Κρητο-κυπριακό συνέδριο Ρευματολογίας

Χανιά 9-11 Νοεμβρίου 2018

Josef's email

Αγαπητοί,

Επισυνάπτεται το πρόγραμμα.

Σας παρακαλώ ΠΟΛΥ να θυμάστε (παράκληση από τον Πρόδρομο και όλους τους διοργανωτές) τα cases να είναι 8 λεπτά ομιλία και 2 λεπτά ερωτήσεις. **ΟΚΤΩ ομιλία και ΔΥΟ για ερωτήσεις (ανά περιστατικό)**

Joseph


7:55
DEFUSABLE
CLOCK
nootropic
design
ALARM
COUNTDOWN BOMB

The Trilogy

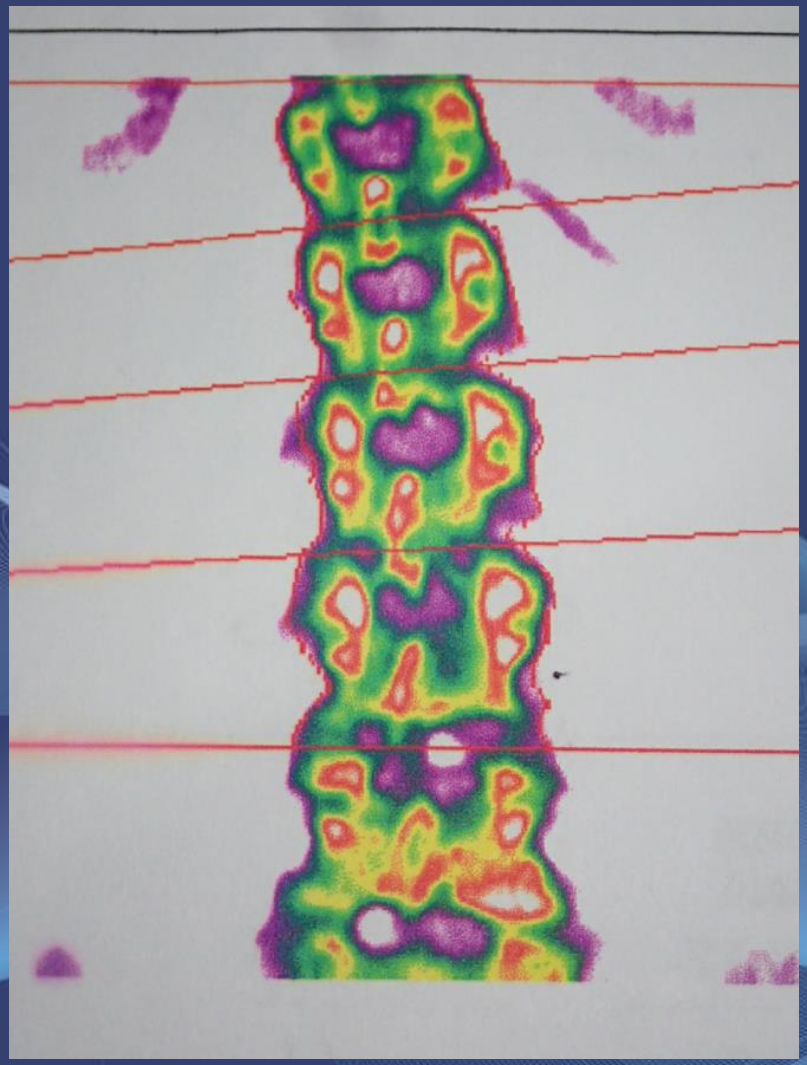
The ugly

- Mrs. Ch. A is a 60 year old lawyer mother of two children.
- Hysterectomy at age 45 (2003) with preservation of one ovary.
- Menopause in 2005 (age 47) according to her gyno.
- Never received HRT.

The Ugly

DATE	L1-L4	L2-L4	NECK	TOTAL	COMMENTS
14.09.01	-0.3	-0.1	-1.3	-1.0	Wrong numbering of vertebra (T12 as L1) – Good positioning of neck ROI with good internal rotation
20.02.03	-0.4	-0.3	-1.6	-1.0	Wrong numbering of vertebra(T12 as L1) – Good positioning of neck ROI with good internal rotation
07.02.04	-0.6	-0.6	-1.3	-1.1	Wrong numbering of vertebra.(T12 as L1) – Good positioning of neck ROI with good internal rotation
10.12.05	-0.6	-0.5	-1.6	-1.5	Wrong numbering of vertebra. (T12 as L1) - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
24.03.07	-0.3	-0.3	-1.6	-1.2	Wrong numbering of vertebra(T12 as L1). - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
27.08.08	-1.1	-1.0	-2.3	-1.6	Wrong numbering of vertebra(T12 as L1). - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
20.02.10	-0.9	-0.8	-2.4	-1.6	Correct numbering of vertebra - Good positioning of neck ROI with good internal rotation
14.05.11	-1.2	-1.2	-2.2	-1.6	Correct numbering of vertebra - Wrong positioning of neck ROI (lower, towards the trochanter major)with good internal rotation
28.04.12	-1.3	-1.3	-2.4	-1.9	Correct numbering of vertebra - Good positioning of neck ROI with good internal rotation
11.05.13	-1.6	-1.5	-2.7	-2.3	Correct numbering of vertebra. Part of L4 not included - Good positioning of neck ROI with good internal rotation
07.01.15	-0.8	-0.8	-2.6	-1.9	Correct numbering of vertebra - Wrong positioning of neck ROI (lower, towards the trochanter major)with good internal rotation
14.07.16	-0.3	-0.3	-2.6	-1.9	Correct numbering of vertebra - Good positioning of neck ROI with good internal rotation
03.07.17	-0.3	-0.4	-2.6	-2.0	Correct numbering of vertebra - Good positioning of neck ROI with good internal rotation
05.07.18	-0.9	-0.9	-2.7	-1.9	Wrong numbering of vertebra(T12 as L1). - Part of 'L1' not included. – Wrong positioning of neck ROI (very close to trochanter major) with good internal rotation. Part of the shaft not included

The Ugly



The Ugly

28.04.12 (age 54)

L1-L4 T-score = -1.3

Neck T-score = -2.4

Which would have been your treatment choice: SERMs -BPs – DSM - TPT?

The ugly

The real question is:

When to start treatment?

The answer is:

Fracture risk assessment

The ugly

FRACTURE RISK PREDICTION TOOLS

- History of fractures in the patient
- Evaluation of co-morbidities
- Bone mineral density (BMD)measurement
- Evaluation of the fall risk
- Absolute fracture risk prediction tools e.g. FRAX
- Trabecular Bone Score (TBS)
- Measurement of bone strength
- Bone Turnover Markers (BTM)

There is insufficient evidence that bone turnover markers help to predict the fracture risk in clinical practice(1).

(1) Vasikaran S et al. Osteoporos Int. 22 391-420.

The ugly

Measurements of bone strength

Hip structural analysis (HSA) } DXA

Trabecular bone score (TBS) } DXA

Finite element analysis (FEA) } DXA + CT

Greek guidelines for diagnosis and osteoporosis treatment 2017

Indications of drug therapy for postmenopausal osteoporosis

- Σπονδυλικό κάταγμα χαμηλής βίας.
- Κάταγμα ισχίου χαμηλής βίας.
- Περισσότερα από ένα έτερα κατάγματα χαμηλής βίας (π.χ. κάταγμα κερκίδας).
- Μέτρηση οστικής πυκνότητας ισχίου (ολικό ισχίο ή αυχένας μηριαίου) ή/και Ο.Μ.Σ.Σ. με T score ≤-2,5.
- Μέτρηση οστικής πυκνότητας με T score μεταξύ -1,0 και -2,5 (οστεοπενία) αλλά με 10-ετή καταγματικό κίνδυνο (FRAX) ≥10% για μείζον οστεοπορωτικό κάταγμα ή/και ≥ 2,5% για κάταγμα ισχίου, για άτομα ηλικίας 50-75 ετών.
- Μέτρηση οστικής πυκνότητας με T score μεταξύ -1,0 και -2,5 (οστεοπενία) αλλά με 10-ετή καταγματικό κίνδυνο (FRAX) ≥ 15% για μείζον οστεοπορωτικό κάταγμα ή/και ≥5% για κάταγμα ισχίου, για άτομα ηλικίας άνω των 75 ετών.

The Ugly

Country: Greece Name/ID: Ch.A About the risk factors

Questionnaire:

1. Age (between 40 and 90 years) or Date of Birth

   Age: 60 Date of Birth: Y: 1958 M: 03 D: 30

2. Sex — Male / Female

3. Weight (kg): 50

4. Height (cm): 159

5. Previous Fracture — No / Yes

6. Parent Fractured Hip — No / Yes

7. Current Smoking — No / Yes

8. Glucocorticoids — No / Yes

9. Rheumatoid arthritis — No / Yes

10. Secondary osteoporosis — No / Yes

11. Alcohol 3 or more units/day — No / Yes

12. Femoral neck BMD (g/cm^2)

GE-Lunar 0.689 T-score: -2.5

Clear Calculate

BMI: 19.8

The ten year probability of fracture (%)

with BMD

Major osteoporotic	7.2
Hip Fracture	2.4

If you have a TBS value, click here: Adjust with TBS

Cost-effective osteoporosis treatment thresholds in Greece.

Makras P. et al Osteoporos Int 2015 Jul:26(7):1949-1957

< 75 y.o

MOF ≥ 10%

HF ≥ 2.5%

> 75 y.o

MOF ≥ 15%

HF ≥ 5%

2018 update of French recommendations on the management of postmenopausal osteoporosis

Briot K. et al . Joint Bone Spine (2017), https://doi.org/10.1016/j.jbspin.2018.02.009

Indications of drug therapy for postmenopausal osteoporosis.

Based on T-score at site where the value is lowest	Severe fractures (femur, spine, humerus, pelvis, proximal tibia)	Non-severe fractures	No fracture but risk factors for osteoporosis and/or falls
>-1	Advice from a specialist	No treatment	No treatment
≤-1 and >-2	**Treatment**	Advice from a specialist	No treatment
≤-2 and >-3	**Treatment**	**Treatment**	Advice from a specialist
≤-3	**Treatment**	**Treatment**	**Treatment**

The Ugly

Do BMD changes over time matter? Are they crucial for your decision?

From 14.09.01 to 28.04.12 we had a decrease in BMD :

L1-L4 = -12.2% (Not comparable) ~1.2%/year

Neck = - 16.3% (Comparable) ~ 1.55/year

The Ugly

Following her endocrinologist's advice…

- June 2012 started Denosumab 60mg/6mo
- Last Denosumab injection in mid-December 2017.

03.07.17	Change (28.04.12)
L1-L4 T-score = -0.3	↑ 10.2%
Neck T-score = -2.6	↓ 1.8%

Are you happy with the response?

Would you stop or continue?

Deciding to continue, which would have been your choice? DSM, BPs, TPT, TPT+DSM?

The Ugly

The real question is…

For how long do we have to treat?

When do we have to continue treatment?

Treatment duration

- The decision for how long to treat with anti-resorptive drugs is largely dependent on their long-term efficacy and safety.

- Generally agreed duration of treatment is:

  Oral BPs → 5 years

  IV BPs → 3 years

  DSM → 4-5 years

When do we have to continue treatment

- Reassessment of fracture risk is essential for decision making.
- A patient is considered to remain at high risk of fracture if:

1.) History of hip, spine or multiple osteoporotic fractures within 5 years before and/or during therapy.

2.) In the absence of fracture, has persistently low BMD :

- Hip (neck or total) < 2.5 if < 65 years
- Hip (neck or total) < 2.0 if >65 years and/or are frequent fallers

3.) BMD decrease > 0.03g/cm2 at the spine or hip

4.) Persistently high fracture risk based on clinical judgment or comorbidities.

Continue with what and for how long?

- Data on fracture risk reduction during long-term treatment are mainly available for antiresorptive drugs.
- Among antiresorptives, the results of extension studies with alendronate, risedronate ,zoledronate and denosumab have been analysed.
- Notably, these extension studies were not primarily designed for fracture outcomes, but to look at BMD changes upon continuation or discontinuation of therapy and were also limited in the number of patients who were enrolled long-term.

Continue with what and for how long?

RISEDRONATE

VERT extension 3 → 7 years

ALENDRONATE

FIT extension study (FLEX) 5 → 10 years

ZOLENDRONATE

HORIZON extension study 3 → 6 → 9 years

DENOSUMAB

FREEDOM extension study 3 → 5 → 10 years

Drug holiday for how long?

- Risedronate : 1 year
- Alendronate : 2 – 3 years
- Zolendronate : 3 years

The Ugly

In late August 2018 started experiencing severe back pain.

- 05.09.18 MRI : 4 vertebral fractures
- 20.09.18 MRI : Additional 3 fractures
- 01.10.18 MRI : A total of **13 vertebral fractures.**

Denosumab-discontinuation associated fractures

- Discontinuation of denosumab results in a rebound response of bone turnover markers, which rise above baseline at 3 months and remain elevated until reaching again baseline levels approximately 30 months after the last dose.
- Bone mineral density (BMD) gains are also lost, and BMD values reach baseline values after 1- 2 years off-treatment.

Bone HG, et al. J Clin Endocrinol Metab. 2011;96(4):972–80.

Miller PD, et al. Bone. 2008;43(2):222–9.

Denosumab-discontinuation associated fractures

"Discontinuation of denosumab and associated fracture incidence: analysis from the Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) trial".

Brown PJ et al. J Bone Miner Res 2013 Apr;28(4):746-52

In 2016 a cascade of case reports of vertebral fractures following denosumab discontinuation was published, soon followed by an editorial calling for "Cancel the denosumab holiday".

McClung M.R Osteoporos Int (2016) 27:1677-1682)

Early 2017 , Anastasilakis et al. analyze in a systematic review the published case reports aiming to identify clinical or imaging characteristics that could be associated with increased risk of vertebral fractures upon denosumab discontinuation.

Anastasilakis A. et al. JBMR, Vol. 32, No. 6, June 2017, pp 1291–1296

Denosumab-discontinuation associated fractures

- None of the cases reported herein sustained any non-vertebral fractures (Rebound-Associated Vertebral Fractures, RAVFs).
- The majority of the patients had multiple fractures (92%).
- The number of fractures per patient was 4.7 (mean) / 5.0 (median) with a range from 1 to 9.
- Vertebra T12 was the most commonly affected (17/24) followed by L1 (14/24), L3 (13/24), T11 (12/24), and L2 (12/24). Location being similar to common osteoporotic fractures suggests that these are typical insufficiency fractures, albeit in a rather magnified scale.
- Patients treated for ≤ 2 years had less fractures than those treated for > 2 years.

Denosumab-discontinuation associated fractures

- Twenty of the 24 patients (83%) were treatment naive. The remaining 4 had received previous treatment for osteoporosis (1 STR + RAL, 1 TPT, 2 BPs).

- It had been proposed that these incidents occur in treatment naive patients only and that previous use of BPs decrease the risk for this alarming phenomenon.

  Lamy O et al. J Clin Endocrinol Metab. Epub 2016 Oct 12: jc20163170.

- However, as more cases are reported, it seems that previous treatment might not necessarily avert the risk of fracture.

  Liana Tripto-Shkolnik et al. Cal Tiss Int July 2018, Volume 103, Issue 1, pp 44–49

Denosumab-discontinuation associated fractures

- Eight patients (33%) had previous prevalent vertebral fractures, that may suggest impaired bone strength and tendency to new fractures.
- Prevalent vertebral fractures, before or during the treatment period, were the strongest predictor of new vertebral fractures after discontinuation in the 2016 analysis of denosumab's pivotal study.

Brown JP et al. J Bone Miner Res. 2016;31(Suppl 1)

- All cases occurred 8 to 16 months after the last denosumab injection.
- Patient's age is probably of minimal importance because these incidents have been described in a wide range of age.

Denosumab-discontinuation associated fractures

- After the incident fracture, several treatment strategies were followed: most patients received teriparatide, some reinitiated denosumab, a few received zoledronic acid, and others received a combination of teriparatide and denosumab or zoledronic acid.

- Five patients underwent vertebroplasty. In all cases, several new fractures occurred in the month after vertebroplasty, questioning the utility of this procedure in these patients.

- The recent post-hoc analysis of FREEDOM trial and its extension confirmed the increased vertebral fracture risk in patients who discontinued denosumab and that more than half of these patients had multiple fractures.

Cummings SR. et al. JBMR, Vol.33, No 2, February 2018, pp 190-198

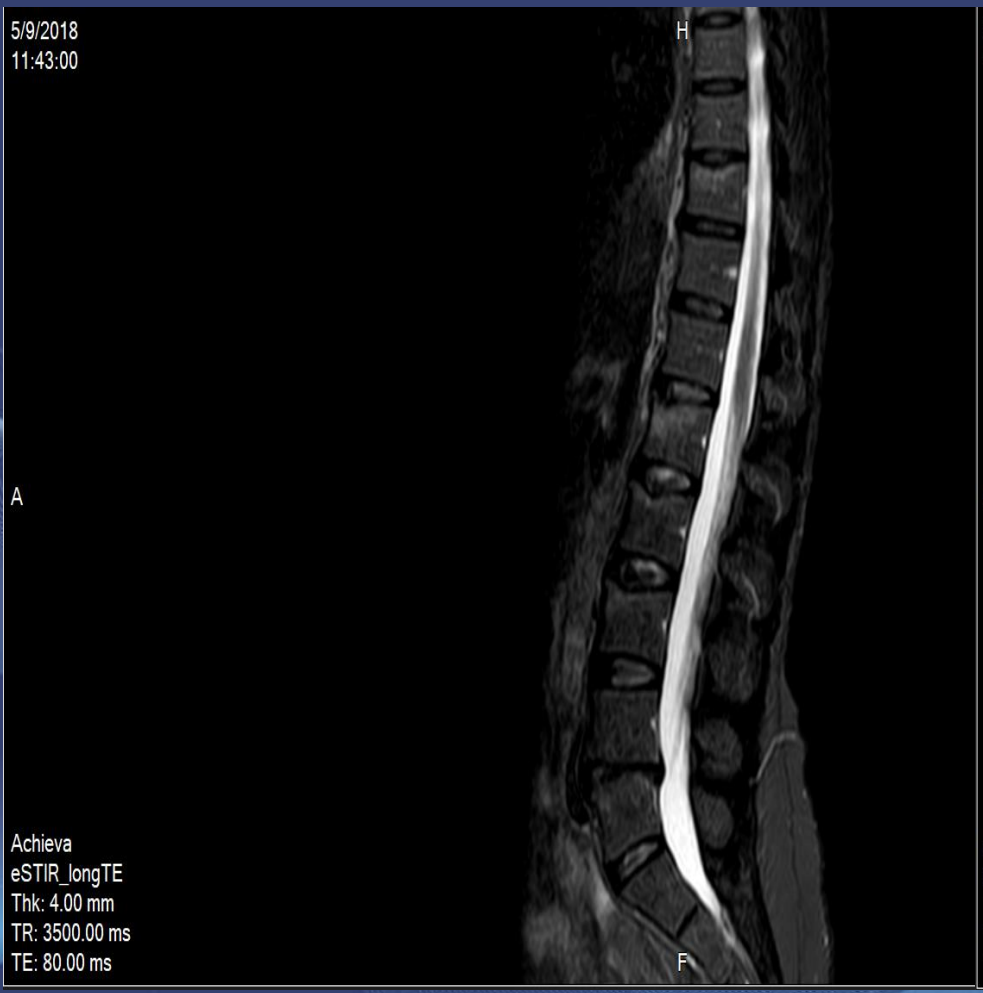
The Ugly

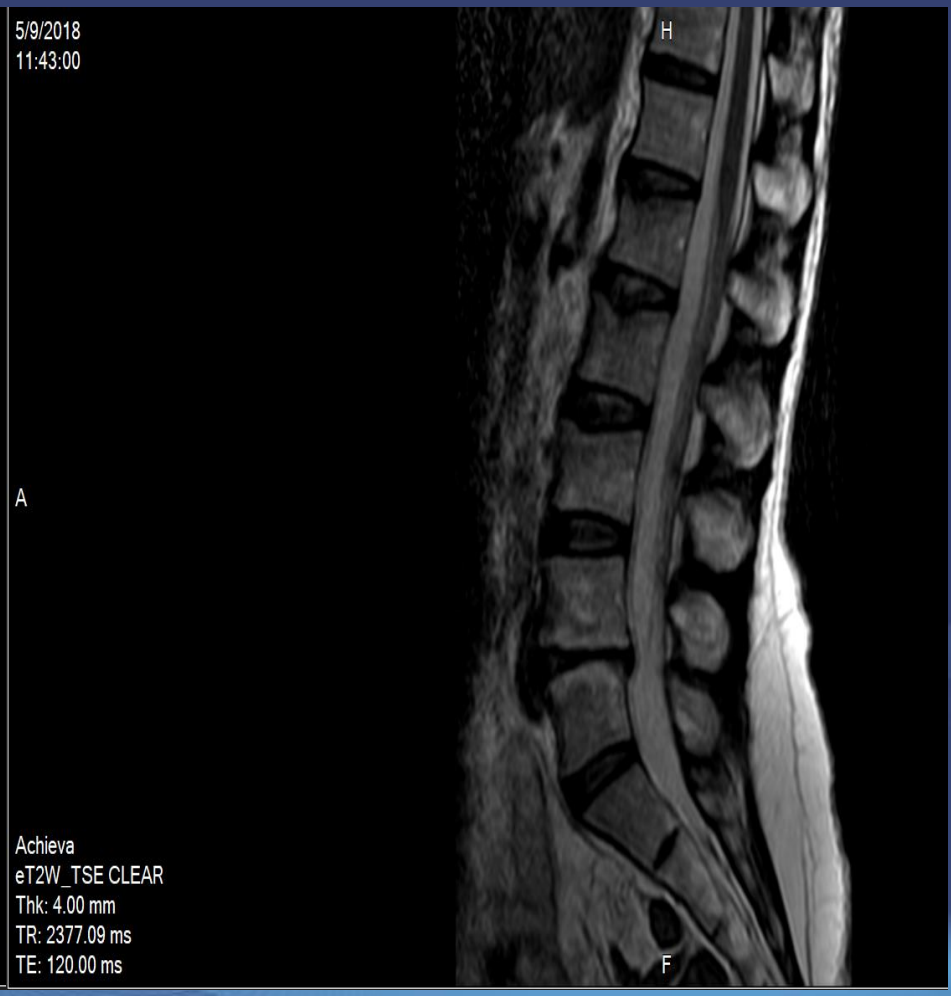
- How would you manage her pain?
  - Conservative treatment: Pain killers, spinal brace
  - Percutaneous Vertebral Augmentation: PVP, PKP, PIT
- Will you treat her with anti-osteoporotic medications?
- If yes what would have been your choice: BPs, DSM, TPT, TPT+ DSM, TPT+ZOL?

The Ugly

05.09.18

T10, L1, L2, L3

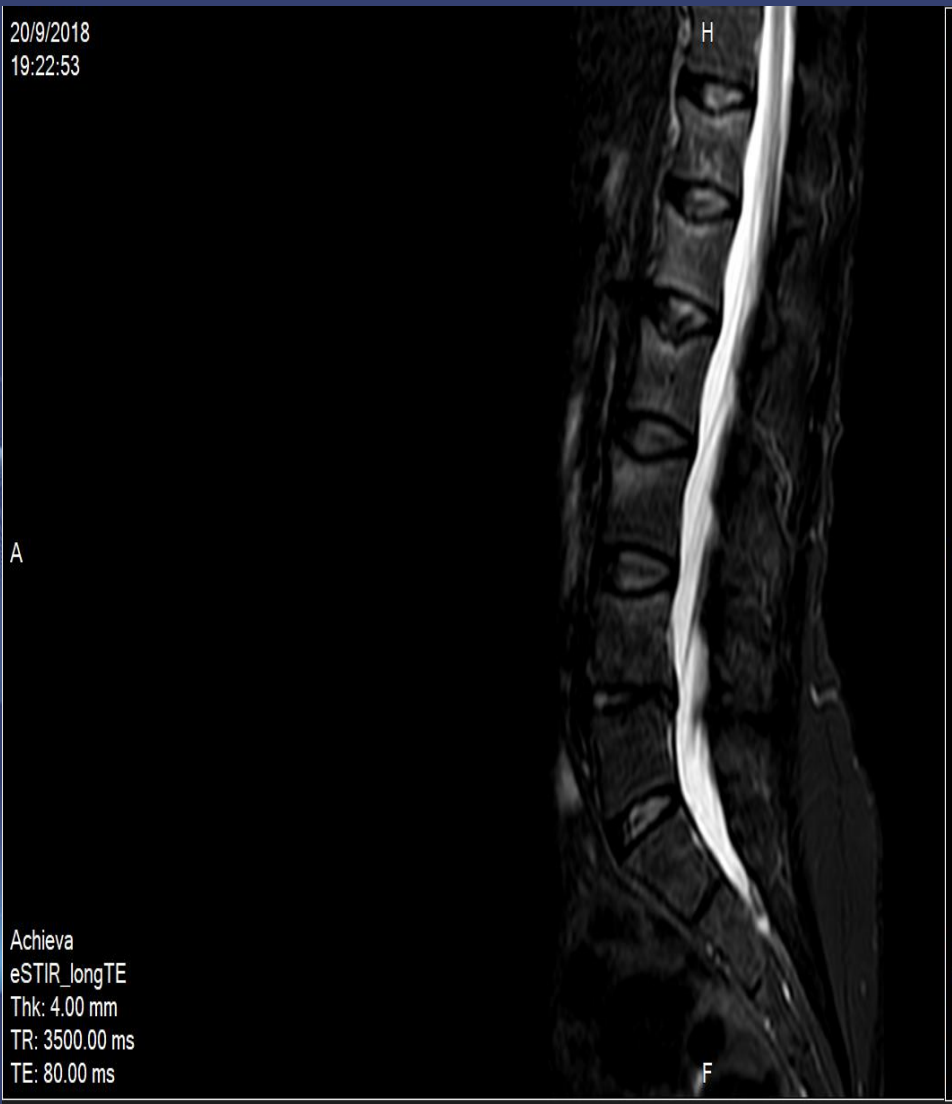


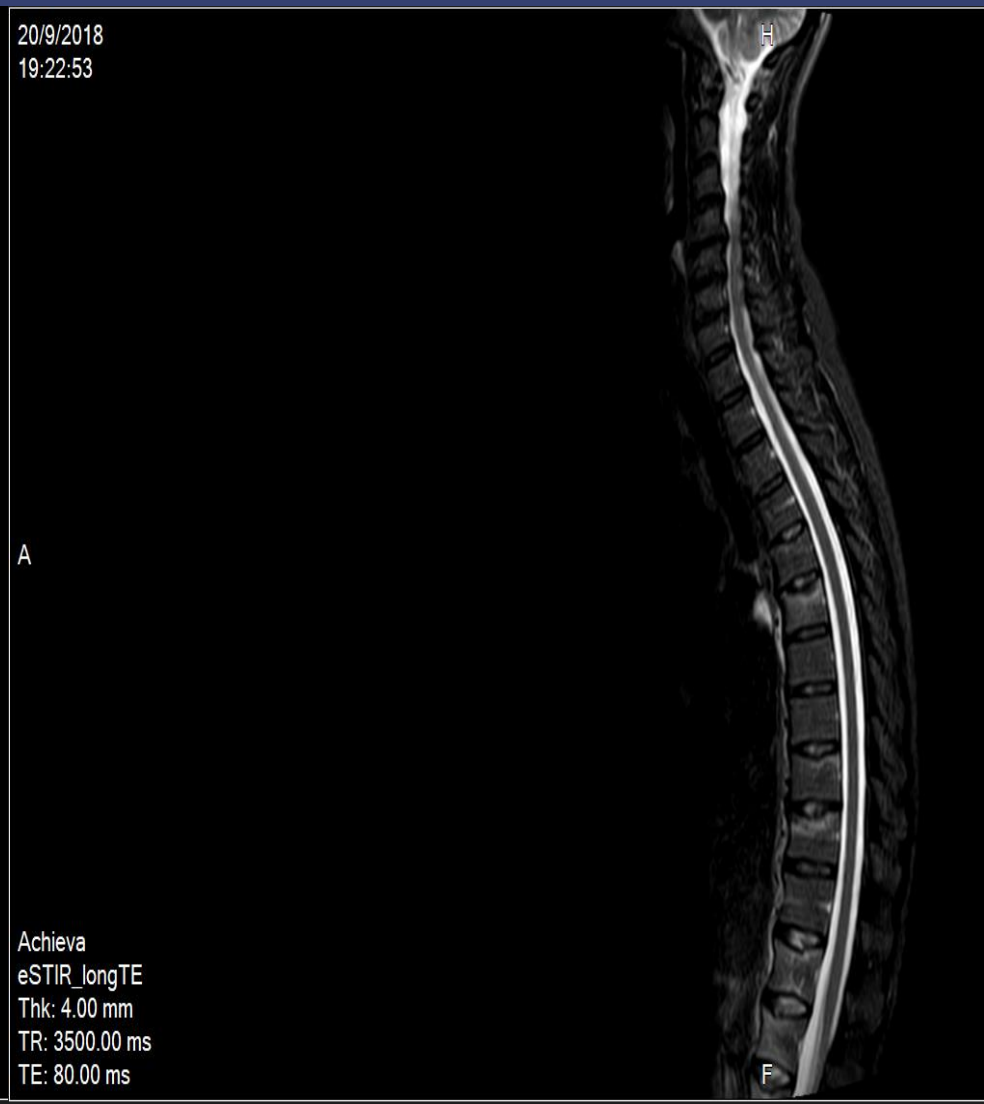


The Ugly

20.09.18

T6, T9, T10, T12, L1, L2, L3

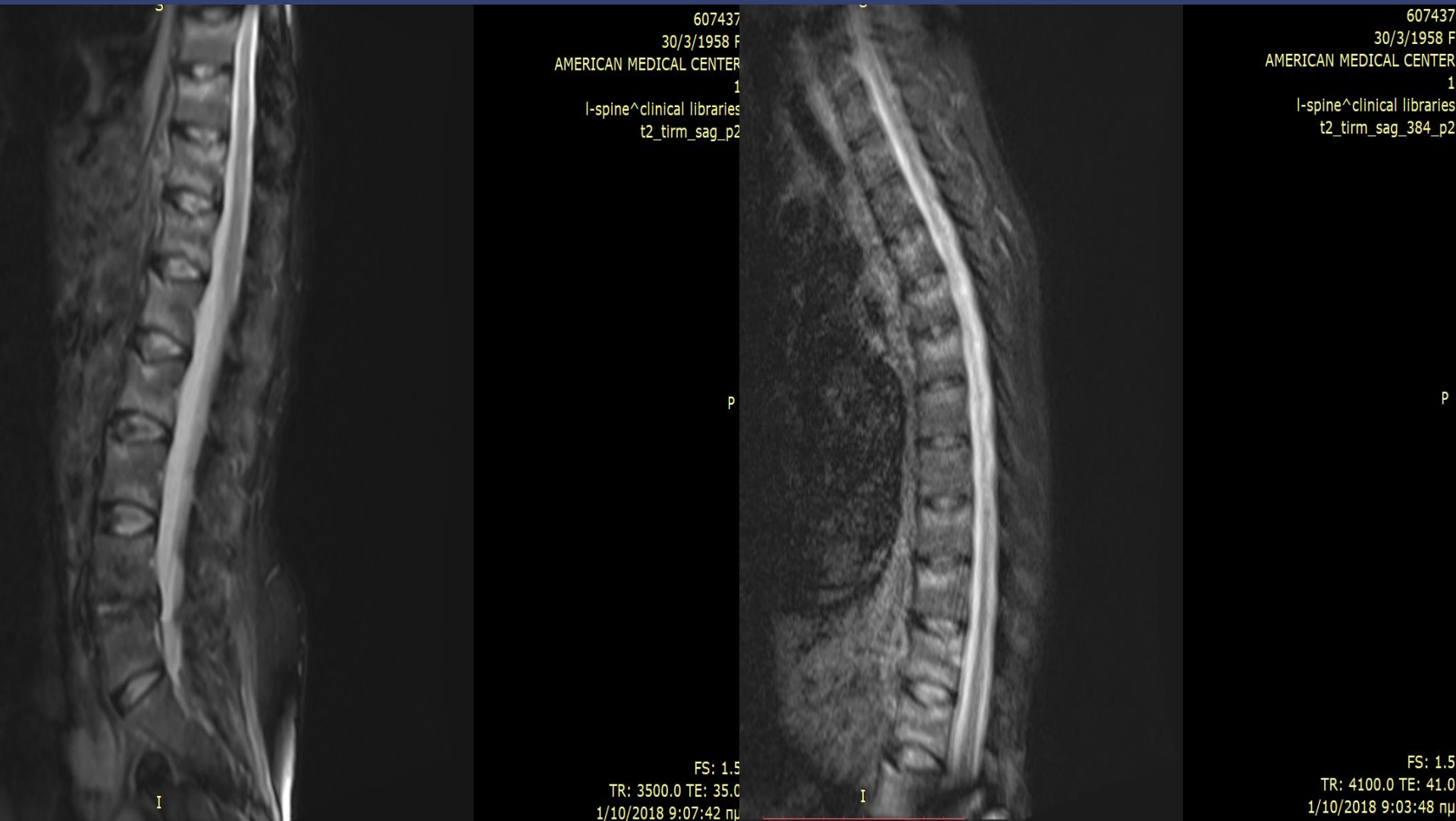




The Ugly

01.10.18

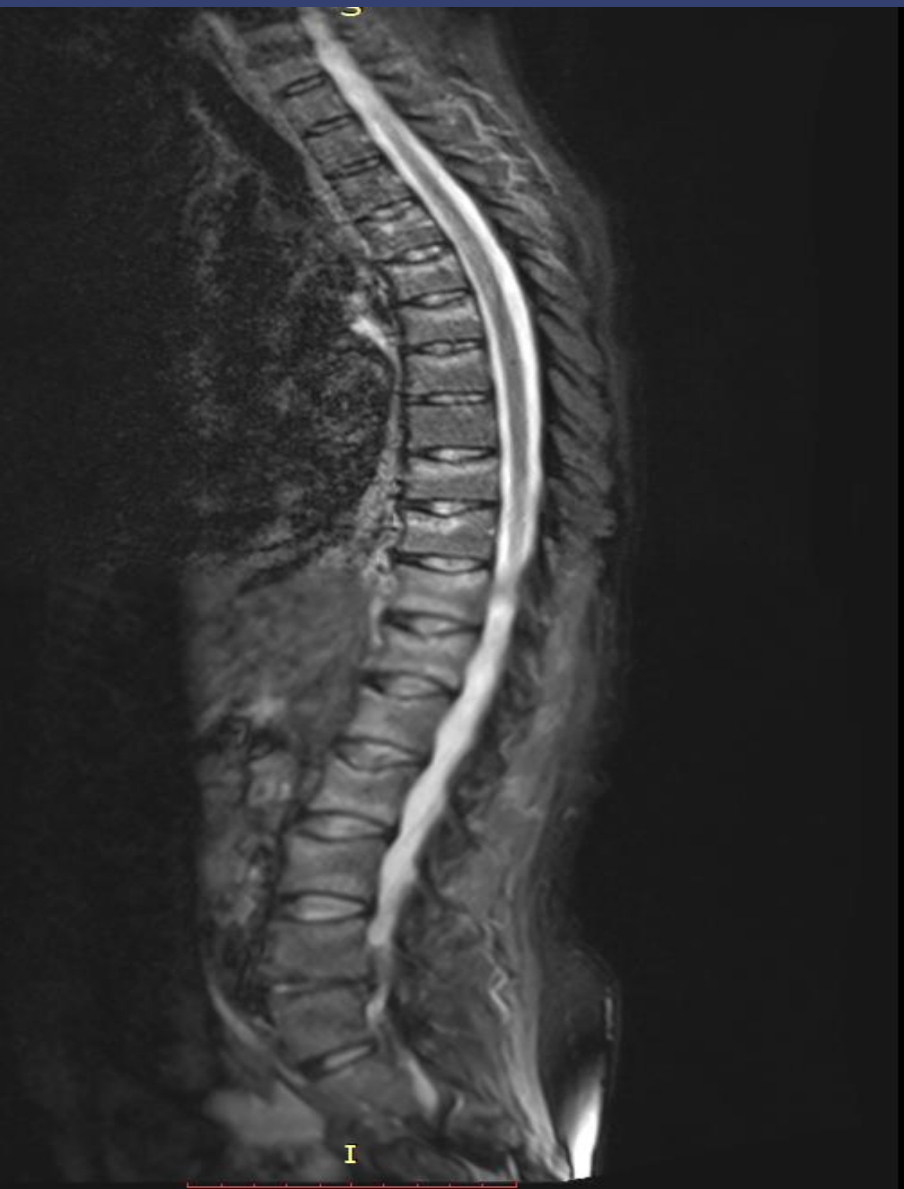
T4, T5, T6, T7, T8, T9, T10, T11, T12, L1, L2, L3, L4



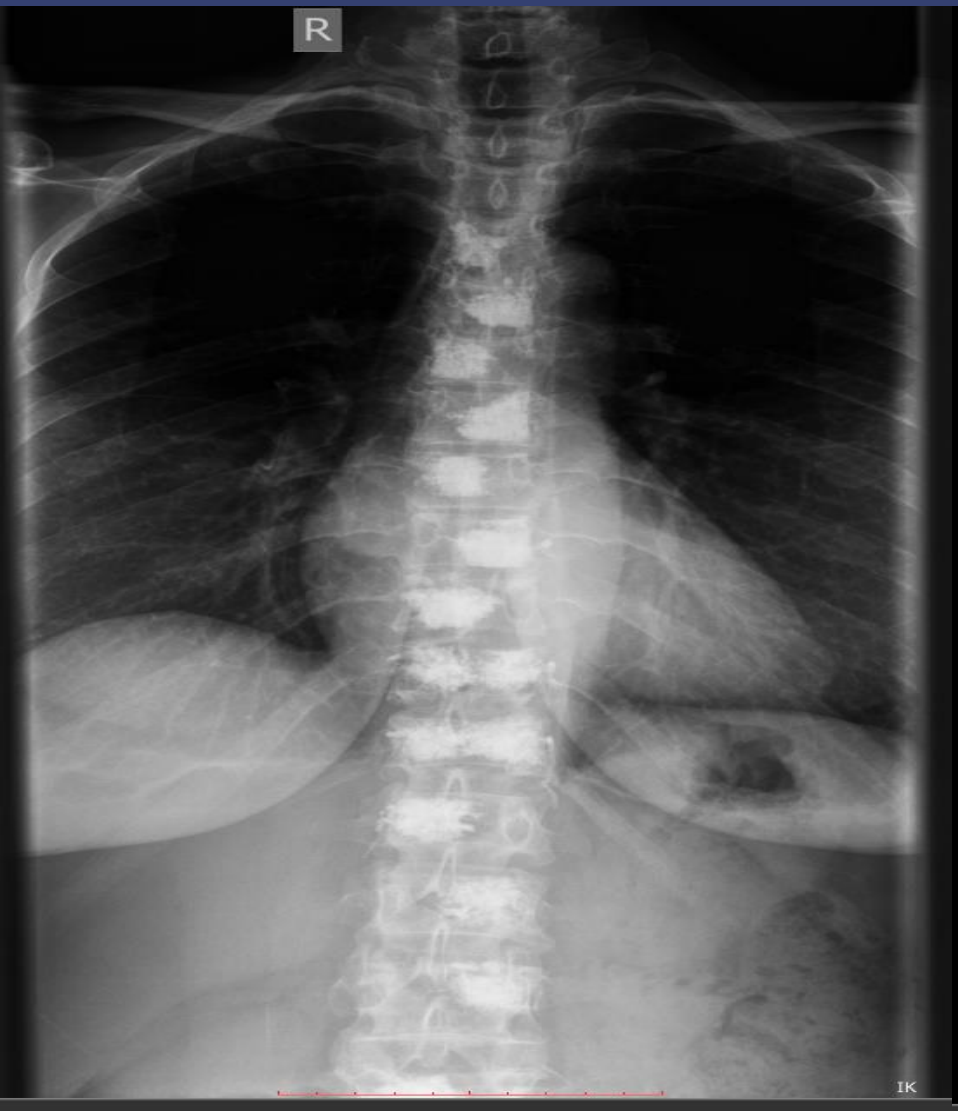
The Ugly

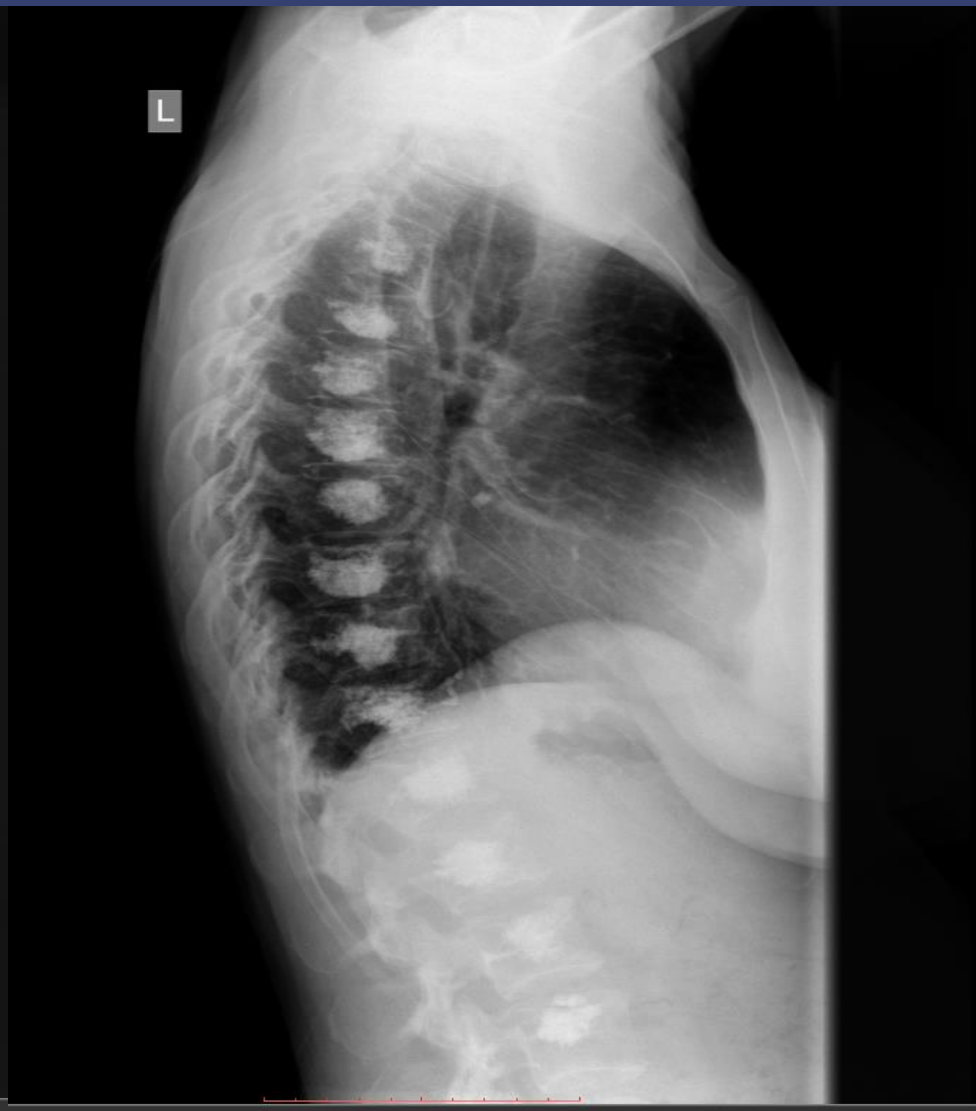
01.10.18

T4, T5, T6, T7, T8, T9, T10, T11, T12, L1, L2, L3, L4

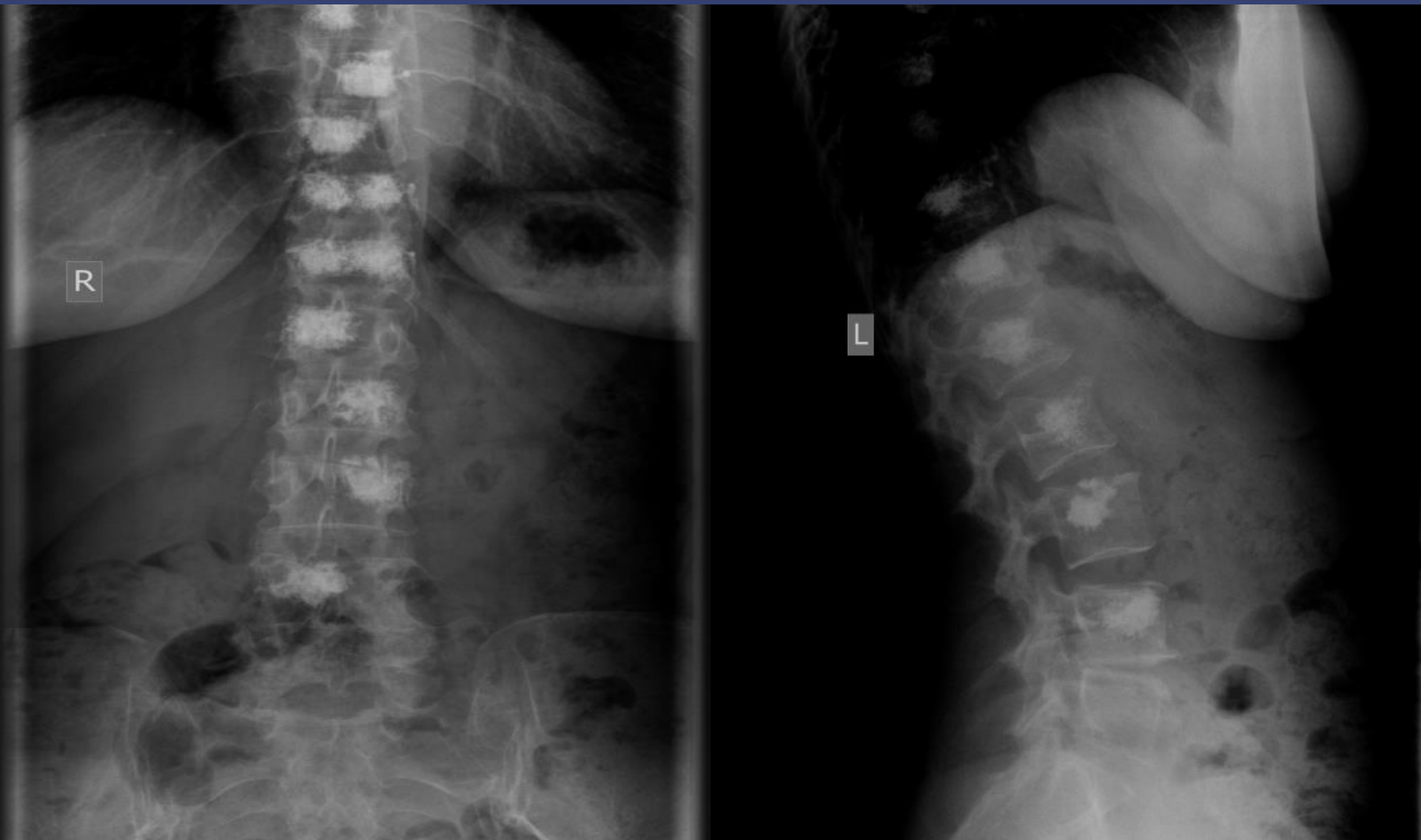


The Ugly





The Ugly



The Ugly

31.10.18 : Zolendronic acid 5mg iv

Was it a good choice?

For how long do we have to treat her?

Would you switch to TPT or combine ZOL with TPT at some time?

If yes, when is the best time to do so?

Discontinuation of Denosumab therapy for osteoporosis: A systematic review and position statement by ECTS.

Tsourdi E. et al .Bone 2017 Dec;105:11-17. doi: 10.1016/j.bone.2017.08.003. Epub 2017 Aug 5.

CONCLUSION

- There appears to be an increased risk of multiple vertebral fractures after discontinuation of denosumab although strong evidence for such an effect and for measures to prevent the occurring bone loss is lacking.

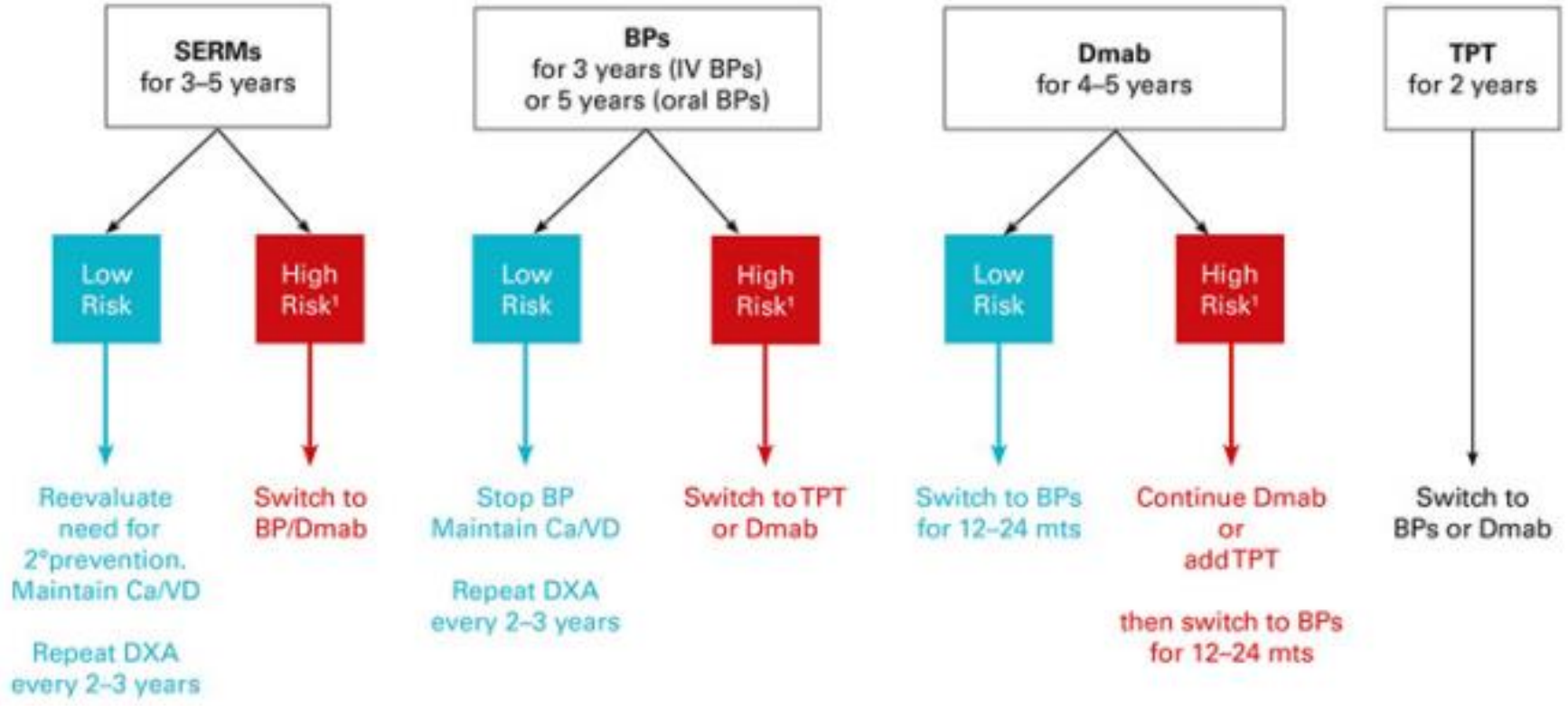
- Following discontinuation of denosumab, bisphosphonate therapy should be considered to reduce or prevent the rebound increase in bone turnover.

- The optimal bisphosphonate regimen post-denosumab is currently unknown (ongoing trials).

For how long and continue with what?

Osteoporosis drug treatment: duration and management after discontinuation. A position statement from the Swiss Association against Osteoporosis (SVGO/ASCO)

Meier C. et al. Swiss Med Wkly. 2017;147:w14484



Trilogy of skeleton revenge

- ONJ (Osteonecrosis of the Jaw)
- AFF (Atypical femoral fractures)
- DDAF (Denosumab-discontinuation associated fractures)

Ouffff… Too much adrenaline!

S.E.Papapoulos@lumc.nl
Tue 10/30/2018, 8:59 PM

Dear Andrea,

This unfortunate patient started treatment without really needing it (unless she had prevalent vertebral fractures; did she?). The development of multiple vertebral fractures following denosumab discontinuation has been well described in the literature (see, for example Tsourdi E, Langdahl B, Cohen-Solal M, et al. Discontinuation of Denosumab therapy for osteoporosis: A systematic review and position statement by ECTS. Bone 2017;105:11-7) or articles by Anastasilakis A; this being the reason that bisphosphonates are recommended for patients discontinuing denosumab. There is a number of clinical trials going on at present with zoledronate but results are not yet available.

I believe that giving Zoledronate to this patient is the right, but late, decision. Most probably she will not need a second infusion but we discuss this when the time comes. I don't think she needs teriparatide, certainly not at this stage.

Let me know if you have other questions.

Best wishes

Socrates

Personal Experience

- Female 74 years, treatment naïve, with mild kidney failure, received 4 doses of denosumab. Next dose due date: July 2017. Despite calling her twice and warning her for increased risk for fractures by delaying her treatment she never came (too busy!!!). January 2018 sustained 3 vertebral fractures. Came back in April 2018. We reinstituted Denosumab.
- Female 54 years did not want to take BPs (inta en na perno ta idia poy perni i mana moy!!!) . Very good response after 5 years. Stopped treatment 21/2 years ago, but refused to take BPs despite our strong advice. A few months later sustained 2 vertebral fractures. Her BMD gains were lost (as measured recently) and still refusing to take BPs.

Personal Drama

- Orthopedic's statement: " BPs are dead. Why are they giving you BPs? Take Denosumab"
- But my friends are taking denosumab. Why do you suggest to take BPs?
- But my gyno, my orthopedic, my GP, my hairdresser told me to take denosumab…
- Ease of use and negligence of how to use ZOL by most physicians led to the boom of denosumab in Cyprus.
- Every physician, regardless of specialty, is giving OP treatment without deep knowledge of the topic.
- " Hey!! You have taken 5 years of BPs (or whatever) so you have to stop" a common statement by many GPs and other physicians.

HIGHLIGHTS OF PRESCRIBING INFORMATION

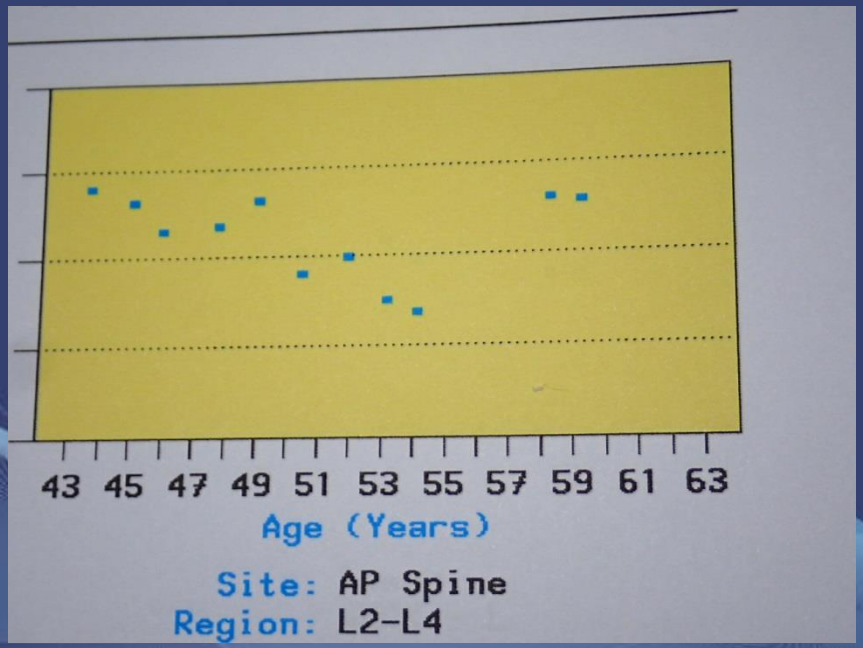
USA

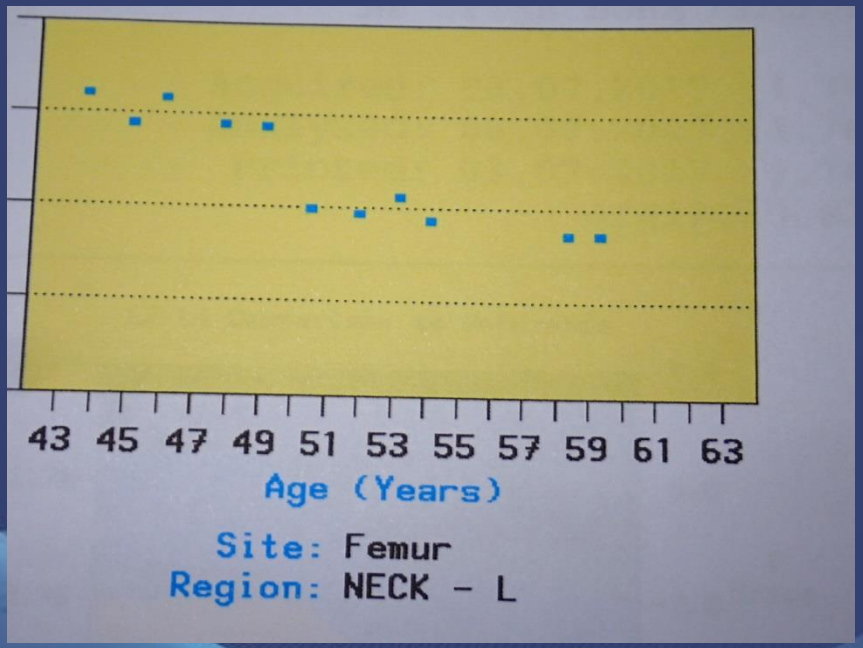
5.6 Multiple Vertebral Fractures (MVF)

- Following Discontinuation of Prolia Treatment Following discontinuation of Prolia treatment, fracture risk increases, including the risk of multiple vertebral fractures.
- Cessation of Prolia treatment results in markers of bone resorption increasing above pretreatment values then returning to pretreatment values 24 months after the last dose of Prolia.
- In addition, bone mineral density returns to pretreatment values within 18 months after the last injection. [see Pharmacodynamics (12.2) and Clinical Studies (14.1)].
- New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of Prolia.
- Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia discontinuation.
- Evaluate an individual's benefit-risk before initiating treatment with Prolia.
- If Prolia treatment is discontinued, consider transitioning to an alternative antiresorptive therapy [see Adverse Reactions (6.1)].

EUROPE

The ugly


43 45 47 49 51 53 55 57 59 61 63
Age (Years)
Site: AP Spine
Region: L2-L4


43 45 47 49 51 53 55 57 59 61 63
Age (Years)
Site: Femur
Region: NECK - L


00:00:05

The Ugly

The real question is…

For how long do we have to treat?

When do we have to continue treatment?

The Ugly

20.09.18

ALP = 124 (39-117)

Ca = 10.27 (8.80-10.60)

31.10.18

b-CTX = 143pg/mL (0-1000)

P1NP = 38 ng/mL (20-76)

FREEDOM STUDY : 11.08.2009

EMEA APPROVAL : 28.05.2010

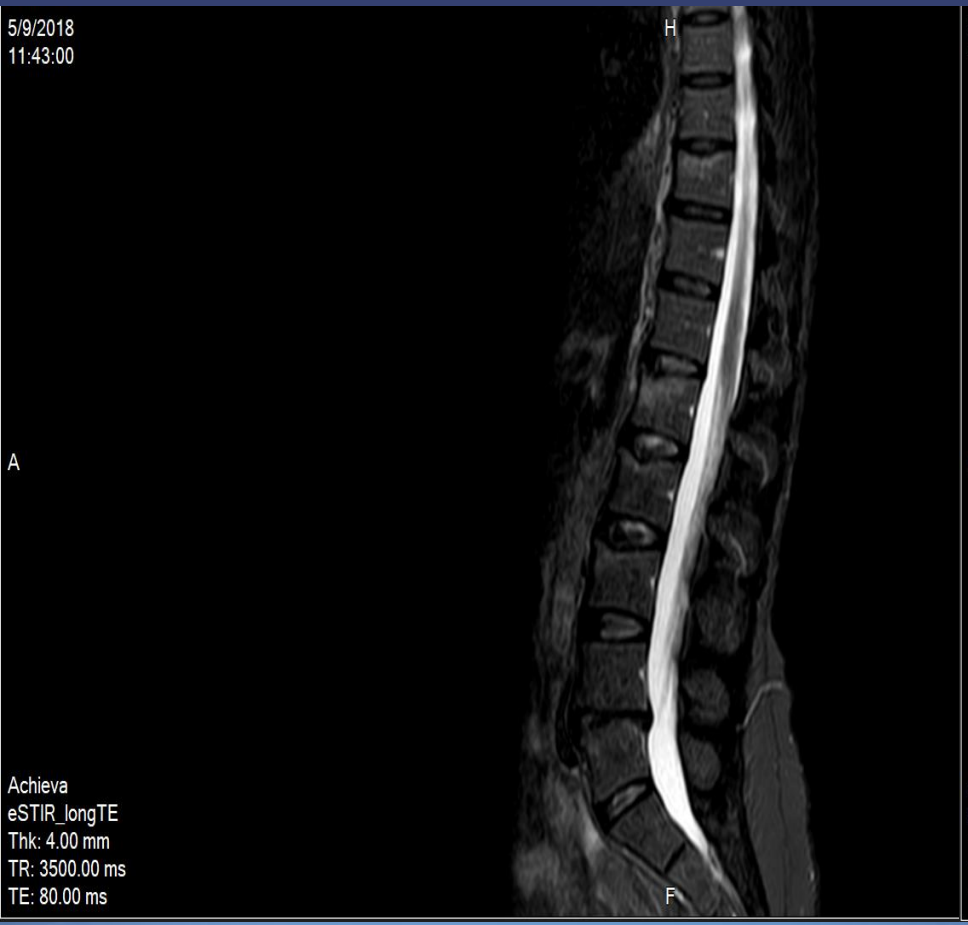
FDA APPROVAL : 01.06.10

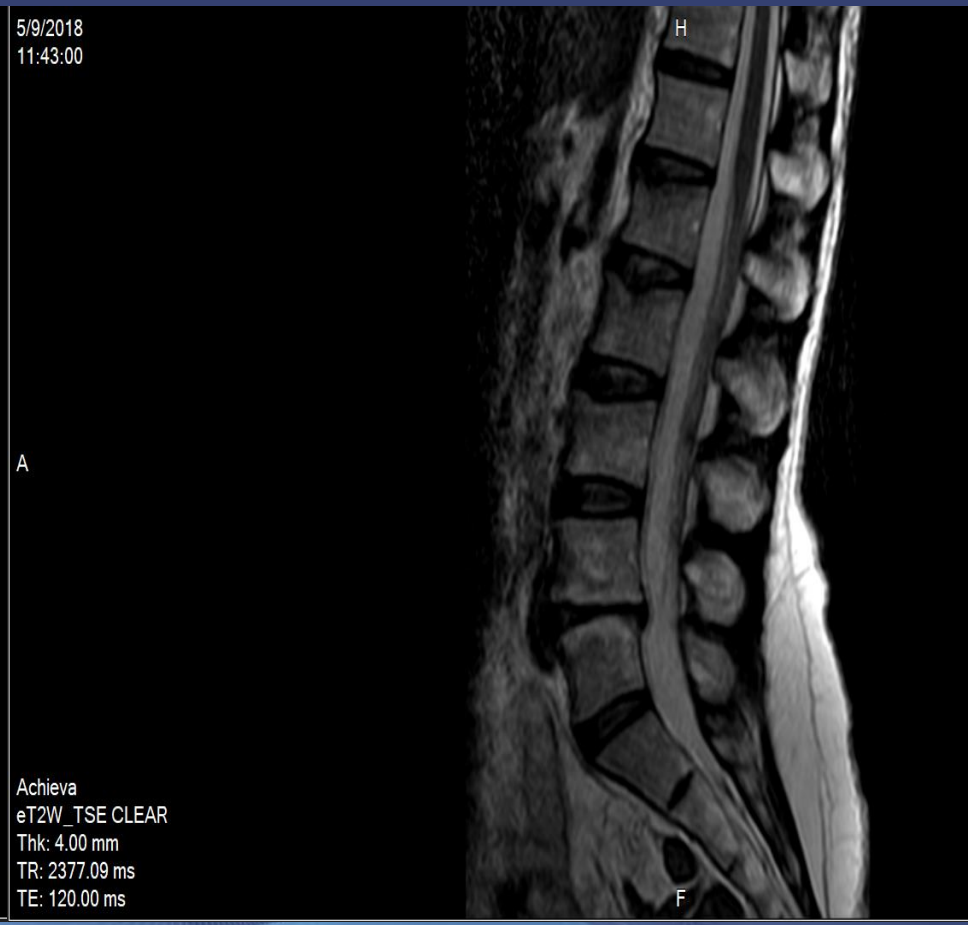
FREEDOM extension study (8 or 5 years) : 23.07.15

FR EEDOM extension study (10 years) : 22.05.17

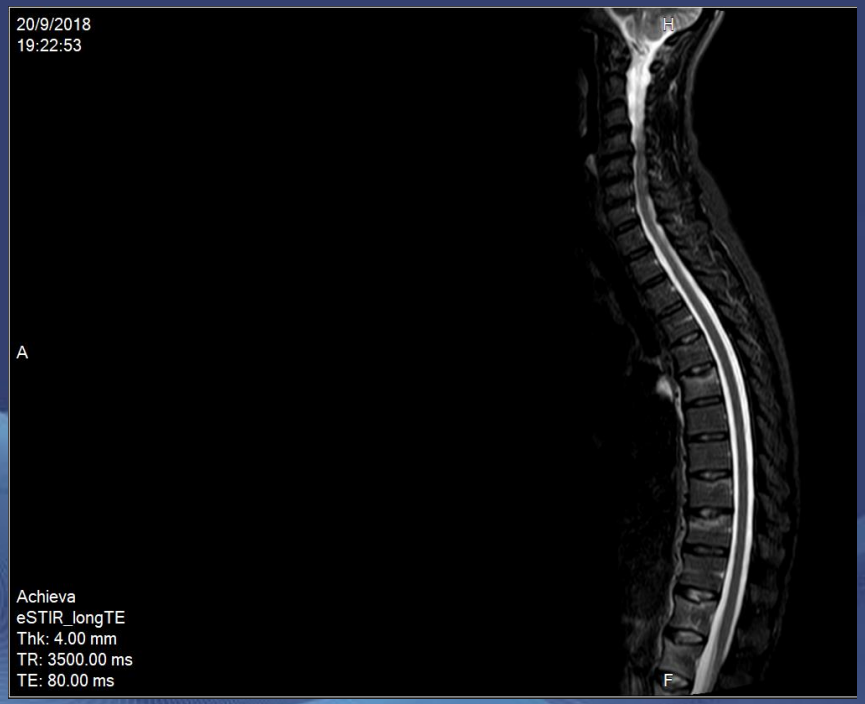
05.09.18

T10, L1, L2, L3

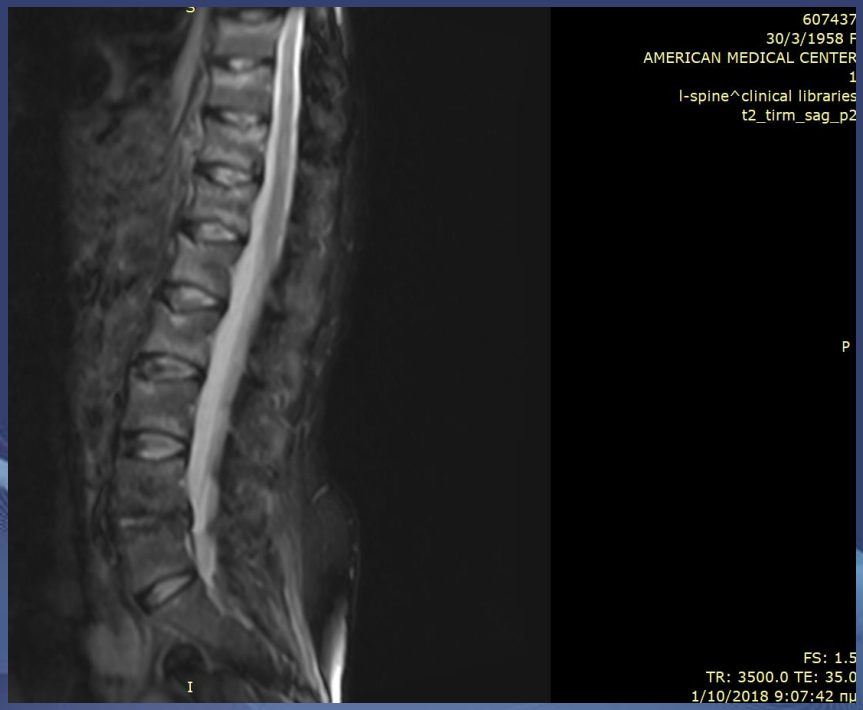


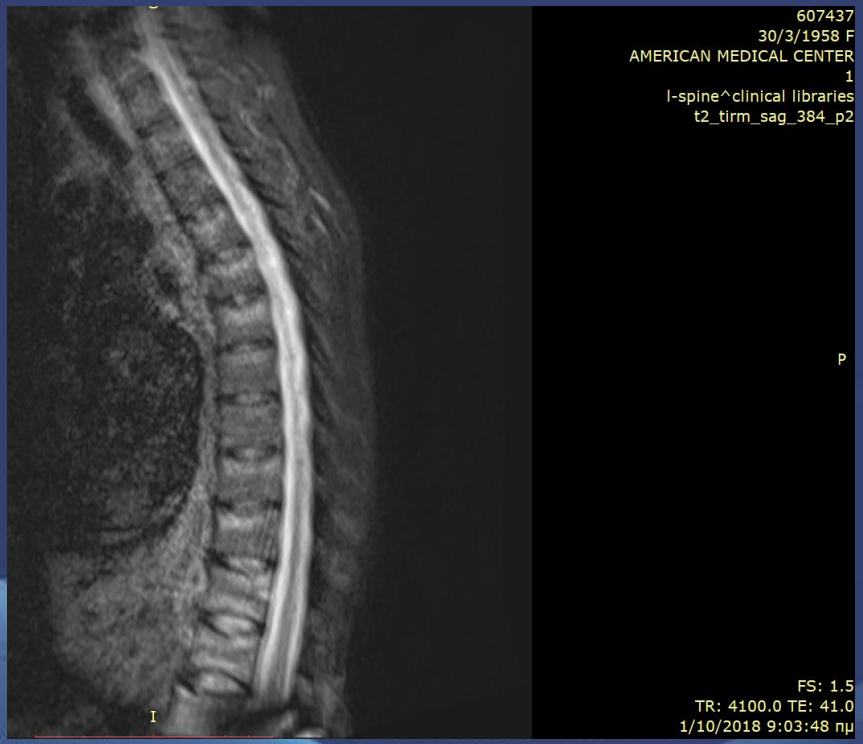


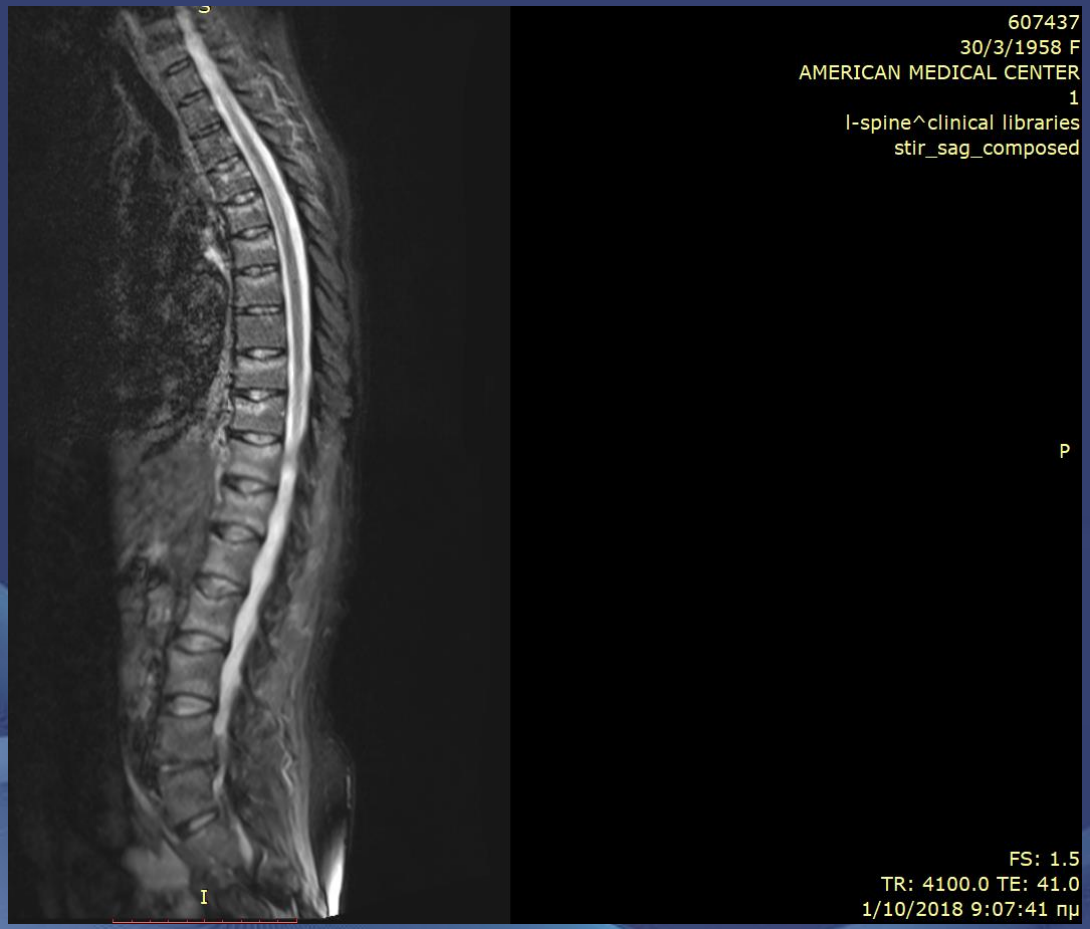

20/9/2018
19:22:53
H
A
Achieva
eSTIR_longTE
Thk: 4.00 mm
TR: 3500.00 ms
TE: 80.00 ms
F

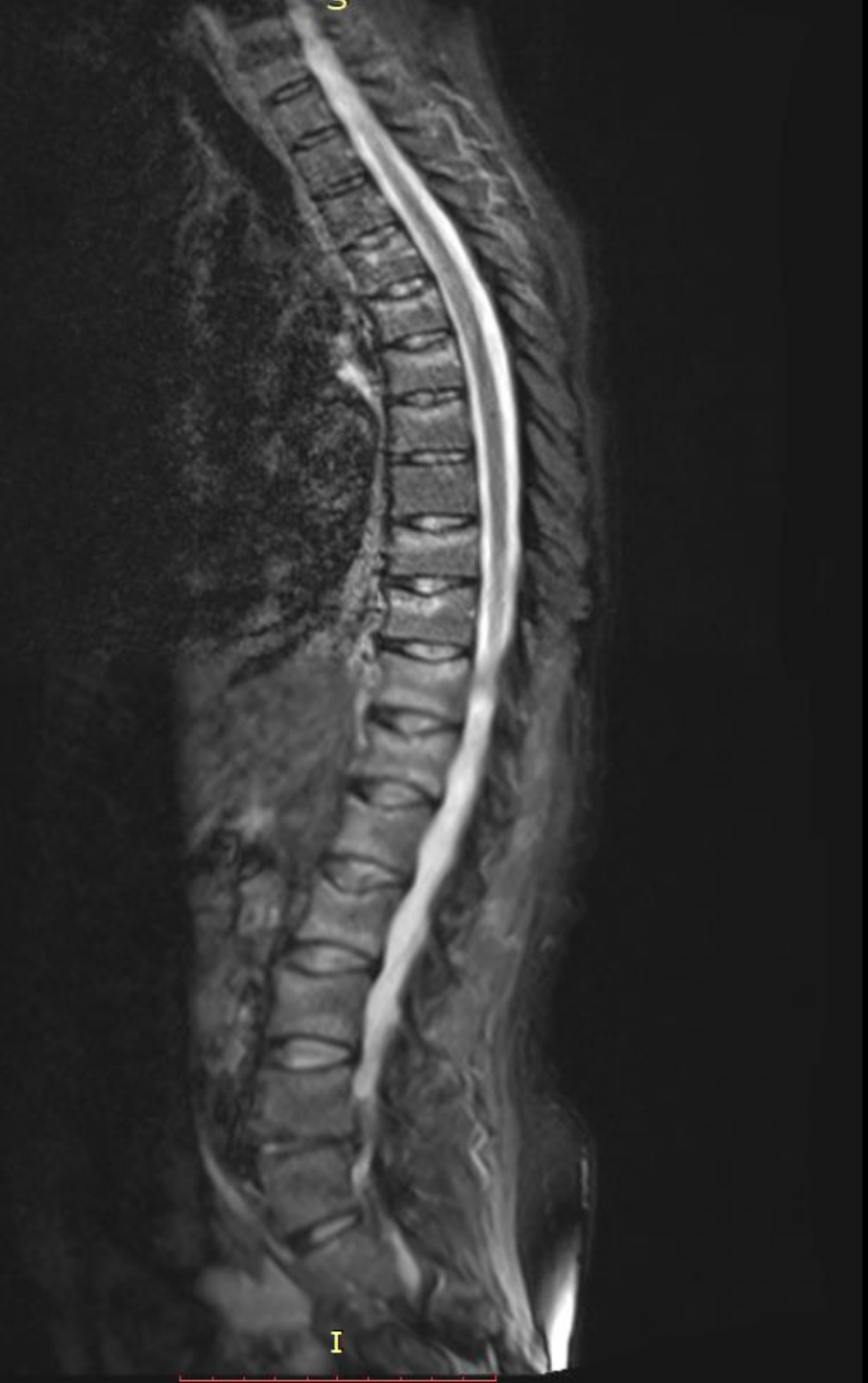

20/9/2018
19:22:53
H
A
Achieva
eSTIR_longTE
Thk: 4.00 mm
TR: 3500.00 ms
TE: 80.00 ms
F

The Ugly


607437
30/3/1958 F
AMERICAN MEDICAL CENTER
1
l-spine^clinical libraries
t2_tirm_sag_p2
P
FS: 1.5
TR: 3500.0 TE: 35.0
1/10/2018 9:07:42 пµ
I


607437
30/3/1958 F
AMERICAN MEDICAL CENTER
1
l-spine^clinical libraries
t2_tirm_sag_384_p2
P
FS: 1.5
TR: 4100.0 TE: 41.0
1/10/2018 9:03:48 пµ
I


607437
30/3/1958 F
AMERICAN MEDICAL CENTER
1
l-spine^clinical libraries
stir_sag_composed
P
FS: 1.5
TR: 4100.0 TE: 41.0
1/10/2018 9:07:41 πμ
I



607437
30/3/1958 F
AMERICAN MEDICAL CENTER
1
l-spine^clinical libraries
stir_sag_composed

P

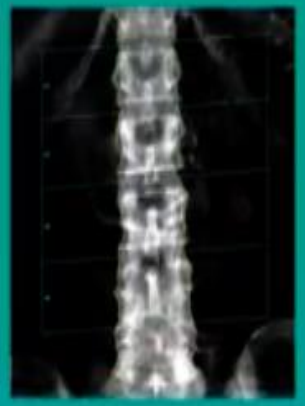
FS: 1.5
TR: 4100.0 TE: 41.0
1/10/2018 9:07:41 πμ

Trabecular Bone Score (TBS)

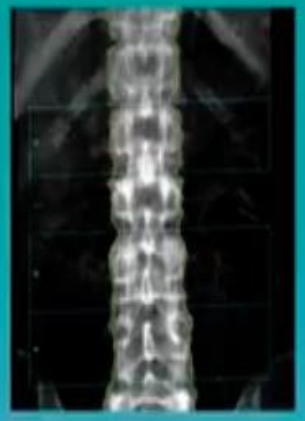
- TBS is derived from a software program that using a gray-level of two-dimensional AP DXA images calculates the bone texture.
- TBS is closely associated to bone microarchitecture as it relies on the mean thickness and volume fraction of trabecular bone.
- TBS provides information about bone strength and bone fracture risk beyond BMD and clinical risk factors and FRAX.

Principle of TBS

Patient 1:
BMD L1-L4:
T-score: - 2.2



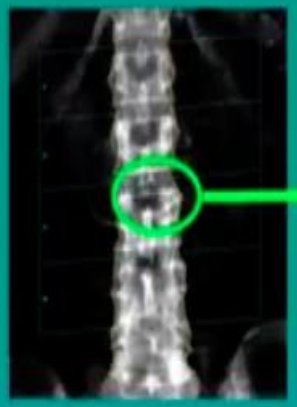
Patient 2:
BMD L1-L4:
T-score:- 2.2



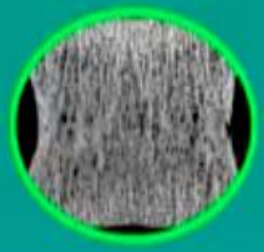
2 patients display the same BMD T-score…

Principle of TBS

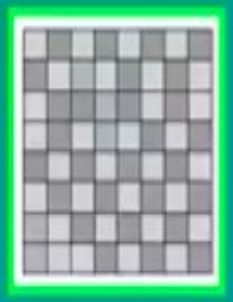
Patient 1:
BMD L1-L4:
T-score: - 2.2



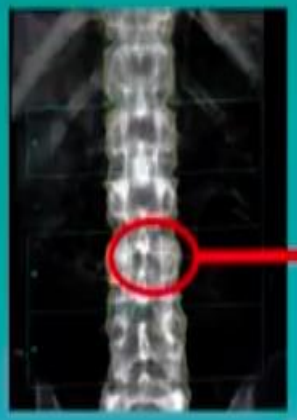
Normal



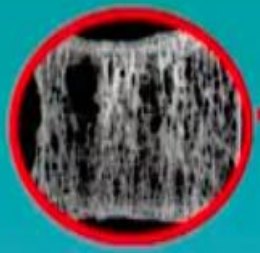
Homogeneous



Patient 2:
BMD L1-L4:
T-score: - 2.2



Degraded



Heterogeneous

TBS algorithm analyses the texture of the DXA bone image using a fractal approach called experimental variogram.

TBS explores the spatial variability of the pixels intensity in the image.

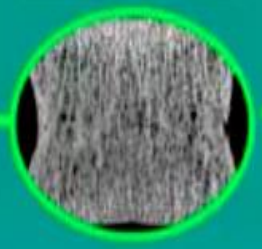
These two patients display
a different bone texture.

Principle of TBS

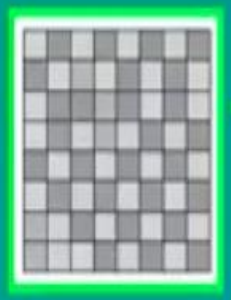
A high TBS reflects better bone microstructure

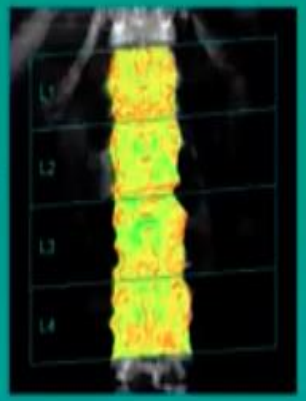
a low TBS reflects worse bone microstructure

Normal



Homogeneous

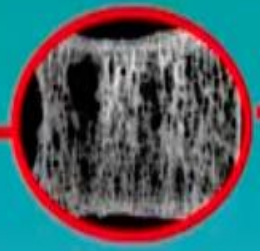




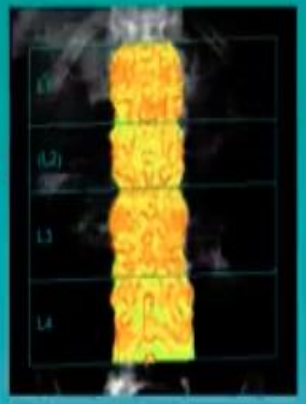
High TBS

TBS L1-L4: 1.457

Degraded



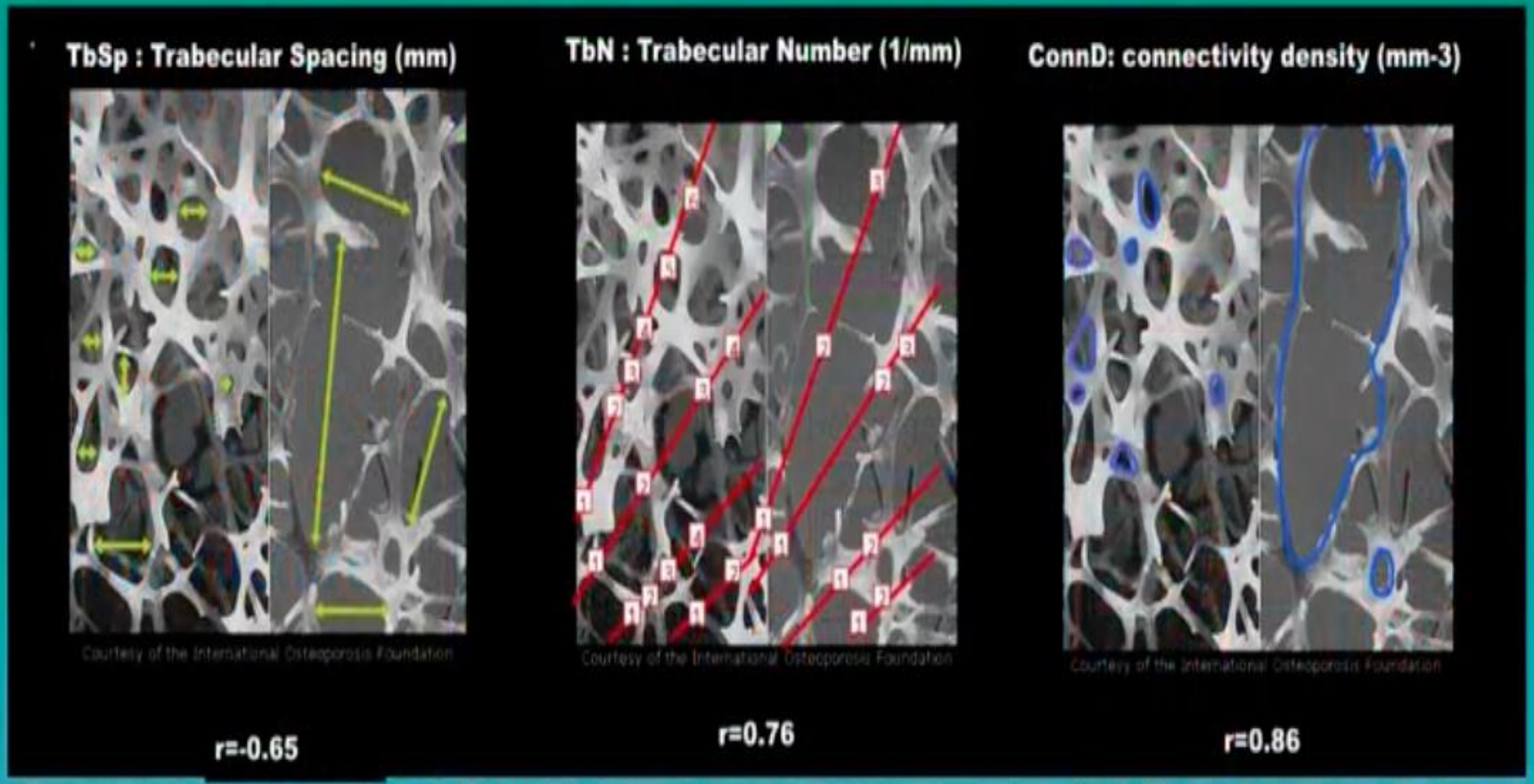
Heterogeneous



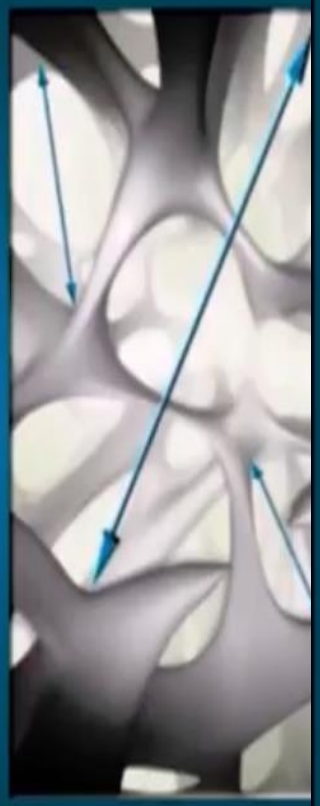
Low TBS

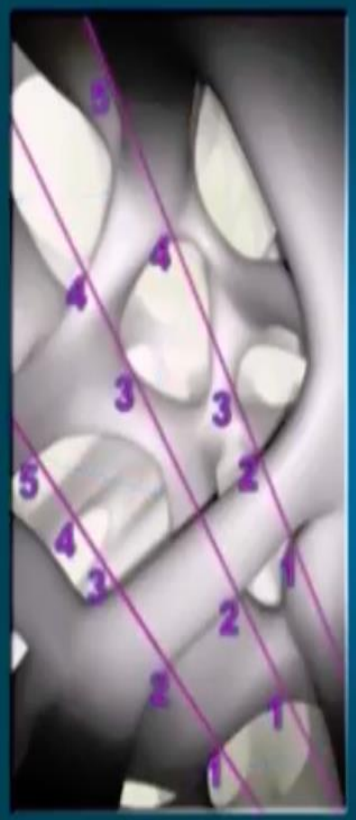
TBS L1-L4: 1.132

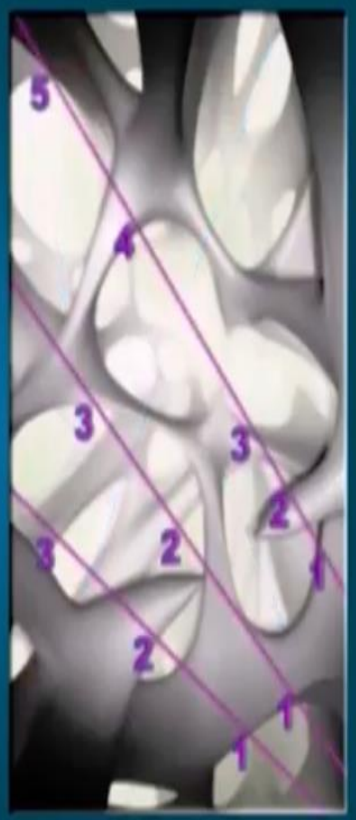
TBS' Relation to Microarchitecture Parameters

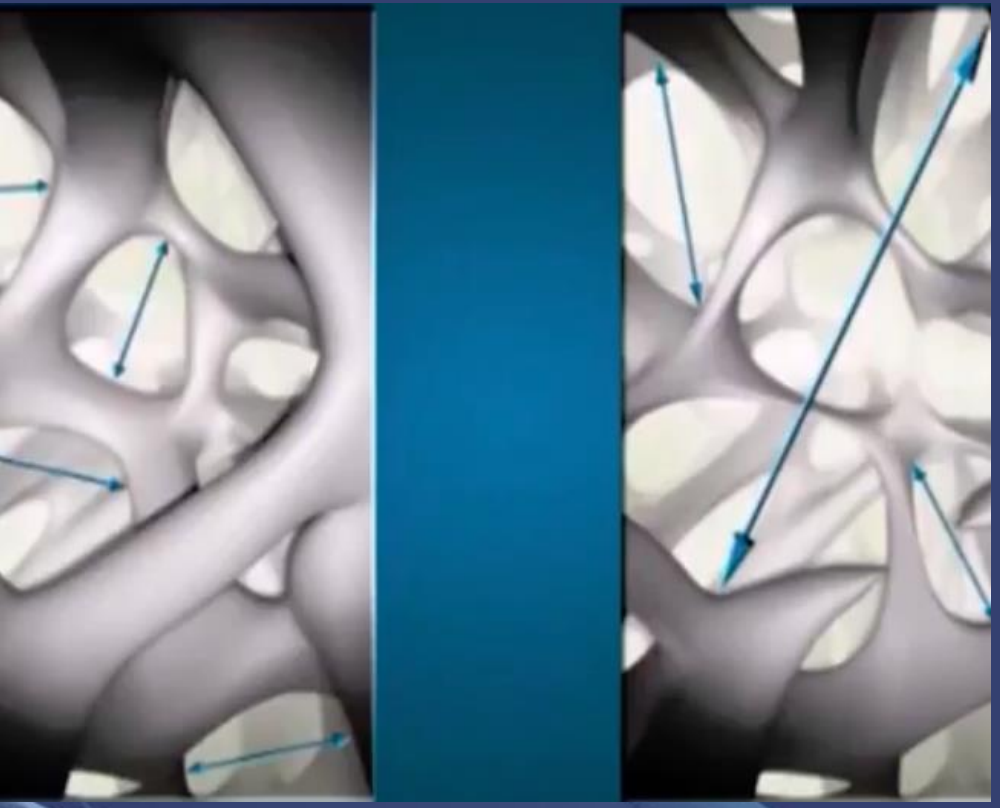


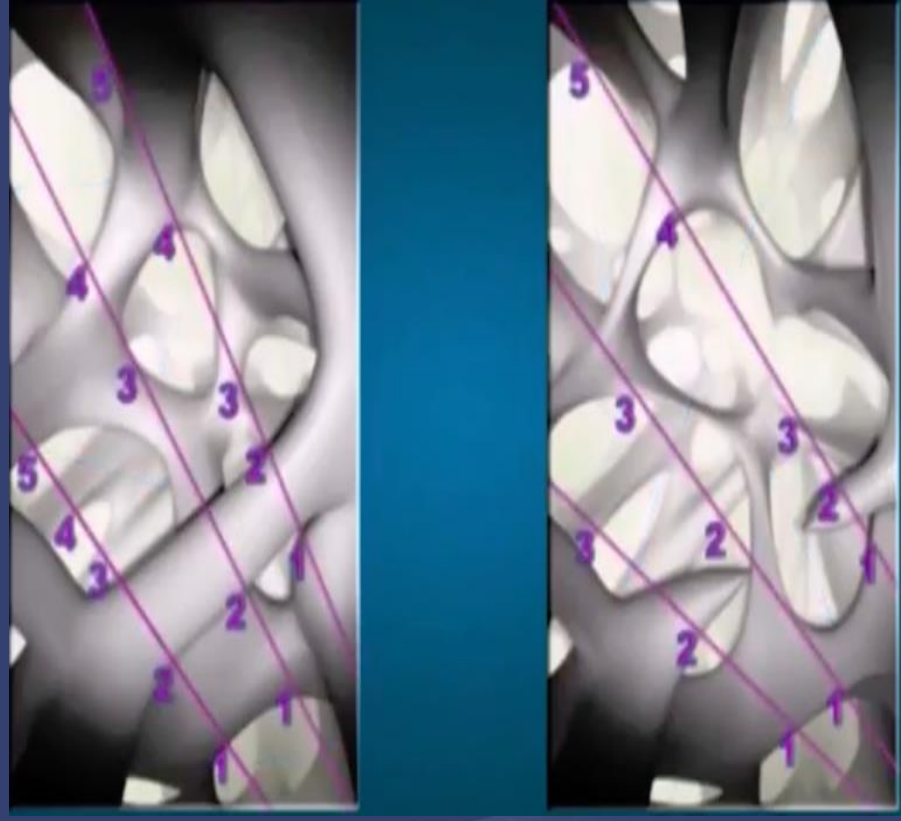
Hans et al. JCD 2011; Winzenrieth et al. JCD. 2012; Roux JP et al. ASBMR 2012, Resch et al. ASBMR 2012, Bilezikian JCEM 2013




5
4
4
3
3
5
4
3
2
2
1
2
1
1


5
4
3
3
2
3
2
1
2
1
1





TBS

TBS correlates with the parameters of the microarchitecture of "Parfitt"-parameters such as the connectivity density, the trabecular space and the trabecular number.

TBS in Guidelines and Endorsement by International Scientific Societies

TBS in Guidelines and Endorsement by International Scientific Societies

TBS is a worldwide acknowledged independent parameter for fracture prediction.

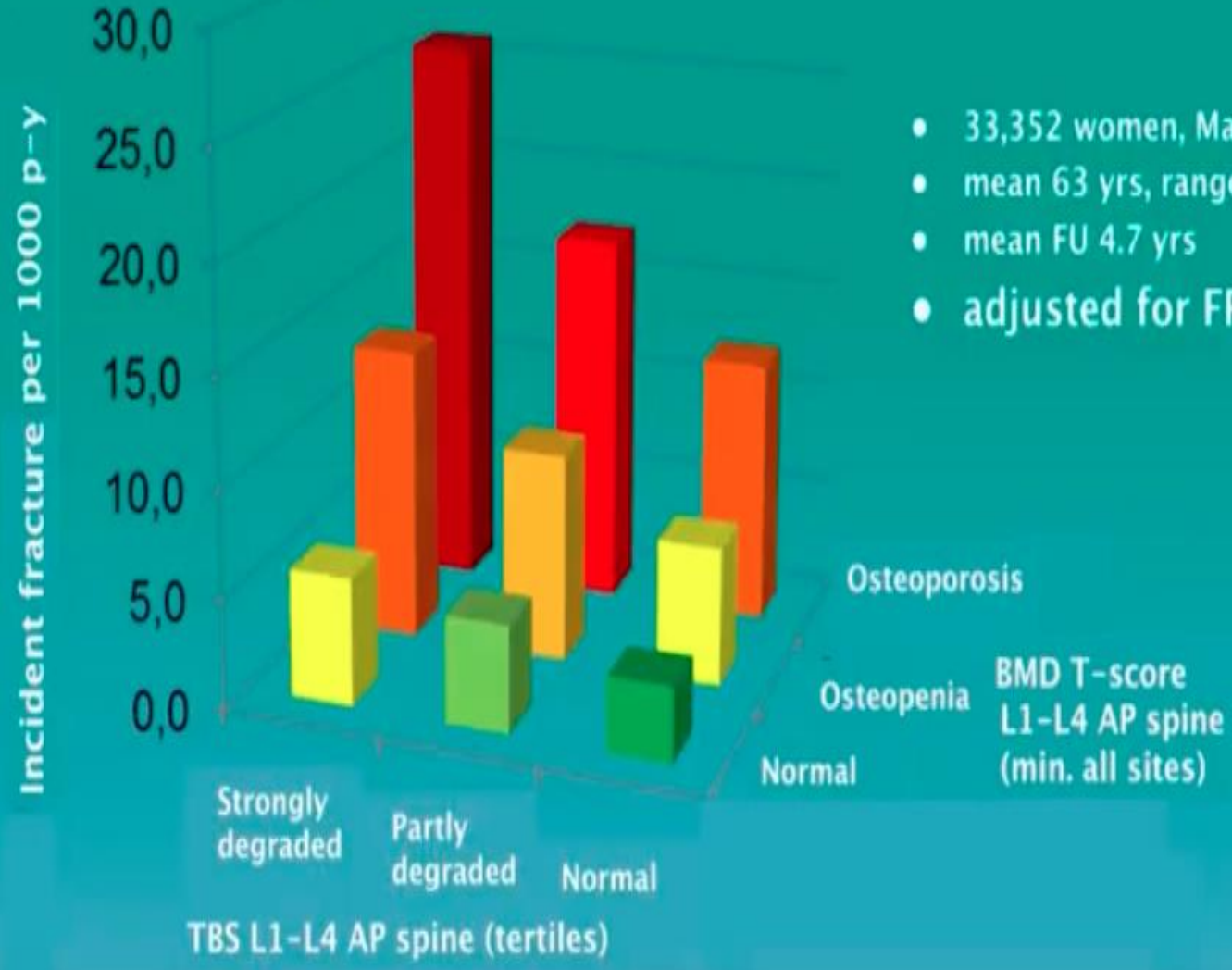
TBS

and

Fracture Prediction

TBS helps Identify New Patients at Risk of Fracture

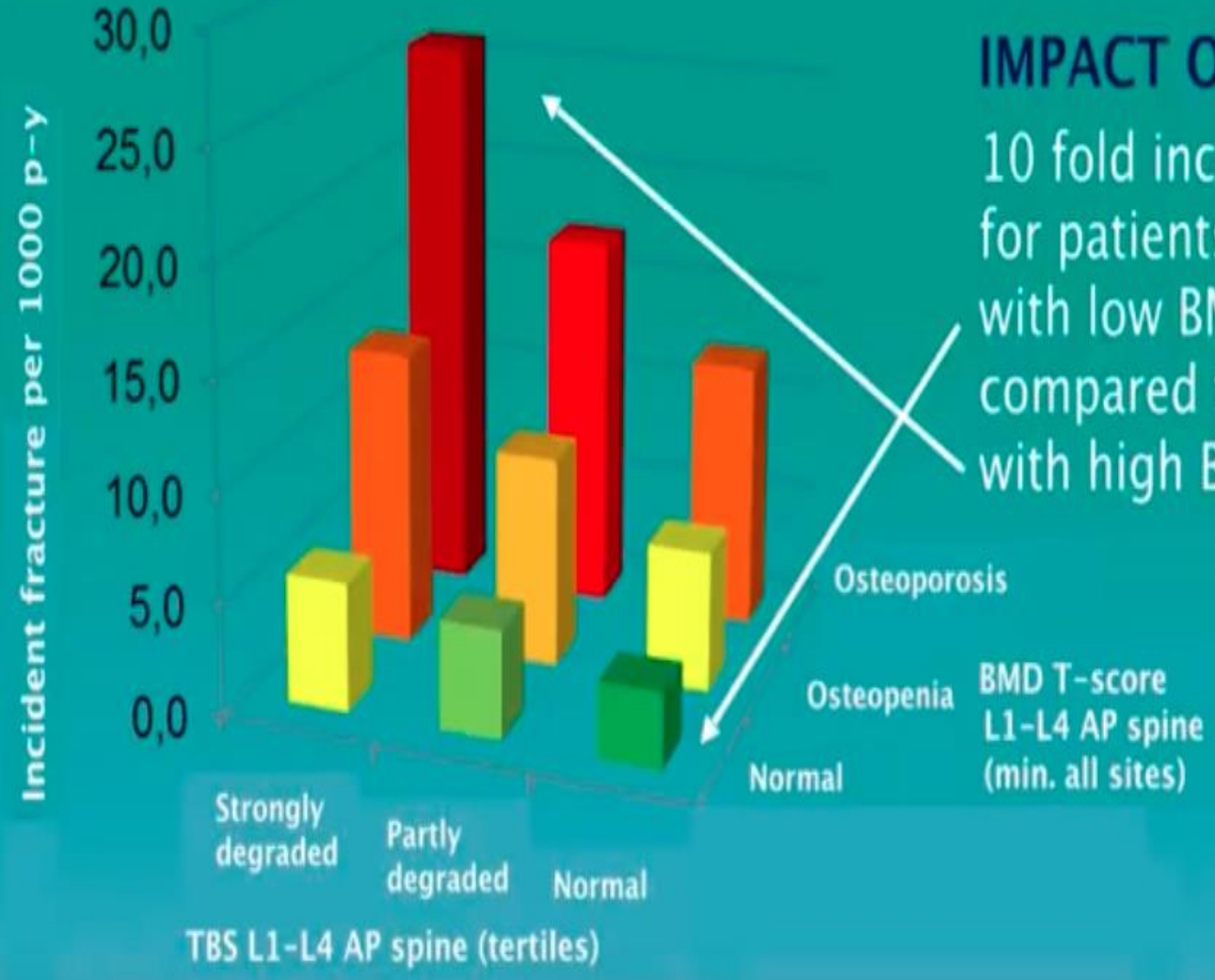
TBS and BMD evaluate different bone properties



- 33,352 women, Manitoba
- mean 63 yrs, range: 40-100 yrs
- mean FU 4.7 yrs
- adjusted for FRAX clinical risk factors

TBS helps Identify New Patients at Risk of Fracture

TBS and BMD evaluate different bone properties

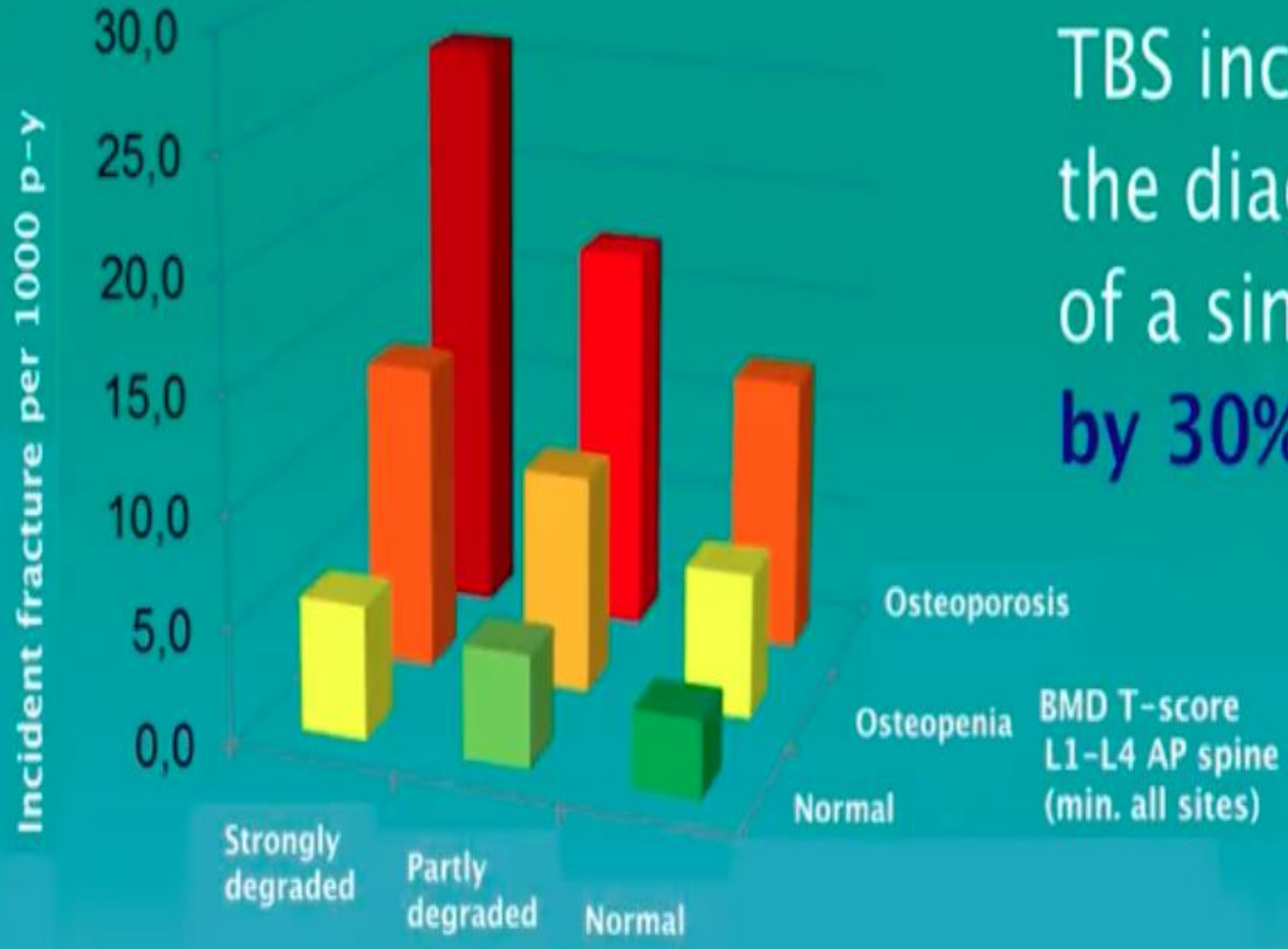


IMPACT ON FRACTURE RISK

10 fold increase in risk for patients with low BMD & low TBS compared to patients with high BMD and high TBS

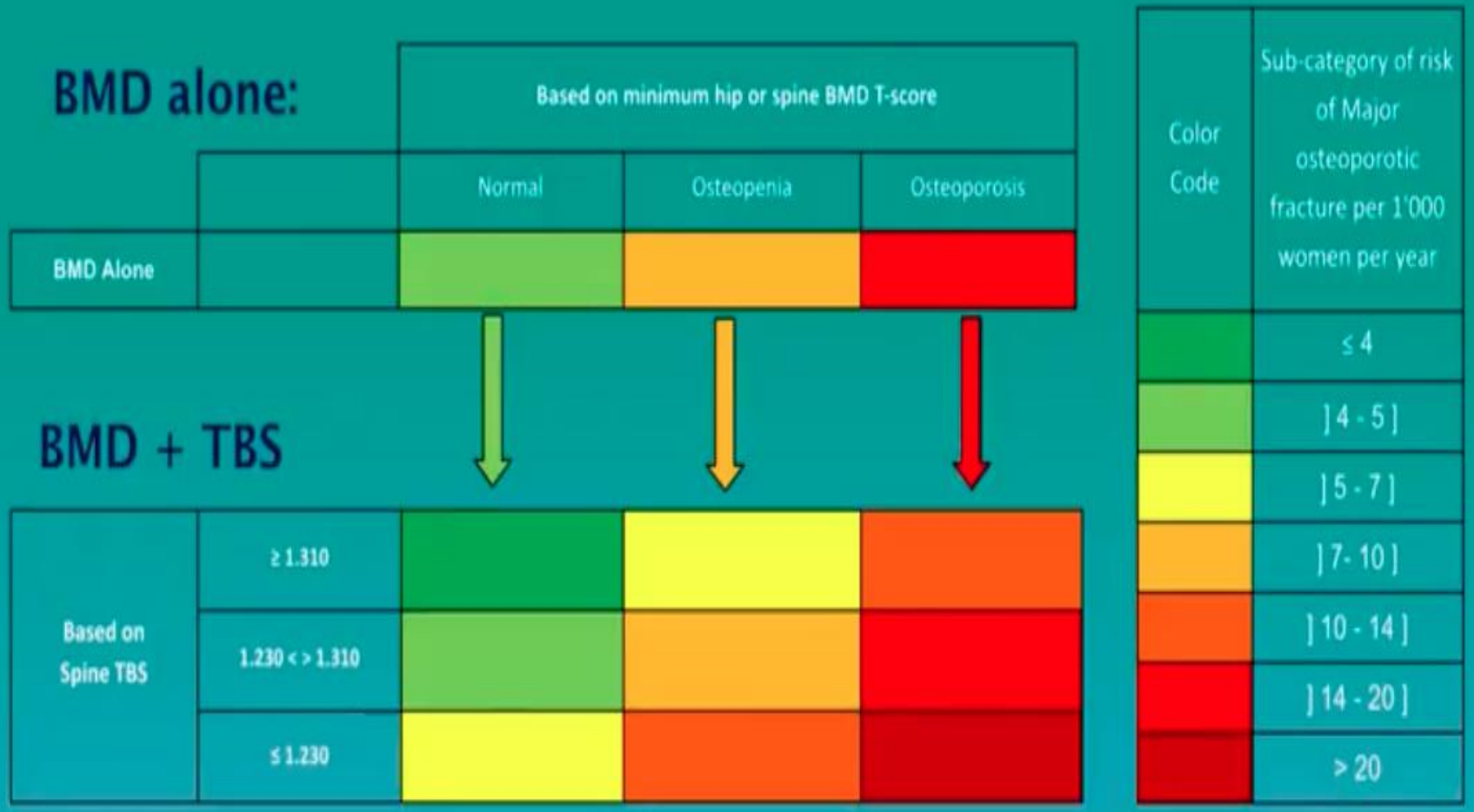
TBS helps Identify New Patients at Risk of Fracture

TBS and BMD evaluate different bone properties



TBS increases the diagnosis ability of a single BMD exam **by 30%.**

BMD and TBS are Complementary Needed



Adapted from Hans et al. JBMR 2011 Nov;26(11):2762-9 and A Meta-Analysis of Trabecular Bone Score in Fracture Risk Prediction and Its Relationship to FRAX. (McCloskey et al 2016; JBMR)

TBS

and

FRAX®

TBS adjusted FRAX®

FRAX is a calculation tool for assessment of fracture risk based on clinical risk factors with and without BMD.

TBS can be used as a FRAX modifier to refine the patients risk profile as TBS is independent of BMD and clinical risk factors.

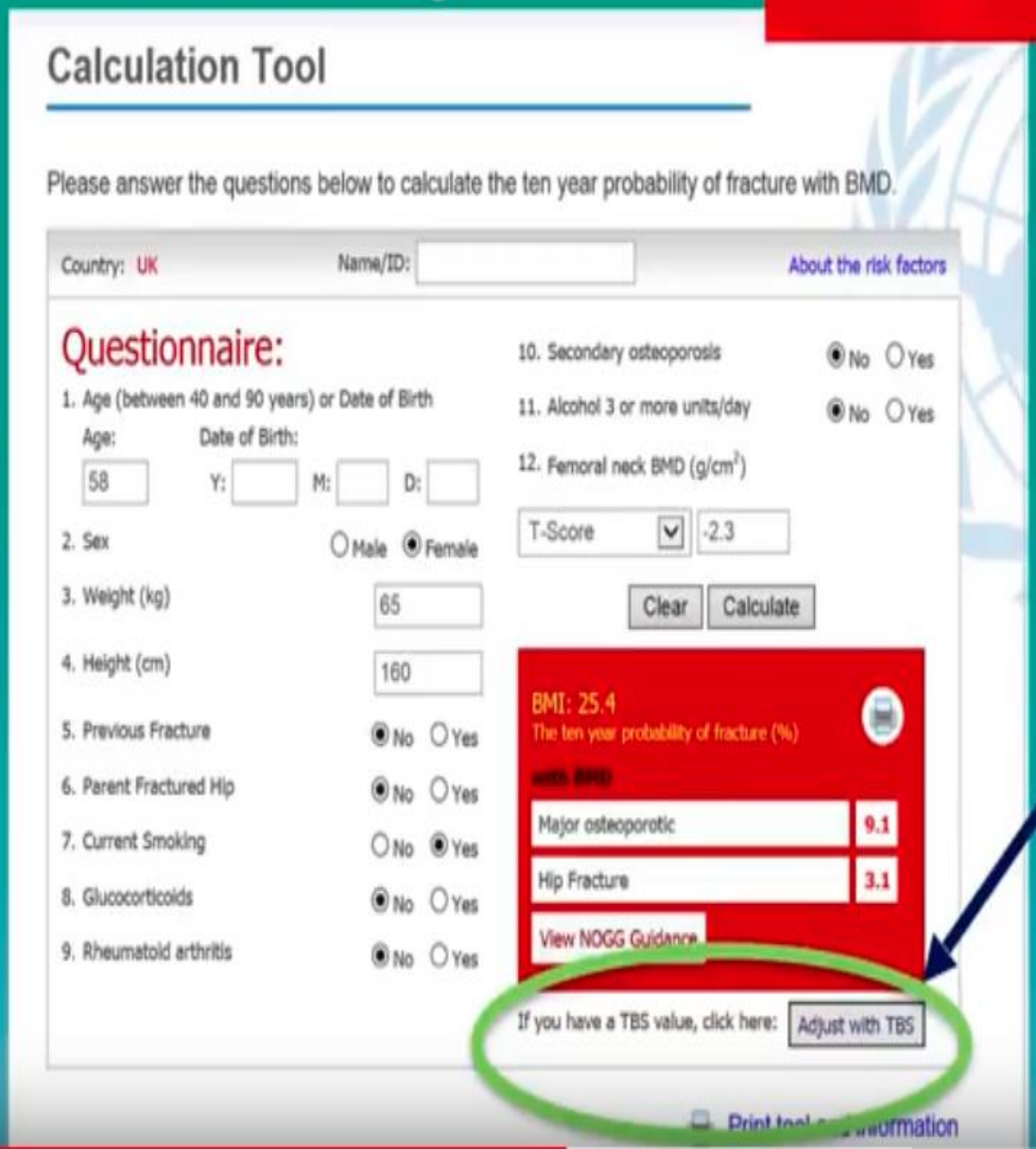
1 (Model): McCloskey et all. CTI 2015" Adjust fracture probability by Trabecular Bone Score" 2 (Validation): McCloskey et al. JBMR 2015: "A meta-analysis of trabecular bone score in fracture risk prediction

TBS adjusted FRAX®

"By fine tuning the information provided by FRAX, TBS adjusted FRAX gives clinicians more precise information that can aid them in making informed treatment decisions within the course of a clinical assessment." (E. McCloskey Quote: IOF Press Release - April 2014)

TBS adjusted FRAX®

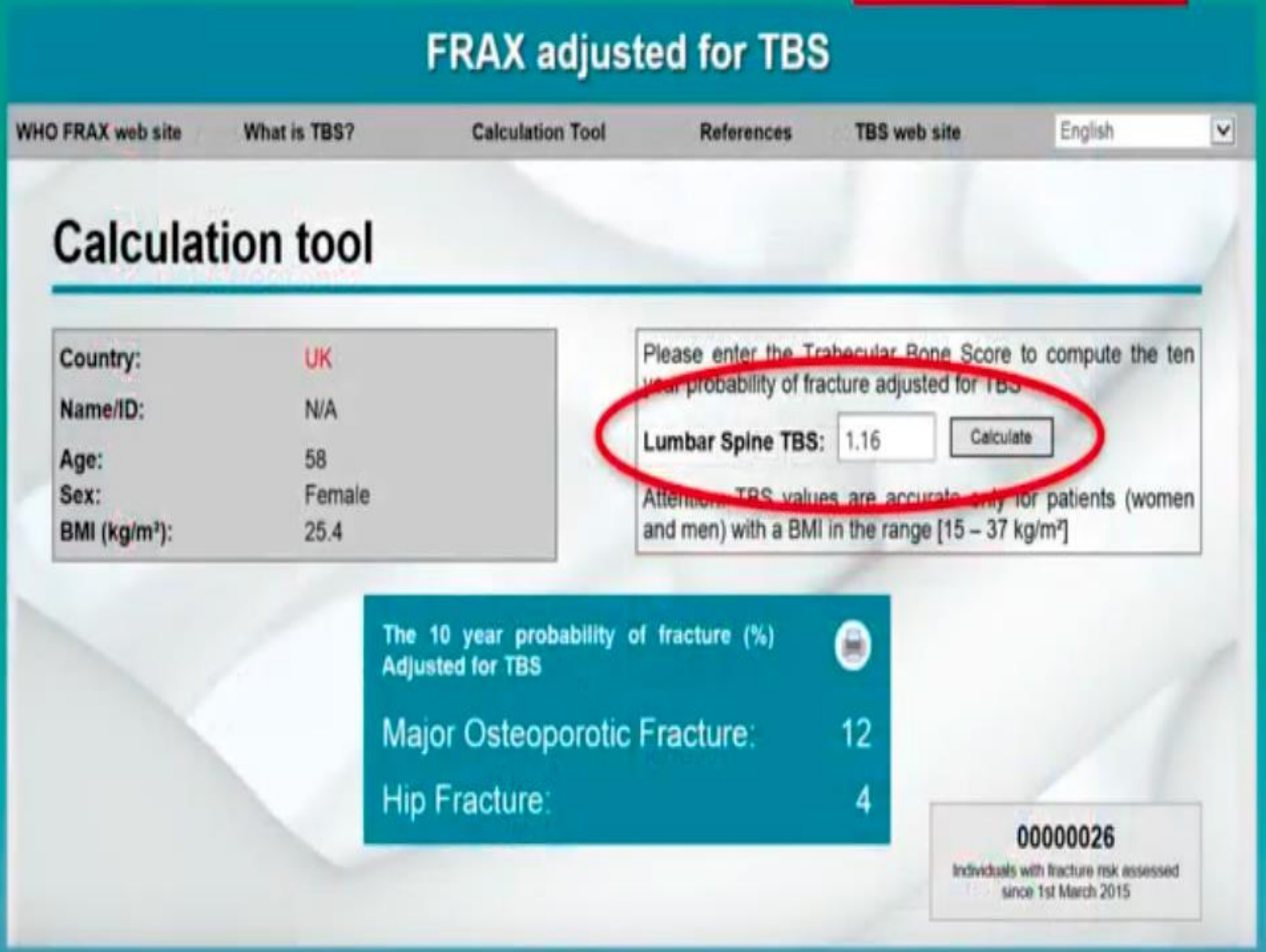
www. Shef.ac.uk/FRAX



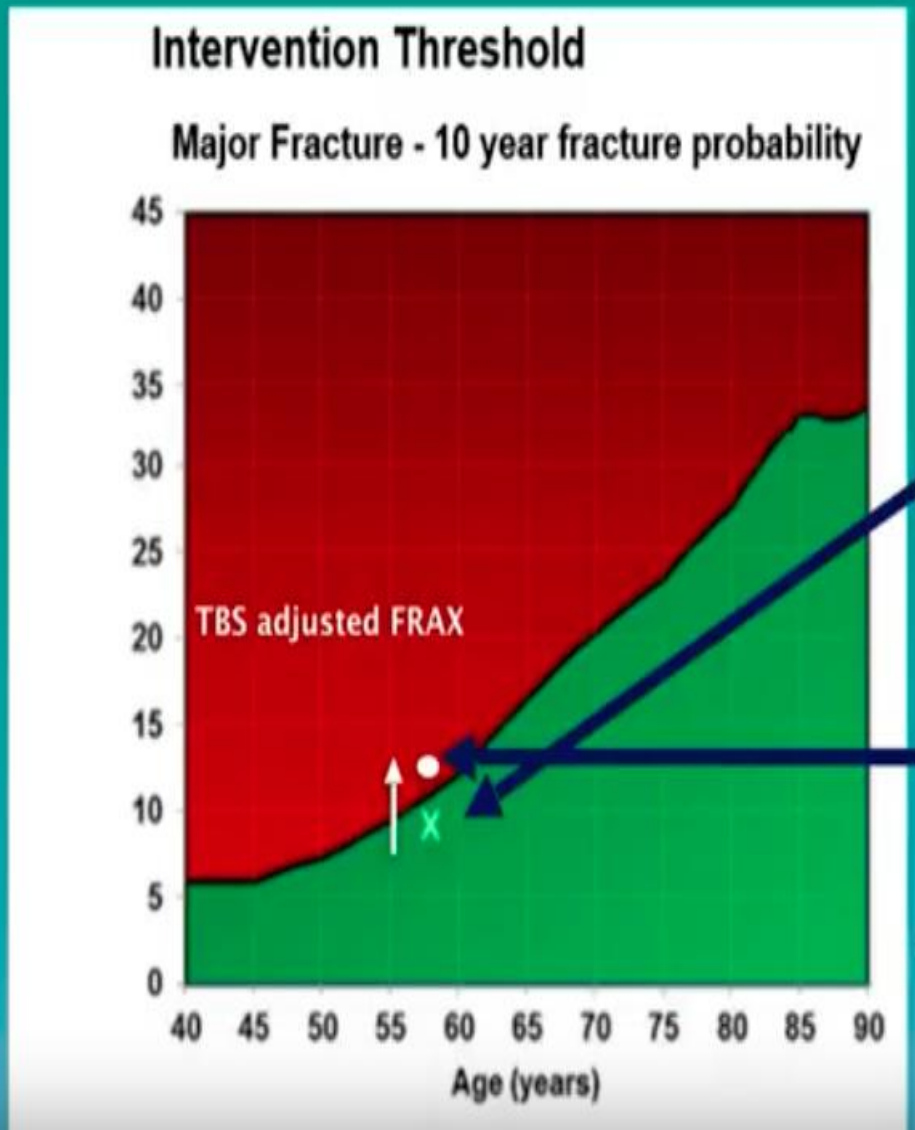
Adjust with TBS

TBS adjusted FRAX®

www.Shef.ac.uk/FRAX



TBS adjusted FRAX®



Who to treat?

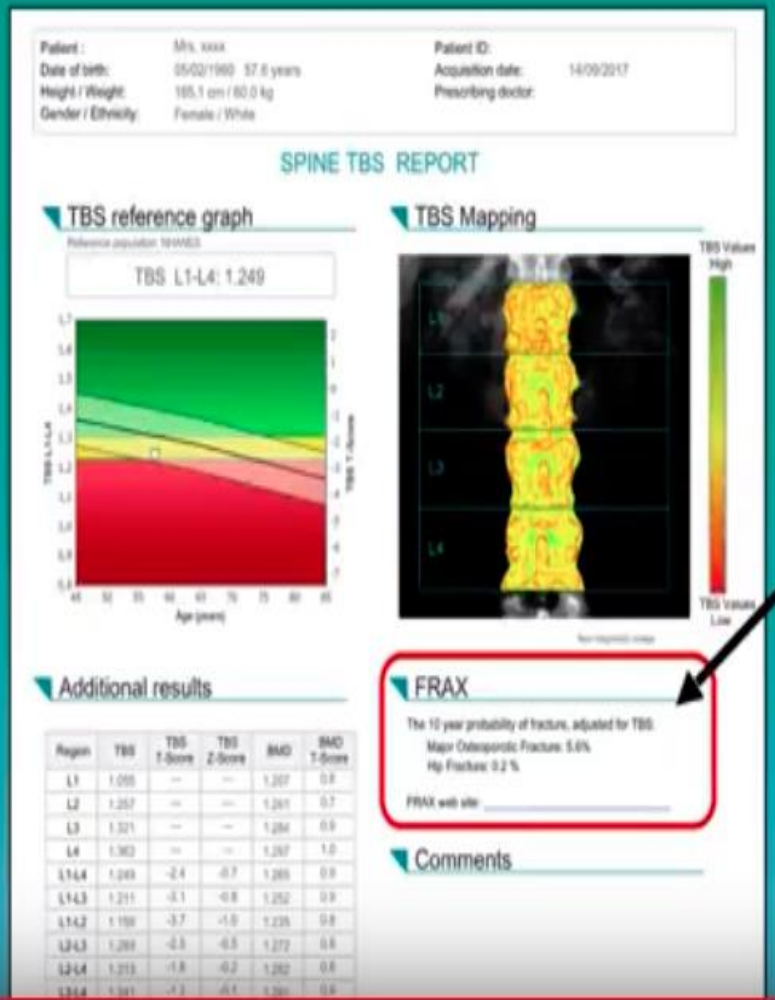
FRAX without TBS: no intervention

FRAX with TBS: intervention

- Refinement of therapy decision

TBS adjusted FRAX®

… also directly incorporated in the TBS printout


Patient : Mrs. xxxx
Date of birth: 05/02/1960 57.6 years
Height / Weight: 165.1 cm / 60.0 kg
Gender / Ethnicity: Female / White
Patient ID:
Acquisition date: 14/09/2017
Prescribing doctor:

SPINE TBS REPORT

TBS reference graph

TBS L1-L4: 1.249

TBS Mapping

TBS Values High

TBS Values Low

Additional results

Region	TBS	TBS T-Score	TBS Z-Score	BMD	BMD T-Score
L1	1.055	--	--	1.207	0.8
L2	1.257	--	--	1.261	0.7
L3	1.321	--	--	1.284	0.9
L4	1.362	--	--	1.287	1.0
L1-L4	1.249	-2.4	-0.7	1.265	0.9
L1-L3	1.211	-3.1	-0.8	1.252	0.9
L1-L2	1.159	-3.7	-1.0	1.235	0.8
L2-L3	1.289	-2.5	-0.5	1.272	0.8
L2-L4	1.213	-1.8	-0.2	1.282	0.8
L3-L4	1.341	-1.1	-0.1	1.291	0.9

FRAX

The 10 year probability of fracture, adjusted for TBS:
Major Osteoporotic Fracture: 5.6%
Hip Fracture: 0.2 %

FRAX web site:

Comments

FRAX

The 10 year probability of fracture, adjusted for TBS:

Major Osteoporotic Fracture: 5.6 %

Hip Fracture: 0.2 %

FRAX web site: https://www.shef.ac.uk/FRAX/?lang=en

TBS for Treatment Monitoring?

TBS: ISCD position statement

- **TBS is associated with vertebral, hip and major osteoporotic fracture risk in postmenopausal women.**
- **TBS is associated with hip fracture risk in men over the age of 50 years.**
- **TBS is associated with major osteoporotic fracture risk in men over the age of 50 years.**
- **TBS should not be used alone to determine treatment recommendations in clinical practice.**
- **TBS can be used in association with FRAX and BMD to adjust FRAX-probability of fracture in postmenopausal women and older men.**
- **TBS is not useful for monitoring bisphosphonate treatment in postmenopausal women with osteoporosis.**
- **TBS is associated with major osteoporotic fracture risk in postmenopausal women with type II diabetes.**

Hip Geometry: ISCD position statement

- Hip axis length (HAL) derived from DXA is associated with hip fracture risk in postmenopausal women.
- The following hip geometry parameters derived from DXA (CSA, OD, SM, BR, CSMI, NSA) should not be used to assess hip fracture risk.
- Hip geometry parameters derived from DXA (CSA, OD, SM, BR, CSMI, HAL, NSA) should not be used to initiate treatment.
- Hip geometry parameters derived from DXA (CSA, OD, SM, BR, CSMI, HAL, NSA) should not be used for monitoring.

QCT-based Finite Element Analysis ISCD position statement

- **Vertebral strength as estimated by QCT-based FEA predicts vertebral fracture in postmenopausal women.**
- **Vertebral strength as estimated by QCT-based FEA is comparable to spine DXA for prediction of vertebral fractures in older men.**
- **Femoral strength as estimated by QCT-based FEA is comparable to hip DXA for prediction of hip fractures in postmenopausal women and older men.**

QCT-based Finite Element Analysis ISCD position statement

- **FEA cannot be used to diagnose osteoporosis using the current WHO T-score definition.**

- **Vertebral or femoral strength as estimated by QCT-based FEA can be used to initiate pharmacologic treatment using validated thresholds and in conjunction with clinical risk factors.**

- **Vertebral or femoral strength as estimated by QCT-based FEA can be used to monitor age- and treatment-related changes.**

FRAX INTRODUCTORY STATEMENT

1. FRAX is a computer-based algorithm which uses easily obtained clinical risk factors to estimate an individual's 10-year fracture probability.

It may be utilized by clinicians

to assist in the identification of patients at high risk for fractures.

FRAX CLINICAL STATEMENTS

2. Impaired functional status in patients with rheumatoid arthritis may be a risk factor for clinical fractures. FRAX may underestimate fracture probability in such patients.

3. There is no consistent evidence that non-glucocorticoid medications for rheumatoid arthritis alter fracture risk.

4. While there is evidence that duration and dose of tobacco smoking may impact on fracture risk, quantification of this risk is not possible.

5. Falls are a risk factor for fractures but are not accommodated as an entry variable in the current FRAX model. Fracture probability may be underestimated in individuals with a history of frequent falls, but quantification of this risk is not currently possible.

FRAX CLINICAL STATEMENTS

5. Falls are a risk factor for fractures but are not accommodated as an entry variable in the current FRAX model. Fracture probability may be underestimated in individuals with a history of frequent falls, but quantification of this risk is not currently possible.

6. There is a relationship between number of prior fractures and subsequent fracture risk. FRAX underestimates fracture probability in persons with a history of multiple fractures.

7. There is a relationship between severity of prior vertebral fractures and subsequent fracture risk. FRAX may underestimate fracture probability in individuals with prevalent severe vertebral fractures

FRAX CLINICAL STATEMENTS

8. While there is evidence that hip, vertebral, and humeral fractures appear to confer greater risk of subsequent fracture than fractures at other sites, quantification of this incremental risk in FRAX is not possible.

9. A parental history of non-hip fragility fracture may be a risk factor for fracture. FRAX may underestimate fracture probability in individuals with a parental history of non-hip fragility fracture.

10. Evidence that bone turnover markers predict fracture risk independent of Bone Mineral Density (BMD) is inconclusive. Therefore, bone turnover markers are not included as risk factors in FRAX.

FRAX CLINICAL STATEMENTS

11

- Th
- ere is a dose relationship between glucocorti-
- coid use of greater than 3 months and fracture
- risk. Th
- e average dose exposure captured within
- FRAX is likely to be a prednisone dose of

1 FRAX is a computer-based algorithm which uses easily obtained clinical risk factors to estimate an individual's 10-year fracture probability. It may be utilized by clinicians to assist in the identification of patients at high risk for fractures.

2 Impaired functional status in patients with rheumatoid arthritis may be a risk factor for clinical fractures. FRAX may underestimate fracture probability in such patients.

3 There is no consistent evidence that non-glucocorticoid medications for rheumatoid arthritis alter fracture risk.

4 While there is evidence that duration and dose of tobacco smoking may impact on fracture risk, quantification of this risk is not possible.

5 Falls are a risk factor for fractures but are not accommodated as an entry variable in the current FRAX model. Fracture probability may be underestimated in individuals with a history of frequent falls, but quantification of this risk is not currently possible.

6 There is a relationship between number of prior fractures and subsequent fracture risk. FRAX underestimates fracture probability in persons with a history of multiple fractures.

7 There is a relationship between severity of prior vertebral fractures and subsequent fracture risk. FRAX may underestimate fracture probability in individuals with prevalent severe vertebral fractures.

8 While there is evidence that hip, vertebral, and humeral fractures appear to confer greater risk of subsequent fracture than fractures at other sites, quantification of this incremental risk in FRAX is not possible.

9 A parental history of non-hip fragility fracture may be a risk factor for fracture. FRAX may underestimate fracture probability in individuals with a parental history of non-hip fragility fracture.

10 Evidence that bone turnover markers predict fracture risk independent of Bone Mineral Density (BMD) is inconclusive. Therefore, bone turnover markers are not included as risk factors in FRAX.

11 There is a dose relationship between glucocorticoid use of greater than 3 months and fracture risk. The average dose exposure captured within FRAX is likely to be a prednisone dose of 2.5-7.5 mg/day or its equivalent. Fracture probability is under-estimated when prednisone dose is greater than 7.5 mg/day and is over-estimated when prednisone dose is less than 2.5 mg/day.

12 Frequent intermittent use of higher doses of glucocorticoids increases fracture risk. Because of variability in the dose and dosing schedule, quantification of this risk is not possible.

13 High dose inhaled glucocorticoids may be a risk factor for fracture. FRAX may underestimate fracture probability in users of high dose inhaled glucocorticoids.

14 Appropriate glucocorticoid replacement in individuals with adrenal insufficiency has not been shown to increase fracture risk. In such patients, use of glucocorticoids should not be included in FRAX calculations.

15 Measurements other than BMD or T-score at the femoral neck by Dual-energy X-ray Absorptiometry (DXA) are not recommended for use in FRAX.

16 FRAX may underestimate or overestimate major osteoporotic fracture risk when lumbar spine T-score is much lower or higher (>1 Standard Deviation discrepancy) than femoral neck T-score.

17 A procedure based upon the difference (offset) between the Lumbar Spine and Femoral Neck T-scores can enhance fracture prediction in the current version of FRAX.

18 The ISCD 2007 PDC Statements on fracture risk prediction and application of heel Quantitative Ultrasounds (QUS) are supported by a higher level of evidence in men and women than was available in 2007.

19 Currently validated heel QUS devices, using criteria defined in the 2007 ISCD PDC, predict fracture risk similarly.

20 FRAX with BMD predicts fracture risk better than clinical risk factors or BMD alone. Use of FRAX without BMD is appropriate when BMD is not readily available or to identify individuals who may benefit from a BMD measurement.

21 It is not appropriate to use FRAX to monitor treatment response.

22 Evidence that rate of bone loss may be an independent risk factor for fracture is conflicting. Therefore, rate of bone loss is not included as a FRAX risk factor.

23 Separate FRAX models are available for United States (US) Asians, Blacks and Hispanics because hip and major osteoporotic fracture rates are lower in these ethnic groups than in US Whites. Until additional data are available, the US Caucasian FRAX calculator should be used to assess fracture risk in US Native American women.

24 Changing fracture and mortality rates and improved quality of data are expected. Therefore, periodic review of country-specific fracture rates used in the FRAX model is recommended.

25 There is significant variability in hip fracture rates throughout the world. The minimum requirement for construction of a country-specific FRAX model is hip fracture incidence data that are of high quality and representative of that country.

26 The accuracy of FRAX models is improved by the inclusion of country-, age- and sex-specific rates of other major osteoporotic fractures (clinical vertebral, humerus, distal forearm).

27 In the absence of high quality, national hip fracture data, a country-specific FRAX model can be built using hip fracture incidence rates from a surrogate country, but with incorporation of country-specific mortality rates.

28 In the absence of any hip fracture data, development of FRAX models based on broad categories of fracture risk (e.g. low, medium, high), adjusted for country-specific mortality rates is recommended.

DATE	L1-L4	L2-L4	NECK	TOTAL	COMMENTS
14.09.01	-0.3	-0.1	-1.3	-1.0	Wrong numbering of vertebra (T12 as L1) – Good positioning of neck ROI with good internal rotation
20.02.03	-0.4	-0.3	-1.6	-1.0	Wrong numbering of vertebra(T12 as L1) – Good positioning of neck ROI with good internal rotation
07.02.04	-0.6	-0.6	-1.3	-1.1	Wrong numbering of vertebra.(T12 as L1) – Good positioning of neck ROI with good internal rotation
10.12.05	-0.6	-0.5	-1.6	-1.5	Wrong numbering of vertebra. (T12 as L1) - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
24.03.07	-0.3	-0.3	-1.6	-1.2	Wrong numbering of vertebra(T12 as L1). - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
27.08.08	-1.1	-1.0	-2.3	-1.6	Wrong numbering of vertebra(T12 as L1). - Part of 'L1' not included. – Good positioning of neck ROI with good internal rotation
20.02.10	-0.9	-0.8	-2.4	-1.6	Correct numbering of vertebra - Good positioning of neck ROI with good internal rotation
14.05.11	-1.2	-1.2	-2.2	-1.6	Correct numbering of vertebra - Wrong positioning of neck ROI (lower, towards the trochanter major)with good internal rotation

FRAX 10 year absolute risk

MOF = 7.2

HF =2.4

Will you still insist on treating or not treating?

The patient following her physician’s advice had her last Denosumab injection in mid-December 2017.

03.07.17

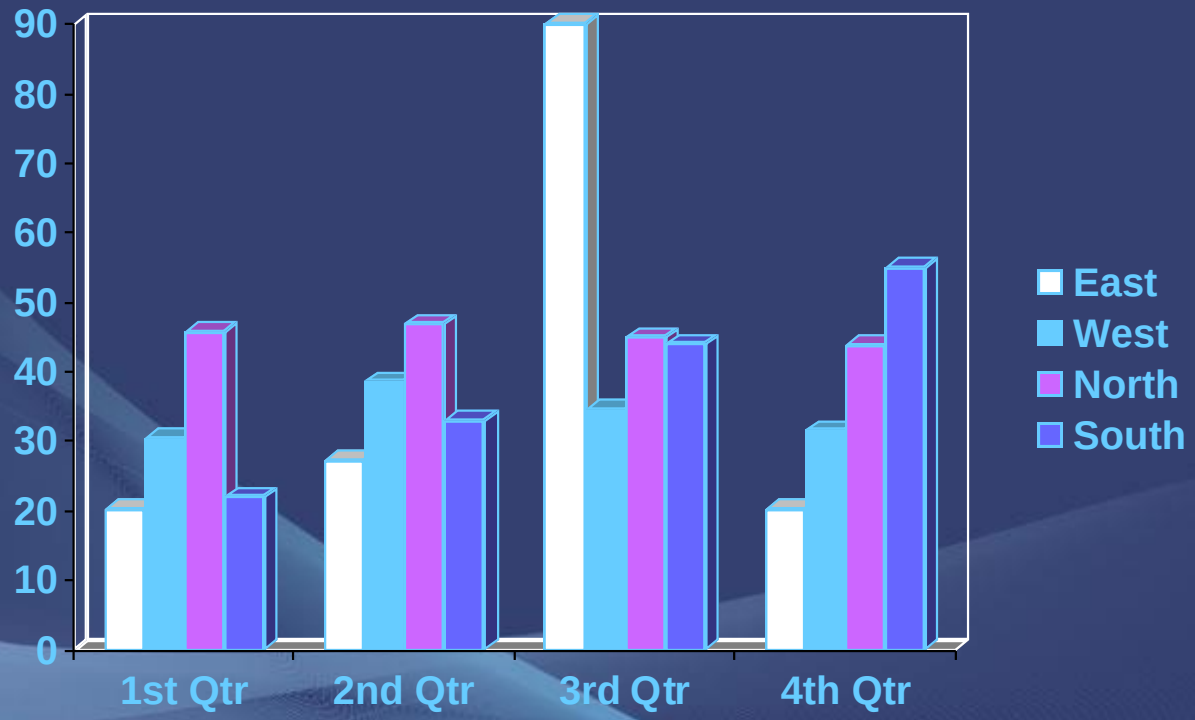
L1-L4 T-score = -0.3

Neck T-score = -2.6

Example of a Bullet Point Slide

- Bullet Point
- Bullet Point
  - Sub Bullet

Example of a chart



Picture slide

- Bullet 1
- Bullet 1

Examples of default styles

- Text and lines are like this
- Hyperlinks like this
- Visited hyperlinks like this

Table	

Text box

Text box
With shadow

Use of templates

You are free to use these templates for your personal and business presentations.

We have put a lot of work into developing all these templates and retain the copyright in them. They are not Open Source templates. You can use them freely providing that you do not redistribute or sell them.

Do

- ✓ Use these templates for your presentations
- ✓ Display your presentation on a web site provided that it is not for the purpose of downloading the template.
- ✓ If you like these templates, we would always appreciate a link back to our website. Many thanks.

Don't

- × Resell or distribute these templates
- × Put these templates on a website for download. This includes uploading them onto file sharing networks like Slideshare, Myspace, Facebook, bit torrent etc
- × Pass off any of our created content as your own work

You can find many more free templates on the Presentation Magazine website
www.presentationmagazine.com