


MAYO CLINIC

Bisphosphonates and the Femur: What Should I Do?


TRAUMA 101 – FRACTURE CARE FOR THE COMMUNITY ORTHOPEDIST

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Disclosures

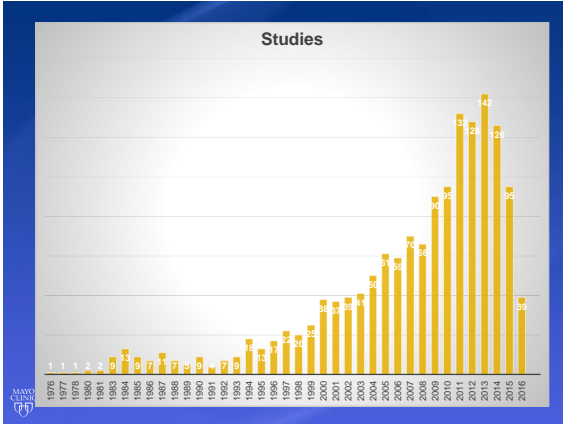
- I have no disclosures



The Routine fx...

- Routine subtroch fx
- Routine cares
- Heal and adios...





Bisphosphonates: A quick primer

- Absorbed systemically and binds to bone surfaces
- Osteoclasts take up Bisphosphonates from bone surface
 - High remodeling centers
- Loss of resorptive function
- Accelerates apoptosis

Binding/Affinity

}

Anti-Resorptive

Long-Term Use of Bisphosphonates in Osteoporosis

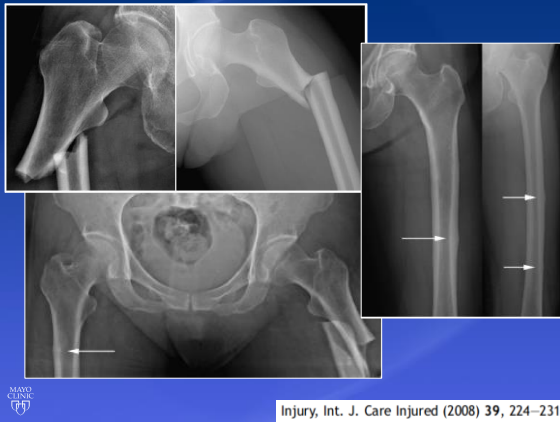
Nelson B. Watts and Dima L. Diab
 University of Cincinnati Bone Health and Osteoporosis Center, Cincinnati, Ohio, 45229

J Clin Endocrinol Metab, April 2010, 95(4):1555-1565

How do they work: "IN DEPTH" review

- Nitrogen containing:
 - Inhibit **farnesyl pyrophosphate synthase**
 - Inhibits prenylation** (stops anchoring of GTP-binding proteins from bonding to the cell membrane)
 - = loss of resorptive capacity
- Non-nitrogen containing:
 - Produce toxic analogs of ATP that cause osteoclast cell death

J Clin Endocrinol Metab, April 2010, 95(4):1555-1565



Injury, Int. J. Care Injured (2008) 39, 224–231

Femoral Cortical Stress Lesions in Long-Term Bisphosphonate Therapy: A Herald of Impending Fracture?

Joyce S. B. Koh, MD, FRCS,* Seo Kiat Goh, MD, FRCS,* Meng Ai Png, MD, FRCR,† Ernest B. K. Kwek, MD, FRCS,‡ and Tet Sen Howe, MD, FRCS*

J Orthop Trauma • Volume 24, Number 2, February 2010

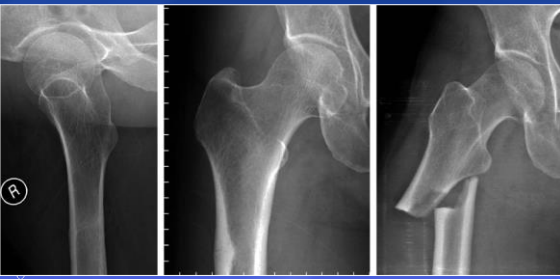
- Reviewed 33 patients with meta-diaphyseal **stress reactions**
- Every patient that fractured had
 - **PRODROMAL PAIN**
 - **“DREADED BLACK LINE”**
- Followed a group with discontinuation of anti-resorptive therapy (12 pts)
 - Stress reactions unchanged
 - Pain improved in 80%



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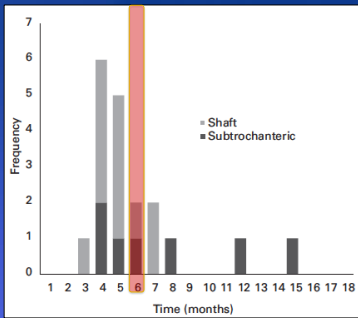
Atypical femoral fractures and bisphosphonate treatment

EXPERIENCE IN TWO LARGE UNITED KINGDOM TEACHING HOSPITALS
R. N. THOMPSON, J. R. A. PHILLIPS, S. H. J. MCCAULEY, J. R. M. ELLIOTT, C. G. MORAN
VOL. 94-B, No. 3, MARCH 2012

- 2008-2010: 22 pts/24 fxs a/w bisphosphonates
- 42% had **PRODROMAL PAIN**
- 14% had **BILATERAL FXS**
- 50% had spontaneous fxs
- Mean duration of use: **4.6 years**



Healing Potential: Is there a delay?



VOL. 94-B, No. 3, MARCH 2012

Healing Delayed But Generally Reliable After Bisphosphonate-associated Complete Femur Fractures Treated with IM Nails

Kenneth A. Egol MD, Ji Hae Park BS, Zehava Salkin Rosenberg MD, Valerie Peck MD, Nirmal C. Tejwani MD
Published online: 20 April 2013

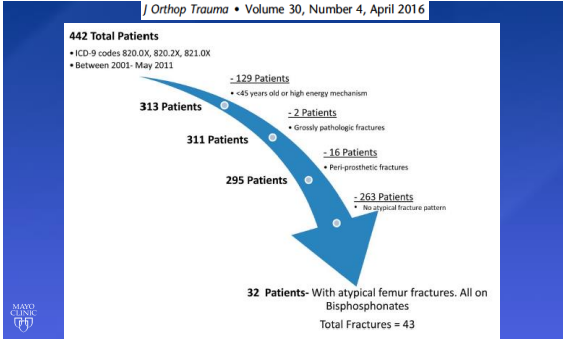
- 33 patients, 41 fractures
- 2004-2011
- ≥5 years bisphosphonate use (8.8 years)
- 6 months prodromal pain (1-8 mo)
- **66% returned to baseline in 12 months**
- **98% healed at 12 months**



A Review of Atypical Femoral Fractures From a Tertiary Care Teaching Hospital: An Alarming Trend?

John-David Black, MD,* Vamsi K. Kancherla, MD,* and William G. De Long, Jr, MD*†

J Orthop Trauma • Volume 30, Number 4, April 2016

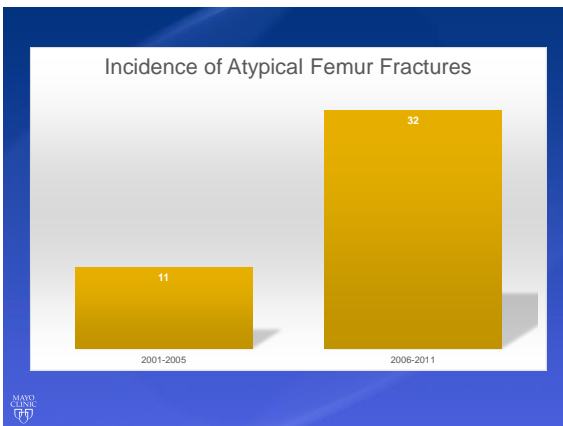


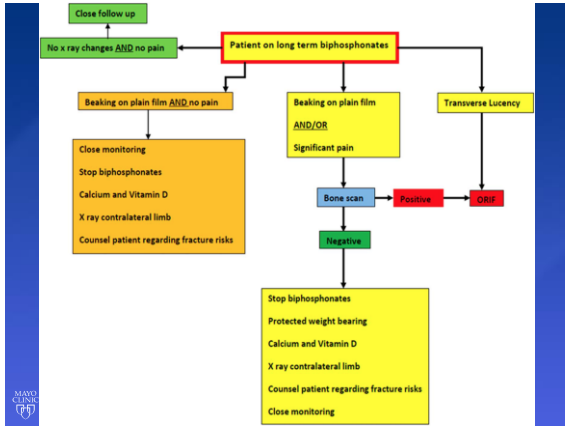
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- 31 F, 1 M
- Age: 71.0 (47–92 years) ± 11 years
- Average duration of bisphosphonate therapy
 - 7.6 (1–12 years) ± 3.07 years
- Prodromal: 10/23 → 46.5%





Newer studies in 2016

Bilateral femur fractures associated with short-term bisphosphonate use.
Rifai A, Pourtafahi S, Carbone A, Callaghan JJ, Stadler CM, Record N, Issa K. Orthopedics. 2015 Feb;38(2):e139-42. doi: 10.3928/01477447-20150204-90. PMID: 25665120

Spontaneous Bilateral Femoral Fractures After High-Dose Zoledronic Acid.
Brin YS, Palmanovich E, Heler Z, Kish BJ, Nyska M, Bismuth H, Coughlin R, Zehavi T, Rotman P. Orthopedics. 2015 Nov;38(11):e1051-4. doi: 10.3928/01477447-20151020-16. PMID: 26558671

Atypical Femoral Fractures Can Happen Even With Short Duration Bisphosphonate Treatment.
Kohli R, Siva C. Conn Med. 2015 Aug;79(7):419-22. PMID: 26411180

Sequential subtrochanteric femoral fracture after atypical diaphyseal fracture in a long-term bisphosphonate user: a case report.
Park KT, Lee KB. Acta Chir Orthop Traumatol Cech. 2015;82(2):157-60. PMID: 26317188

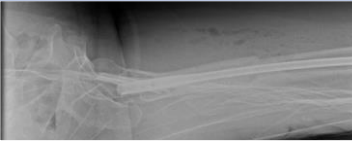
Case examples

Case 1

- 70 y/o F
- 3 weeks of left thigh pain
- 7 years alendronate use
- During interview, also noted very mild right thigh pain

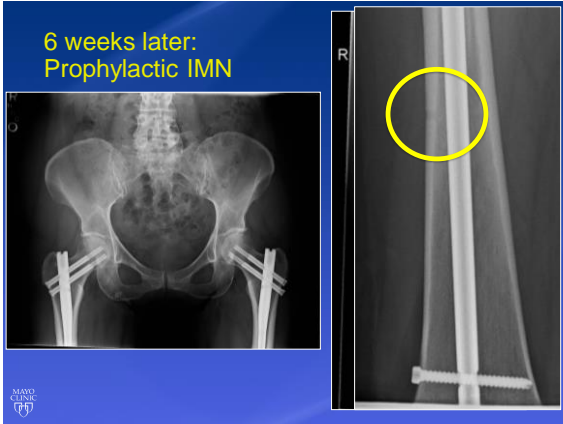


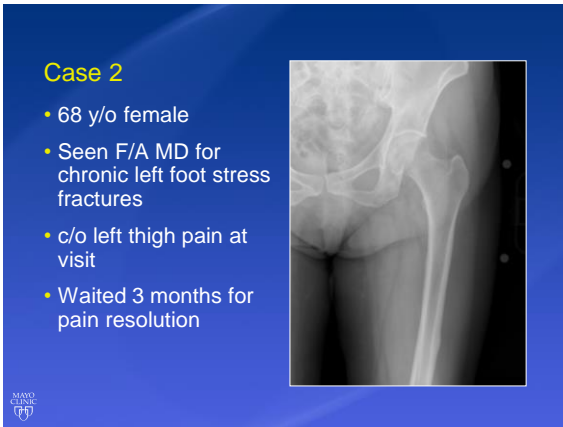
Left leg

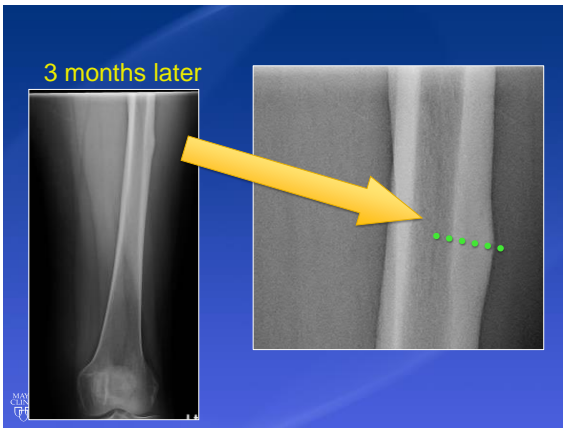


Right leg

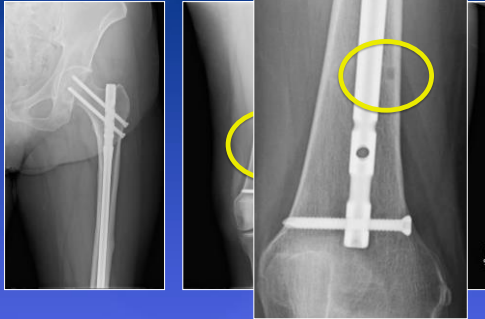








Prophylactic treatment



Case 3

- 69 y/o Female fell at cash register
- c/o right thigh pain for 3 months
- No c/o left thigh pain
- Alendronate use for 6.5 years

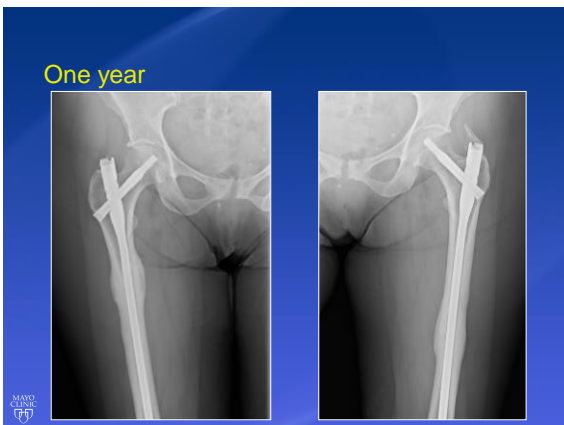


Injury films









Case 4

- 70 y/o F fell at bathroom sink
- Mild right thigh pain for 'months'
- Alendronate use for 8 years



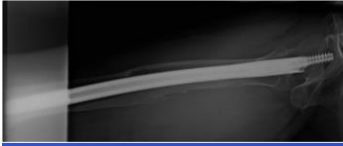
Injury Films



8 months postop



8 months postop

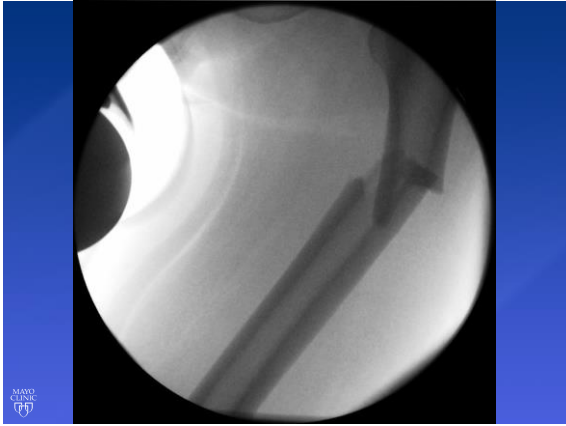


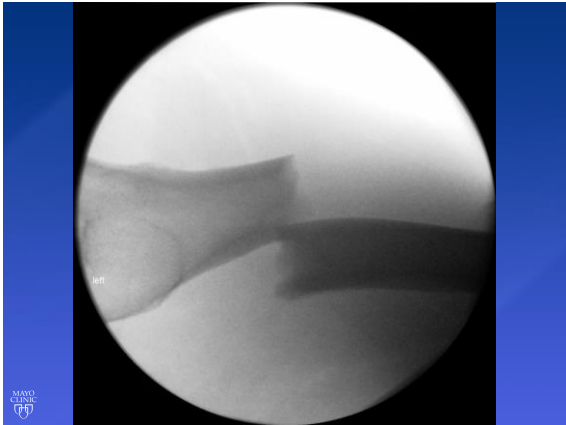
Case 5

- 60 y/o F with bilateral thigh pain
- Pain there for "about a month", Left worse
- Twisted at kitchen sink
- Annual bisphosphonate injections x 5 years

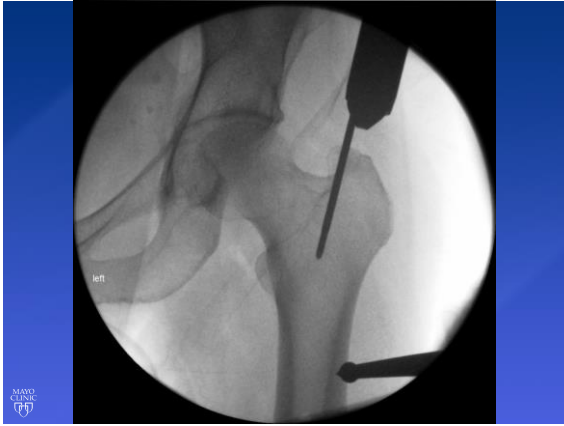


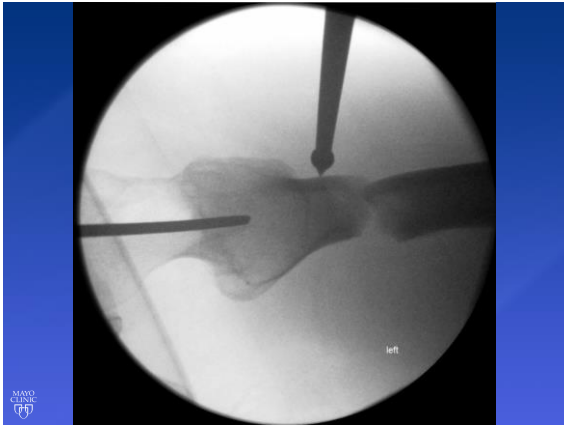




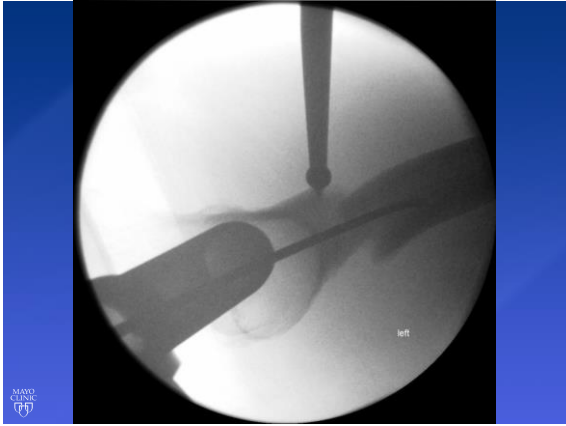






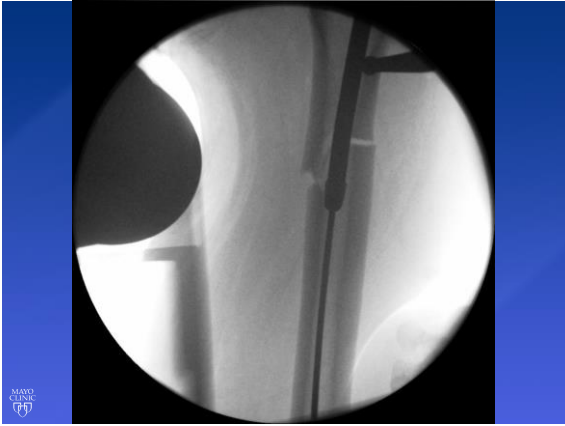






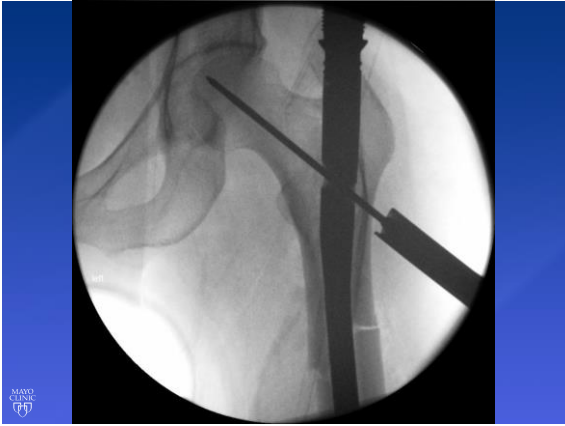






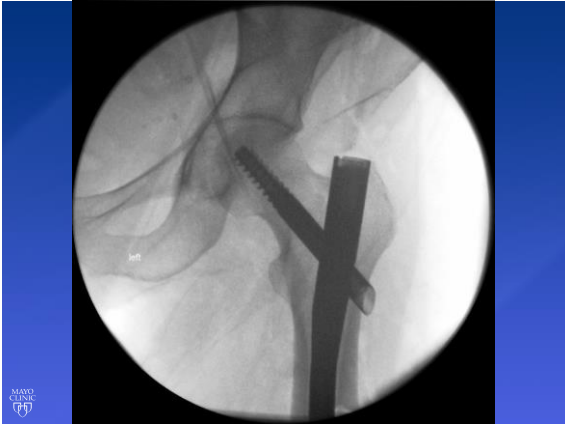


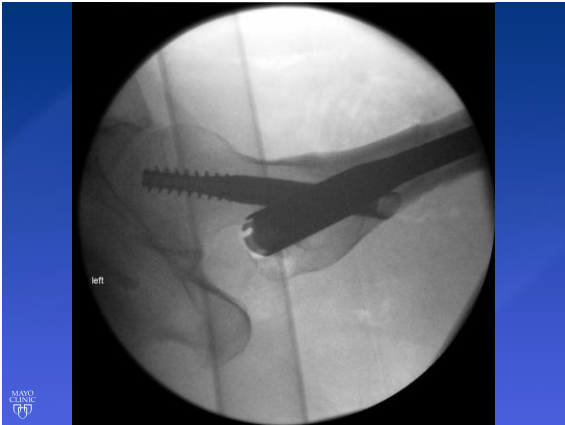


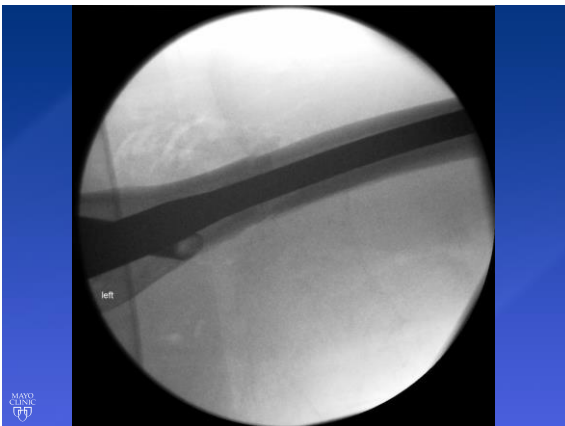


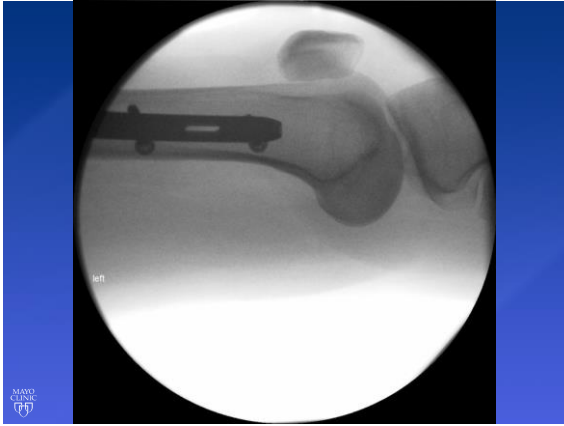




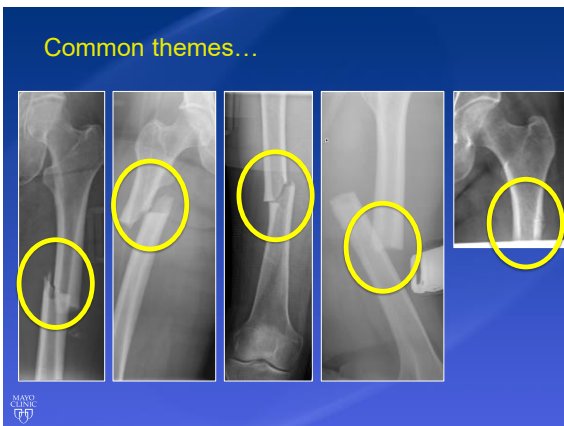












What are the current recommendations?

- 1. Clear evidence: The use of bisphosphonates reduces fractures in osteoporotic patients (T< -2.5)
- 2. Fracture risks are significantly greater in patients taking bisphosphonates for greater than 5 years
- 3. Current evidence shows NO benefit for bisphosphonates beyond 5 years
- 4. May consider anabolic agents (teriparatide) if needed

What is the optimal duration of bisphosphonate therapy?

BISPHOSPHONATE THERAPY AND ATYPICAL FRACTURES
JAMA, October 6, 2010—Vol 304, No. 13

CLEVELAND CLINIC JOURNAL OF MEDICINE
VOLUME 78 • NUMBER 9 • SEPTEMBER 2011

Bisphosphonates and the Femur:
What Should WE Do?

- 1. Treat femur fracture (choice of IM nail)
- 2. Counsel patient on potential delayed healing
- 3. ALWAYS EVALUATE CONTRALATERAL SIDE
- 4. Discontinue bisphosphonate use and consider other agent IF osteoporosis persistent/severe
 - 1. May consider new DEXA scan
 - 2. Can look at bone turnover markers
- 5. Consider referral to endocrine/primary MD if not comfortable managing resorptive therapy