3° INCONTRO - Mercoledì 11 maggio 2016

Metastasi ossee da tumori solidi e tumori primitivi dell'osso: quali novità per il 2016?

Metastasi ossee da tumori solidi: patogenesi, incidenza e manifestazioni cliniche

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Incidence of bone metastases

Prevalence of bone metastases at necroscopy

Tumor site	Prevalence (%) (low and upper rates)
Breast	73
Prostate	68
Thyroid	42
Kidney	35
Lung	36
Gastrointestinal tract	5

Adapted from Galasco CSB. Clin Orthop 1986;210:14-21

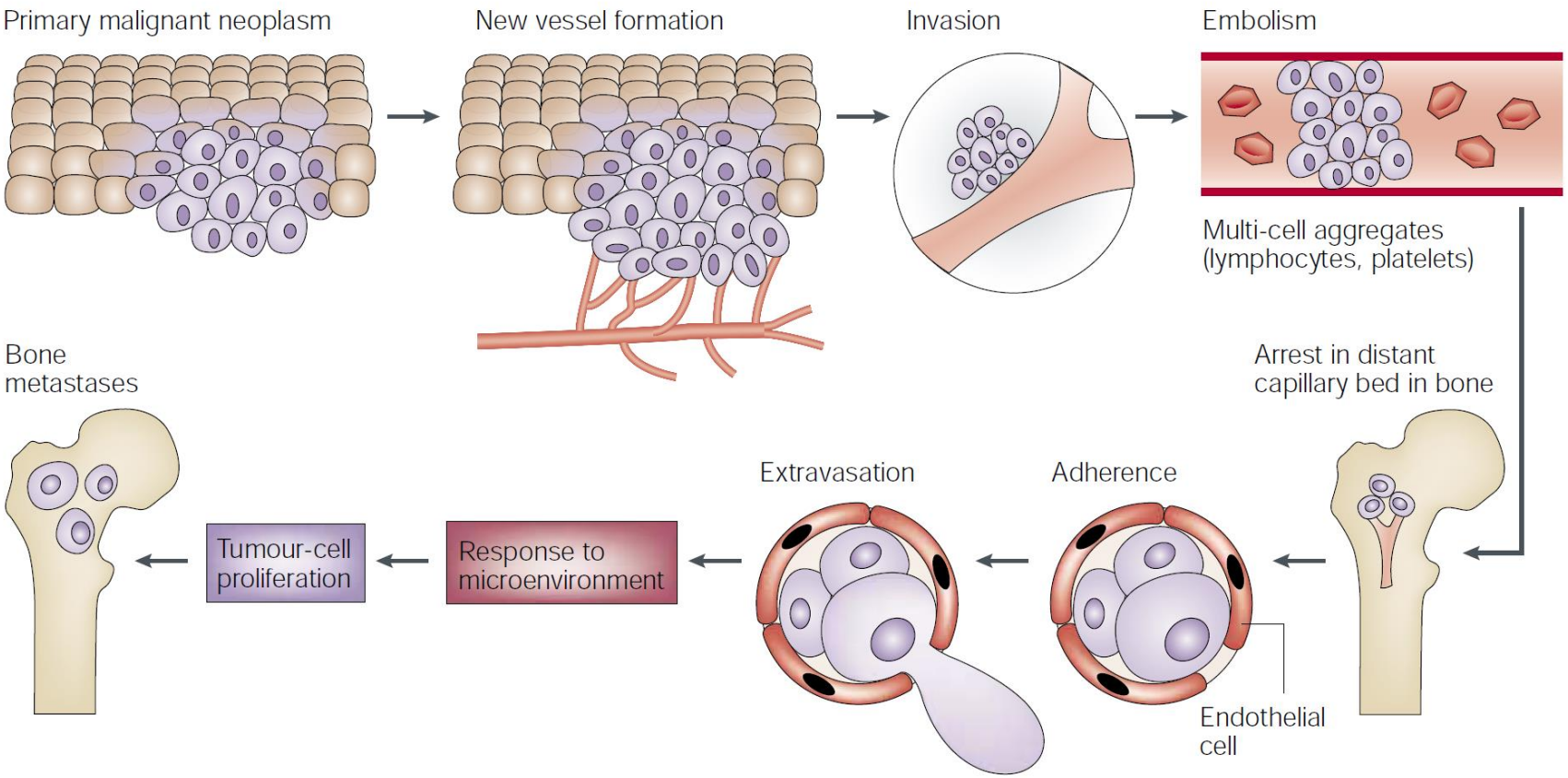
Distribution of bone metastases

Distribution of skeletal metastases in breast cancer (212 pts)

Anatomical site	At any time (% of all patients)
Lumbar spine	59
Dorsal spine	57
Pelvis	49
Ribs	30
Femur	24
Skull	20
Cervical spine	17
Humerus	13
Other	3

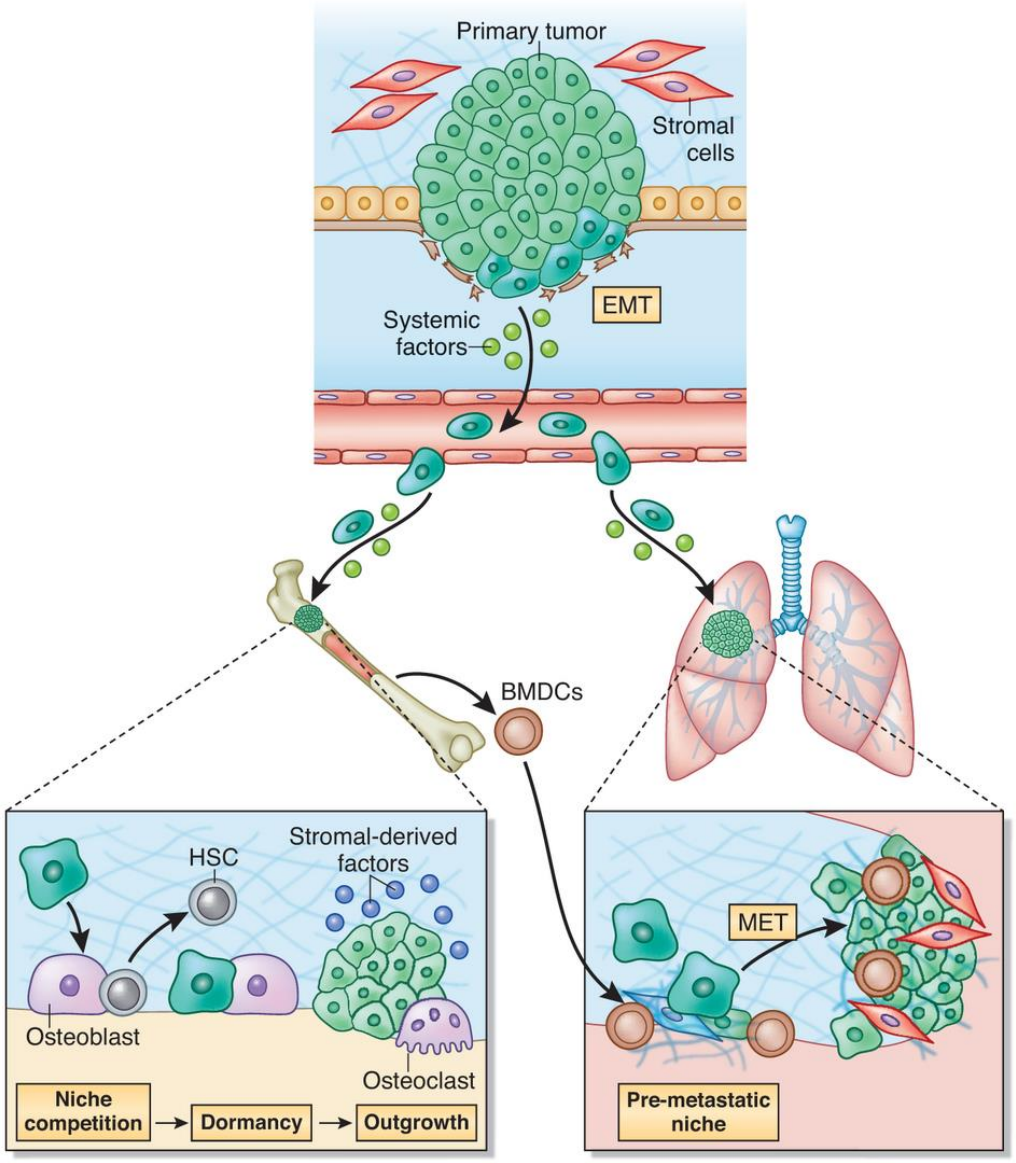
Tubiana-Hulin M. Bone 1991;12:S9-10

Bone metastasis: general mechanisms



Mundy GR. Nat Rev Cancer 2002;2:584-593

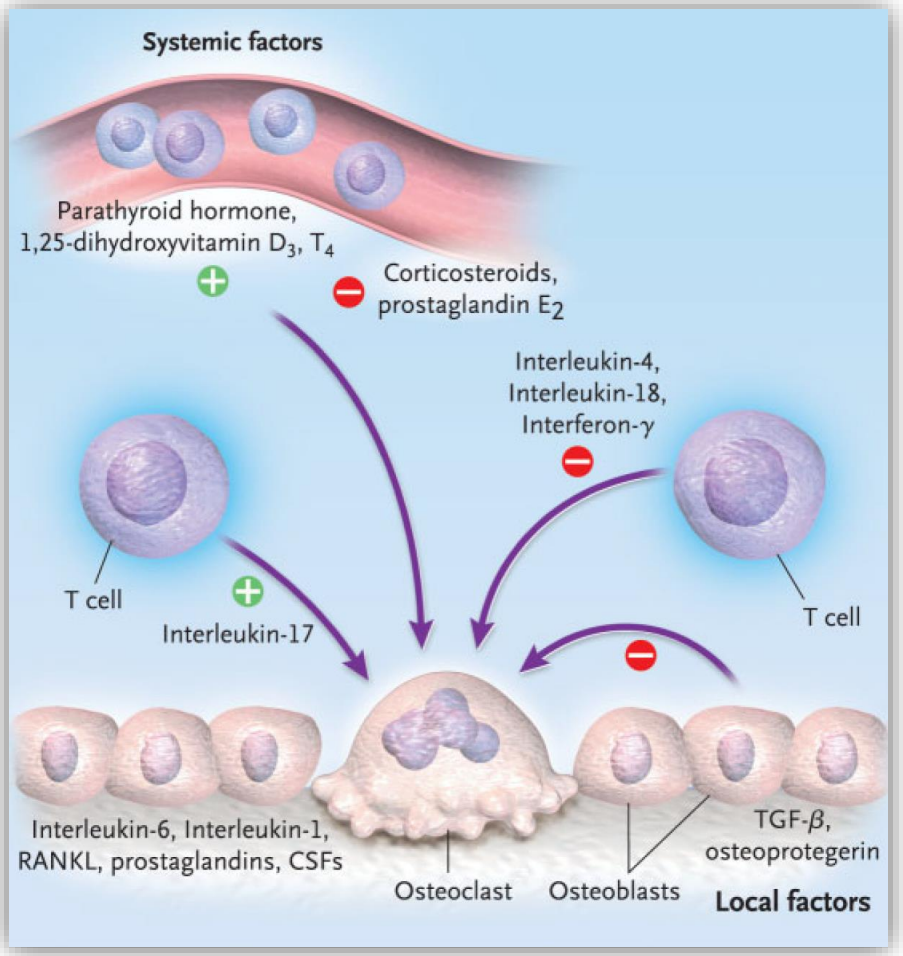
Tumor dormancy and metastatiche niche



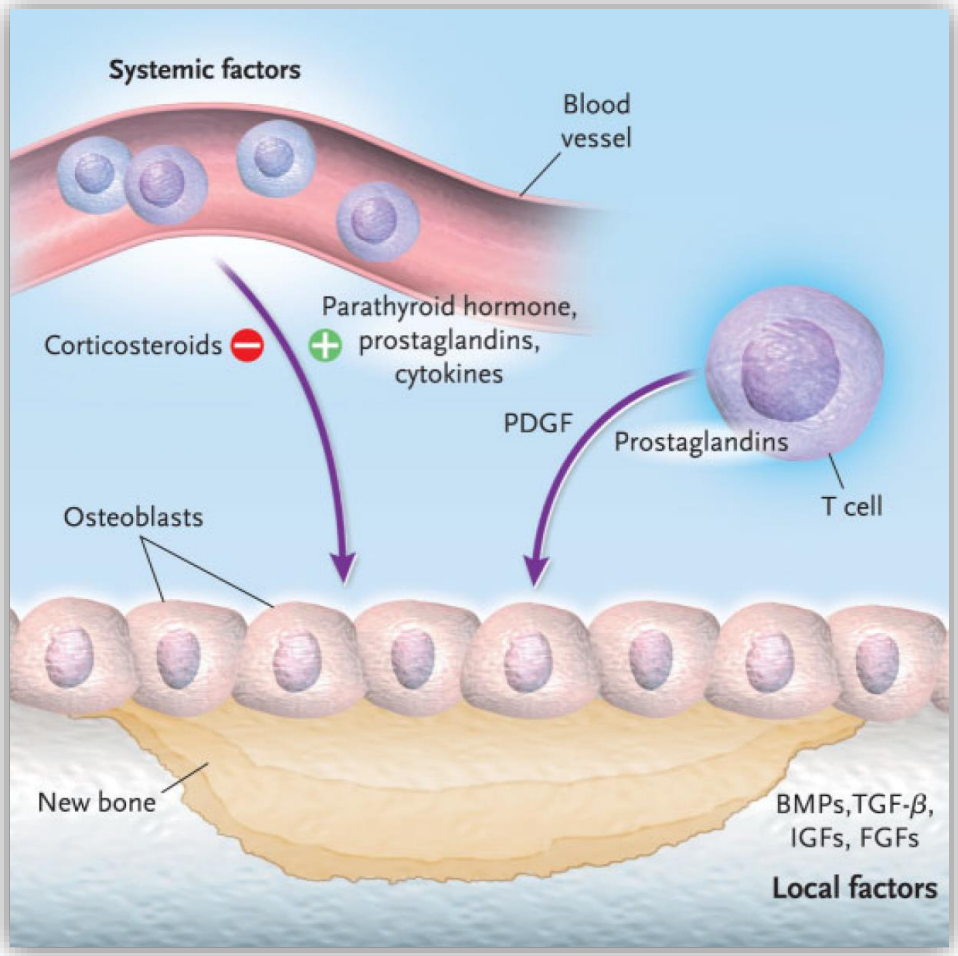
Wan L et al. Nat Med 2013;19:1450-64

Normal bone remodelling process

Bone Resorption

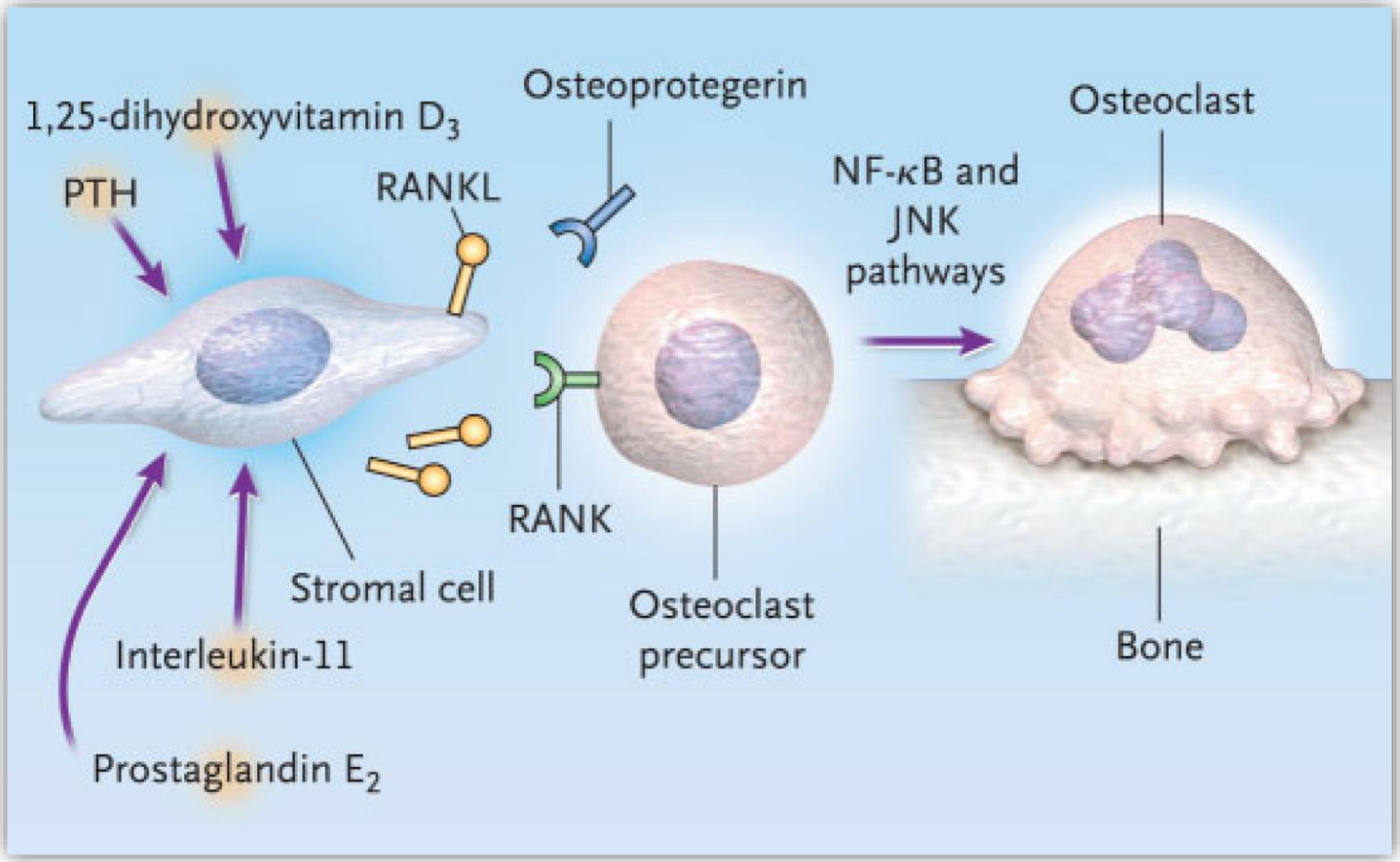


Bone Formation



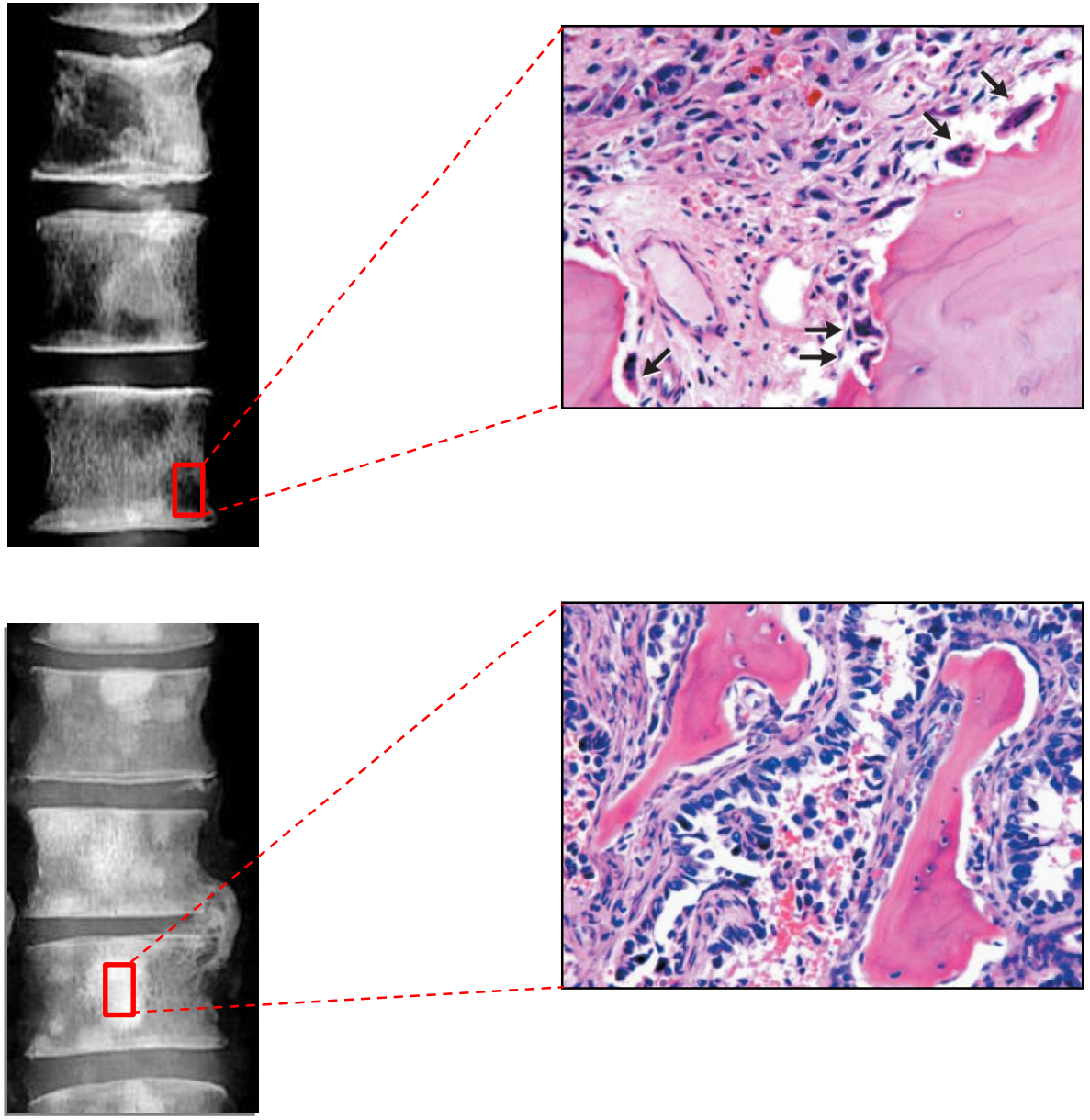
Roodman GD. N Engl J Med 2004;350:1655-64

RANK/RANKL pathway



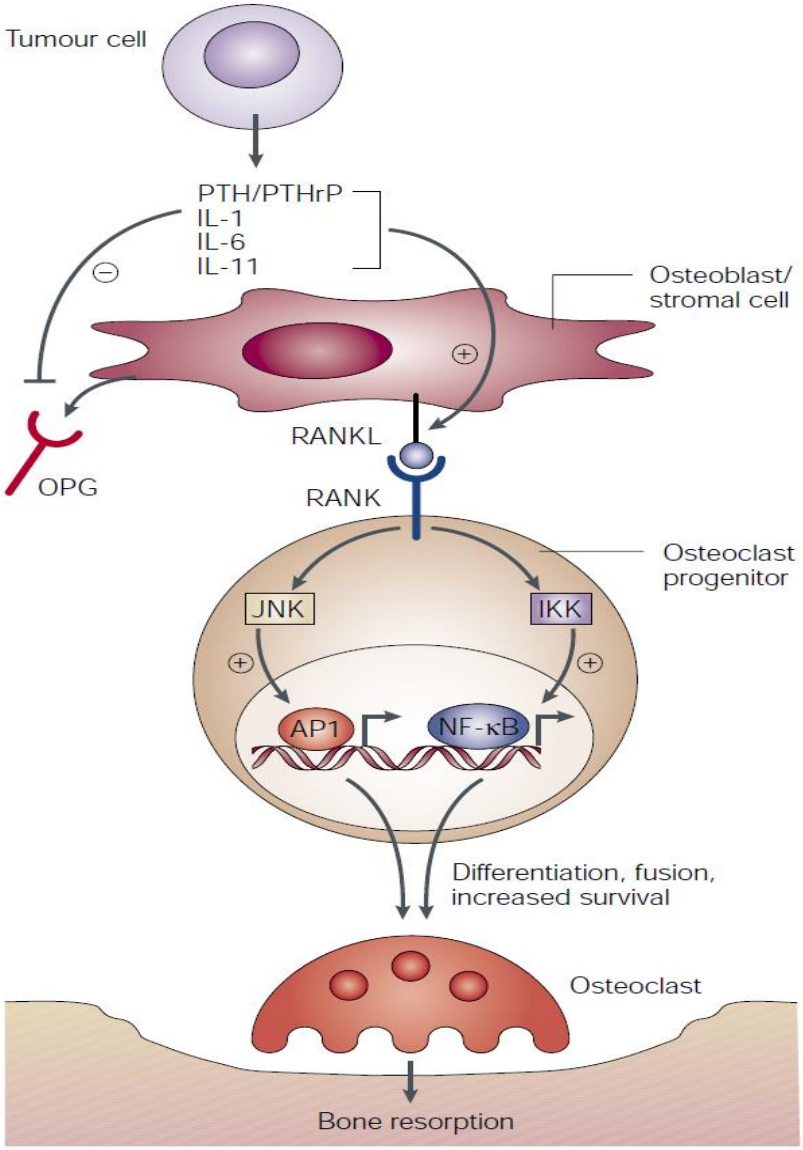
Roodman GD. N Engl J Med 2004;350:1655-64

Osteolytic and osteoblastic bone metastases



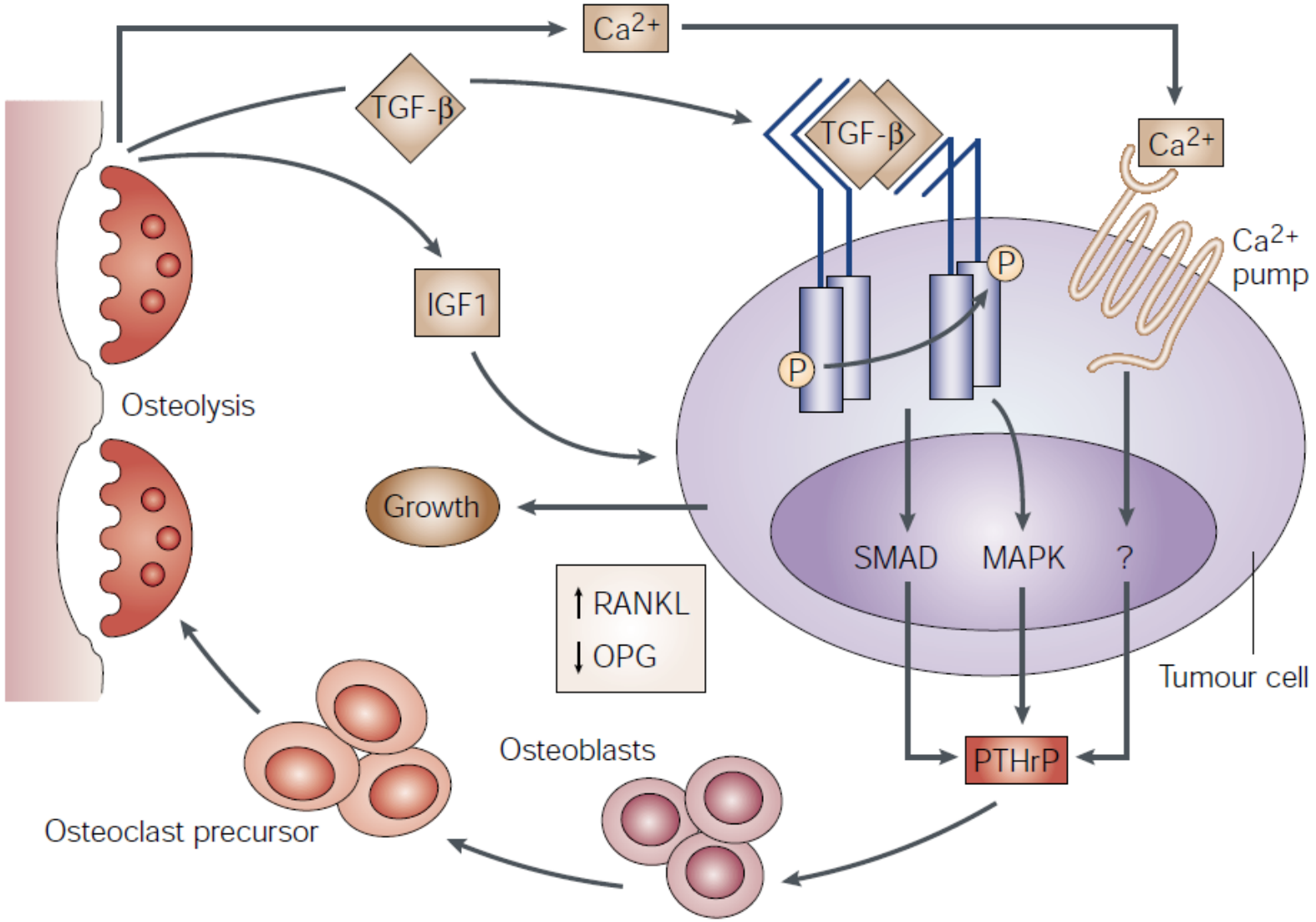
Adapted from Roodman GD. N Engl J Med 2004;350:1655-64

The RANK/RANKL system in osteolytic bone metastases



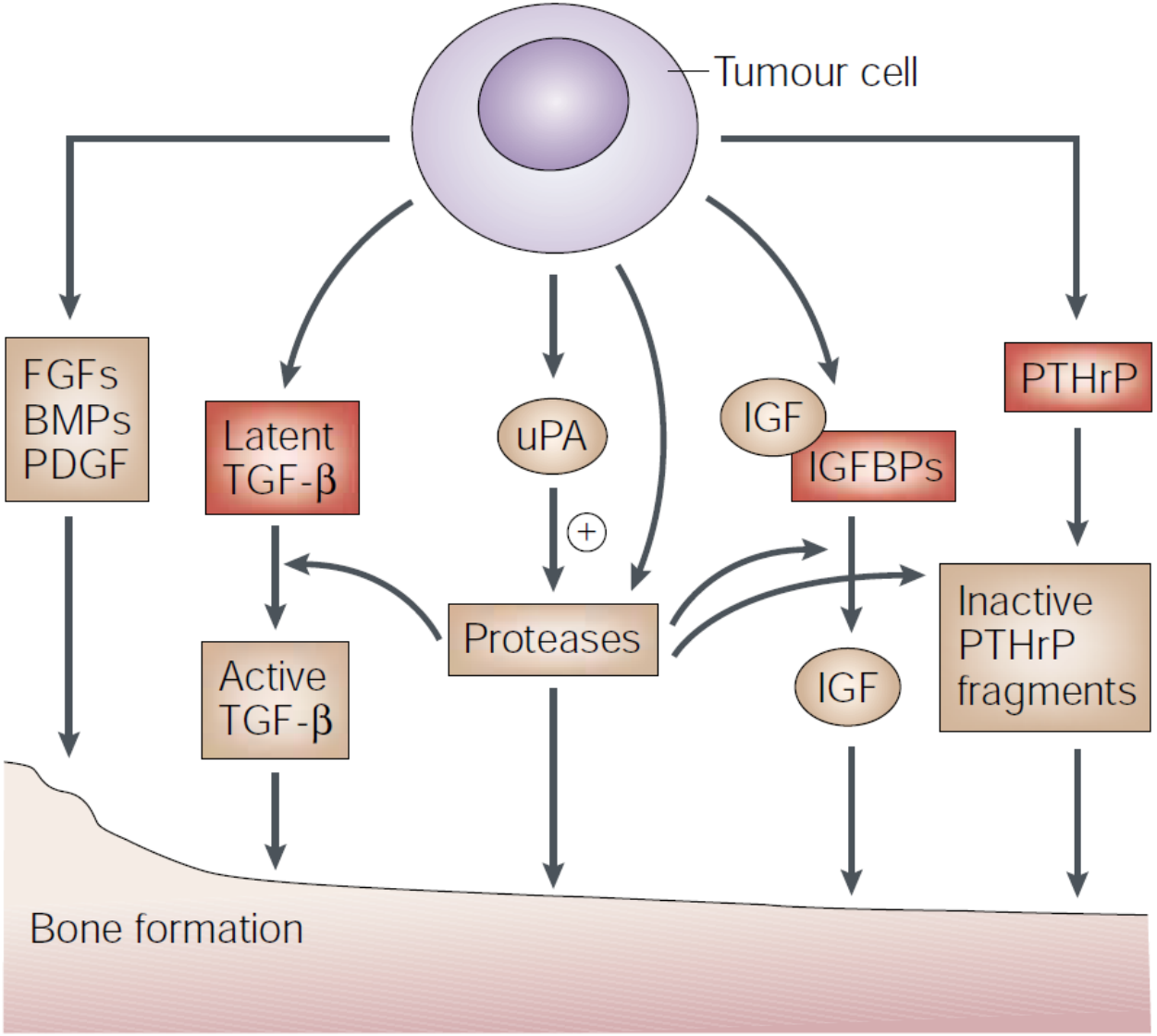
Mundy GR. Nat Rev Cancer 2002;2:584-593

The ‘viciuos cycle’ hypothesis of osteolytic metastasis



Mundy GR. Nat Rev Cancer 2002;2:584-593

Model for osteoblastic bone metastases



Mundy GR. Nat Rev Cancer 2002;2:584-593

Clinical features of bone metastases

- **Pain**
  - The most common cause of cancer-related pain
  - Different sites of bonemetastases are associated with distinct clinical pain syndromes
  - Mechanisms of pain include tumor-induced osteolysis, tumor production of cytokines, direct infiltration of nerves, stimulation of ion channels

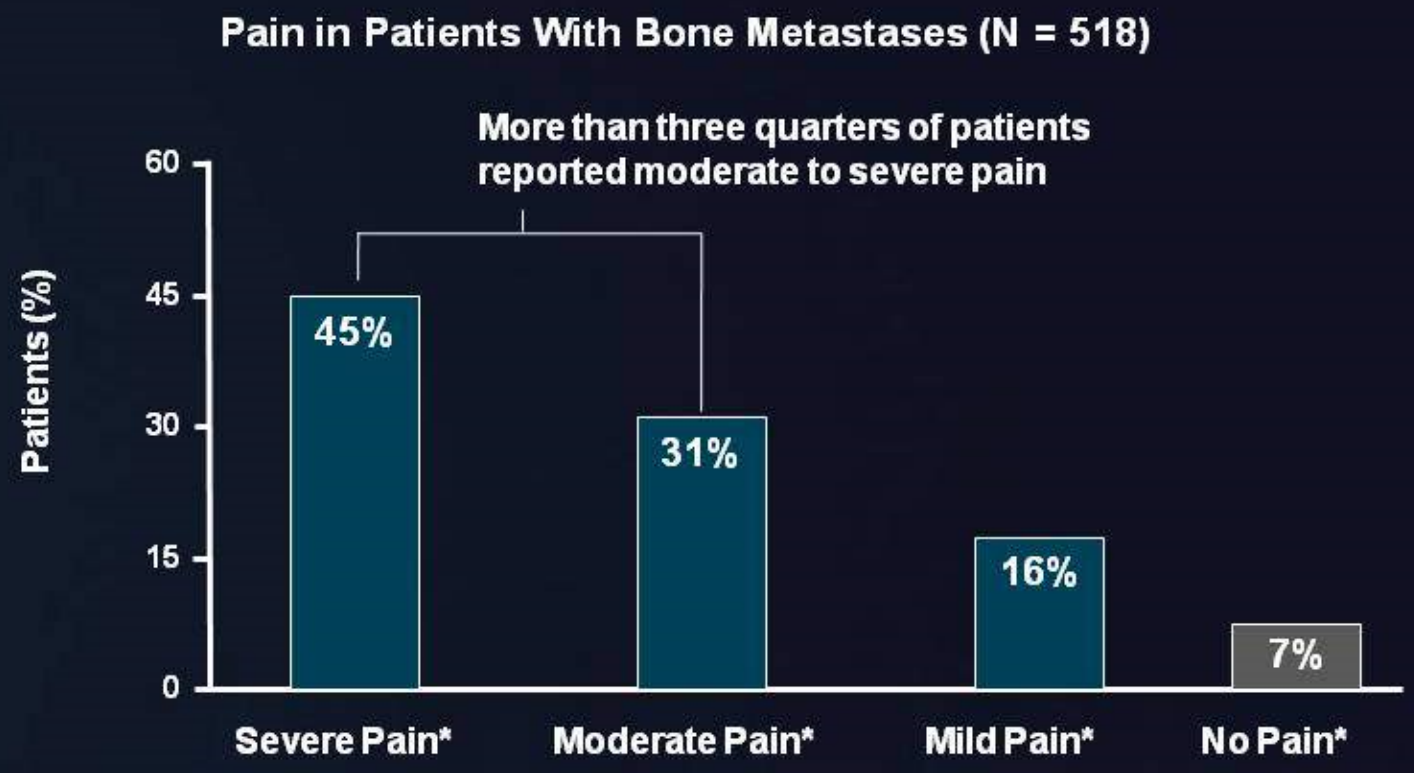
- **Hypercalcemia**
  - It is mainly due to osteolysis but also kindey plays a role
  - PTHrP involved
  - Nonspecific signs and symptoms (fatigue, anorexia, constipation)
  - If untreated: deterioration of renal function and mental status

- **Pathologic fractures**
  - Common through lytic lesions in weight-bearing bones
  - Long bone fractures or epidural extension of tumor into the spine cause the most disability

- **Cord compression**
  - Medical emergency
  - Radicular pain, weakness, paralysis
  - Urinary retention, incontinence and impotence are late manifestations

Coleman RE. Clin Cancer Res 2006;12:6243s-49s

Pain from bone metastases

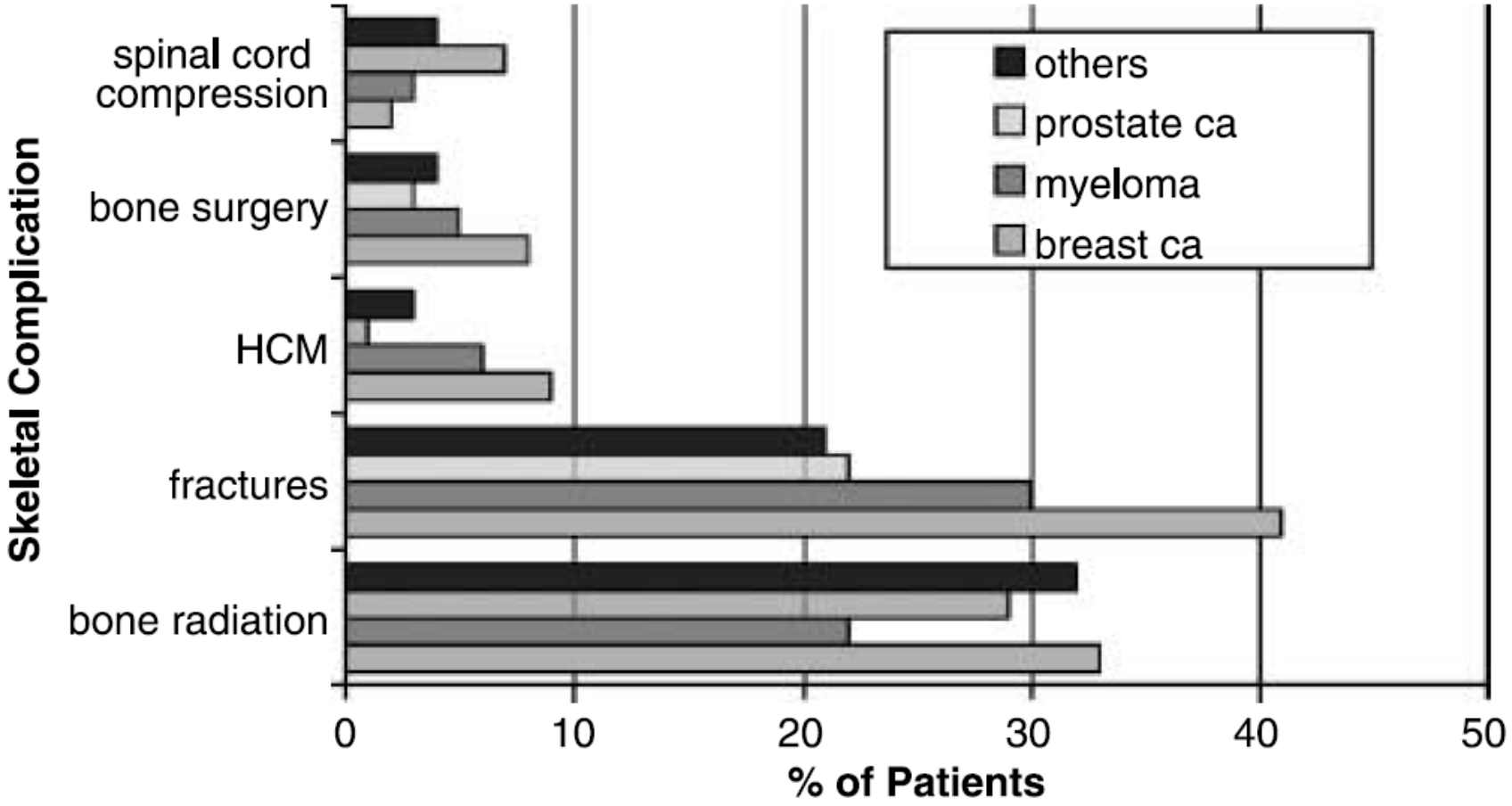


*Brief pain inventory: no pain level 0; mild pain levels 1–3; moderate pain levels 4–7; severe pain levels 8–10.

Data from a survey of 534 patients with cancer and bone metastases, referred to a palliative radiation center including 117 patients with prostate cancer. Sixteen patients were unable to provide their pain score and were excluded from the analysis.

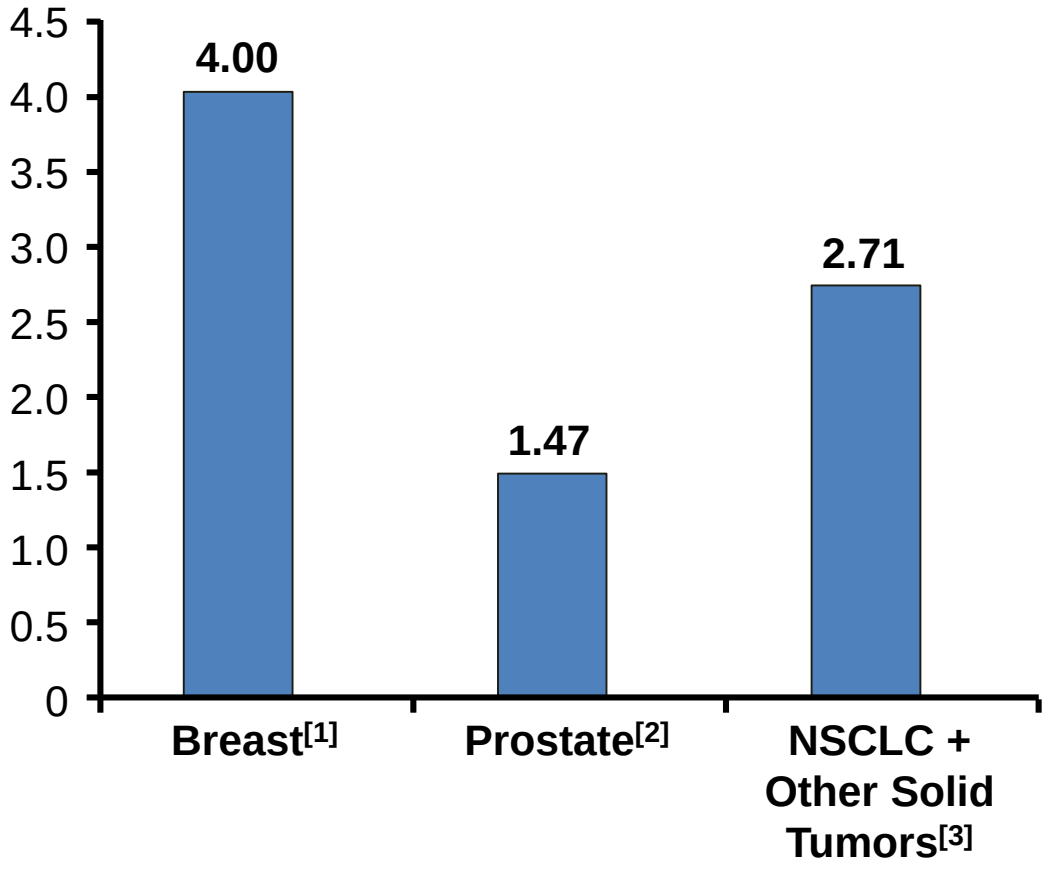
Yau V, et al. *J Pain Symptom Manage*. 2004;27:1–3.

Incidence of SREs



Adapted from Coleman RE, Oncologist 2004;9:14-27

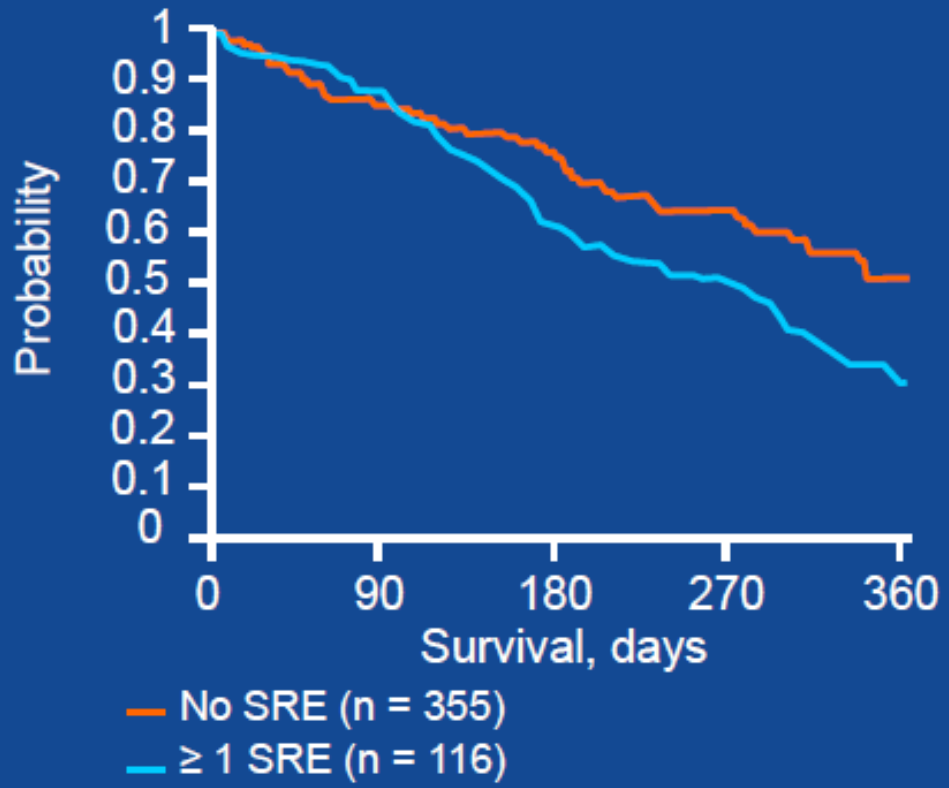
Cancer patients experience multiple SREs



*Mean number of SRE per patient per yr.

1. Lipton A, et al. Cancer. 2000;88:1082-90. 2. Saad F. Clin Prostate Cancer. 2005;4:31-37.
3. Rosen LS, et al. Cancer. 2004;100:2613-21.

SREs are associated with increased mortality



360 Days' Survival

- No SRE: 49.7%
- ≥1 SRE: 28.2%
- *P* = .02

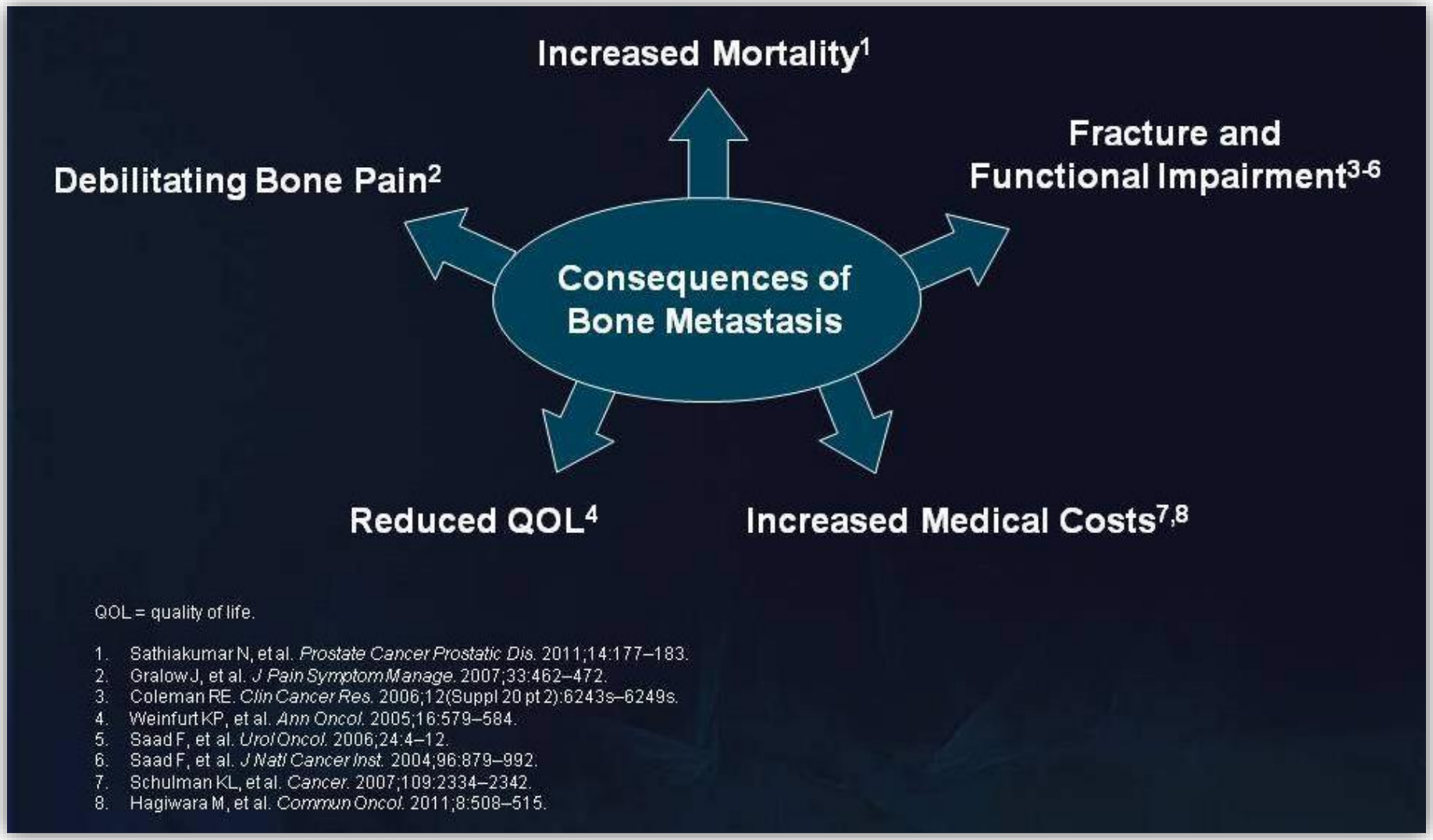
Median Survival Times

- No SRE: 338 days (95% CI = 189, 460)
- ≥ 1 SRE: 248 days (95% CI = 181, 296)

Abbreviation: CI, confidence interval; SRE, skeletal-related event.

Reprinted from DePuy V, et al. *Support Care Cancer*. 2007;15(7):869-876.

Bone metastases are associated with important clinical consequences



QOL = quality of life.

1. Sathiakumar N, et al. *Prostate Cancer Prostatic Dis.* 2011;14:177–183.
2. Gralow J, et al. *J Pain Symptom Manage.* 2007;33:462–472.
3. Coleman RE. *Clin Cancer Res.* 2006;12(Suppl 20 pt 2):6243s–6249s.
4. Weinfurt KP, et al. *Ann Oncol.* 2005;16:579–584.
5. Saad F, et al. *Urol Oncol.* 2006;24:4–12.
6. Saad F, et al. *J Natl Cancer Inst.* 2004;96:879–992.
7. Schulman KL, et al. *Cancer.* 2007;109:2334–2342.
8. Hagiwara M, et al. *Commun Oncol.* 2011;8:508–515.

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