Valutazione strumentale dell'osteoporosi
QUS

ROBERTO CESAREO
LATINA

Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni NON ho avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario.

L'OSSO: UN "SISTEMA COMPLESSO" DALLE CARATTERISTICHE CONTRADDITTORIE …..

- **Sufficientemente rigido per resistere al carico meccanico ma abbastanza flessibile per poter assorbire energia senza fratturarsi**

- **Sufficientemente leggero per favorire la velocita' del movimento ma robusto per permettere il movimento stesso contro la forza di gravita'**

PREVISIONE DEL RISCHIO DI FRATTURA

Site of measurement	Forearm fracture	Hip fracture	Vertebral fracture	All fractures
Distal radius	1.7 (1.4–2.0)	1.8 (1.4–2.2)	1.7 (1.4–2.1)	1.4 (1.3–1.6)
Femoral neck	1.4 (1.4–1.6)	2.6 (2.0–3.5)	1.8 (1.1–2.7)	1.6 (1.4–1.8)
Lumbar spine	1.5 (1.3–1.8)	1.6 (1.2–2.2)	2.3 (1.9–2.8)	1.5 (1.4–1.7)

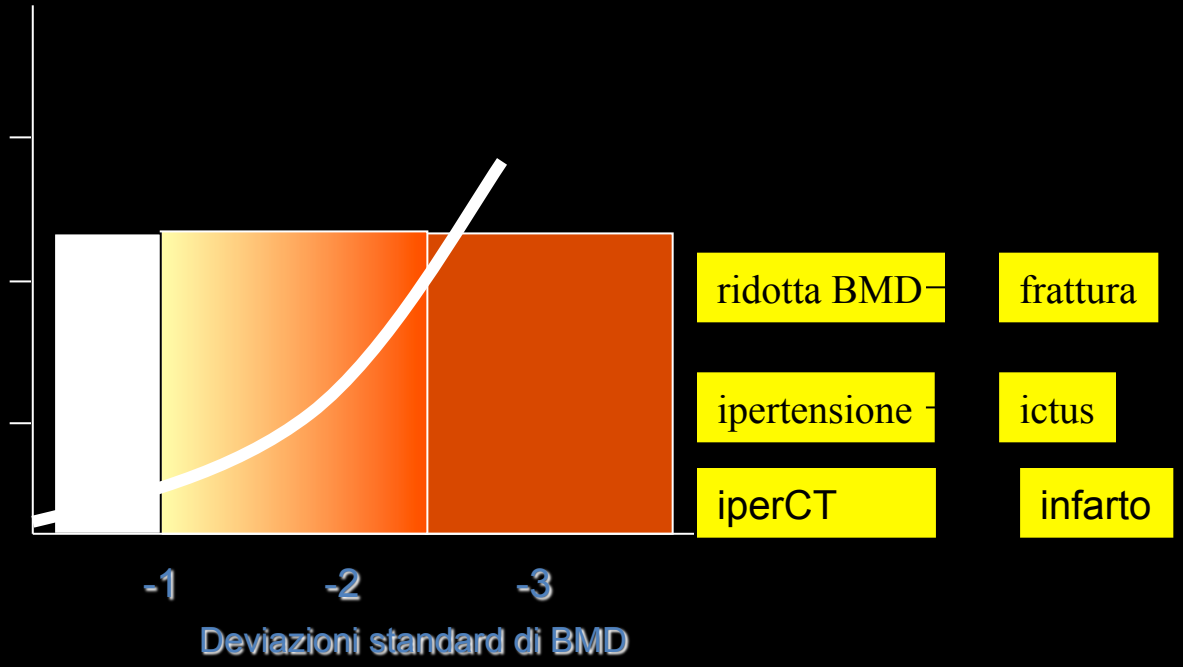
Alla diminuzione di una deviazione standard della BMD il rischio di frattura del femore aumenta di 2,6

T score -3

RISCHIO 15 VOLTE (2.6^3)

MAGGIORE DI UN INDIVIDUO CON T SCORE DI 0

Osteoporosi e rischio di frattura



Marshall D et al, BMJ 1996

Limiti della densitometria

Se si considerano le donne in menopausa, **solo nel 26% delle fratture vertebrali e nel 18% di quelle femorali** è presente un quadro densitometrico di osteoporosi (*T-score* < -2,5 DS)

La frattura è un evento multifattoriale in cui entrano in gioco anche fattori non espressi dall'indagine densitometrica

Gatti D., Adami S.; GIBIS YEARBOOK 2011; Capitolo 8 : Stima del rischio di frattura e soglia di intervento terapeutico

La resistenza scheletrica

ITALIAN CHAPTER

BMD

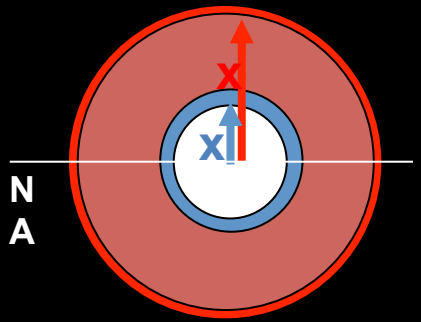
Bone Quality

RESISTENZA

- MACROARCHITETTURA (forma e geometria)
- MICROARCHITETTURA (organizzazione ed integrità delle trabecole)
- MICROCRACS
- MATRICE OSSEA (minerale e collagene)

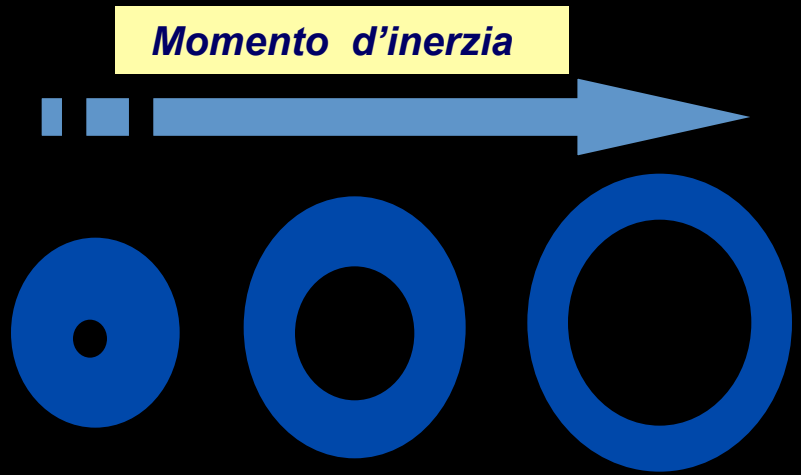
ADATTAMENTO FUNZIONALE OSSO CORTICALE: GEOMETRIA

L'osso rosso
"è meglio" di quello blu
perchè è più lontano
dall'asse neutro (NA)



"Cross-Sectional Moment of Inertia" distribuzione della massa nello spazio

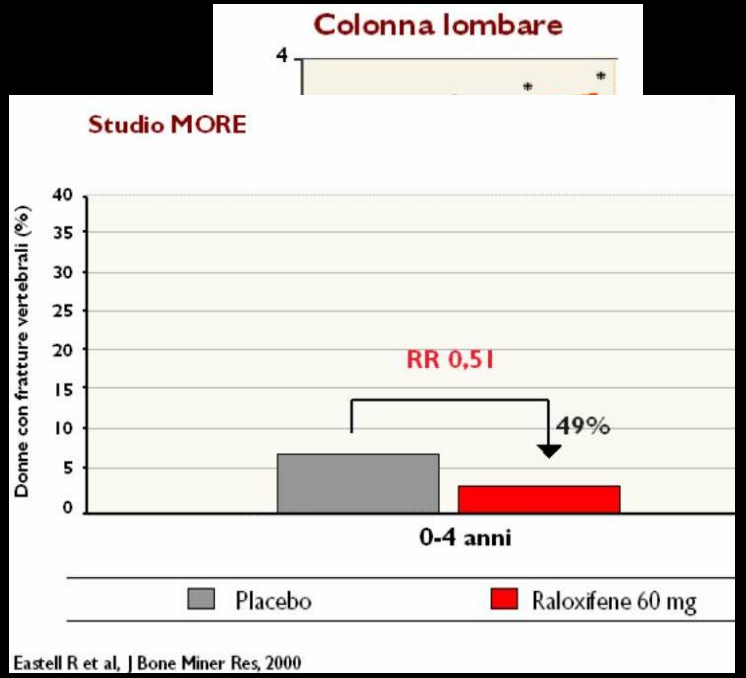
È una funzione del quadrato della distanza dall'asse neutro



	2.77	2.77	2.77
	0.61	1.06	1.54
Resistenza	*100%*	*149%*	*193%*

Il ruolo centrale della BMD nella valutazione del rischio di frattura ?

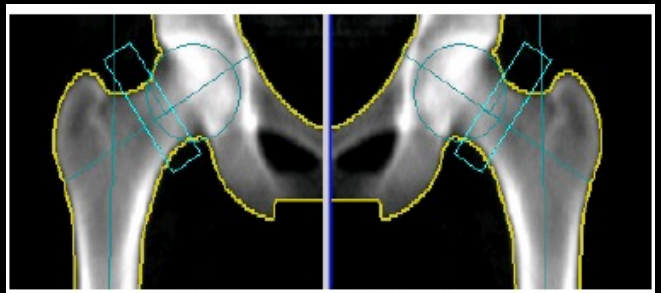
STUDIO MORE
RALOXIFENE



DEXA
INDICE DI RESISTENZA
ALLA ROTTURA FEMORALE

AHA

Caratteristiche geometriche



Calcolo automatico indice resistenza alla rottura femorale

- cross-sectional area (CSA)
- cross-sectional moment of inertia (CSMI)
- the section modulus (Z)
- the buckling ratio (BR)
- cortical thickness

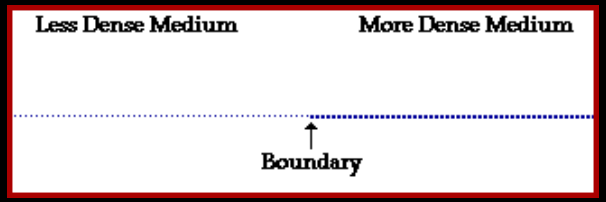
Ultrasuoni: definizione

Con il termine ultrasuoni si definiscono onde meccaniche, elastiche, la cui frequenza è maggiore del limite superiore di udibiltà per l'orecchio umano (20.000 hertz).

Per onda elastica si intende un'onda che utilizza un mezzo materiale per propagarsi.

Infrasuono	campo udibile	ultrasuoni

Quando l'onda ultrasonografica passa attraverso l'osso, le caratteristiche fisiche di questo modificano la velocità e l'intensità dell'onda in uscita.



Ultrasuonografia

Sedi di indagine:

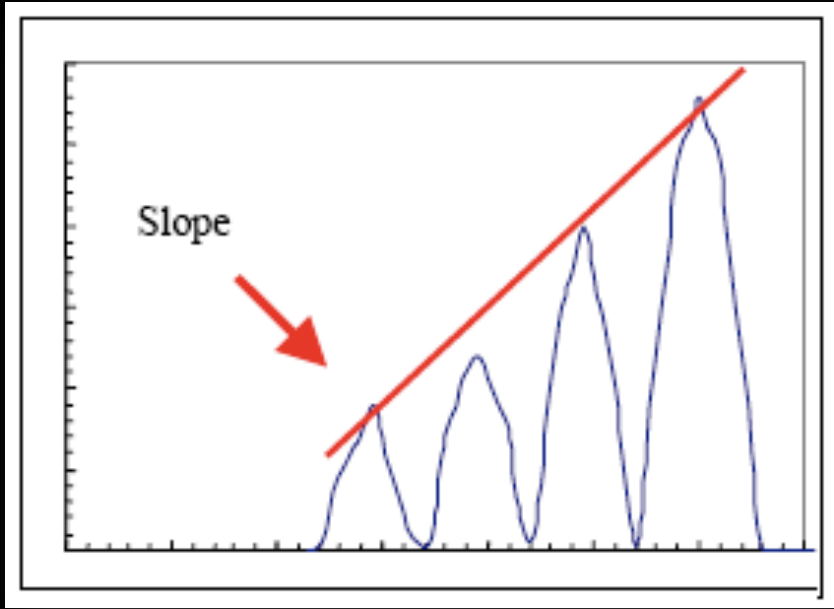
Che cosa si misura con gli apparecchi ad ultrasuoni ?

PARAMETRI MISURATI

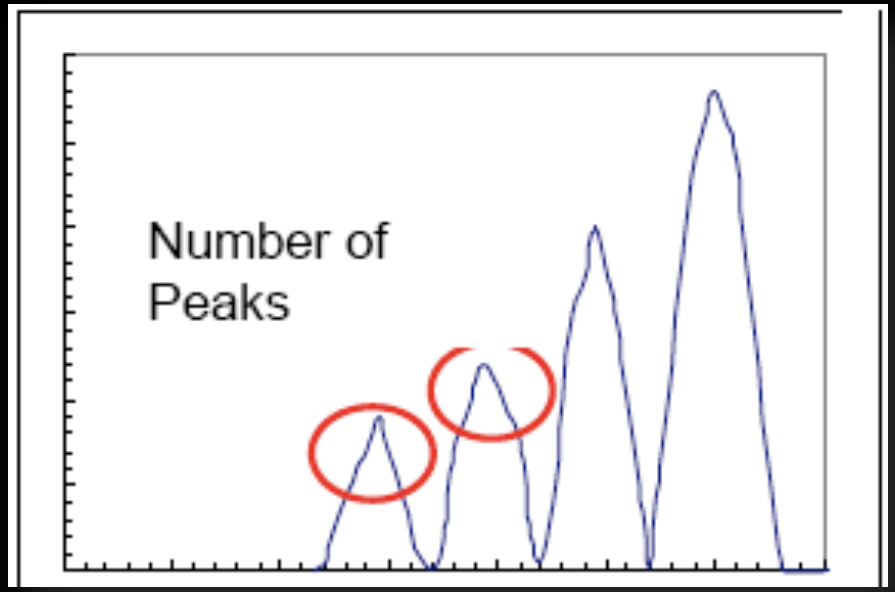
- *VELOCITA'*
- *ATTENUAZIONE*
- *STIFNESS/QUI*

I parametri QUS sono correlati ad aspetti strutturali e geometrici dell'osso e possono fornire informazioni aggiuntive sulla struttura rispetto alla densitometria ossea

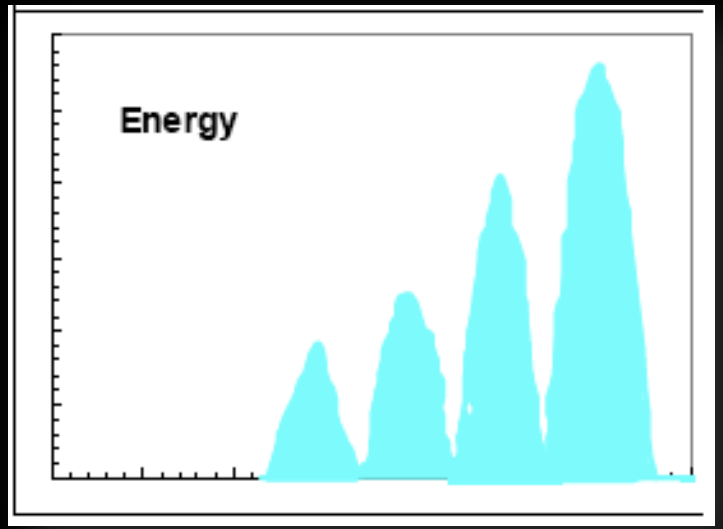
Speed of sound
Sos



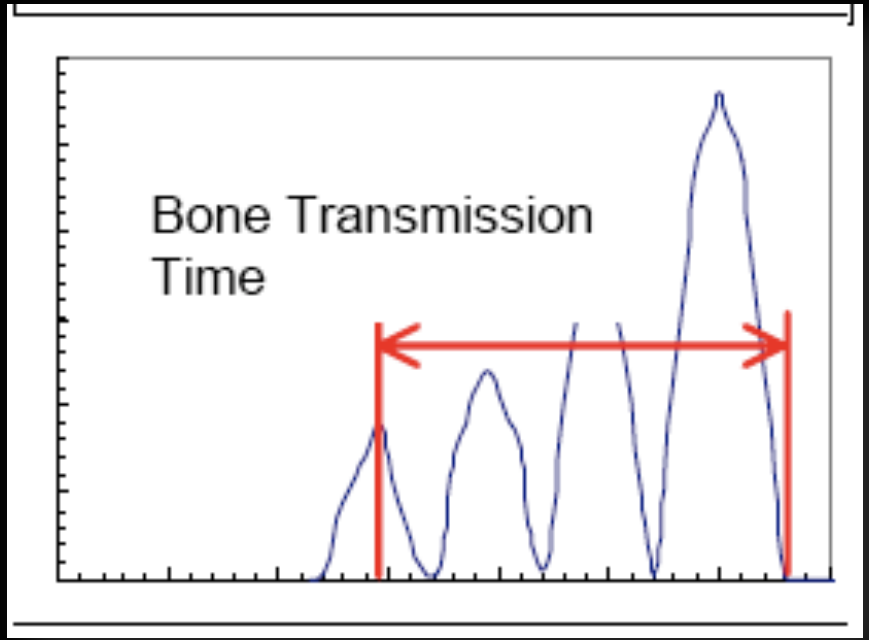
Numero di picchi



Energia



Bone trasmission time



Parametri fisici

Parametro	Caratteristiche del tessuto osseo
Pure Speed of Sound	Densità
Number of Peaks	Continuità strutturale della matrice mineralizzata
Energy	Elasticità
Fast Wave Amplitude	Elasticità, Densità
Ultrasound Peak Amplitude	Spazi mineralizzati (trabecole)
Bone trasmission time	Area corticale, Momento di Inerzia
AD-SoS	Area corticale, Momento di Inerzia, Densità

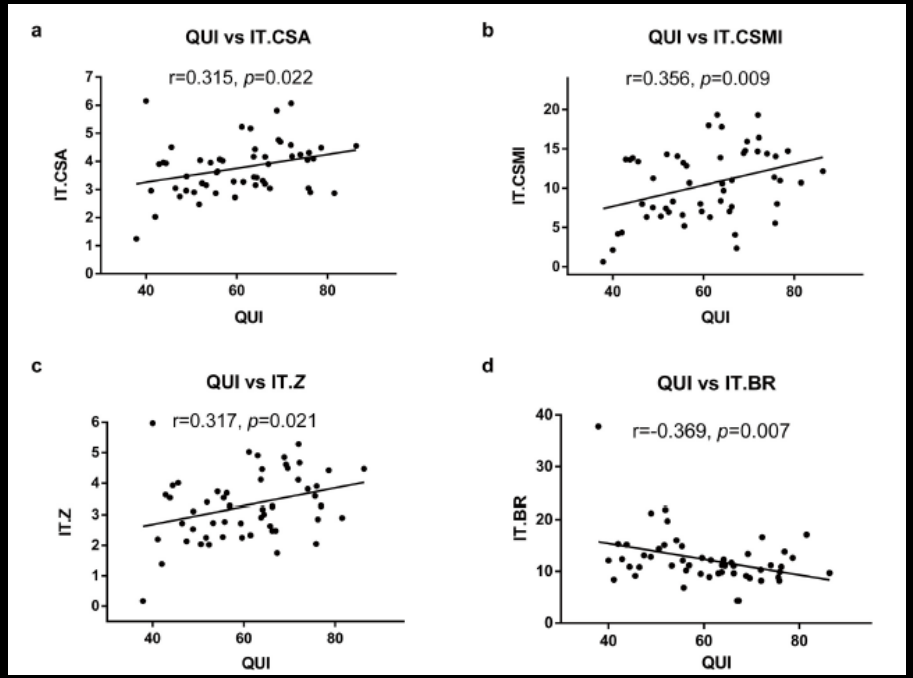
Calcaneal Quantitative Ultrasound as a Determinant of Bone Health Status: What Properties of Bone Does It Reflect?

Int J Med Scie 2013

Researchers (year)	Sample	Findings
Bouxsein and Radoff (1997) (21)	Human cadaveric calcaneal bone	BUA and SOS of intact heel correlated significantly with compressive modulus and ultimate strength, but the correlations were inferior compared to BMD and apparent density. Combining BUA and BMD or apparent density increased the association with elastic modulus. Combining BUA and SOS explained 7-12% of the variance in trabecular bone mechanical properties.
Hans et al. (1999) (14)	Human cadaveric spinal bone	SOS was measured from sagittal, coronal and axial axes. SOS correlated significantly with BMD, BV/TV, Tb.Sp., Tb.N., fractal dimension and elasticity. After adjusting for BMD, the correlation between SOS and elasticity at coronal axis remained significant. Using multivariate regression, most of the variation in SOS was contributed by BMD and the contributions of elasticity and anisotropy were small.
Trebacz and Natali (1999) (19)	Human cadaveric calcaneal and L1 vertebral bone.	The relationships between SOS with bone ash density, BV/TV and Tb.Th. were significant. The combination of the aforementioned factors contributed to 83% of the variation in SOS. BV/TV was a significant predictor for BUA.
Toyras et al. (1999) (16)	Trabecular sample from bovine femur and tibia.	SOS was associated with BMD, Young's modulus or ultimate strength in bovine trabecular sample but BUA was not. *In vivo* study showed that BUA was associated with BMD in human calcaneus. BUA was not suitable in measurement for high density sample.
Toyras et al. (2002) (17)	Trabecular sample from bovine femur and tibia.	BUA correlated negatively with vBMD and storage modulus. SOS correlated positively and strongly with vBMD and storage modulus but negatively with tangent loss. BUA could not predict mechanical properties of the bone with high density.
Cortet et al. (2003) (13)	Human cadaveric calcaneal bone.	SOS was correlated significantly with BMD, BV/TV, Tb.Th., Tb.Sp., and Tb.N. The combination of the factors such as trabecular pattern and fractal dimension contributed to 17.8% variation in SOS other than BMD.
Chaffai et al. (2002) (18)	Human cadaveric calcaneal bone.	All QUS indices (nBUA, UVB and BUB) correlated significantly with BMD and microarchitecture parameters of bone (BV/TV, BS/BV, Tb.Th., Tb.N., Tb.Sp., N.Nd) but all these correlations were independent of BMD. In stepwise regression model, BMD was significant predictor for UVB.
Haİat et al. (2007) (20)	Computer simulation of trabecular sample from human cadaveric femur.	The variation in BV/TV exerted most significant influence on BUA and SOS compared to other factors such as density, stiffness and microarchitecture of the bone. After adjustment for BMD, most variations in SOS and BUA were determined by BV/TV.
Cavani et al. (2008) (12)	Cylindrical bone sample from equine vertebrae.	SOS correlated with volumetric BMD, BV/TV, BS/TV, Tb.N., Tb.Th., Tb.Sp. and Young's Modulus. After adjustment for vBMD, SOS was significantly correlated with BV/TV, BS/TV and Young's modulus. A total of 93.34% of the variation in SOS was contributed by BMD and Young's modulus.
Padilla et al. (2008) (15)	Human cadaveric femoral bone.	All QUS parameters (SOS, BUB and nBUA) were correlated with BMD. SOS was correlated significantly with microarchitecture parameters of the bone (Tb.Th., BS/BV, Tb.N., Tb.Sp., Euler, incidence angle, RV/BV and BV/TV). In multiple regression analysis, microarchitectural parameters contributed 19% of the variation in SOS apart from BMD.

Researcher (year)	Subject and Study Type	Findings
Hernandez et al. (2004) (25)	5195 Spanish women aged 65 years or older. Cross-sectional study.	All QUS parameters (eBMD, BUA, SOS, QUI) were significantly different between Spanish women with and without history of osteoporotic fractures. QUS parameters showed significant association with previous fractures.
Gonnelli et al. (2005) (30)	401 Italian male aged 45-82 years. Cross-sectional study.	All QUS and DXA parameters were significantly different between men with and without fractures. QUS at heel had better discriminatory ability compared to QUS at fingers. As shown by receiver operating characteristics curve, SOS had discriminatory ability same as femoral neck BMD. The association between SOS and previous fractures was significant and higher than BUA but lower than stiffness.
Varenna et al. (2005) (26)	4832 Italian men aged 60-80 years. Cross-sectional study.	Hip and non-spinal fractures were significantly associated with SOS, BUA and SI.
Khaw et al. (2004) (27)	The Norfolk cohort of the European Prospective Investigation into Cancer. 14824 men and women analysed together (42-82 years). Prospective study: follow-up for an average of 1.9 years.	1 SD decrease in VOS caused a 60 % increase in fracture risk (both gender), higher risk for older subjects, and doubled for subjects with previous fractures.
Fujiwara et al. (2005) (28)	1004 Japanese men and 3024 Japanese women. Prospective study: follow-up for an average of 5 years.	SOS, BUA and SI significantly predicted fractures. SOS and SI were better predictors than BUA. The short term prediction (5 years) was better than long term prediction (>5-10 years).
Damilaski et al. (2007) (49)	30 postmenopausal women with hip fractures and 30 healthy women. Cross-sectional study.	ROC curve showed that BUA, SOS and SI were able to differentiate hip-fractured and non-hip-fracture in postmenopausal women. BUA and SI showed significant discriminability at hip fracture but were not superior to BMD at the hip.
Meszaros et al. (2007) (6)	117 men, 27-78 years. Cross-sectional study.	BUA and SOS were significantly correlated with BMD. SOS was better at discriminating between subject with and without fractures. Discriminatory ability of SOS to vertebral fractures was the best as assessed using AUC compared to BMD and BUA.
Bauer et al.(2007) (50)	5607 US men aged ≥ 65 years. Prospective study: follow-up for an average of 4.2 years.	BUA significantly predicted hip fracture and any non-spine fracture. Combining BUA and BMD was not superior to each indicator alone in the prediction. Other QUS indices were the same.
Dane et al. (2008) (23)	351 pre- and postmenopausal women. Cross-sectional study.	BUA, SOS and SI significantly correlated with BMD at lumbar spine and femur in postmenopausal women. Only SOS significantly correlated with BMD spine and femur in pre-menopausal women. AUC showed that the QUS showed poor performance in discriminating osteoporotic and normal subjects.
El Maghraoui et al. (2009) (33)	295 postmenopausal women aged 60 - 84. Cross-sectional study.	BUA correlated weakly and significantly with BMD at the hip, lumbar spine and femur. Only lumbar spine BMD significantly predicted vertebral fracture in asymptomatic women, but QUS did not. Combination of QUS and BMD did not improve the predictability.
Kwok et al. (2012) (32)	1921 Hong Kong Chinese men aged 65-92 years. Prospective study: follow-up for an average of 6.5 years.	BUA and QUI were significantly associated with non-vertebral fractures and major fragility fractures, but the prediction of hip and spine BMD were better in major fragility fractures. Combining hip BMD and QUS indices did not improve the prediction.
Chan et al. (2012) (31)	454 women and 445 men aged 62-89 years. Prospective study: 13 years.	In women, the combination of BUA and femoral neck BMD predicted fragility fractures (hip, vertebral or any fractures) better than BMD alone. In men, the combination did not improve the prediction.

Correlation between Parameters of Calcaneal Quantitative Ultrasound and Hip Structural Analysis in Osteoporotic Fracture Patients



PLOS 2015

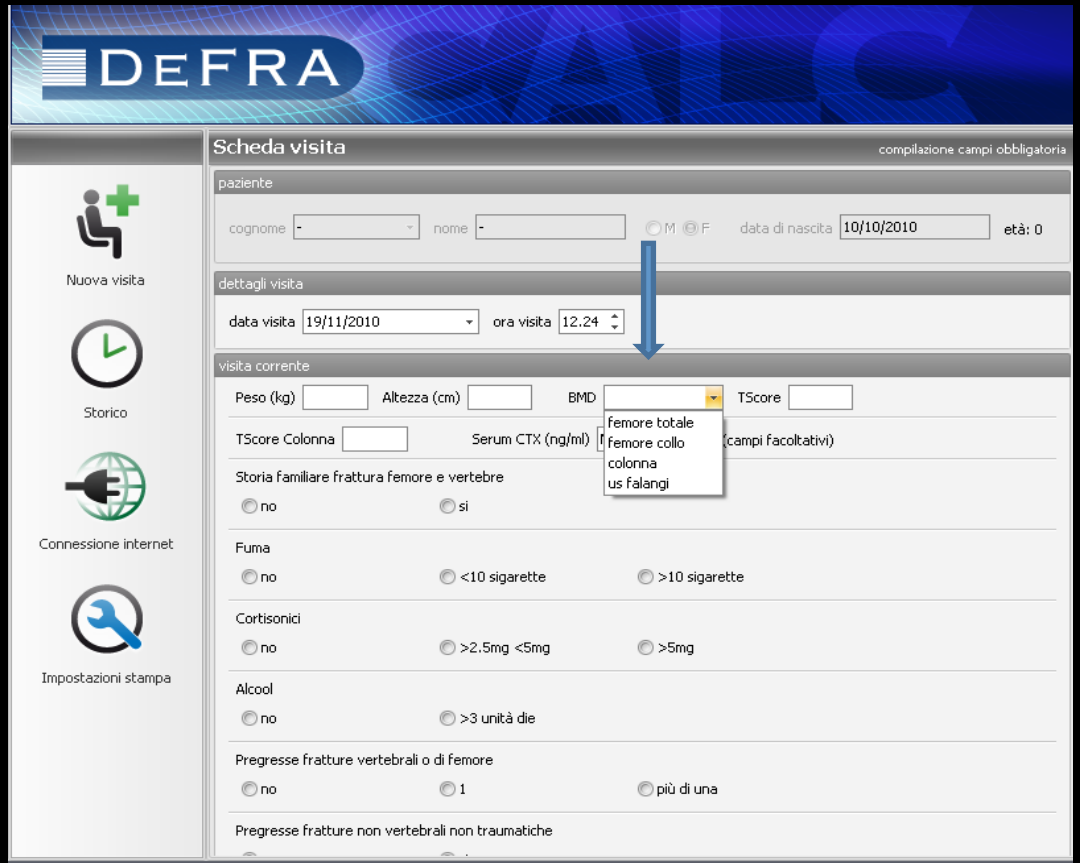
NOTA 79
ESENZIONE DAL PAGAMENTO DEI FARMACI

Terapia steroidea>3 mesi con
Prednisone>5 mg/die o equivalenti

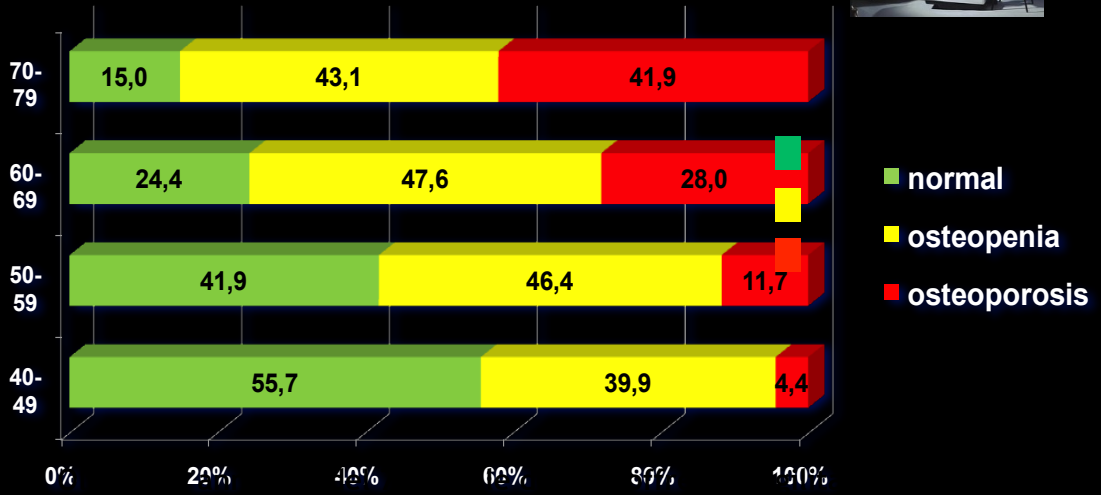
BMD Femorale<-4
QUS Calcagno<-4
QUS falangi<-5

BMD Femorale<-3
QUS Calcagno<-3
QUS falangi<-4
+
Storia familiare di fratture vertebrali
Artrite reumatoide o altre connettiviti
Pregressa frattura osteoporotica del polso
Menopausa prima dei 45 anni di età
Terapia steroidea cronica

PREVENZIONE PRIMARIA


DeFRA
Scheda visita
compilazione campi obbligatoria
Nuova visita
Storico
Connessione internet
Impostazioni stampa
paziente
cognome
nome
M
F
data di nascita
10/10/2010
età: 0
dettagli visita
data visita
19/11/2010
ora visita
12.24
visita corrente
Peso (kg)
Altezza (cm)
BMD
TScore
femore totale
femore collo
colonna
us falangi
TScore Colonna
Serum CTX (ng/ml)
(campi facoltativi)
Storia familiare frattura femore e vertebre
no
si
Fuma
no
<10 sigarette
>10 sigarette
Cortisonici
no
>2.5mg <5mg
>5mg
Alcool
no
>3 unità die
Pregresse fratture vertebrali o di femore
no
1
più di una
Pregresse fratture non vertebrali non traumatiche

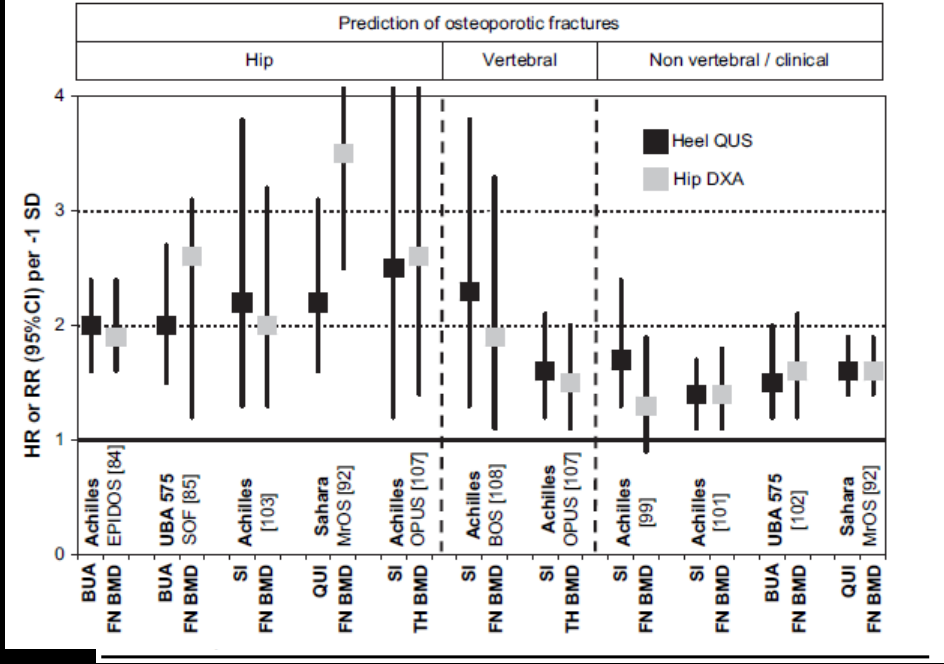
PREVALENZA DI OSTEOPENIA ED OSTEOPOROSI
Popolazione femminile in Italia
Studio E.S.O.P.O.



Adami S et al., Calcif Tissue Int 2004

Position Statement

Quantitative Ultrasound in the Management of Osteoporosis: The 2007 ISCD Official Positions



J Clin Den Ass Sk H 2008

Linee guida per la diagnosi, prevenzione e terapia dell'osteoporosi

Guidelines for the diagnosis, prevention and treatment of osteoporosis

S. Adami, F. Bertoldo, M.L. Brandi, C. Cepollaro, P. Filipponi, E. Fiore, B. Frediani, S. Giannini, S. Gonnelli, G.C. Isaia, G. Luisetto, E. Mannarino, C. Marcocci, L. Masi, C. Mereu, S. Migliaccio, S. Minisola, R. Nuti, G. Rini, M. Rossini, M. Varenna, L. Ventura, G. Bianchi

Siti di misurazione della densità ossea	*Rischio Relativo di frattura*			
	Avambraccio	*Femorale*	*Vertebrale*	*Tutte*
DXA Radio prossimale	1.8 (1.5-2.1)	2.1 (1.6-2.7)	2.2 (1.7-2.6)	1.5 (1.3-1.6)
DXA Radio distale	1.7 (1.4-2.0)	1.8 (1.4-2.2)	1.7 (1.4-2.1)	1.4 (1.3-1.6)
DXA Femore	1.4 (1.4-1.6)	2.6 (2.0-3.5)	1.8 (1.1-2.7)	1.6 (1.4-1.8)
DXA Lombare	1.5 (1.3-1.8)	1.8 (1.2-2.2)	2.3 (1.9-2.8)	1.5 (1.4-1.7)
DXA Calcagno	1.6 (1.4-1.8)	2.0 (1.5-2.7)	2.4 (1.8-3.2)	1.5 (1.3-1.8)
Ultrasuoni calcagno*		2.2 (1.8-2.7)	1.8 (1.5-2.2)	1.5 (1.4-1.7)

*L'ultrasonografia ossea non rappresenta una misura diretta della densità ossea

Linee Guida SIOMMS 2009

ITALIAN CHAPTER

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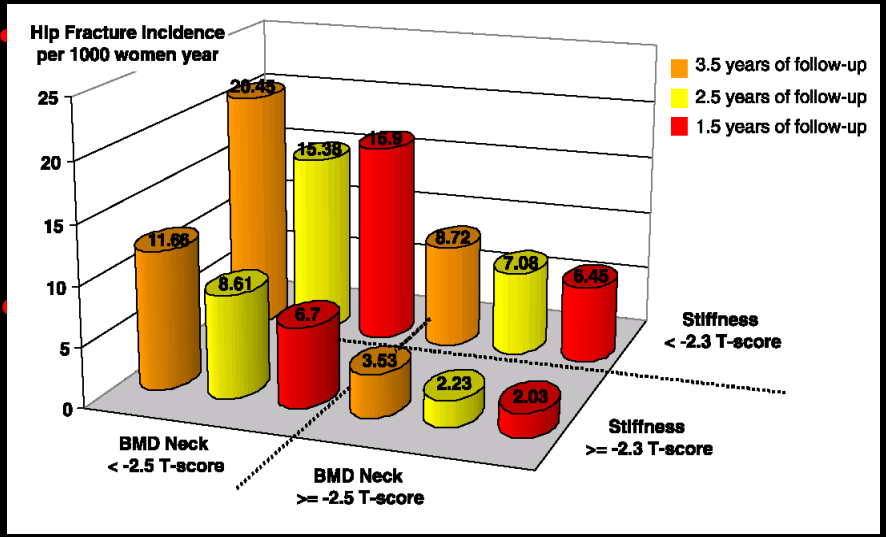
Sito/tecnica	*Rischio frattura vertebrale*	*Rischio frattura non vertebrale*	*Monitoraggio terapeutico*	*Raccomandazione impiego diagnostico*
BMD colonna/DXA	1a	1a	1b	A
BMD collo femore/DXA	1a	1a	1b	A
BMD polso/DXA	1a	1a	1b	A
BMD calcagno/DXA	1b	1a	2	A/B
Ultrasuoni calcagno	1a	1b	2	A/B
Ultrasuoni (altri)	2	1b	3	B

LINEE GUIDA SIOMMS 2009

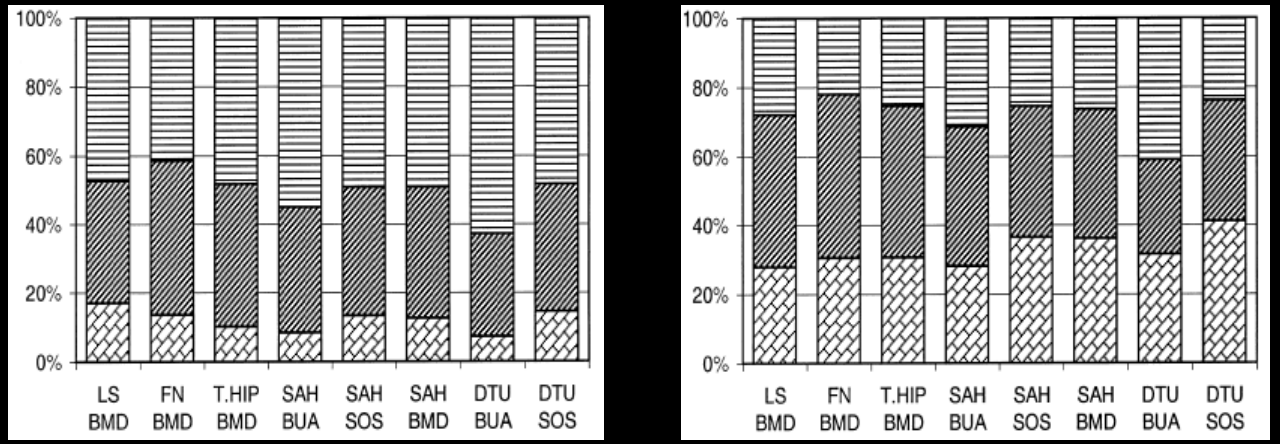
EPIDOS PROSPECTIVE STUDY
Bone. 2004

QUS E DEXA INSIEME

GRUPPO AD ALTO RISCHIO



Quantitative Ultrasound and Bone Mineral Density Are Equally Strongly Associated with Risk Factors for Osteoporosis



Prevalence of osteopenia and osteoporosis in (A) women with no clinical risk factors and (B) women with one or more clinical risk factors using BMD and QUS measurements

MIN RES 2001

Three-Year Prospective Study on Fracture Risk in Postmenopausal Women by Quantitative Ultrasound at the Phalanges

Data Correlation of Fractured and Unfractured Subjects

Parameters	Unfractured (N = 2103)	Hip fractures (n = 23)	Clinical vertebral fractures (n = 51)	No fracture vs hip fracture	No fracture vs vertebral fracture	Hip fracture vs vertebral fracture
Age (yr)	60.3 ± 9.7	74.9 ± 9.0	70.4 ± 9.3	<0.0001	<0.0001	0.03
Age at menopause (yr)	49.4 ± 4.3	48.0 ± 5.0	46.1 ± 5.5	0.23	<0.0001	0.17
BMI (kg/m^2)	26.5 ± 4.6	27.5 ± 4.4	26.8 ± 4.9	0.30	0.65	0.56
Anti-osteoporosis drug (%)	129 (6.1)	9 (39.1)	40 (78.4)	<0.0001	<0.0001	0.002
vitD supplementation (%)	168 (8.0)	9 (39.1)	8 (15.7)	<0.0001	0.08	0.038
AD-SoS T-score	−1.76 ± 1.59	−4.15 ± 1.59	−4.33 ± 1.71	<0.0001	<0.0001	0.67
UBPI T-score	−1.69 ± 1.75	−4.19 ± 1.11	−4.13 ± 1.04	<0.0001	<0.0001	0.82

Clin Dens 2013

Can the WHO Criteria for Diagnosing Osteoporosis be Applied to Calcaneal Quantitative Ultrasound?

In conclusion, the WHO threshold of $T = -2.5$ for diagnosing osteoporosis requires modification when using QUS to assess skeletal status. For the three QUS devices used in this study, a *T*-score threshold of –1.80 would result in the same percentage of postmenopausal women classified as osteoporotic as the WHO threshold for BMD measurements

Osteop Int 2000

Is calcaneal quantitative ultrasound useful as a prescreen stratification tool for osteoporosis?

Table 6 The combined strategy (CS)–Achilles Devices

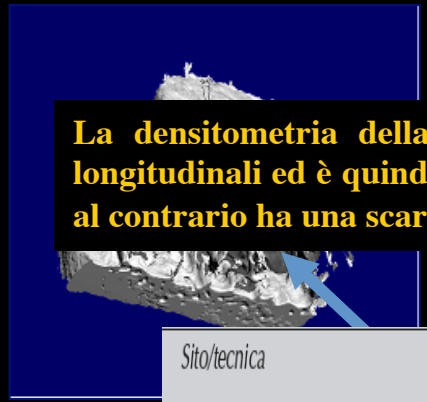
Study	Sample size	Prevalence of osteoporosis *n* (%)	Device	Measured variable	Certainty level sensitivity/specificity	Lower cutoff	Upper cutoff	DXAs saved (%)	Misclassification rate (%)
Clowes [22]	500	49 (9.8)	Achilles Plus	BUA	96/96	94	108	55.8	4.0
Clowes[a] [22]	279	100 (35.8)	Achilles Plus	BUA	96/96	94	108	47.3	3.9
Clowes [22]	500	49 (9.8)	Achilles Plus	SOS	96/95	1486	1529	47.4	4.8
Clowes[a] [22]	279	100 (35.8)	Achilles Plus	SOS	96/95	1486	1529	43.4	4.7
Edelmann-Schäfer [24]	43	8 (18.6)	Achilles plus	SI	100/91	−2.5	−3.68	72.1	7.0
Bachman [21]	314	69 (22.0)	Achilles	SI	89/92	−2.5	−1.0	48.7	4.8
Harrison [27]	207	70 (33.8)	Achilles Insight	T-score	90/90	−2.9	−1.6	51.2	10.1

Study	Sample size	Prevalence of osteoporosis *n* (%)	Device	Measured variable	Certainty level sensitivity/specificity	Lower cutoff	Upper cutoff	DXAs saved (%)	Misclassification rate (%)
Harrison [27]	207	70 (33.8)	CUBA Clinical	T-score	90/90	−2.27	−1.02	43.0	10.1
Naganathan [47]	326	46 (14.1)	CUBA MarkII	VOS T-score	88/96	−2.5	−1.0	52.8	11.0
Clowes [22]	500	49 (9.8)	DTU-ONE	BUA	96/95	35.1	51.2	43.6	4.8
Clowes[a] [22]	279	100 (35.8)	DTU-ONE	BUA	96/95	35.1	51.2	32.0	4.7
Clowes [22]	500	49 (9.8)	DTU-ONE	SOS	96/95	1528	1552	31.2	4.8
Clowes[a] [22]	279	100 (35.8)	DTU-ONE	SOS	96/95	1528	1552	29.0	4.7
Clowes [116]	500	49 (9.8)	UBIS 5000	BUA	96/95	55.7	63.3	57.4	4.8
Clowes[a] [116]	279	100 (35.8)	UBIS 5000	BUA	96/95	55.7	63.3	46.2	4.7
Clowes [116]	500	49 (9.8)	UBIS 5000	SOS	96/95	1453	1502	46.0	4.8
Clowes[a] [116]	279	100 (35.8)	UBIS 5000	SOS	96/95	1453	1502	41.2	4.7
Clowes [116]	500	49 (9.8)	QUS 2	BUA	96/95	54.7	77.8	57.0	4.8
Clowes[a] [116]	279	100 (35.8)	QUS 2	BUA	96/95	54.7	77.8	51.3	3.9

However, there is no consensus for type of devices, measured variables, or cutoffs. Overall, there is no sufficient evidence to recommend a specific cutoff for calcaneal QUS that provides a certainty level high enough to rule in or out osteoporosis.

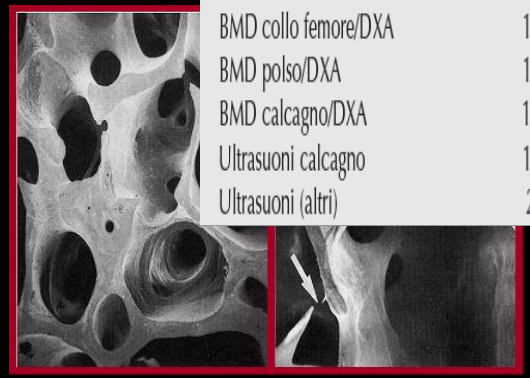
Osteop Int 2015

MONITORAGGIO



La densitometria della colonna lombare è più sensibile alle modificazioni longitudinali ed è quindi preferita nel monitoraggio della massa ossea. La QUS al contrario ha una scarsa accuratezza.

Sito/tecnica	Rischio frattura vertebrale	Rischio frattura non vertebrale	Monitoraggio terapeutico	Raccomandazione impiego diagnostico
BMD colonna/DXA	1a	1a	1b	A
BMD collo femore/DXA	1a	1a	1b	A
BMD polso/DXA	1a	1a	1b	A
BMD calcagno/DXA	1b	1a	2	A/B
Ultrasuoni calcagno	1a	1b	2	A/B
Ultrasuoni (altri)	2	1b	3	B



nuto

25-30%

Quantitative Ultrasound (QUS)

VANTAGGI

- Metodo non invasivo
- Velocità di esecuzione
- Costo contenuto
- Trasportabile
- Qualità dell'osso
- Facile Utilizzo

SVANTAGGI

- Diversità di apparecchiature
- Carenza dati di normalità
- Difficoltà di standardizzazione
- Precisione long-term
- Accuratezza
- Solo misure qualitative

TAKE HOME MESSAGES

- **I parametri ultrasonografici sono in grado di predire il rischio di fratture osteoporotiche (femorali, vertebrali, non vertebrali) in maniera non inferiore alla DEXA lombare o femorale sia nelle donne che negli uomini.**

- **L'uso combinato dei parametri ultrasonografici e dei fattori di rischio migliora la predizione del rischio di frattura.**

- **La QUS non può essere utilizzata per la diagnosi di osteoporosi secondo i criteri OMS attualmente in uso (T-score <-2.5).**

- **I limiti della QUS si correlano alla non omogeneità dei dati tra i vari devices in uso e alla scarsa accuratezza in corso di follow-up osservazionale rispetto all'esame DEXA**

THANKS!!!