Surgical Considerations for Bone Metastasis from Breast Cancer

Wanlim Kim MD

Department of Orthopaedic Surgery Bone and Soft Tissue Sarcoma Center Asan Medial Center, Seoul

Annual cancer registration in AMC



Estimated bone metastasis

- 20~25% develop clinically evident bone mets.
- Up to 75% in breast, prostate Ca. (autopsy study)

		Total number			evelop bo	op bolle metastasis			
	Year of cancer	patients with cancer n	Total		At primary cancer diagnosis		More than 3 months after primary diagnosis		
Cancer type	be diagnosis		n	%	n	%	n	%	
Lung	1994–1997	13713	445	3	291	2	154	1	
	1998–2001	14419	633	4	333	2	300	2	
	2002–2006	19504	1188	6	755	4	433	2	
	2007-2010	17270	1137	7	785	5	352	2	
Breast	1994–1997	13623	936	7	143	1	793	6	
	1998–2001	15145	1001	7	172	1	829	5	
	2002–2006	20348	1223	6	314	2	909	4	
	2007-2010	19893	629	3	236	1	393	2	
Prostate	1994–1997	6041	1034	17	308	5	726	12	
	1998–2001	7774	1602	21	352	5	1250	16	
	2002–2006	13588	2181	16	652	5	1529	11	
	2007–2010	15454	1124	7	325	2	799	5	

(Svensson, 2017, BMJ)

Improved survival, but...



* 증감: '93-'95년 대비 '11-'15년 암발생자의 생존율 차이

- 1. Underestimation of bone metastasis
- 2. Optimal treatment?

3. QOL?



Impact of bone metastasis

- 1. Decreased mobility
 - \downarrow Performance
 - \downarrow Tolerance to medical treatment
 - Thromboembolic events
- 2. Poor QOL
 - Pain, weakness, emotional stress, independence $\downarrow \dots$
- 3. Poor survival



Problems

- 1. Inadequate recognition
- 2. Inadequate evaluation
- 3. Inadequate referral and treatment
 - 1. Excessive delays / Long waiting lists
 - 2. Indirect communication



Contents

- 1. Indication for surgical treatment
- 2. Pre-Op evaluation
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Incidence

✓ Primary cancers

Breast > lung > prostate ...thyroid, kidney

✓ Common metastatic organs

Lymphatic system > lung > liver > bone

✓ Site of bone metastasis

✓ Spine > pelvis > ribs...skull, long bones

Acral metastasis

- \checkmark distal to elbow or knee
- ✓ lung cancer, mostly



Radiologic evaluation

✓ X ray (AP/lateral)!

✓ Structural integrity

✓ MRI

✓ Local extent, soft tissue involvement

✓ CT

- ✓ Bone integrity
- ✓ Poor soft tissue & bone marrow resolution

Patterns of destruction



X-ray findings

Primary Tumor	Common Type of Bone Destruction
Breast	Mixed
Lung	Lytic
Thyroid	Lytic
Kidney	Lytic
Prostate	Blastic
Melanoma	Lytic



F/64 colon cancer



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Treatment options for bone metastasis

✓ Surgery

✓ Radiation therapy

✓ Medical management

✓ Bone modifying agents: denosumab, bisphosphonate

✓ Intervention

 \checkmark RFA, cryoablation

Indication for surgery

Impending Fracture Painful mets. Location factor fracture



Predicting risk of pathologic fracture

- ✓ Lesions ≥ 2.5cm (LARGE lesion)
- ✓ Involvement of bone diameter \ge 50%
- ✓ Accompanying lesser trochanter fracture
- ✓ Location (esp. L/E, trochanteric)
- ✓ Failure of radiation therapy
- ✓ Progression rate



Predicting risk of pathologic fracture

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Mirels scoring system

Mirels Rating System for the Prediction of Pathologic Fracture Risk

Score	SIte	Nature	Slze ^a	Pain
1	Upper extremity	Blastic	< 1/3	Mild
2	Lower extremity ^b	Mixed	1/3 to 2/3	Moderate
3	Peritrochanteric	Lytic	> 2/3	Functional

^aRelative proportion of bone width involved by tumor. ^bNonperitrochanteric lower extremity.

- ✓ Score ≥ 9: Consider prophylactic fixation
- ✓ Sensitivity 91%, Specificity 35%





SYMPOSIUM: 2014 MUSCULOSKELETAL TUMOR SOCIETY

CT-based Structural Rigidity Analysis Is More Accurate Than Mirels Scoring for Fracture Prediction in Metastatic Femoral Lesions

Timothy A. Damron MD, Ara Nazarian PhD, Vahid Entezari MD, Carlos Brown MD, William Grant EdD, Nathan Calderon MSc, David Zurakowski PhD, Richard M. Terek MD, Megan E. Anderson MD, Edward Y. Cheng MD, Albert J. Aboulafia MD, Mark C. Gebhardt MD, Brian D. Snyder MD, PhD

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Fracture risk: Importance

- ✓ Patients undergoing prophylactic fixation
 - ✓ Shorter hospitalization
 - ✓ Discharge to home more likely
 - ✓ Quicker return to pre-morbid function
 - ✓ Improved survival
 - ✓ Less hardware complications



(Katzer, 2002, Arch Orthop Trauma Surg)

F/54, Breast cancer Disseminated bone mets Weight bearing pain -











Full weight bearing No pain (1.5y)

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Factors in decision-making

- ✓ Life expectancy
- ✓ Concurrent oncologic treatments (CTx, RT)
- Comorbidities, performance status
- ✓ Fracture pattern, bone destruction
- Tumor histology (healing, bleeding risk)

Life expectancy

Primary Tumor	Common Type of Bone Destruction	Fracture Healing ^a (%)	5-Year Relative Survival Rates With Distant Metastases ^b (%)	Radiosensitivity ^c
Breast	Mixed	37	23.8	+++
Lung	Lytic	0	3.7	++
Thyroid	Lytic	NA	53.9	++
Kidney	Lytic	44	11.6	-
Prostate	Blastic	42	27.8	+++
Melanoma	Lytic	NA	15.1	++

✓ More than 6-12 wks → consider Op

✓ Conservative Tx. is more acceptable in UE

✓ Op or not / Fixation modality

Op or not / Fixation modality





F/57 Breast ca, LE> 6mo

















Healing of pathologic fracture

Primary Tumor	Common Type of Bone Destruction	Fracture Healing ^a (%)
Breast	Mixed	37
Lung	Lytic	0
Thyroid	Lytic	NA
Kidney	Lytic	44
Prostate	Blastic	42
Melanoma	Lytic	NA

✓ Fracture healing rate 34%

(Gainor, 1983, Clin Orthop)



F/64, Breast cancer ORIF 2y













Concurrent oncologic treatments

- 1. Chemotherapy
- 2. Radiation therapy
- 3. Intervention
- 4. Etc.



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Goals of Surgical Treatment

- ✓ Restore skeletal stability
- ✓ Regain functional independence
- ✓ Alleviate pain
- ✓ Reduce narcotic use
Practical Goal of Surgery

No second Op

Internal fixation

✓ Intramedullary nail

- Static interlocking
- Bone cement
 - Unaffected by radiotherapy
 - Bridging segmental defect
 - Provide immediate stability
- Cover the entire bone













F/68, Lung ca





Prosthesis

- ✓ Severe bone destruction
- ✓ Epiphyseal lesion
- ✓ Cemented implants
- Long-stemmed implants





Clin Orthop Relat Res (2012) 470:684–691 DOI 10.1007/s11999-011-2038-0

SYMPOSIUM: 2010 MUSCULOSKELETAL TUMOR SOCIETY

Endoprostheses Last Longer Than Intramedullary Devices in Proximal Femur Metastases



Clinical Orthopaedics

and Related Research

A Publication of The Association of Bone and

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5. Cases

Post-op care

✓ Rehabilitation

- ✓ Standing/walking after removal of drain
- ROM: immediately after op, except prosthetic recon.

✓ Hospitalization

✓ Internal fixation: 3-4 days (U/E), 5 days (L/E)

✓ Prosthetic reconstruction: 7-10 days

Post-op care

✓ Radiation therapy

- ✓ Stable wound, no discharge
- ✓ 3wks after op.

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JBMR

Incidence of Atypical Nontraumatic Diaphyseal Fractures of the Femur

Richard M Dell,¹ Annette L Adams,² Denise F Greene,¹ Tadashi T Funahashi,¹ Stuart L Silverman,³



Fig. 4. Incidence of atypical femur fractures according to duration of bisphosphonate exposure (unadjusted and age-adjusted, showing incidence and 95% confidence intervals).









Summary

- 1. X rays
- 2. Pain
 - severity, aggravation factor
- 3. Direct communication
 - LE, concurrent Tx

4. Long term BP use

- Atypical femoral fracture

Thank you for your attention



Pathophysiology of atypical femoral fractures and osteonecrosis of the jaw

J. Compston

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Abstract In recent years, atypical femoral fractures and osteonecrosis of the jaw have emerged as potential complications of long-term bisphosphonate therapy; osteonecrosis of the jaw has also been reported in patients receiving high doses of denosumab. The pathophysiology of both conditions is poorly defined, and the underlying mechanisms are likely to differ. The initiation of atypical fractures in the lateral femoral shaft suggests that reduced tensile strength, possibly secondary to alterations in the material properties of bone resulting from low bone turnover, may be an important pathogenetic factor. Osteonecrosis of the jaw is characterised by infection, inflammation, bone resorption and bone necrosis, but the sequence in which these occur has not been established. However, the observation that bone resorption occurs in close proximity to microbial structures suggests that infection may be the most important trigger, often as a result of dental disease. Other possible pathogenetic factors include suppression of bone turnover, altered immune status and adverse effects of bisphosphonates on the oral mucosa.

bisphosphonates, appear to be related to the duration of therapy. However, whilst ONJ has also been reported in patients taking denosumab, AFFs have so far only been associated with bisphosphonate therapy, and whereas the incidence of ONJ is higher in patients receiving larger doses of bisphosphonates or denosumab for oncological indications than in those receiving smaller doses for osteoporosis, this dose response is not apparent for bisphosphonates and AFFs. These latter differences indicate distinct pathophysiological mechanisms, and in this review, the two conditions will be considered separately.

Atypical femoral fractures

Clinical and radiological features

AFFs have strikingly characteristic clinical and radiological features that may provide some clues as to their pathogenesis. They occur in the subtrochanteric or diaphyseal region of the

Bisphosphonate drug holiday: who, when and how long

Dima L. Diab and Nelson B. Watts

Abstract: Bisphosphonates have been widely used in the treatment of osteoporosis with robust data from numerous placebo-controlled trials demonstrating efficacy in fracture risk reduction over 3–5 years of treatment. Although bisphosphonates are generally safe and well tolerated, concerns have emerged about adverse effects related to long-term use. For most patients with osteoporosis, the benefits of treatment outweigh the risks. Because these agents accumulate in bone with some persistent antifracture efficacy after therapy is stopped, it is reasonable to consider a 'drug holiday.' There is considerable controversy regarding the optimal duration of therapy and the length of the holiday, both of which should be based on individual assessments of risk and benefit.

Keywords: bisphosphonates, drug holidays, fractures, osteoporosis

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JOURNAL OF CLINICAL ONCOLOGY

Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study

Alison T. Stopeck, Allan Lipton, Jean-Jacques Body, Guenther G. Steger, Katia Tonkin, Richard H. de Boer, Mikhail Lichinitser, Yasuhiro Fujiwara, Denise A. Yardley, María Viniegra, Michelle Fan, Qi Jiang, Roger Dansey, Susie Jun, and Ada Braun

See accompanying editorial on page 5127

Purpose

This randomized study compared denosumab, a fully human monoclonal antibody against receptor activator of nuclear factor κ B (RANK) ligand, with zoledronic acid in delaying or preventing skeletal-related events (SREs) in patients with breast cancer with bone metastases.

A B S T R A C T

Patients and Methods

Patients were randomly assigned to receive either subcutaneous denosumab 120 mg and intravenous placebo (n = 1,026) or intravenous zoledronic acid 4 mg adjusted for creatinine clearance and subcutaneous placebo (n = 1,020) every 4 weeks. All patients were strongly recommended to take daily calcium and vitamin D supplements. The primary end point was time to first on-study SRE (defined as pathologic fracture, radiation or surgery to bone, or spinal cord compression).

Results

Denosumab was superior to zoledronic acid in delaying time to first on-study SRE (hazard ratio, 0.82; 95% CI, 0.71 to 0.95; P = .01 superiority) and time to first and subsequent (multiple) on-study SREs (rate ratio, 0.77; 95% CI, 0.66 to 0.89; P = .001). Reduction in bone turnover markers was greater with denosumab. Overall survival, disease progression, and rates of adverse events (AEs) and serious AEs were similar between groups. An excess of renal AEs and acute-phase reactions occurred with zoledronic acid; hypocalcemia occurred more frequently with denosumab. Osteonecrosis of the jaw occurred infrequently (2.0%, denosumab; 1.4%, zoledronic acid; P = .39).

From the University of Arizona, Arizona Cancer Center, Tucson, AZ: Penn State Milton S. Hershey Medical Center, Hershey, PA; Centre Hospitalier Universitaire Brugmann, Université Libre de Bruxelles, Brussels, Belgium; Medical University of Vienna, Vienna, Austria; Cross Cancer Institute, Edmonton Alberta, Canada; Western and Royal Melbourne Hospitals, Melbourne, Victoria, Australia; Blokhin Cancer Research Center, Moscow, Russia; National Cancer Center Hospital, Tokyo, Japan: Sarah Cannon Research Institute, Nashville, TN; Corporacion Medica de General San Martin, San Martin, Argentina; and Amgen, Thousand Oaks, CA.

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Written on behalf of the 20050136 Breast Cancer Skeletal-Related Events Study Investigators.

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F/70, Multiple myeloma

K



Solid bone union





F/64 Pancreas cancer





M/78 Small cell lung cancer



M/54 CBD cancer







M/69 RCC















7m after RT

Metastatic bone tumors

- ✓ 400,000/year (US)
- ✓ Majority treated by general orthopedic surgeons
- ✓ 70% in metastatic breast or prostate cancer
- ✓ 20-30% in metastatic lung or GI cancer

Fracture pattern, bone destruction







8M

F/57 breast cancer





Cases
























M/55 RCC Single bone meta









F/45, Lung cancer (ADC) Painful left hip













M/47, NSCLC







