buona Differenziazione**
  - **Ca prostata: scarsa differenziazione**
- **Terapia antitumorale**



# DIAGNOSI ED EVOLUZIONE

- Clinica:
  - SINTOMI: dolore, fratture, anemizzazione ...
  - ESAMI EMATOCHIM: ipercalcemia, PTH, fosfatasi alcalina...
- Strumentale:

	<b>SENSIBILITA'</b>	<b>SPECIFICITA'</b>	<b>VALORE PREDITTIVO POSITIVO</b>	<b>VALORE PREDITTIVO NEGATIVO</b>
<b>RX</b>	44-81	78	34	93
<b>SPECT (<sup>99</sup>Tc)</b>	62-98.2	95.2	72.8	99.8
<b>PET</b>	73-92	88-99	46-92	97-99
<b>TAC</b>	71-100			
<b>RMN</b>	82-100	73-100		

# DIAGNOSI ED EVOLUZIONE

## Quale ruolo per markers biochimici

TABLE 2  
Biochemical Evidence of Increased Bone Resorption in Solid Tumors<sup>a</sup> (Coleman, '01)

	Breast (n = 29)	Prostate (n = 10)	Other (n = 7)
Ntx	→ 2.55	→ 7.61 ←	→ 3.19
Crosslaps	1.84	4.93	2.86
Free Dpd	2.22	3.19	2.47
Hydroxyproline	1.66	2.92	2.27
Urinary calcium	0.78	1.77	2.46

<sup>a</sup>Data are expressed as ratios of the mean value in patients to the mean value in age- and gender-matched controls. Ntx: N-terminal telopeptide of type I collagen. Dpd: deoxydipicolinate.

Fosfatasi alcalina

Crosslinks del piridinio

Ntx: N-telopeptide del collagene di tipo I (urine)

Table 3. Relative risks (RRs) and 95% confidence intervals (CIs) associated with negative outcomes for patients with prostate cancer, non-small-cell lung cancer (NSCLC), and other solid tumors considered separately and together, according to bone marker level category

Outcome	Prostate cancer			NSCLC and other solid tumors			Total patient population		
	RR	95% CI	P	RR	95% CI	P	RR	95% CI	P
<b>Baseline N-telopeptide</b>									
SRE	1.57	1.09 to 2.26	.015	1.62	0.96 to 2.74	.073	1.59	1.17 to 2.14	.003
Time to first SRE	1.72	1.15 to 2.57	.008	1.85	1.08 to 3.18	.026	1.76	1.28 to 2.44	.001
Disease progression	1.56	1.13 to 2.15	.006	1.76	1.06 to 2.93	.029	1.60	1.22 to 2.11	.001
Death	2.40	1.73 to 3.33	<.001	3.03	2.06 to 4.46	<.001	2.65	2.06 to 3.42	<.001
<b>On-study N-telopeptide</b>									
SRE	3.25	2.26 to 4.68	<.001	1.79	1.15 to 2.79	.010	2.54	1.95 to 3.32	<.001
Time to first SRE	3.05	1.96 to 4.72	<.001	1.97	1.22 to 3.20	.006	2.53	1.84 to 3.47	<.001
Disease progression	2.02	1.48 to 2.74	<.001	1.91	1.16 to 3.15	.011	1.99	1.53 to 2.58	<.001
Death	4.59	2.82 to 7.46	<.001	2.67	1.85 to 3.85	<.001	3.29	2.49 to 4.36	<.001
<b>Baseline bone-specific alkaline phosphatase</b>									
SRE	1.85	1.15 to 2.98	.012	1.32	0.92 to 1.89	.135	1.50	1.14 to 1.99	.004
Time to first SRE	1.88	1.11 to 3.18	.018	1.49	1.02 to 2.17	.041	1.62	1.20 to 2.19	.002
Disease progression	1.27	0.88 to 1.83	.205	1.77	1.19 to 2.64	.005	1.49	1.13 to 1.96	.004
Death	1.83	1.19 to 2.83	.006	1.53	1.15 to 2.03	.003	1.62	1.28 to 2.04	<.001
<b>On-study bone-specific alkaline phosphatase</b>									
SRE	3.03	1.67 to 5.51	<.001	1.87	1.30 to 2.69	.001	2.20	1.63 to 2.96	<.001
Time to first SRE	3.10	1.66 to 5.81	<.001	1.83	1.23 to 2.70	.003	2.16	1.57 to 2.97	<.001
Disease progression	1.64	1.09 to 2.48	.018	2.01	1.31 to 3.10	.001	1.81	1.34 to 2.45	<.001
Death	3.19	1.58 to 6.42	.001	1.79	1.30 to 2.46	<.001	2.02	1.52 to 2.67	<.001

<sup>a</sup>High bone-specific alkaline phosphatase ( $\geq 146$  IU/L) versus low bone-specific alkaline phosphatase ( $< 146$  IU/L) levels. Referent group = patients in the low-level category.

(Brown et al, '05)



# PROGNOSI E DECORSO CLINICO

Sopravvivenza mediana in soggetti con malattia avanzata

	<b>Esclusivamente Metastasi ossee</b>	<b>Metastasi ossee + altre sedi</b>
<b>Cancro prostata</b>	<b>53 mesi</b>	<b>30 mesi</b>
<b>Cancro della mammella</b>	<b>25 mesi</b>	<b>18 mesi</b>
<b>Cancro del polmone</b>	<b>3-6 mesi</b>	
<b>Mieloma multiplo</b>	<b>24-36 mesi</b>	

(Coleman '01)

# PROGNOSI E DECORSO CLINICO

**TABLE 4**  
Well-Established Prognostic Factors in Metastatic Bone Disease<sup>a</sup>

Prostate	Myeloma	Breast
Skeletal distribution	$\beta_2$ -microglobulin	Extraosseus disease
Performance status	Proliferative activity	Disease free interval
Extraosseous disease	C-reactive protein	Performance status
Alkaline phosphatase	Immunologic phenotype	Estrogen receptor status
Hemoglobin	LDH	Age
PSA fall	Serum creatinine	Histologic grade
	Hypercalcemia	

PSA: prostate specific antigen; LDH: lactate dehydrogenase.

<sup>a</sup>Data from Coleman et al.,<sup>10</sup> Eisenberger et al.,<sup>12</sup> and Kyle and Blade.<sup>13</sup>

**FATTORI PREDITTIVI  
DI EVOLUZIONE DELLA  
MALATTIA  
METASTATICA OSSEA**

**TABLE 3**  
Evolution of Bone Metastases in **Breast Carcinoma**, Showing Factors That Predict for Disease Remaining Confined to the Skeleton<sup>a</sup>

	Bone only (n = 139)	Bone + other sites (n = 228)	P value
Postmenopausal	63% ←←←	43%	0.0002
Lymph node negative	29% ←←←	18%	0.02
Lobular	21% ←←←	12%	0.04
Premenopausal	24%	37%	0.009
<4 lymph nodes positive	16%	30%	0.001
Grade 3	19%	32%	0.001

<sup>a</sup>Data from Coleman et al.<sup>10</sup>

**FATTORI ASSOCIATI  
ALLA  
LOCALIZZAZIONE  
DELLE METASTASI NEL  
CA MAMMARIO**

# DECORSO CLINICO

## COMPLICANZE delle METASTASI OSSEE

**TABLE 6**  
Frequency of Major Complications of Skeletal Involvement<sup>a</sup>

Complication	No. (%) of patients
Hypercalcemia of malignancy	70 (19%)
Pathologic fracture of a long bone	68 (19%)
Spinal cord compression	36 (10%)
Bone marrow failure/leukoerythroblastic anemia	33 (9%)

<sup>a</sup>Data from Coleman et al.<sup>10</sup> (Ca mammario)

**+ DOLORE**

(10% DELLE INSTABILITÀ SPINALI  
SONO CAUSA DI DOLORE ALLA  
SCHIENA)

**Table 2.** Number of skeletal-related events (SREs) among patients with prostate cancer, non-small-cell lung cancer (NSCLC), or other solid tumors enrolled in the placebo arms of two randomized trials of zoledronic acid to treat bone metastases\*

Category	Prostate cancer	NSCLC and other solid tumors			(441 100%) Total patient population
		Overall	NSCLC	Other solid tumors	
All pathologic fractures	73	70	30	40	143 <b>32%</b>
Vertebral fractures	24	34	19	15	58 <b>13%</b>
Nonvertebral fractures	49	36	11	25	85 <b>19%</b>
Radiotherapy to bone	110	130	69	61	240 <b>54%</b>
Surgery to bone	11	13	4	9	24 <b>5.4%</b>
Spinal cord compression	19	10	7	3	29 <b>6.5%</b>
Change in antineoplastic therapy	18	—	—	—	18 <b>4%</b>
Total No. of SREs	231	223	110	113	454 <b>103%</b>

(Brown et al, '05)





# TERAPIA

TERAPIA	INDICAZIONI	SCOPO	NOTE
CHIRURGICA	<ul style="list-style-type: none"> <li>■ frattura</li> <li>■ Rischio di frattura</li> <li>■ Mielopatia</li> </ul>	<ul style="list-style-type: none"> <li>■ CONTROLLO LOCALE</li> <li>■ PALLIAZIONE</li> </ul>	Condizioni generali, Aspettativa di vita, N° metastasi ossee, Altri siti coinvolti, Stato e rischio di frattura, Rischio di mielopatia
RADIOTERAPIA (Selvaggi et al '03)	<ul style="list-style-type: none"> <li>■ Dolore</li> <li>■ frattura o Rischio</li> <li>■ Mielopatia</li> <li>■ associazione con chirurgia</li> <li>■ non chirurgica</li> </ul>	<ul style="list-style-type: none"> <li>■ CONTROLLO LOCALE</li> <li>■ PALLIAZIONE</li> </ul>	
RADIOFARMACEUTICA	<ul style="list-style-type: none"> <li>■ dolore</li> </ul>	<ul style="list-style-type: none"> <li>■ PALLIAZIONE</li> </ul>	
FARMACOLOGICA ■ ANTITUMORALE ■ BIFOSFONATI	<ul style="list-style-type: none"> <li>■ Prevenzione dell'evoluzione o peggioramento</li> <li>■ trattamento di un peggioramento</li> <li>■ dolore</li> </ul>	<ul style="list-style-type: none"> <li>■ CONTROLLO LOCALE</li> <li>■ PALLIAZIONE</li> </ul>	
ALTERNATIVA ■ RIABILITAZIONE ■ SUPPORTO PSICOLOGICO ■ NURSING	<ul style="list-style-type: none"> <li>■ periodo di mantenimento</li> <li>■ Trattamento fase ACUTA post chirurgica</li> <li>■ Trattamento lesioni non operabili</li> </ul>	<ul style="list-style-type: none"> <li>■ Promozione salute,</li> <li>■ benessere psico-fisico</li> <li>■ RECUPERO Funzionale</li> <li>■ Prevenzione complicanze</li> <li>■ PALLIAZION</li> </ul>	<b>SETTING TIMING MODALITA' DIFFERENTI</b>

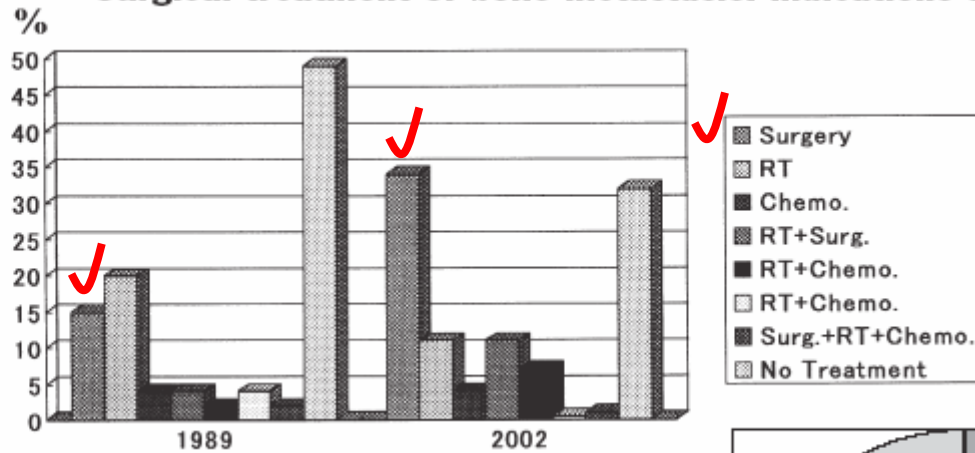
# Terapia chirurgica

REVIEW ARTICLE

Jun Manabe · Noriyoshi Kawaguchi · Seiichi Matsumoto  
Taisuke Tanizawa

## Surgical treatment of bone metastasis: indications and outcomes

Fig. 1. Changes in treatment modalities for bone metastasis (Bone Tumor Registry in Japan). RT, radiotherapy; chemo, chemotherapy

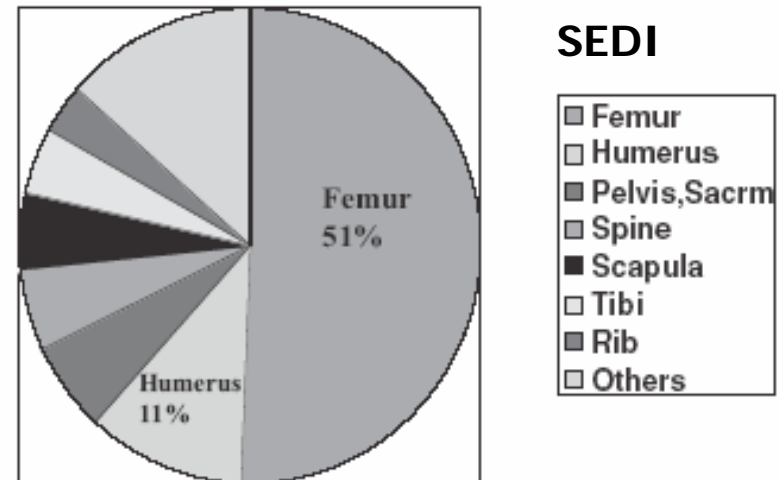


### TUMORI PRIMITIVI

Table 1. Patients with surgery for bone metastases at the Cancer Institute Hospital (CIH)\*

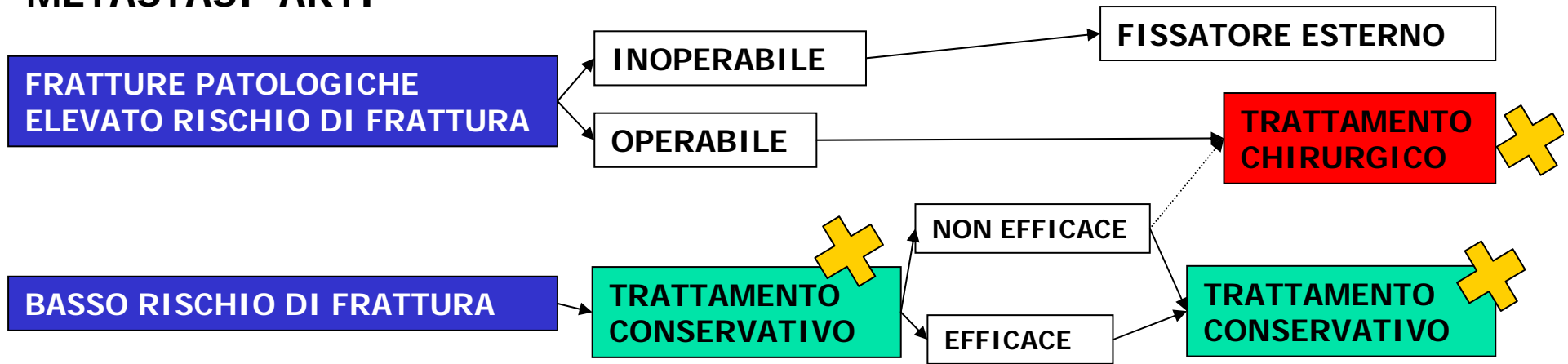
Primary tumor (n)			
Breast Ca.	52	Renal Ca.	39
Lung Ca.	34	Lymphoma	16
Liver Ca.	14	Thyroid Ca.	13
Sarcoma	9	Colon Ca.	6
Unknown	10	Others	39

\*Between 1980 and 2002, 220 patients were treated (115 males and 105 females; age, 4-86 years; mean age 64 years)

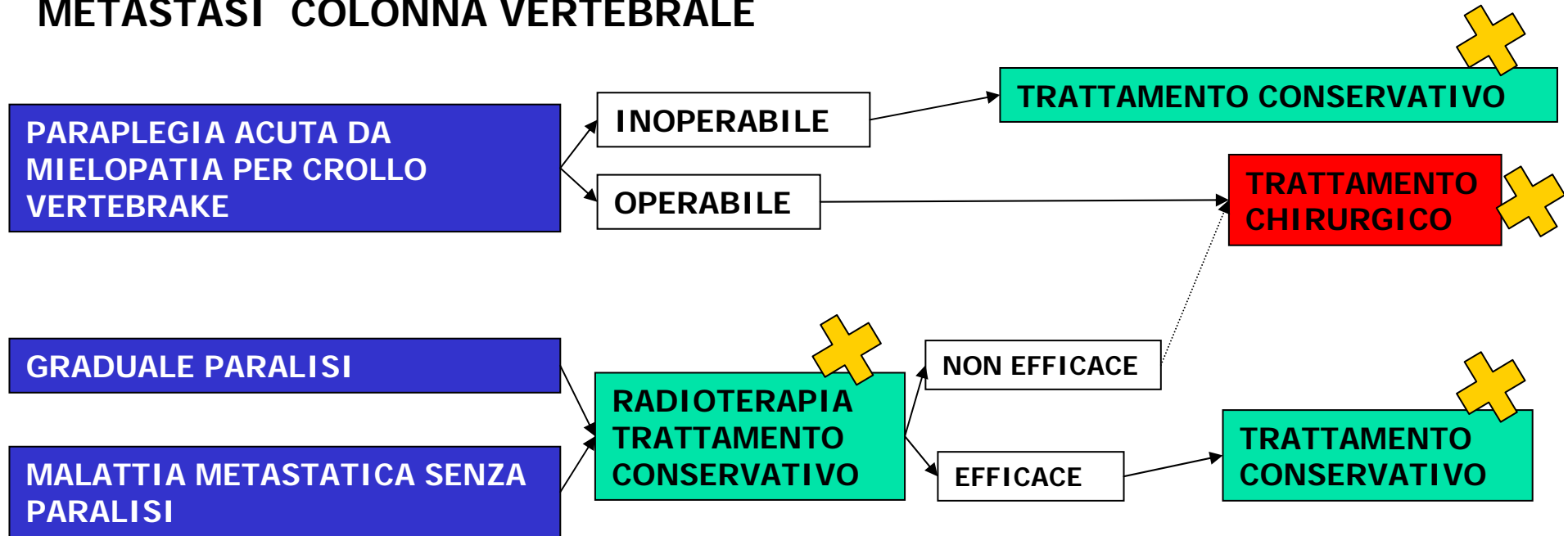


### SEDI

## METASTASI ARTI



## METASTASI COLONNA VERTEBRALE



**+ RIABILITAZIONE**

(Manabe et al '05)



# TERAPIA - riabilitazione

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- Obiettivi della fase avanzata:
  - Gestione fase acuta della complicate: es. riabilitazione post-chirurgica
  - Gestione problematiche emergenti durante terapie palliative: conseguenze immobilizzazione, fatica, ..
  
- Monitoraggio funzionale
- Conservazione autonomia e mobilità
- Promozione
  - salute
  - attività vocazionali
- Integrazione sociale
  
- Prevenzione complicanze terziarie da ipomobilità in fase terminale

***durante  
terapie***

***post-  
trattamento***

# TERAPIA - riabilitazione

SCENARIO	OBIETTIVO	SETTING	TIMING	Modalita'	Referenze
<p><b>MALATTIA METASTATICA SENZA EVIDENTE RISCHIO DI FRATTURA imminente</b></p>	<p><b>LUNGO TERMINE:</b> Conservazione - ottimizzazione funzionale globale (indipendenza nelle adl) e abil. selettiva: destrezza, cammino, Promozione salute: fitness Promozione attività vocazionali e sociali</p>	<p>ambulatoriale Home-based</p>	<p>Estensivo</p>	<p>Trattamenti multidisciplinare (intervento cognitivo, emotivo fisico sociale spirituale) FKT =</p> <ul style="list-style-type: none"> <li>■ Mobilizzazione attiva</li> <li>■ Attività aerobica</li> <li>■ Ginnastica respiratoria</li> <li>■ Qicong – Tai Qi</li> <li>■ ? Prescrizione Ortesi</li> </ul>	<p>Schmitz '05 Rummans '06</p>

# TERAPIA - riabilitazione

SCENARIO	OBIETTIVO	SETTING	TIMING	REFERENZA	
PERIODO POST CHIRURGICO RIPARAZIONE LESIONE MIELICA COLONNA	<b>BREVE-MEDIO TERMINE</b> recupero condizione precedente l'evento acuto: - funzionale globale (indipendenza nelle ...	DEGENZA	Intensivo - estensivo a seconda dei fattori prognostici	D unche) ✓ Protocolli intensivi neuromotori: ✓ training del cammino .... Precoce con ORTESI ✓ Training ai corretti cambi posturali ✓ Training all'uso di ausili ed ortesi	Narazachi '06 Coleman '03

**FATTORI PREDITTIVI Dell'OUTCOME FUNZIONALE:**

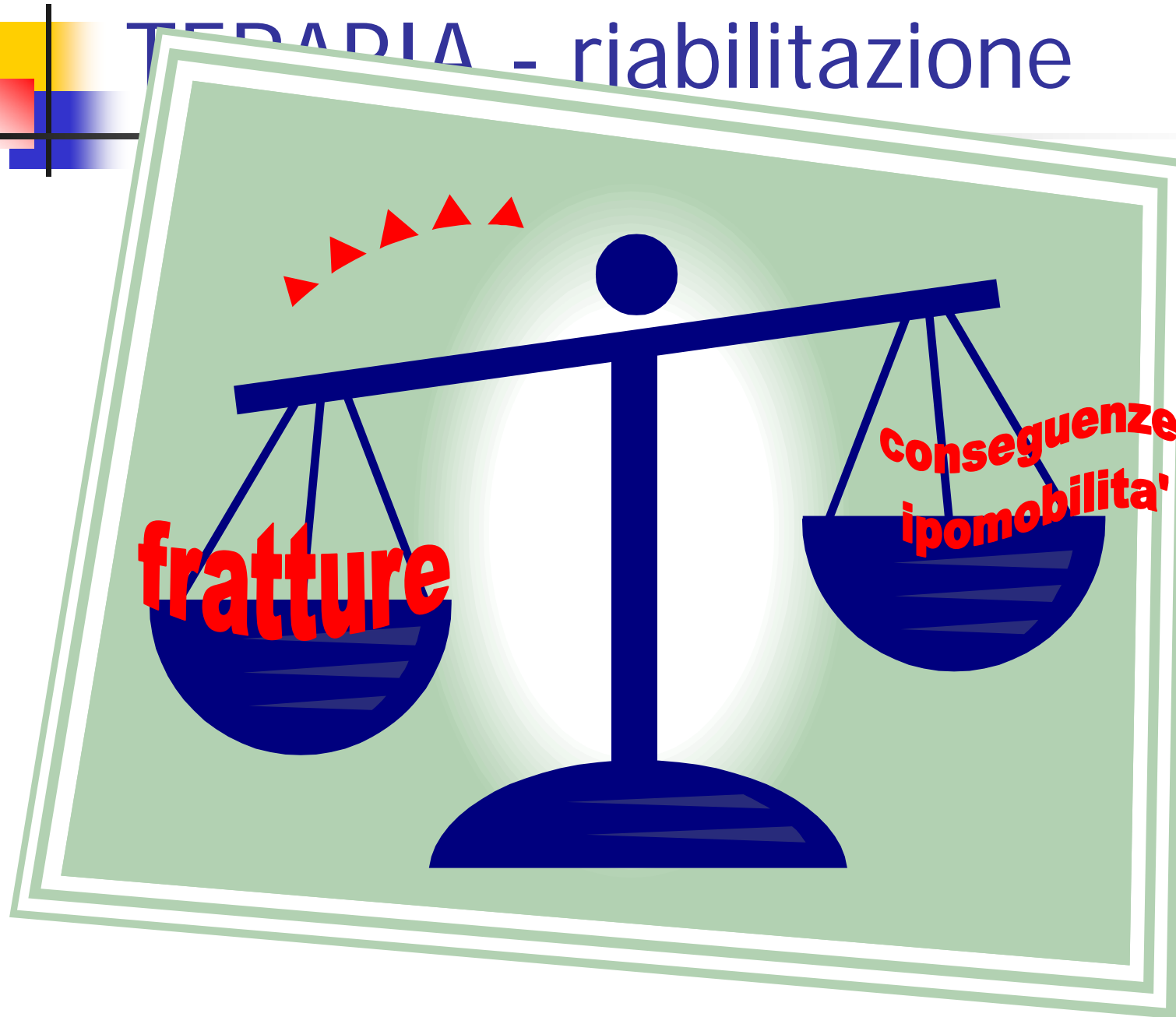
- Dg precoce
- Ter. Corticosteroidea
- Decompressoine urgente Per via chirurgica o radiante e stabilizzazione
- Recupero clinico-funzionale entro 48 ore

**ORTESI PER LA COLONNA:**

- SIGNIFICATO FUNZIONALE: PREVENZIONE E CONTENIMENTO DEL DOLORE
- NELLA FASE ACUTA,
- POST CHIRURGICA,
- DURANTE E DOPO TRATTAMENTO RADIANTE PALLIATIVO

•Non influenza lioutcome a lungo termine (Schen '99)

# TERAPIA - riabilitazione





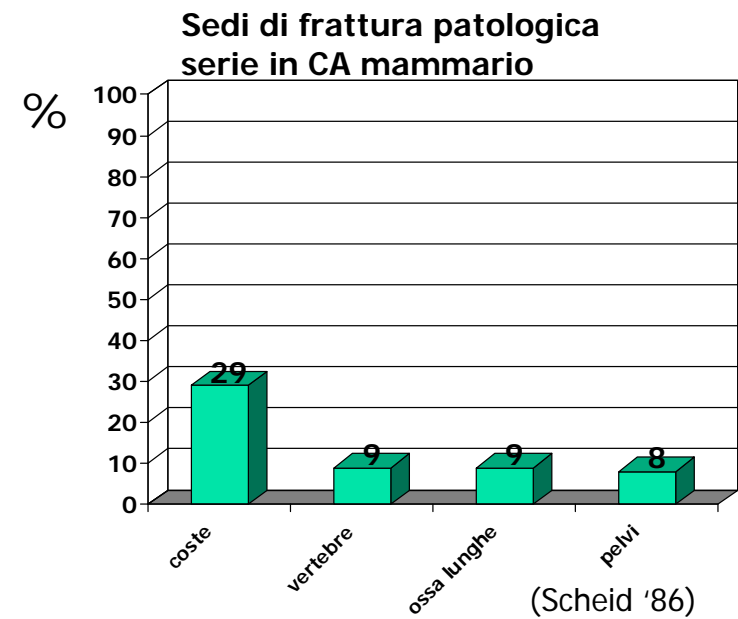
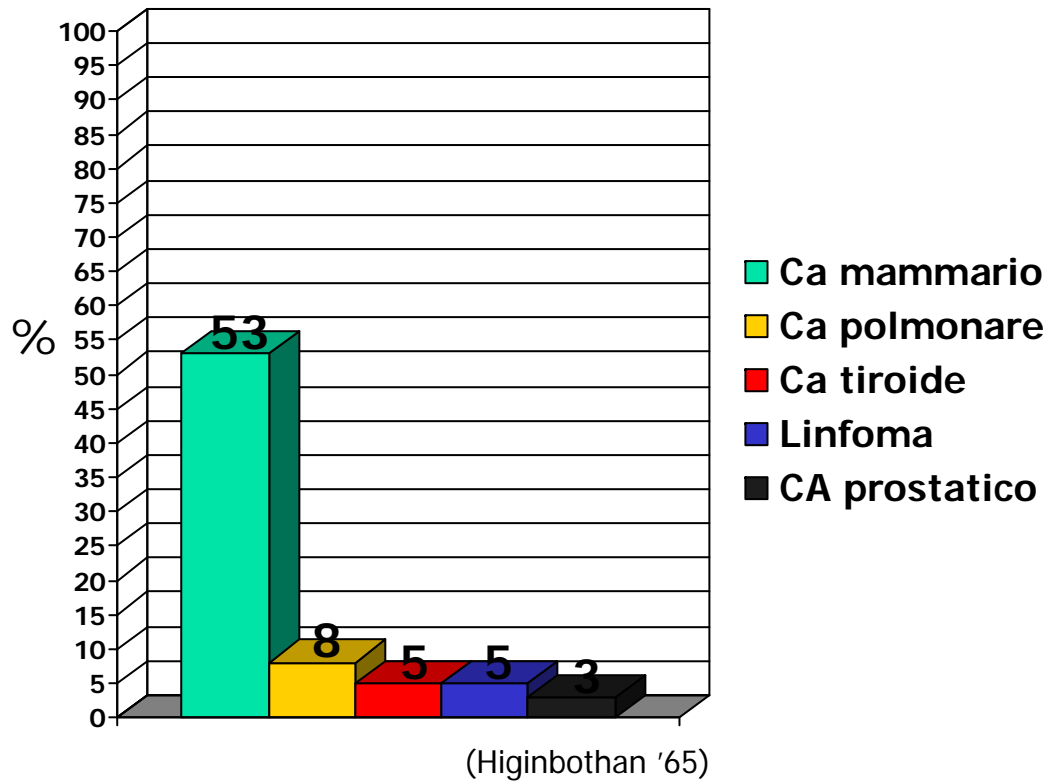
# TERAPIA – riabilitazione (Bunting '01)

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- Alcune linee guida generali per il paziente con malattia metastatica dell'osso:
  - ESAME OBIETTIVO del segmento affetto:
    - NO test forza muscolare
    - NO ROM passivo o attivo
    - Si' movimenti attivi
  - TRATTAMENTO:
    - NO esercizi contro resistenza
    - NO percussione o vibrazione del torace



# COMPLICANZE – FRATTURE (prevalenza)



COMPLICANZE DELLE METASTASI OSSEE –

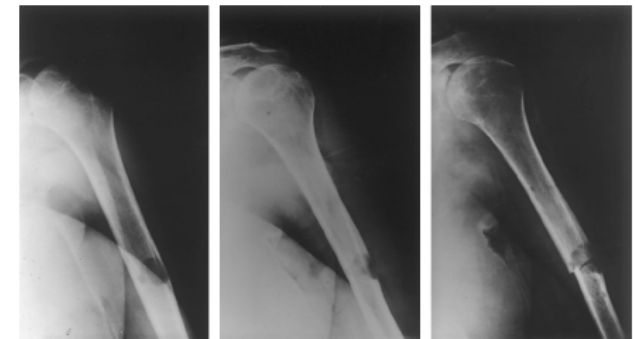
# FRATTURE (VALUTAZIONE DEL RISCHIO)

AUTORE	CRITERIO principale	MISURA	Cut-off
Snell & Beals '64	Dimensione (corollari: dolore, tipologia, coinvolgimento corticale)	<b>Dimensione assoluta della lesione</b>	1 inch (=2.56 cm)
Fidler '73, '81	Dimensione	<b>Percentuale della corteccia coinvolta</b>	50%
Mireles '89	SEDE <b>DOLORE</b> DIMENSIONE TIPOLOGIA	PUNTEGGIO 1 – 3 AD OGNI ITEMs (max 12)	> 7 = PEGGIORE PROGNOSI



FIGURE 2. A punched-out lytic lesion of the femur is shown in a female age 76 years with breast cancer.

**LA MALATTIA METASTATICA  
è EVOLUTIVA**



**Criteria non affidabili (Hipp '95, Van der Linden '04)  
e non applicabili alla colonna**

# FRATTURE (VALUTAZIONE DEL RISCHIO)

AUTORE	CRITERIO principale	MISURA	Cut-off
Brown et al'05	Biochimico	<b>[Ntelopeptide] urinario</b>	> 100 nmol/mmol creatinina
Roth '04	Caratteristiche biomeccaniche (colonna)	<b>Parametri indicativi della capacità di sostenere il peso (TAC)</b>	
Spruijt' 06	Caratteristiche biomeccaniche (ossa lunghe)	<b>Parametri indicativi della capacità di sostenere il peso (TAC) mediante ricostruzione tridimensionale</b>	

COMPLICANZE DELLE METASTASI OSSEE –

# FRATTURE (VALUTAZIONE DEL RISCHIO)

## Pathologic Fracture Risk in Rehabilitation of Patients with Bony Metastases

ROBERT BUNTING, M.D., WENDY LAMONT-HAVERS, R.P.T.,  
DONNA SCHWEON, R.P.T., AND ALLAN KLIMAN, M.D.

STUDIO PROSPETTICO, non controllato		
Pazienti	54 consecutivi per la riabilitazione	<ul style="list-style-type: none"><li>■14 esiti di mielopatia compressiva</li><li>■12 decondizionamento</li><li>■11 esiti di patologia vertebrale senza mielopatia</li><li>■7 chirurgia di fratture patologiche</li><li>■10 altro</li></ul>
RIABILITAZIONE		
Setting	Degenti ospedale per acuti	
Timing	1 volta/giorno x 5 giorni alla settimana	
Obiettivo	Recupero funzionale, indipendenza funzionale (destrezza e deambulazione)	
Modalità	Multidisciplinare (training della deambulazione)	
Fattori prognostici valutati		
età, sesso, tumore primitivo, terapia per il tumore primitivo o per fratture patologiche, uso di ortesi, tipologia delle lesioni ossee, massima mobilità all'ingresso, n° sedi ossee coinvolte.		

# Pathologic Fracture Risk in Rehabilitation of Patients with Bony Metastases

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Number 192  
January-February, 1985

Fracture Risk with Bony Metastases 223

TABLE 1. Summary of Patients

Patient	Sex	Age	Primary Cancer	Activity at the Time of Fracture	Site of Fracture
1	F	60	Breast	1. Fell out of bed 2. Unknown 3. Rolling in bed	1. Left humerus 2. Right humerus 3. Rib
2	F	57	Lung	Unknown	Further compression, L2-4
3	F	52	Breast	Rolling in bed	Rib
4	F	42	Lung	Unknown	Further compression T9
5	F	91	Multiple myeloma	1. Unknown 2. Unknown 3. Unknown	1. Further compression, L1-4 2. Further compression, dorsal spine 3. Left knee
6	F	49	Breast	Rolling in bed	Right femur
7	F	61	Multiple myeloma	Sit-stand transfer	Left humerus
8	F	58	Breast	Lying in bed	Right humerus
9	F	58	Breast	Unknown	Rib
10	F	72	Lung	Lying in bed	Left humerus
11	M	69	Multiple myeloma	Unknown	Further compression, lumbar spine
12	F	43	Breast	Sliding-board transfer	Further compression, L4

FRATTURE (N°)	Attività eseguita	sede
1	riabilitazione	1 VERTEBRA
8	? (fratture silenti)	5 VERTEBRA, 1 OMERO 1 GINOCCHIO, 1 COSTA
6	letto	2 COSTE 1 OMERO 1 FEMORE
1	passaggio posturale	2 OMERO
<b>TOT: 16 (IN 12 PATIENTI)</b>		<b>6 VERTEBRA 4 OMERO 4 COSTE 1 FEMORE 1 GINOCCHIO</b>

# Pathologic Fracture Risk in Rehabilitation of Patients with Bony Metastases

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Clinical Orthopaedics  
and Related Research

TABLE 2. Medical Parameters

	<i>Fracture Patients</i>	<i>Nonfracture Patients</i>	
Sex	M (1) F (11)	M (16) F (26)	<b>n.s.</b>
Age	<b>59.3 ± 12.9 years</b> (range, 42–91)	69.3 ± 10.6 years (range 52–90)	<b>&lt;.05</b>
Site of primary cancer	Breast (6) Lung (3) Multiple myeloma (3)	Breast (15) Lung (4) Multiple myeloma (3) Prostate (4) Kidney (2) Endometrium (2) Other (12)	<b>&lt;.01</b> ↑ MM Ca Polmone Ca mammella
Previous treatment for primary cancer	Chemotherapy (9) (75%) Surgery (4) (33.3%) Radiation (5) (41.7%) None (1) (8.3%)	Chemotherapy (28) (66.6%) Surgery (22) (52.4%) Radiation (11) (26.1%) None (4) (9.5%)	<b>n.s.</b>

The number of patients is in parentheses.

# Pathologic Fracture Risk in Rehabilitation of Patients with Bony Metastases

ROBERT BUNTING, M.D., WENDY LAMONT-HAVERS, R.P.T.,  
DONNA SCHWEON, R.P.T., AND ALLAN KLIMAN, M.D.

Number 192  
January-February, 1985

Fracture Risk with Bony Metastases 225

TABLE 3. Orthopaedic Parameters

	<i>Fracture Patients</i>	<i>Nonfracture Patients</i>
Previous treatment for pathologic fracture		
No previous episode	5 (41.6%)	21 (50%)
One fracture	4 (33.3%)	18 (42.9%)
More than one fracture	3 (25%)	3 (7.1%)
Number of metastatic sites	6.3 ± 3.3 (range, 1-11)	4.3 ± 2.8 (range, 1-16)
Lytic <i>versus</i> blastic lesions		
Lytic	6 (50%)	16 (38%)
Mixed lytic and blastic	3 (25%)	6 (14.3%)
Blastic	0 (0%)	7 (16.7%)
Not available	3 (25%)	13 (31%)

Risultati dell'analisi  
statistica

**n.s.**

**<.01**

**<.05**

# Pathologic Fracture Risk in Rehabilitation of Patients with Bony Metastases

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DONNA SCHWEON, R.P.T., AND ALLAN KLIMAN, M.D.

TABLE 4. Rehabilitation Parameters

	<i>Fracture Patients</i>	<i>Nonfracture Patients</i>
<b>Maximal mobility</b>		
Ambulation without a device	0 (0%)	11 (23.8%)
Ambulation with a device	9 (23.8%)	21 (50%)
Wheelchair	3 (25%)	10 (23.8%)
Use of orthotic device	4 (33.3%)	7 (16.6%)
Positive ability to follow directions	11 (91.7%)	38 (90.5%)
<b>Outcome</b>		
Home	2 (16.7%)	12 (28.6%)
Another facility	5 (41.7%)	6 (14.3%)
Expired	3 (25%)	24 (57.1%)
In house	2 (16.7%)	0 (0%)

Risultati dell'analisi  
statistica

**n.s.**

**n.s.**

**n.s.**





## COMPLICANZE - IPERCALCEMIA

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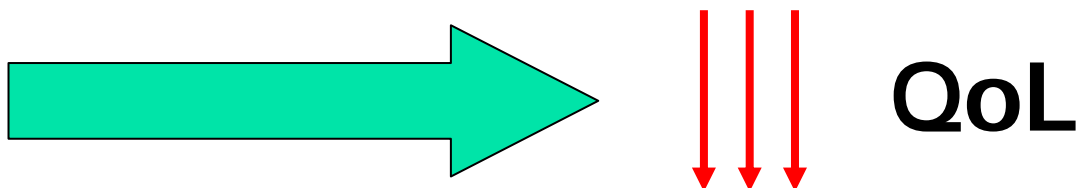
- Complicanza metabolica più frequente
- Moderata – severa = [Calcio] > 3.0mmol/l)
- Causa disfunzioni gastroenteriche e cardio vascolari >>>> morte
- Tumori a rischio: Ca a cellule squamose del polmone, adenoCa di mammella e rene, mielomi e linfomi
- Terapia = bifosfonati e.v.



## COMPLICANZE - DOLORE

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- Complicanza frequente,
- sintomo d'esordio
- EZIOPATOGENESI:
  - Biologica: citochine ed altri mediatori chimici
  - Meccanica: compressione, invasione
- Localizzato, riflesso, drug-resistant, notturno,
- Associato ad ansia e depressione

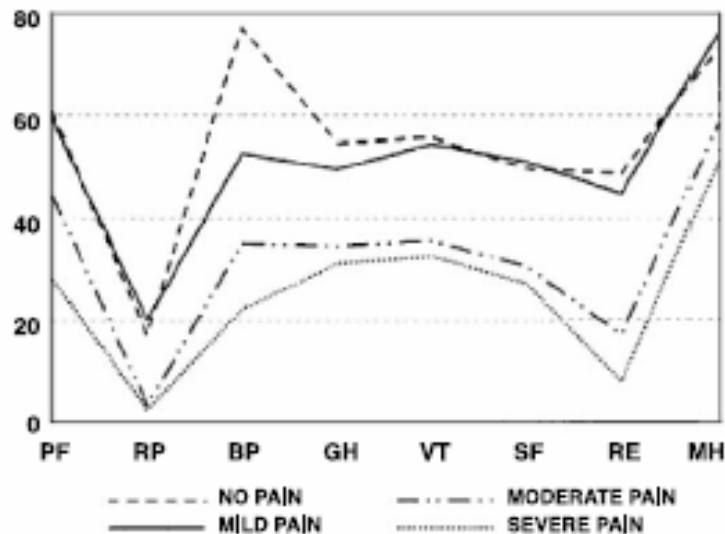


## COMPLICANZE DELLE METASTASI OSSEE –

# DOLORE

La correlazione con la funzione non è lineare

SF-36



Mean SF-36-C (Medical Outcomes Study 36-Item Short-Form Health Survey, Chinese translation) subscale scores are shown by pain severity level.

**PF = physical functioning;**

**RP = role limitations caused by physical problems,**

**BP = bodily pain;**

**GH = general health perceptions;**

**VT = vitality; SF = social functioning;**

**RE = role limitations caused by emotional problems;**

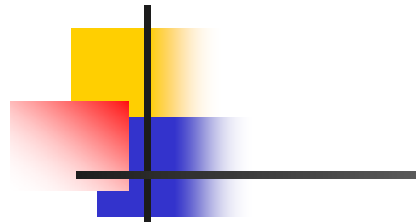
**MH = mental health.**

from Wang XS et al, Cancer 86:1848–1855,1999.)

**TABLE 1. Instruments for Measuring Patient Status, Pain, and Quality of Life\***

Instrument	Year
<b>Performance status</b>	
Karnofsky scale	1949
ECOG performance status	1982
<b>Pain index</b>	
McGill Pain Questionnaire (MPQ)	1980
Brief Pain Inventory (BPI)	1983
Memorial Pain Assessment Card (MPAC)	1986
<b>Functional outcomes</b>	
ISOLS-MSTS score	1993
Toronto Extremity Salvage Score (TESS)	1999
<b>QoL instruments</b>	
<b>General</b>	
Spitzer QoL index	1981
SF-36	1993
<b>Cancer specific</b>	
Functional Living Index-Cancer (FLIC)	1984
Rotterdam Symptom Checklist (RSCL)	1987
Functional Assessment of Cancer Therapy (FACT)	1993
EORTC QLQ-C30	1993
Prostate Cancer Specific Quality of Life Instrument (PROSQOLI)	1995
EORTC QLQ-MY24 (Myeloma)	1998

\*ECOG = Eastern Cooperative Oncology Group; ISOLS: International Society of Limb Salvage; MSTS = Musculoskeletal Tumor Society; EORTC = European Organization for Research and Treatment of Cancer



**TABLE 2. Clinical Studies on Quality of Life in Skeletal Metastases**

Authors	Year	QoL Instrument	Criteria of Success	Disease	n	Treatment	Results
Gilbert et al <sup>13</sup>	1977	Kamofsky Score every 3 months Level 1 => > 70% (independent ADL's)	Good = level 1 for > 50% of remaining life	Breast 68 Lung 27 Prostate 16 Other 47	158	RT 400cGy x 5	Good = 63%
Broos et al <sup>9</sup>	1992	Physician pain assessment, ambulatory status	No regular pain med usage, Ambulation by any means	Pathologic femur fracture, METCA	40	ORIF/Prostheses	67%, recovery of ambulation  75%, effective pain relief
Porter et al <sup>21</sup>	1993	PROSQOLI	Statistically significant change in PROSQOLI	Prostate CA	126	Strontium-89 + RT vs. RT alone	Pain relief and functional improvement greater in Strontium-89 treated group
Wisloff and Gulbrandsen <sup>35</sup>	2000	QLQ-C30 (EORTC)	Statistically significant change in QLQ-C30	Myeloma	484	interferon alpha-2b + melphalan and prednisone	Initial 12 months of treatment, higher complications with interferon. After 12 months, no difference in QoL or complications.
Graupe et al <sup>15</sup>	1996	Standardized self evaluation scheme	Compared surgery prophylactically vs after fx	METCA	67	ORIF/Prostheses	41/60 patients regained normal life. 7 inpatient deaths. Hospital days and OR time > for fx's versus prophylactic Rx
Gaze et al <sup>12</sup>	1997	Spitzer QoL Index	Change in score	METCA	209	RT 1000 cGy vs. 5 x 450 cGy	No difference in RT regimen
Okuyama et al <sup>18</sup>	1999	ECOG performance status	Any improvement in perf status	METCA spine	7	Spinal stabilization	5 of 7 patient's performance status improved
Clohisy et al <sup>6</sup>	1999	FLIC, SF36	Any improvement in health status	METCA	52	ORIF	Trend for improvement in physical and mental health. Any improvement at 6 weeks postoperative predicted longer survival. Floor effect?
Wedin et al <sup>33</sup>	2001	ECOG performance status	Any improvement in status	METCA-Breast	107	ORIF, prosthesis	Pain ↓ in 77%. ECOG performance status improved in 65%
Vitale et al <sup>30</sup>	2001	Pain VAS, FACT, ECOG performance status	Pamidronate	METCA-thyroid	10	Pamidronate 90 mg q month	FACT-G improved over baseline p = 0.006. Maximum response was ↑ 17%. Maximum pain reduction at 3 months = 31%.
Popken et al <sup>20</sup>	2002	Surgical complications	Compared surgery prophylactically vs. after fracture.	METCA-breast	79	ORIF/prosthesis	Intraoperative complication only occurred in the fracture group. Postoperative complications were > in the fracture group 29% versus 11%, p < 0.02; higher usability in nonfracture group.

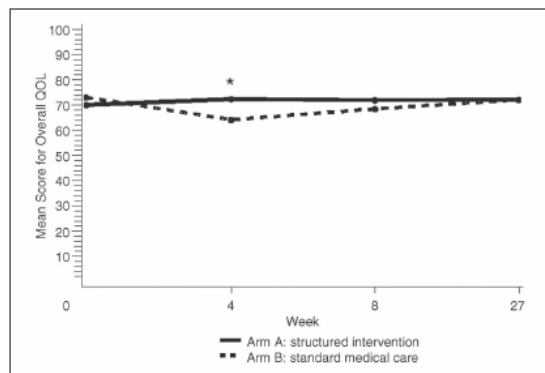
ADL = activities of daily living, cGy = centigray; CA = cancer; METCA = metastatic carcinoma; RT = radiation therapy; ORIF = Open reduction and internal fixation; QoL instrument acronyms = see Table 1.

## Impacting Quality of Life for Patients With Advanced Cancer With a Structured Multidisciplinary Intervention: A Randomized Controlled Trial

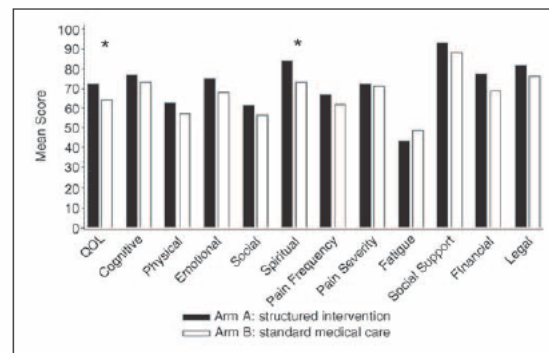
Teresa A. Rummans, Matthew M. Clark, Jeff A. Sloan, Marlene H. Frost, John Michael Bostwick, Pamela J. Atherton, Mary E. Johnson, Gail Gamble, Jarrett Richardson, Paul Brown, James Martensen, Janis Miller, Katherine Piderman, Mashele Huschka, Jean Girardi, and Jean Hanson

**Table 1.** Structured Multidisciplinary Intervention Sessions

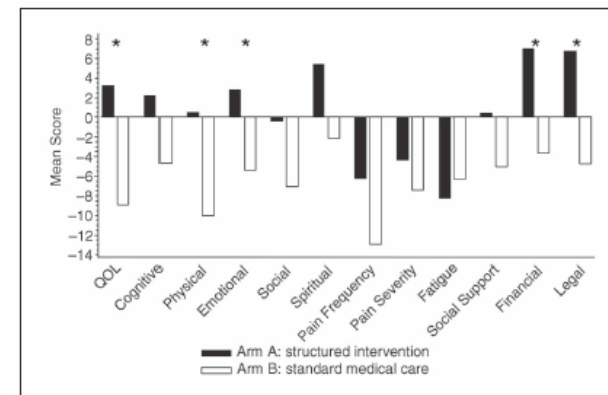
Session	Cognitive Intervention	Emotional Intervention	Physical Intervention	Social Intervention	Spiritual Intervention
1	Education: adjustment phases	Problem solving	Physical therapy	Empathy from providers; unconditional positive regard	Grief
2	Prioritizing and journals	Goal setting	Physical therapy	Sources of support	Guilt
3	Active coping: using support	Stress management	Physical therapy	Using support: communication strategies	Hope
4	Taking charge	Stress management	Physical therapy	Emotional expressiveness	Death and afterlife
5	Lifestyle changes	Assertiveness	Physical therapy	Role playing	Challenged belief system
6	Healthy lifestyle	Irrational thoughts	Physical therapy	Interpersonal relationships	Religious beliefs and treatment
7	Revisiting coping	Challenging thoughts	Physical therapy	Body image and sexuality	Ritual
8	Goal setting	Relapse prevention	Physical therapy	Closure and termination	Meaning and purpose



**Fig 3.** Patient-reported overall quality of life (QOL) mean score by arm over 27 weeks. (\*) Statistically significant.



**Fig 2.** Patient-completed Linear Analog Scales of Assessment mean score by arm at week 4. (\*) Statistically significant. QOL, quality of life.



**Fig 4.** Difference in Linear Analog Scales of Assessment percentage of theoretical range scores between week 4 and baseline. (\*) Statistically significant. QOL, quality of life.

# PATOFISIOLOGIA (Selvaggi et al '05 revised)

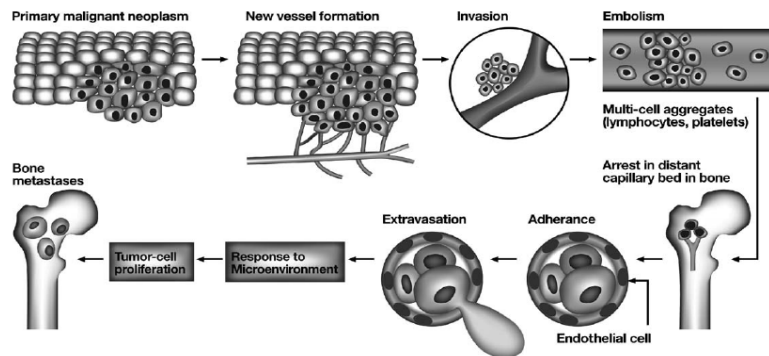


Fig. 1. Putative mechanism by which tumor cells disseminate to bone.

- Vascolarizzazione arteriosa
- Vascolarizzazione venosa (circolazione sec. Batson)
- Caratteristiche del tessuto target
- Caratteristiche biologiche del tessuto tumorale

## RIASSORBIMENTO DELL'OSSO

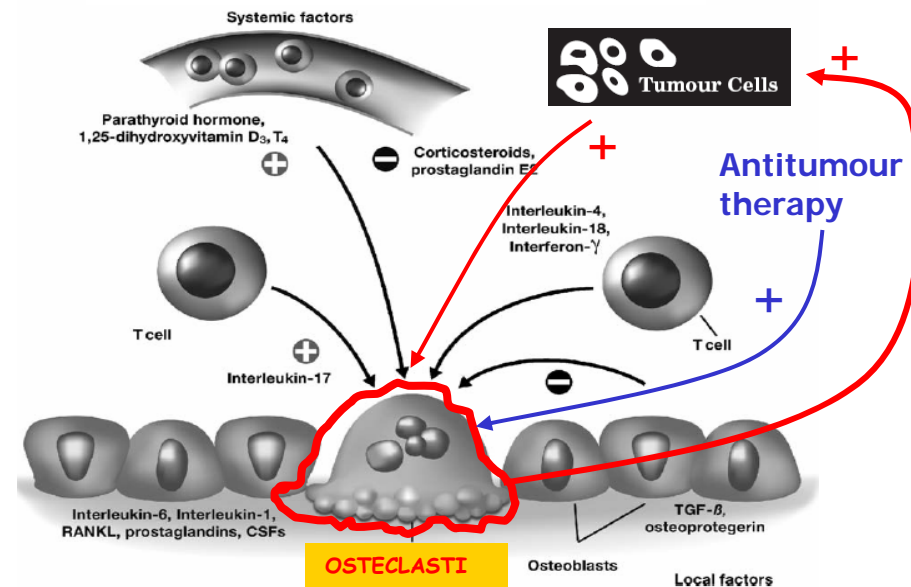


Fig. 2. Role of osteoclasts as mediators of bone resorption.

- Caratteristiche del tessuto target
- Caratteristiche biologiche del tessuto tumorale
  - Ca mammario: PrPTH, + recettori per gli steroidi, buona Differenziazione
  - Ca prostata: scarsa differenziazione
- Terapia antitumorale