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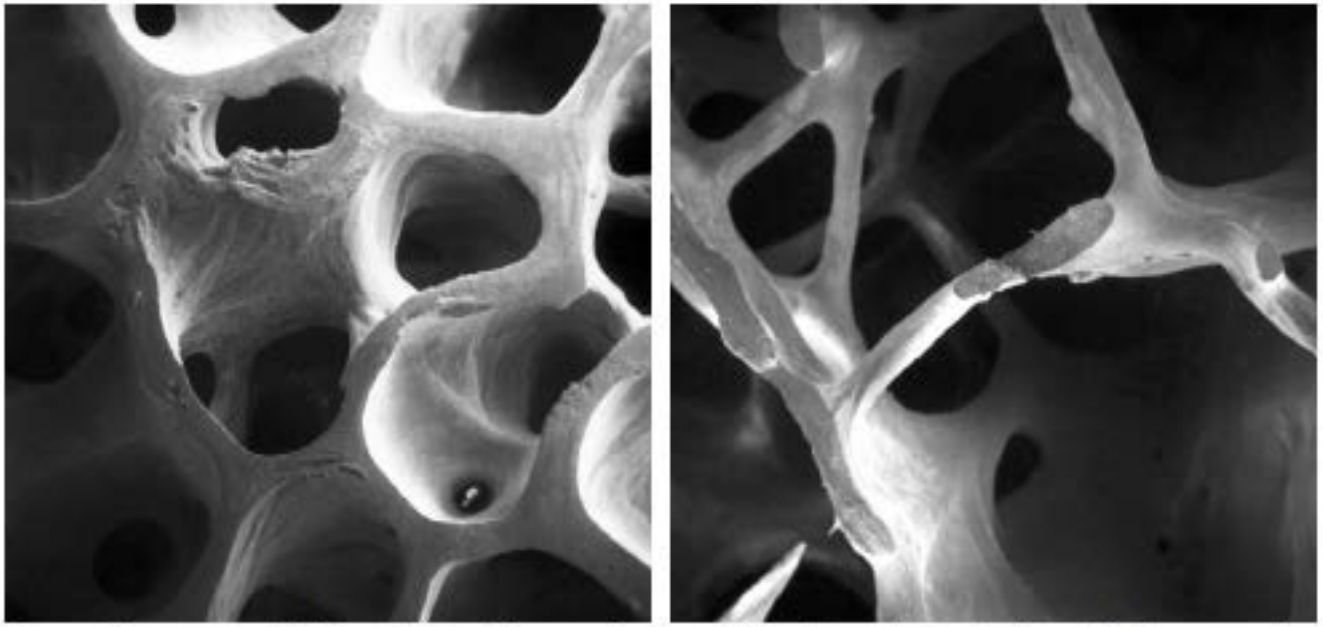
Osteoporosis- Review of 2 cases

FIGURE 1. Micrographs of Normal vs. Osteoporotic Bone

Normal bone *Osteoporotic bone*



From: Dempster, DW et al.[6], with permission of the American Society for Bone and Mineral Research.

Case: C.T. – H & P

- 86 year old consulted for management of osteoporosis by Dr. O Malley.

- What history will you ask?
- What is osteoporosis?
- What are the causes for osteoporosis?
- Is patient at risk for fall?

Case: C.T. – H &P

- Osteoporosis:
- Sustained bilateral hip fracture last year. She was trying to move a recliner, twisted and fell, fracturing her hip. Hip fracture was managed conservatively. Surgical intervention or casting were not done.

- Causes:
- Vitamin D intake . On vitamin D 2000 IU QD
- Menopause- TAH with BSO- 1957.
- Hormone replacement therapy- Was on HRT for 3 years after hysterectomy.

- Exercise- moves around the house using a cane. Does not go out often.
- Smoking history- Never smoked.

- Denies history of eating disorder, kidney stones, blood disorders, use of drugs (immunosuppressants, steroids, heparin), celiac sprue, acromegaly, Cushing's syndrome, bariatric surgery, cancer.

- Hx of hypothyroidism treated with levothyroxine 112 mcg QD. Has type 2 DM.

- Has history of rheumatoid arthritis since 1980. Treated with prednisone for several years. Currently on prednisone 5 mg QD. Has history of steroid injections to shoulder.

Case: C.T. - H &P

- **Fall risk: high**
- History of falls- Denies frequent falls
- Medications -On oxycodone. On Lasix for edema. Wears diapers because she cannot go the bathroom as soon as she would like to.
- Visual problem- yes. Wears glasses. Is not able to see well inspite of using glasses.
- Vestibular problem- Has light headedness and confusion when she is in pain.
- Chronic medical conditions- DM- present, osteoarthritis- present, Parkinson absent, chronic musculoskeletal pain- yes.
- Cognitive dysfunction- only when she has severe pain.
- Vitamin D deficiency- no recent level.
- Musculoskeletal deformities- yes, due to RA and OA.

Case: C.T- H&P

- Her chief concern today is increased musculoskeletal pain. Recently Norco dose was decreased and medication was changed. Since then , she has been in lot of pain. She was in tears due to pain.

- PMHx: Type 2 DM, rheumatoid arthritis, osteoarthritis, chronic pain, anxiety, hypothyroidism, hyperlipidemia, HTN, esophageal stricture-s/p dilation.

- PSHx: Appendectomy, cholecystectomy, thyroidectomy.

- FMHx: Mother died during child birth when she was 27 years old. Father had CAD.

- Social history: Divorced, on SSI, lives at home with her son (Rick). Used to work in farms/. Also, was a waitress and seamstress. Worked till she was 75 years old. Denies tobacco, alcohol and recreational drug use.

Case: C.T- Physical exam

- BP= 144/67 mm of HG; HR= 82/min
- Height=4 feet, 11 inches, Weight=149 lbs, BMI=24.58
- Very pleasant elderly lady in wheel chair
- Has Bouchard's nodes, Heberden's nodes. Has abduction of metacarpals, has feet deformities as well. No tremors.
- Gait- Has difficulty walking without cane.
- No spinal tenderness, kyphosis present.
- CVS, RS, abdomen- unremarkable

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Case: C.T- Labs:

CBC	Feb 2015
WBC	10.1
Hemoglobin	11.6
Platelet count	212
CMP	
Sodium	132
Potassium	4.8
Bicarbonate	26
Chloride	91
Creatinine	0.69
GFR	79
Calcium	9.7
Albumin	3.7
Alkaline phosphatase	89
AST	16
ALT	14
Vitamin D	28

Case: C.T- Imaging:

SOLIS BenOra Mammography

1313 East Osborn Road
Suite 213
Phoenix, AZ 85014

Phone: (602) 234-2601
FAX: (602) 234-3183

Bone Density: Exam date 12/15/2014				
Region	**BMD** (g/cm^2)	**T-Score**	**Z-Score**	**Classification**
AP Spine (L1-L4)	0.967	-0.7	2.1	Normal
Femoral Neck (Left)	0.513	-3.0	-0.6	Osteoporosis
Total Hip (Left)	0.553	-3.2	-0.8	Osteoporosis
Total Hip Bilateral Average	0.532	-3.4	-1.0	Osteoporosis
Femoral Neck (Right)	0.448	-3.6	-1.1	Osteoporosis
Total Hip (Right)	0.510	-3.5	-1.1	Osteoporosis

Case: C.T- Treatment:

Assessment/Plan

#	Detail Type	Description
1.	Assessment	Osteoporosis, unspecified (733.00).
	Patient Plan	- Do following blood work - I will call you with results. - You will need treatment with reclast for osteoporosis. - If vitamin D is normal, I will make arrangements for reclast.
	Provider Plan	- Hx of bilateral hip fracture and T-score in hips (-3.2 and -3.5). DXA done in December 2014. Personally reviewed images and report. - Risk factors- early menopause, senility, chronic steroid use. - At very high risk for fall. - Risk factors for fall- chronic musculoskeletal pain, RA, OA resulting in feet deformities, decreased vision. - Does not have contra- indications for reclast. - Has dentures . Does not need dental work - Will check vitamin D, PTH, CMP. If vitamin D is normal will proceed with reclast infusion. Will not be able to do 24 hour urine calcium because she wears diapers.
	Plan Orders	CMP, Vitamin D, 25-Hydroxy today and TSH to be performed today.

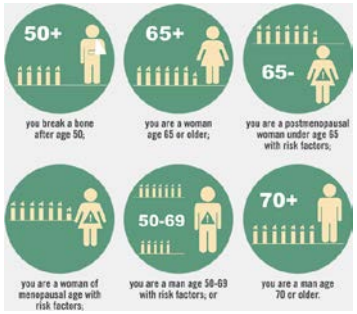
Case: C.T- Treatment:

.	Assessment	Rheumatoid Arthritis (714.0).
	Provider Plan	- On chronic steroid therapy. - Does not appear Cushingoid. - Sent script for med alert bracelet. - Will give sick day rules in next visit and talk about exogenous adrenal insufficiency.
.	Assessment	Esophageal stricture (530.3).
	Provider Plan	- S/p dilatation. - Not candidate for PO fosamax.
.	Assessment	Osteoarthritis (715.90).
	Provider Plan	- Limited ability to walk.
.	Assessment	Hypothyroidism (244.9).
	Provider Plan	- TSH normal in Jan 2015= 2 - Continue levothyroxine 112 mcg QD

What is osteoporosis?

Category	Bone mass
Normal	T-score greater than or equal to -1 SD.
Low bone mass (osteopenia)	T-score less than -1 and greater than -2.5 SD.
Osteoporosis	T-score less than or equal to -2.5 SD Fragility fracture- hip or vertebral fracture, due to fall from a standing position
Severe (established) osteoporosis	T-score less than -2.5 SD in the presence of one or more fragility fractures

Who should be screened?



- Women >65 and men > 70 years
- Younger postmenopausal women and men whom you have concern based on their clinical risk factor profile

- <u>Medicare covers BMD testing for many individuals age 65 and older, and patients with:</u>

- Estrogen deficient women at clinical risk for osteoporosis
- Individuals receiving, or planning to receive, long-term glucocorticoid therapy in a daily dose ≥ 5 mg prednisone or equivalent for ≥ three months
- Individuals with vertebral abnormalities
- Individuals with primary hyperparathyroidism
- Individuals being monitored to assess the response or efficacy of an approved osteoporosis drug therapy

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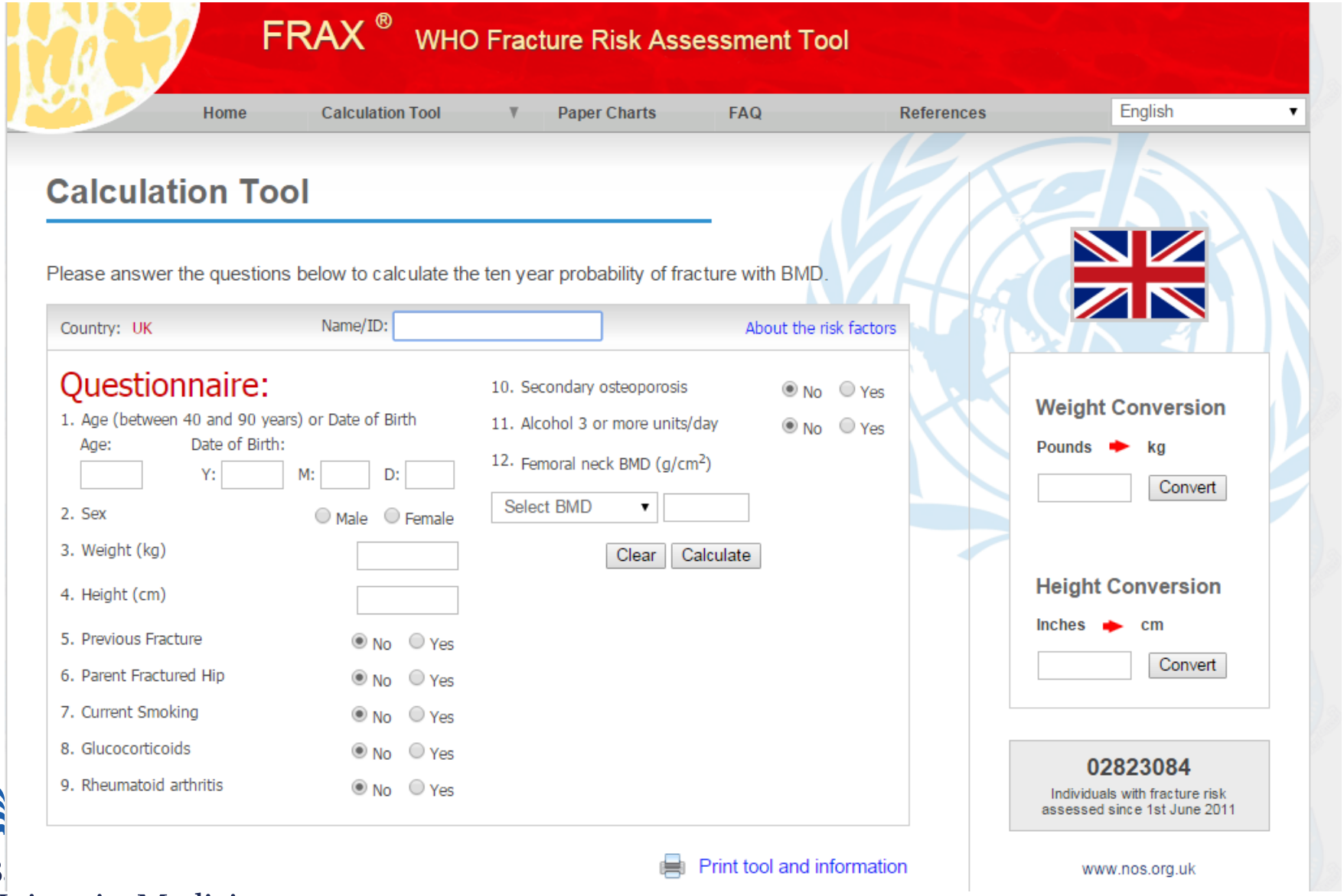
Who should be treated?

- Postmenopausal women and men age 50 and older with:
- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at the femoral neck or spine after appropriate evaluation to exclude secondary causes
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on FRAX score.

FRAX score:



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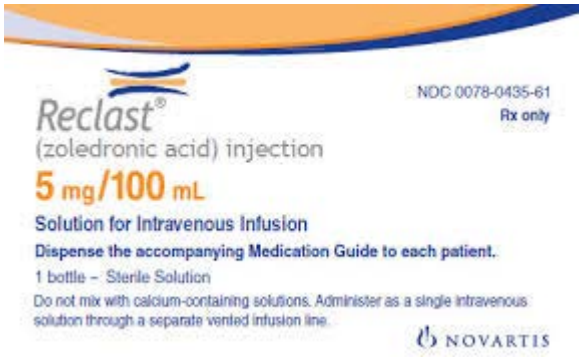
Treatment options-First line medication:

- <u>Bisphosphonates:</u>
- Alendronate is a bisphosphonate that
  - binds to bone hydroxyapatite and
  - specifically inhibits the activity of osteoclasts, the bone-resorbing cells. Alendronate reduces bone resorption with no direct effect on bone formation.



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Fosamax:

- Indications:
  - Prevention and treatment of post menopausal osteoporosis
  - Treatment of male osteoporosis
  - Treatment of steroid induced osteoporosis
  - Treatment of Pagets disease of bone

- Contra-indications:
  - Any esophageal disorder- stricture, achalasia, Barrett's, gastritis, duodenitis, ulcers
  - Pt cannot sit or stand upright for 30 minutes
  - Pt's with increased risk for aspiration
  - Hypocalcemia
  - ? Vitamin D deficiency
  - Creatinine clearance< 35 ml/min/m2

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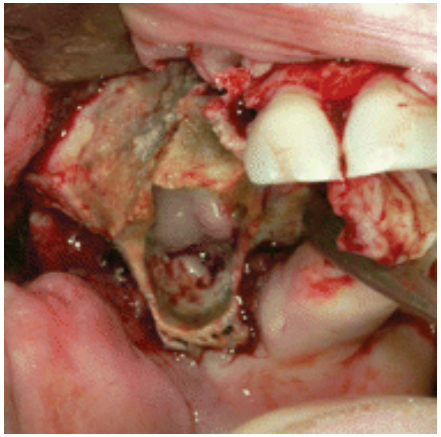
Fosamax: Side effects:

- Upper GI side effects:
  - Abdominal pain, esophageal erosions, bleeding.

- Musculoskeletal Pain:
  - Incapacitating bone, joint, and/or muscle pain
  - Time to onset of symptoms varied from one day to several months after starting the drug
  - Most patients had relief of symptoms after stopping.

Fosamax: Side effects:



- Osteonecrosis of the Jaw:

- Risk factors :
  - -invasive dental procedures (e.g., tooth extraction, dental implants, boney surgery),
  - ill-fitting dentures, pre-existing dental disease,
  - diagnosis of cancer, anemia, coagulopathy
  - concomitant therapies (e.g., chemotherapy, corticosteroids, angiogenesis inhibitors)
  - discontinuation of bisphosphonate treatment may reduce the risk for ONJ

- Patients who develop osteonecrosis of the jaw while on bisphosphonate therapy should receive care by an oral surgeon.
- Extensive dental surgery to treat ONJ may exacerbate the condition.

Fosamax: Side effects:

- Atypical Subtrochanteric and Diaphyseal Femoral Fractures :
- Possible cause:
  - long term oversuppression of bone turnover
  - leading to impaired bone remodeling,
  - accumulation of microdamage in bone and increased skeletal fragility

- Atypical fractures were more likely due to osteoporosis rather than the bisphosphonate therapy itself.

- Low-energy, or low trauma fractures of the femoral shaft
- Can occur anywhere in the femoral shaft
- Transverse or short oblique in orientation without evidence of comminution
- May be bilateral
- Dull, aching thigh pain, weeks to months before a complete fracture occurs.
- Interruption of bisphosphonate therapy

Case 2: I.H- H &P

- 57 year old with hx of GERD, depression, anxiety, eating disorder during adolesence has severe osteoporosis.
- Diagnosed with osteoporosis in 2002 by a DXA scan finding . She recently had T8 compression fracture when she was trying to push her bike in to the car. Has history of multiple rib fracture.
- Has strong family history of osteoporosis and family members do not respond to bisphosphonates.
- Was on bisphosphonate therapy for atleast 10 years. T-score of lumbar spine in May 2014 was -4 and in hip was -2.9.
- Risk factors for osteoporosis:
- Bulimia during adolescence, surgical menopause but she was treated with HRT for 10-12 years, lean built, Caucasian lady, strong family history of osteoporosis, history of proton pump inhibitor use.
- No falls since last visit.

Case 2: I.H- H &P

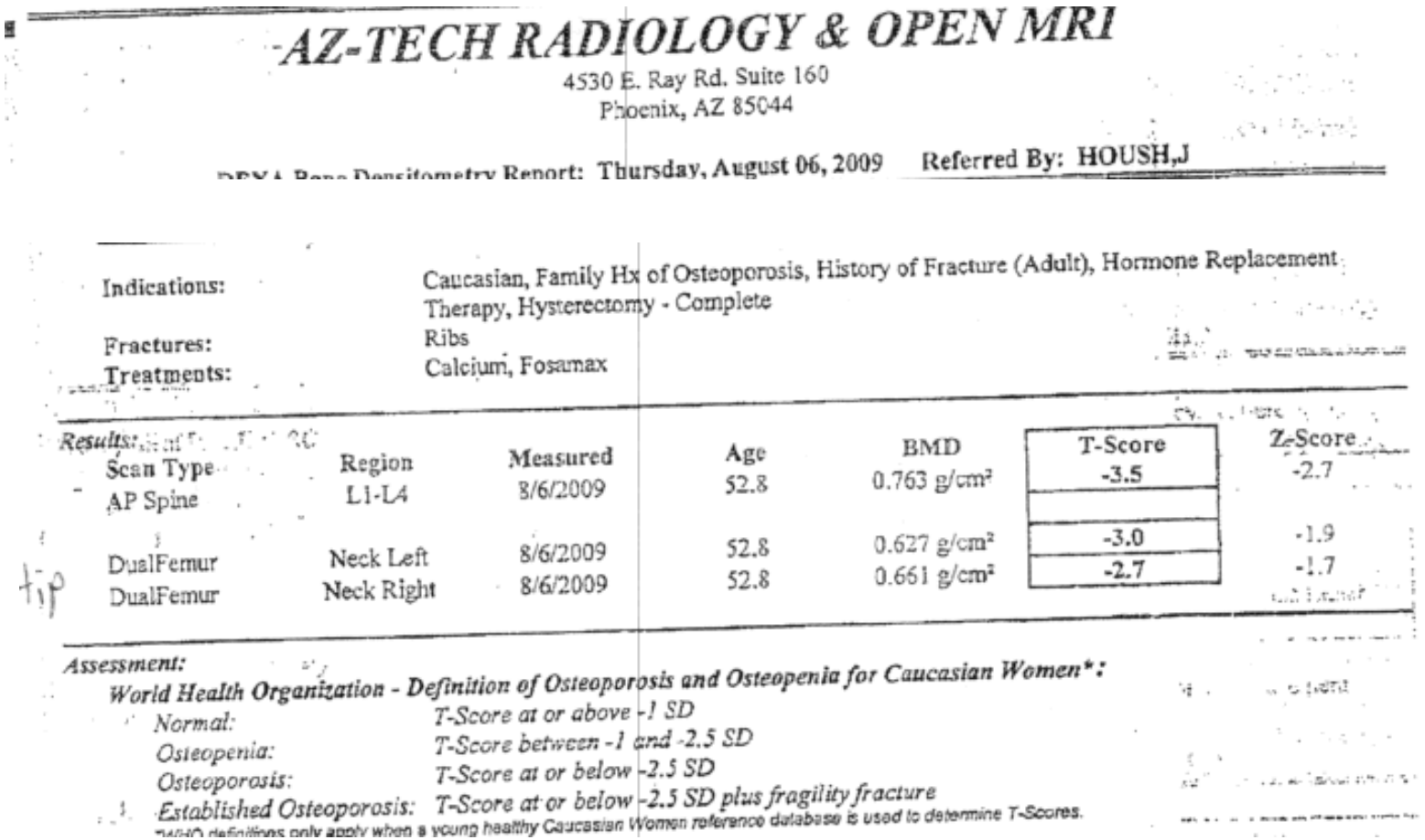
- BP= 110/90 mm of HG, HR= 60 /minute Weight=127.00, BMI= 21.80

- Skin: Thin skin present, no acanthosis, no vitiligo. No stretch marks.
- Musculoskeletal: Able to do tandem walking. Balance is good. Kyphosis present. No spinal tenderness. Not double-jointed.
- Extremity: No edema.
- CVS, RS, abdomen- unremarkable

Case 2: I.H- Labs:

Creatinine	**0.64 mg/dl**
BUN	12 mg/dl
Sodium	141 mmol/L
Potassium	4 mmol/L
Calcium	9.2 mg/dl
Alkaline phosphatase	73 IU/L
AST	18 IU/L
ALT	10 IU/L
PTH	48 (15-65 pg/ml)
Vitamin D	48 (30-100 ng/ml)
TSH	1.3 (0.45-4.5 uIU/ml)
Phosphorus	3.4 (2.5-4.5 mg/dl)

Case 2: I.H- Imaging:



AZ-TECH RADIOLOGY & OPEN MRI

4530 E. Ray Rd. Suite 160
Phoenix, AZ 85044

DEXA Bone Densitometry Report: Thursday, August 06, 2009 Referred By: HOUSH,J

Indications: Caucasian, Family Hx of Osteoporosis, History of Fracture (Adult), Hormone Replacement Therapy, Hysterectomy - Complete
Fractures: Ribs
Treatments: Calcium, Fosamax

Results:

Scan Type	Region	Measured	Age	BMD	T-Score	Z-Score
AP Spine	L1-L4	8/6/2009	52.8	0.763 g/cm²	-3.5	-2.7
DualFemur	Neck Left	8/6/2009	52.8	0.627 g/cm²	-3.0	-1.9
DualFemur	Neck Right	8/6/2009	52.8	0.661 g/cm²	-2.7	-1.7

Assessment:

World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women:*

- *Normal:* T-Score at or above -1 SD
- *Osteopenia:* T-Score between -1 and -2.5 SD
- *Osteoporosis:* T-Score at or below -2.5 SD
- *Established Osteoporosis:* T-Score at or below -2.5 SD plus fragility fracture

**WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.*

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Case 2: I.H- Summary:

- 57 year old with following risk factors for osteoporosis
  - Eating disorder during adolescence
  - Strong family hx of osteoporosis
- S/p treatment with bisphosphonate for 10 years
- Presented with new T8 compression fracture

- What is the next step?

Case 2: I.H- Evaluate for secondary causes for osteoporosis:

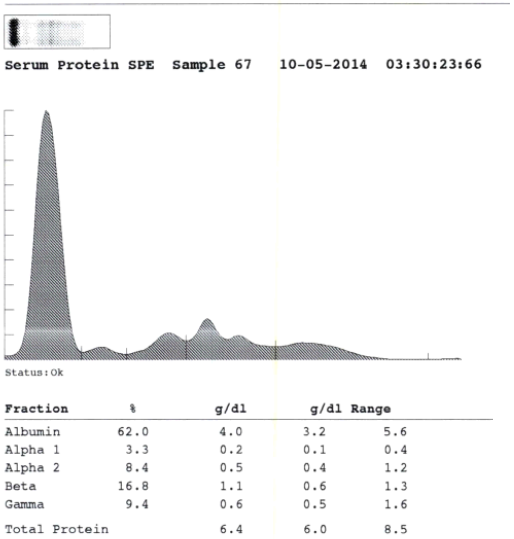
TESTS	RESULT	FLAG
CBC With Differential/Platelet		
WBC	5.6	
RBC	4.50	
Hemoglobin	13.5	
Hematocrit	40.5	
MCV	90	
MCH	30.0	
MCHC	33.3	
RDW	14.0	
Platelets	257	
Neutrophils	61	
Lymphs	29	
Monocytes	9	
Eos	1	
Basos	0	
Neutrophils (Absolute)	3.4	
Lymphs (Absolute)	1.6	
Monocytes(Absolute)	0.5	
Eos (Absolute)	0.1	
Baso (Absolute)	0.0	
Immature Granulocytes	0	
Immature Grans (Abs)	0.0	
Protein Electro.,S		
Protein, Total, Serum	6.4	
Albumin	4.0	
Alpha-1-Globulin	0.2	
Alpha-2-Globulin	0.5	
Beta Globulin	1.1	
Gamma Globulin	0.6	
M-Spike	Not Observed	
Globulin, Total	2.4	
A/G Ratio	1.7	
Please note:		

Protein electrophoresis scan will follow via computer, mail, or courier delivery.

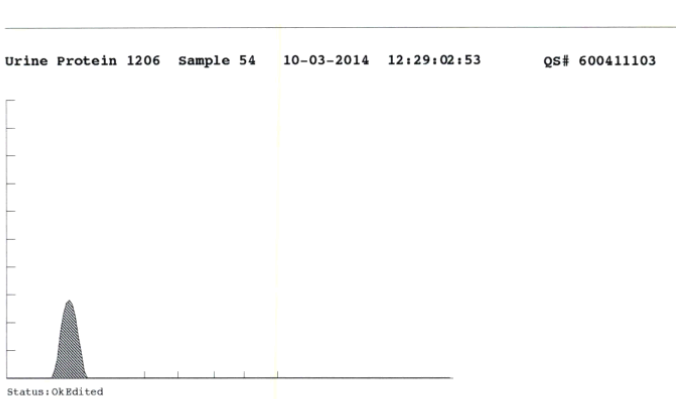
Protein Electro, Random Urine				
Protein,Total,Urine	5.1	mg/dL	0.0 - 15.0	01
Albumin, U	100.0	%		02
Alpha-1-Globulin, U	0.0	%		02
Alpha-2-Globulin, U	0.0	%		02
Beta Globulin, U	0.0	%		02
Gamma Globulin, U	0.0	%		02
M-Spike, %	Not Observed	%	Not Observed	02
Please note:				02

Protein electrophoresis scan will follow via computer, mail, or courier delivery.

Prolactin	19.0	ng/mL	4.8 - 23.3	01
t-Transglutaminase (tTG) IgA	<2	U/mL	0 - 3	02
		Negative	0 - 3	
		Weak Positive	4 - 10	
		Positive	>10	



Fraction	%	g/dl	g/dl Range	
Albumin	62.0	4.0	3.2	5.6
Alpha 1	3.3	0.2	0.1	0.4
Alpha 2	8.4	0.5	0.4	1.2
Beta	16.8	1.1	0.6	1.3
Gamma	9.4	0.6	0.5	1.6
Total Protein		6.4	6.0	8.5



Fraction	%
RAlbumin	100.0
RAlpha 1	0.0
RAlpha 2	0.0
RBeta	0.0
RGamma	0.0
Total Protein	

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What is the treatment option?

Secondary causes for osteoporosis:

- Endocrine disorders :
  - Cushing's syndrome , Hyperprolactinemia, Panhypopituitarism
  - Thyrotoxicosis
  - Hyperparathyroidism
  - Adrenal insufficiency
  - Type 1 Diabetes mellitus
  - Premature ovarian failure, Turner's & Klinefelter's syndromes, hypogonadism, Anorexia nervosa and bulimia

- Gastrointestinal disorders:
  - Celiac disease
  - Malabsorption, gastric bypass surgery, pancreatitis, PBC

- Hematologic disorders:
  - Lymphoma, sickle cell, thalassemia, hemophilia, any cancer

Secondary causes for osteoporosis:

Medications :

-Anticoagulants (heparin)
-Cancer chemotherapeutic drugs
- Gonadotropin releasing hormone agonists
-Anticonvulsants
-Cyclosporine A and tacrolimus
-Lithium
-Aromatase inhibitors
-Depo-medroxyprogesterone
-Glucocorticoids (≥ 5 mg/d of prednisone or equivalent for ≥ 3 mo)

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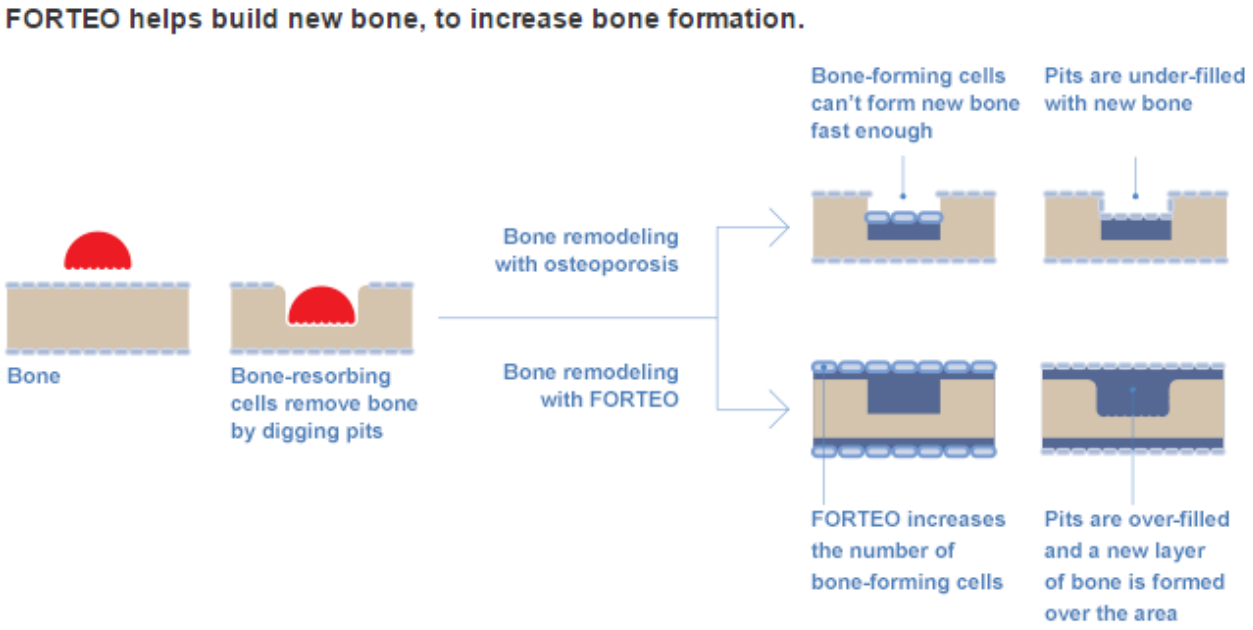
Forteo (Teriparatide- synthetic PTH 1-34):

- PTH maintains serum ionized calcium concentrations within a narrow range,
  - through its actions to stimulate renal tubular calcium reabsorption and bone resorption.

- Chronic exposure to high serum PTH concentrations (as seen with primary or secondary hyperparathyroidism) results in bone resorption.

- Intermittent administration of recombinant human PTH (both full-length 1-84 or fragment 1-34) has been shown to stimulate bone formation more than resorption, at least over the first 12 months of treatment.



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Case 2: I.H- Treatment:

- Candidates — Potential candidates for PTH therapy include

- Men or postmenopausal women with severe osteoporosis
  - T-score of -3.5 or below even in the absence of fractures
  - T-score of -2.5 or below plus a fragility fracture
- Patients with osteoporosis who are
  - unable to tolerate bisphosphonates or
  - have relative contraindications to bisphosphonates (achalasia, scleroderma esophagus, esophageal strictures)
- Patients who fail other osteoporosis therapies
  - fracture with loss of BMD in spite of compliance with therapy

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Forteo:

- Precautions
- Patients with primary or secondary hyperparathyroidism should not receive PTH, even if they have low BMD.

- Patients who are at increased baseline risk for osteosarcoma,
  - such as those with Paget disease of bone,
  - history of prior radiation therapy, or
  - unexplained elevation of alkaline phosphatase, should not receive PTH.

- In patients with
  - pre-existing malignancies,
  - renal stones,
  - gout, or
  - renal insufficiency, PTH should not be considered unless other drugs have failed.

- Caution about calcium supplementation is warranted although clinical trials have used at least 500 mg elemental calcium and at least 400 int. units of vitamin D per day

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Forteo: Teriparatide- synthetic PTH 1-34

- Pretreatment evaluation :
- CMP, vitamin D, phosphorus, uric acid
- 24-hour urine Ca, creatinine

- Patients who are vitamin D deficient should be replaced with vitamin D prior to starting PTH therapy.

- If baseline hypercalcemia or hypercalciuria are present, further evaluation for primary hyperparathyroidism is necessary. PTH therapy should not be started unless hypercalciuria is resolved.

- If the uric acid pre-treatment is >7.5 mg/dL (446 micromol/L), or if there is a history of gout, PTH probably should not be used.

Forteo: Teriparatide- synthetic PTH 1-34

- Administered as once daily injection- 20mcg.
- Recommended duration- 2 years

- Monitoring:
- In patients with vascular insufficiency, or orthostatic hypotension, pulse and blood pressure should be monitored carefully following the first PTH injection.

- Can measure calcium at baseline, 1, 6, 12 months

- Uric acid should be monitored at baseline and at six months.

- BMD in 1 year

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Case 2: I.H- Treatment:

Uric Acid, Serum				
Uric Acid, Serum	5.0	mg/dL	2.5 - 7.1	01
Please Note:				01
	Therapeutic target for gout patients: <6.0			

- Started on Forteo.
- No contra-indications for Forteo.

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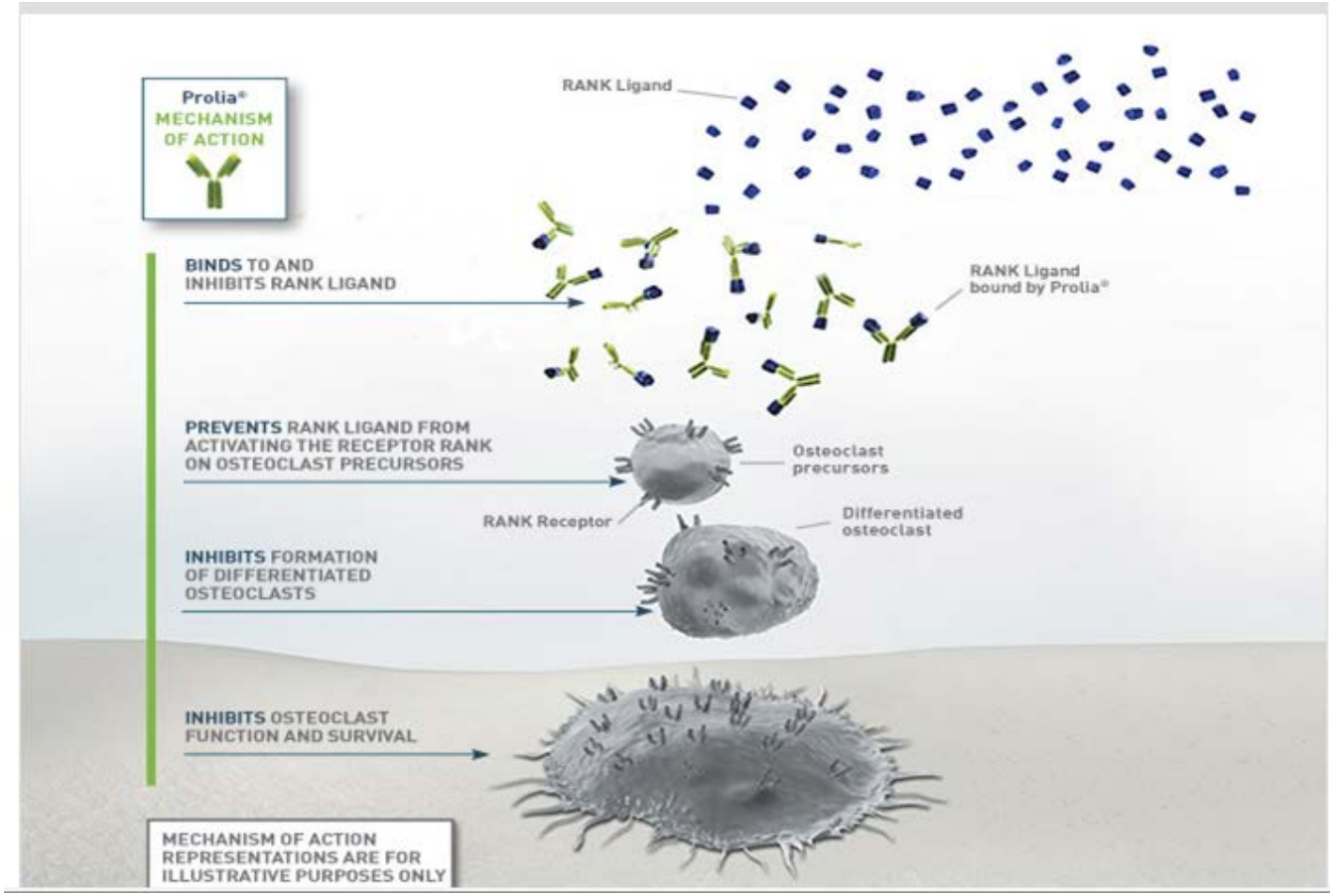
Prolia: Denosumab



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Prolia: Denosumab

- Candidates:
  - No consensus on the optimal use of denosumab
  - May have a role in patients who are intolerant of or unresponsive to other therapies and in those with impaired renal function
  - Men receiving androgen deprivation therapy –non-metastatic prostate cancer
  - Women undergoing breast cancer treatment with aromatase inhibitors
  - Bone metastases
  - Multiple myeloma patients

- Pre-treatment evaluation:
  - Same as bisphosphonates

- Dosing:
  - 60 mg SQ Q 6 months

Prolia: Denosumab

- <u>Monitoring:</u>

- Patients with
  - CKD, CrCl< 30 ml/min/ m2
  - Hypoparathyroidism
  - Malabsorption
- Are at increased risk for hypocalcemia
- Calcium should be checked 10 days after denosumab administration

- Increased frequency of infection:

  -diverticulitis, pneumonia, atypical pneumonia, appendicitis, cellulitis, and labyrinthitis

- ONJ and atypical fractures – over suppression of bone remodelling

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Calcium and vitamin D:

- Optimal intake of calcium and vitamin
  - In 1200 mg of calcium daily (total diet plus supplement) . Elemental calcium. Preferrably in split doses.
  - 800 int. units of vitamin D daily

- Goal Vitamin D> 30
  - When level > 30, secondary hyperparathyroidism begins to occur.