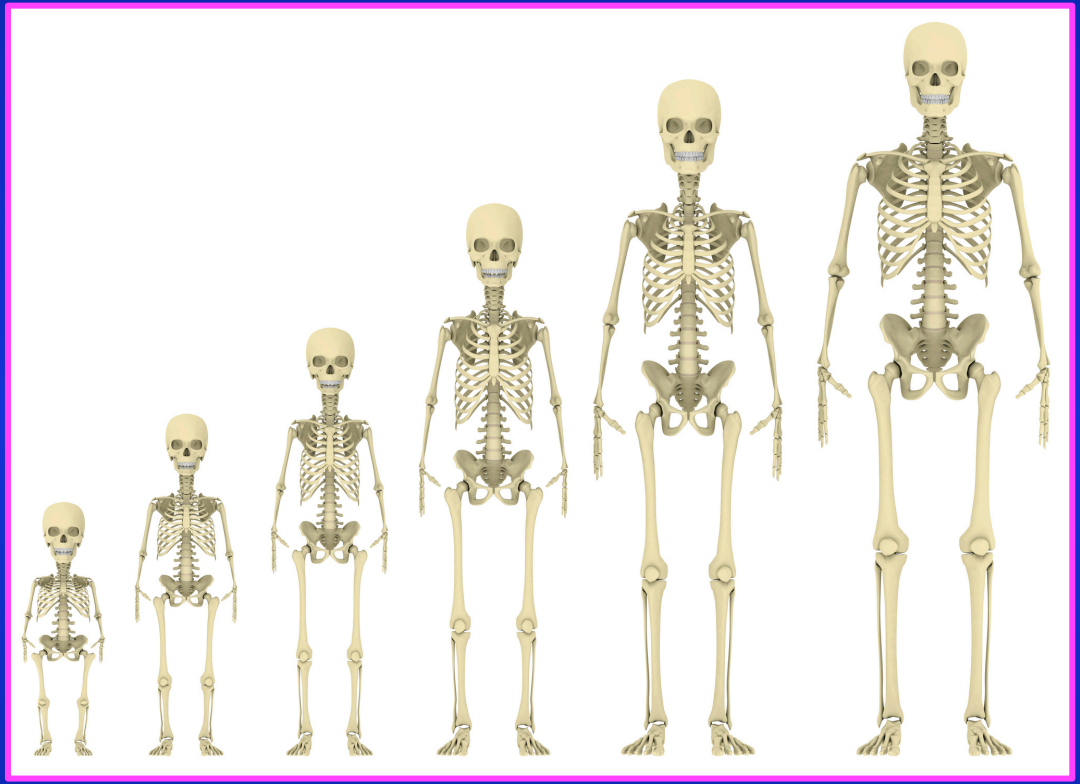
Evaluation of Bone Mineral Density in Children



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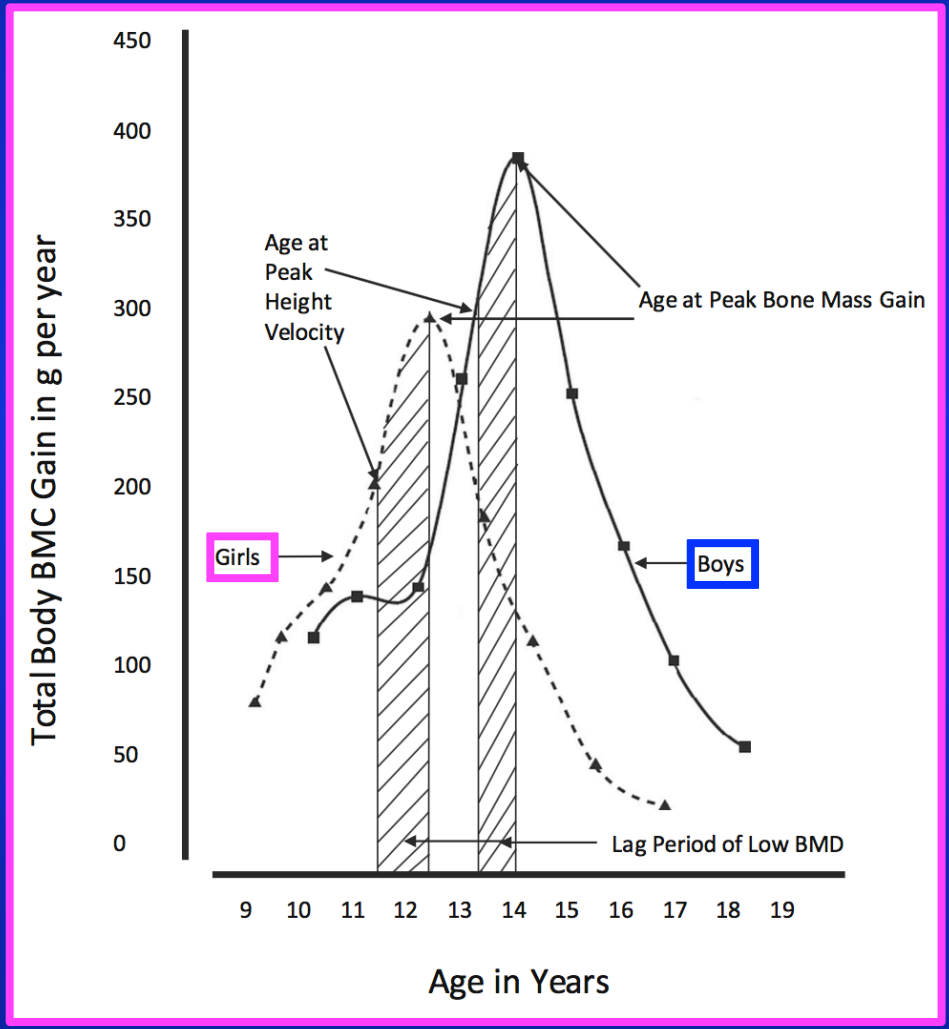
Disclosure: None

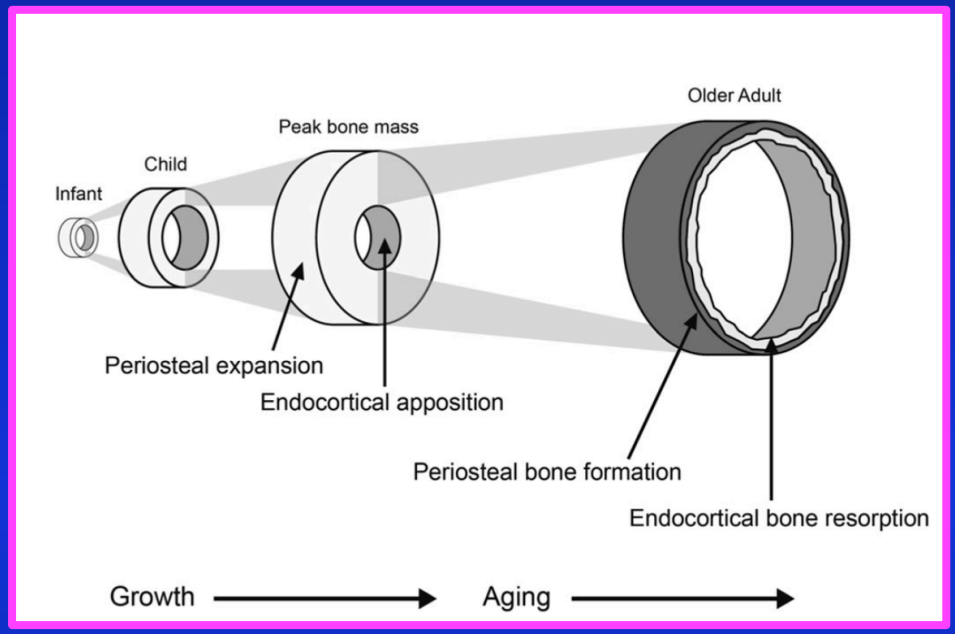
- I have no relevant financial relationship with manufactures of any commercial products and/or providers of commercial services discussed in this CME activity
- I do not intend to discuss an unapproved/ investigative use of a commercial product/device in my presentation

Background

95% bone mass accrued by end of adolescence



Structure and composition change

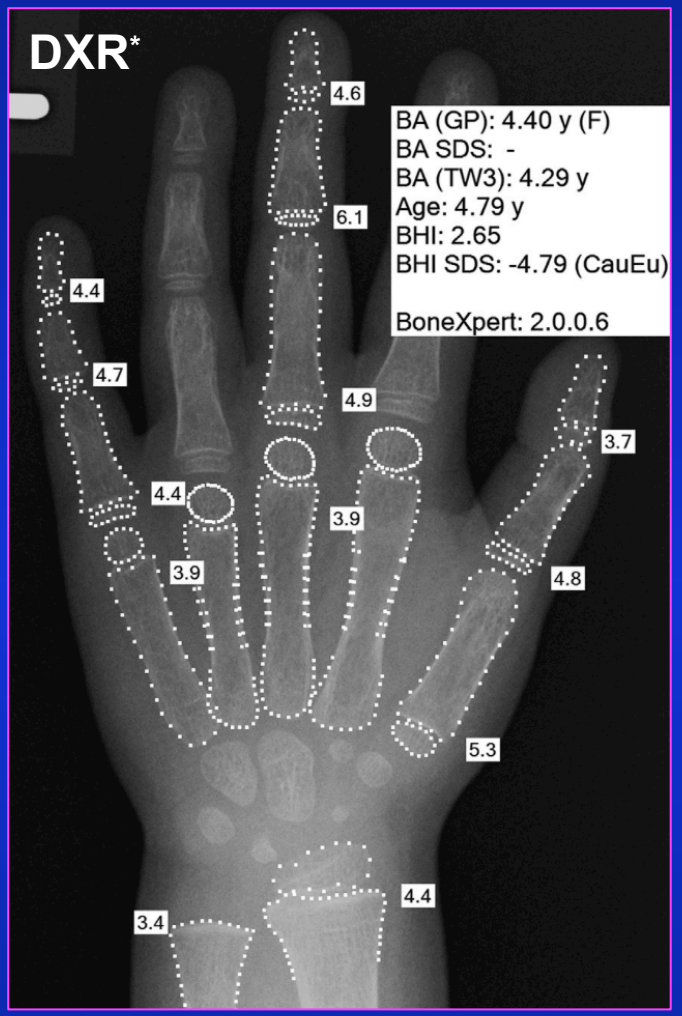


- Chronic childhood diseases result in poor bone accrual or bone loss
- Identify children at risk of fractures
- Treatment and monitoring

Weaver et al (2016) Osteoporos Int 27:1281
Baxter-Jones et al (2011) J Bone Miner Res 26:1729

Demineralization Radiography

- **Qualitative: Visual and Morphology**
  - Cortical thinning
  - Altered trabecular pattern and geometry
  - Radiolucency of the bone
- **Genant's Semi-quantitative Assessment**
  - Decrease height of vertebral bodies
  - Vertebral endplate changes
- **Digital X-Ray Radiogrammetry (DXR)**
  - Metacarpal cortical thickness
- **Vertebral fracture assessment (VFA)**
  - Lateral spine image obtain during DXA



Neelis (2017) Clin Nutr. In press
Renz (2014.) J Bone Miner Metab 34:55
Nusman (2015) Eur J Radiol 84:1999
Adiotomre (2017) Eur Radiol 27:2188

25 OHD = 7 ng/mL
Thacher Score = 0
Demineralization = ?

Demineralization Intra-and Inter-Observer Agreement

Variability	% Agreement	Kappa	Interpretation
Inter-observer	12	0.25 (95% CI: 0.13-0.38)	Fair
Intra-observer (Pooled 3 readers)	66	0.29 (95% CI: 0.11-0.47)	Fair

- 360 healthy infants and toddlers (8-24 mo)
- 44 (12%) had Vit D deficiency (25 OHD<20 ng/mL)
- Demineralization reported frequently: 'questionable' or mild
- Considerable inter- and intra-observer variability
- When demineralization present, Vit D levels lower (p=.02)

Perez-Rossello (2012) Radiology 262:234

ACR Appropriateness Criteria Osteoporosis and Bone Mineral Density

Variant 1. Asymptomatic BMD screening or individuals with established or clinically suspected low BMD.

Radiologic Procedure	Rating	Comments	RRL
DXA lumbar spine and ~~hip(s)~~ **Total Body Less Head**	9		☢
QCT lumbar spine and ~~hip~~ **Forearm, Femur, Tibia**	6		☢☢☢
DXA distal forearm	5		☢
TBS lumbar spine	4		☢
QUS calcaneus	2		○
SXA distal forearm	2		☢
pQCT distal forearm	2		☢
X-ray axial skeleton	1		Varies
X-ray appendicular skeleton	1		☢☢

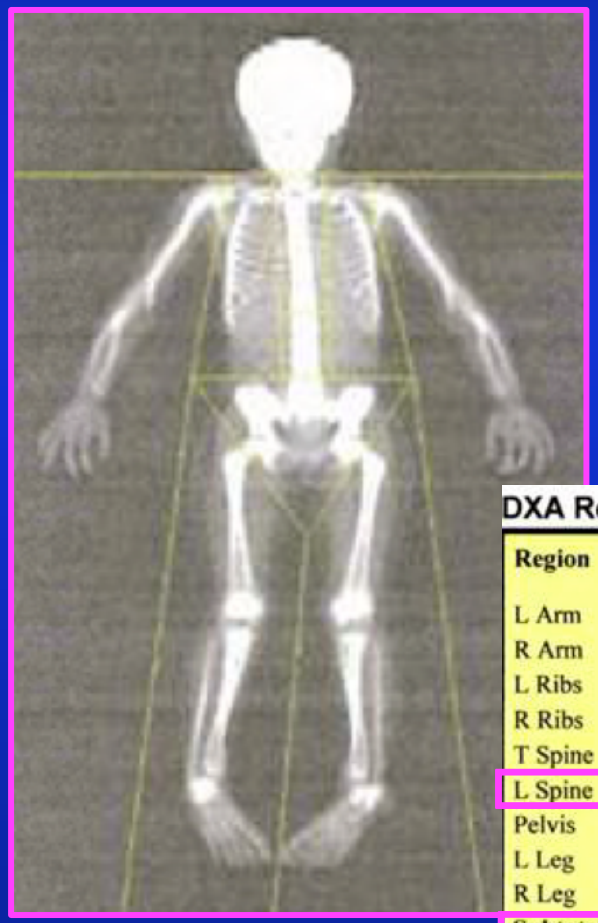
Note: Rating Scale 1,2,3 = usually not appropriate; 4,5,6 = may be appropriate; 7,8,9 = usually appropriate. DXA = dual-energy x-ray absorptiometry; pQCT = peripheral QCT; QCT = quantitative CT; QUS = peripheral ultrasound; RRL = relative radiation level; SXA = single x-ray absorptiometry; TBS = trabecular bone score.

J Am Coll Radiol 2017;14:S189

Difference between DXA and QCT

DXA: 2-Dimentional

$_{areal}BMD = g/cm^2$

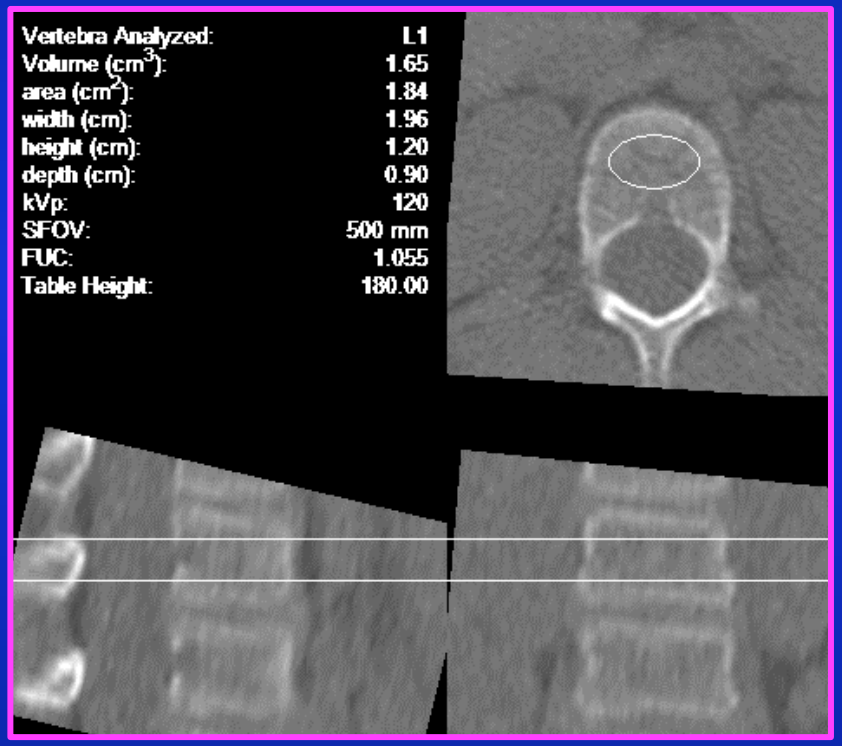


DXA Results Summary:

Region	Area (cm^2)	BMC (g)	BMD (g/cm^2)
L Arm	110.53	45.84	0.415
R Arm	116.00	48.11	0.415
L Ribs	56.24	27.28	0.485
R Ribs	53.51	25.54	0.477
T Spine	65.61	51.73	0.788
L Spine	31.25	27.72	0.887
Pelvis	123.42	112.74	0.914
L Leg	209.34	120.03	0.573
R Leg	212.47	125.19	0.589
Subtotal	**978.36**	**584.18**	**0.597**
Head	180.83	219.49	1.214
Total	1159.19	803.67	0.693

QCT: 3-Dimentional

$_{Volumetric}BMD = g/cm^3$



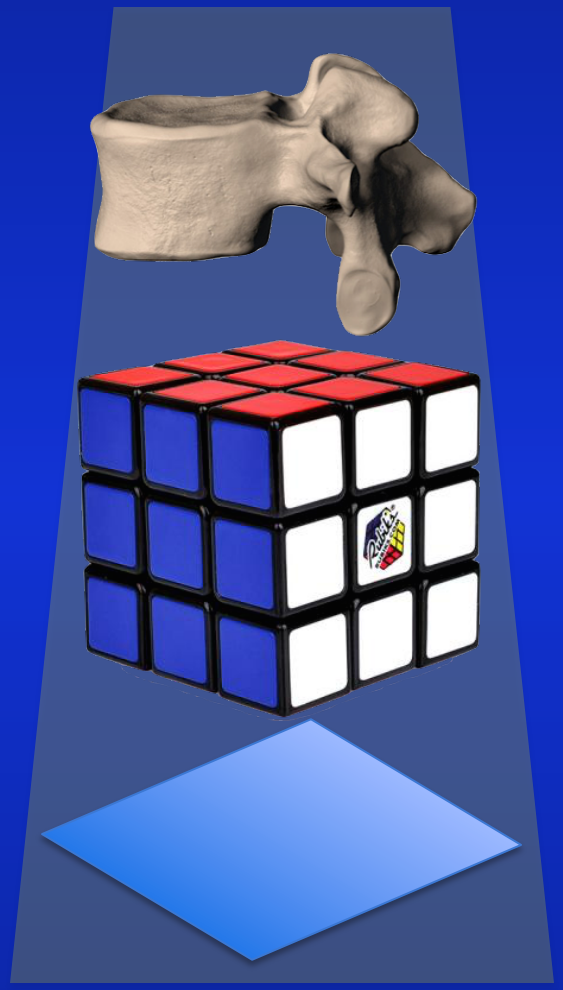
16	Mineral weight (g)	54

QCT

8	Volume (cm3)	27
2	vBMD (g/cm3)	2

DXA

4	Projected Area (cm2)	9
4	aBMD (g/cm2)	6



Bone density measurement affected by...

Gender, ethnicity, body composition, pubertal status, skeletal maturity, disease

Pediatric Guidelines

2013 Pediatric Position Development Conference

J Clin Densitom 2014;17:225

Dual-Energy X-Ray Absorptiometry Interpretation and Reporting in Children and Adolescents: The Revised 2013 ISCD Pediatric Official Positions

Nicola J. Crabtree,[*,1,a] *Asma Arabi,*[2,b] *Laura K. Bachrach,*[3,b] *Mary Fewtrell,*[4,b] *Ghada El-Hajj Fuleihan,*[2,b] *Heidi H. Kecskemethy,*[5,b] *Maciej Jaworski,*[6,b] *and Catherine M. Gordon*[7,c]

2013 Pediatric Position Development Conference

J Clin Densitom 2014;17:258

Quantitative Computer Tomography in Children and Adolescents: The 2013 ISCD Pediatric Official Positions

Judith E. Adams,[*,1,a] *Klaus Engelke,*[2,b] *Babette S. Zemel,*[3,b] *and Kate A. Ward*[4,b]

Pediatrics 2016;138(4):e20

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

Bone Densitometry in Children and Adolescents

Laura K. Bachrach, MD, Catherine M. Gordon, MD, MS, SECTION ON ENDOCRINOLOGY

Revised 2018 (Resolution 8)*

ACR–SPR–SSR PRACTICE PARAMETER FOR THE PERFORMANCE OF DUAL-ENERGY X-RAY ABSORPTIOMETRY (DXA)

https://www.acr.org/-/media/ACR/Files/Practice-Parameters/dxa.pdf?la=en

- Lumbar spine and total body less head (TBLH); lateral distal femur in selected cases
- Z-score BMD: compare to normal pediatric database age, sex and race. (Never use T-scores!)
- Z-scores < 2.0 : “low bone mineral density for age”
- Bone mineral content (BMC)
- Adjustment for body size, height, pubertal status

Zemel, Kalkwarf, Gilsanz. J Clin Endocrinol Metab 2011;96:3160
Binkovitz & Henwood. Pediatr Radiol 2007;37:21
Wildman & Henwood. J Am Osteopath Coll Radiol 2012;1:17

SPR
S. Kaste, MD, MS
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J. Perez-Rossello, MD

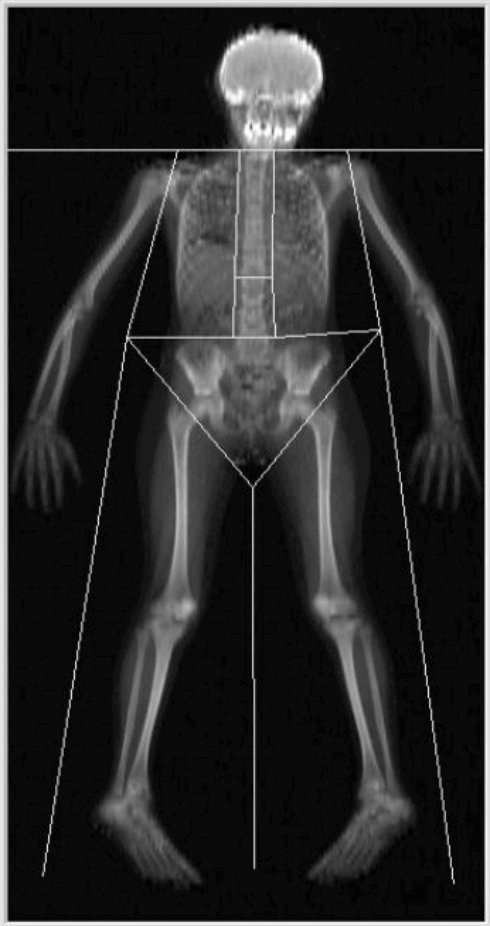
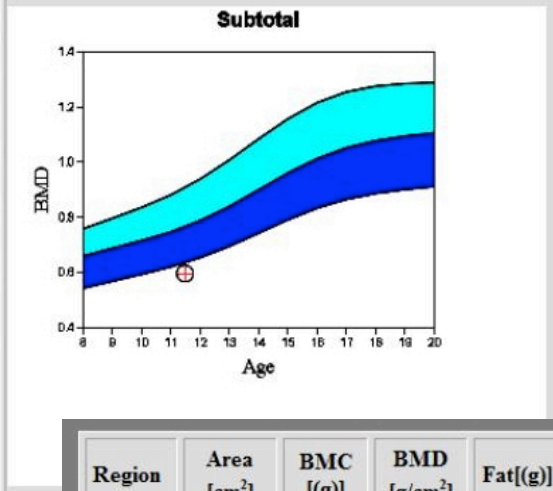


Image not for diagnostic use
318 x 122
k = 1.188, d0 = 48.8
DAP: 17.7 cGy*cm²



CDC
Monitoring the Nation's Health

NHANES III

Vital and Health Statistics
Series 11, Number 253
August 2013

Total Body Bone Area, Bone Mineral Content, and Bone Mineral Density for Individuals Aged 8 Years and Over: United States, 1999–2006

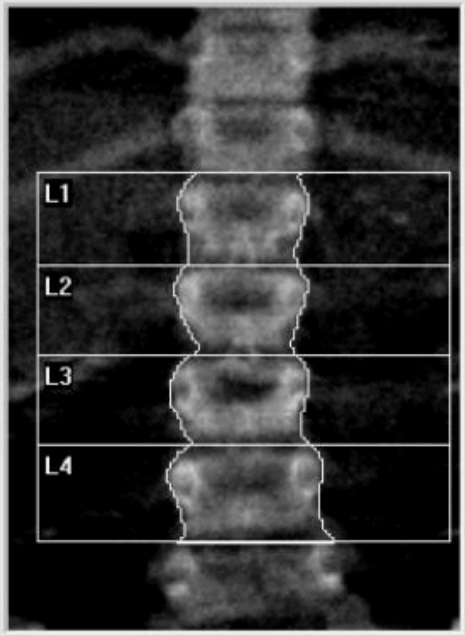
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Center for Health Statistics

Region	Area [cm²]	BMC [(g)]	BMD [g/cm²]	Fat[(g)]	Lean [(g)]	Lean + BMC[(g)]	Total [(g)]	% Fat [(%)]	T-score	PR (Peak Reference)	Z-score	AM (Age ched)
L Arm	104.66	51.36	0.491	599.3	976.9	1028.2	1627.5	36.8				
R Arm	118.67	59.60	0.502	627.0	1143.5	1203.1	1830.1	34.3				
L Ribs	93.38	44.23	0.474									
R Ribs	82.48	39.66	0.481									
T Spine	68.48	37.32	0.545									
L Spine	30.74	18.77	0.611									
Pelvis	131.89	90.24	0.684									
Trunk		230		4343.4	9816.4	10046.6	14390.0	30.2				
L Leg	233.05	152.65	0.655	2744.7	2957.6	3110.3	5855.0	46.9				
R Leg	244.72	165.51	0.676	2816.5	3098.6	3264.1	6080.7	46.3				
Subtotal	**1108.06**	**659.33**	**0.595**	**11130.9**	**17993.0**	**18652.3**	**29783.2**	**37.4**			**-2.6**	**78**
Head	228.77	330.09	1.443	902.0	2734.7	3064.8	3966.8	22.7				
Total	1336.83	989.41	0.740	12032.9	20727.7	21717.2	33750.1	35.7			-2.1	85

Total BMD CV 1.0%, ACF = 1.026, BCF = 1.004
TBAR1904 - NHANES BCA calibration

Total Body Less Head (TBLH)

https://www.cdc.gov/nchs/data/series/sr_11/sr11_253.pdf



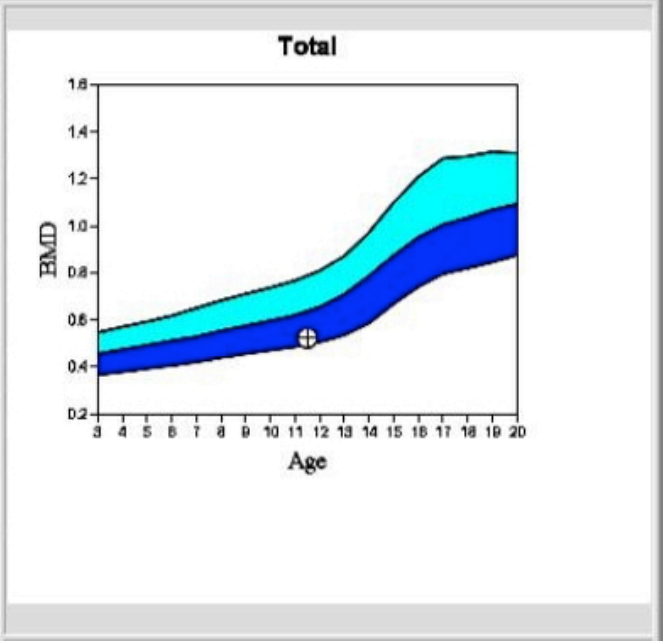
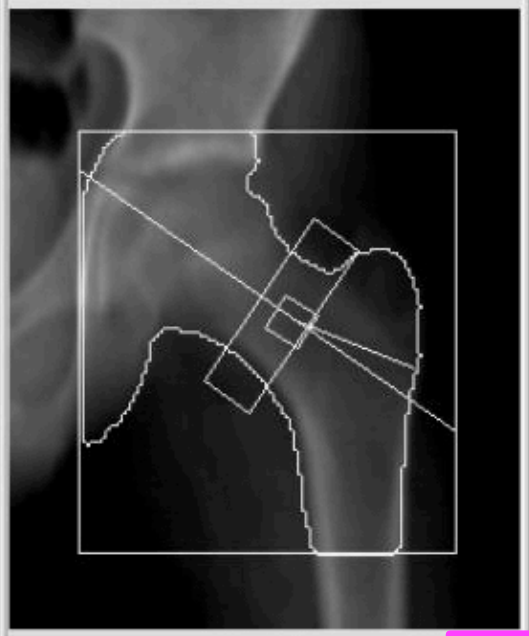


Image not for diagnostic use	
116 x 104	T-score vs. White Male; Z-score vs. White Male. Source:BMDCS/Hologic White Male.
k = 1.151, d0 = 45.6	
DAP: 1.4 cGy*cm^2	

Results Summary:

Region	Area[cm^2]	BMC[(g)]	BMD[g/cm^2]	T-score	PR (Peak Reference)	Z-score	M (Age Matched)
L1	8.64	3.80	0.440				
L2	8.25	4.34	0.526				
L3	9.00	5.19	0.577				
L4	11.48	6.19	0.539				
Total	**37.37**	**19.52**	**0.522**			**-1.6**	**82**

Total BMD CV 1.0%, ACF = 1.026, BCF = 1.004, TH = 5.382



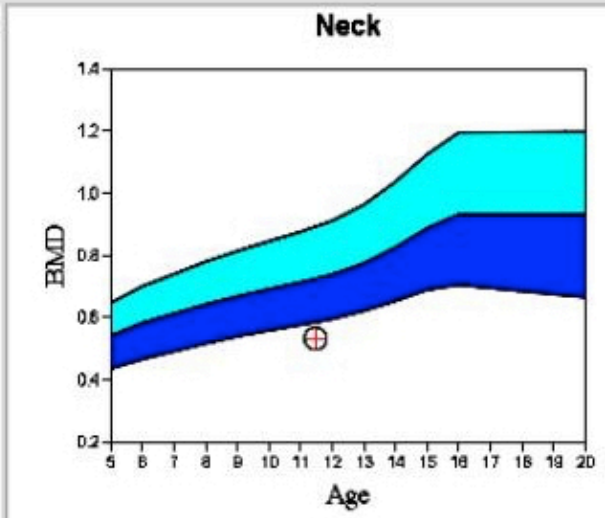


Image not for diagnostic use

94 x 105

NECK: 49 x 15

k = 1.158, d0 = 50.3

DAP: 1.2 cGy*cm^2

Not recommended

Children trabecular pattern and landmarks not fully developed and measurements are difficult to replicated

Results Summary:

Region	Area[cm^2]	BMC[(g)]					
Neck	4.41	2.34	0.531			-2.8	73
Total	24.27	15.40	0.634			-1.9	82

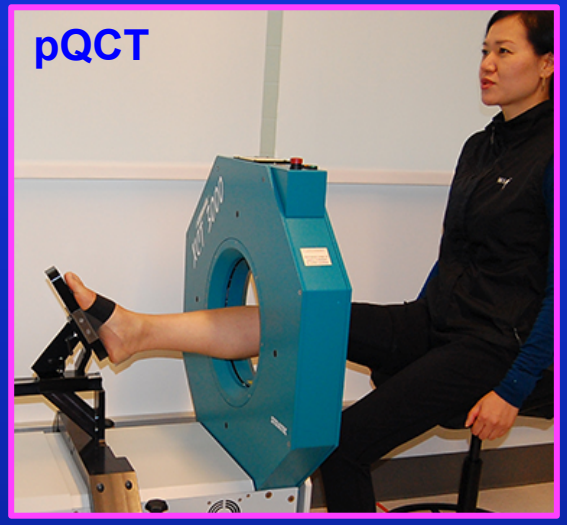
Total BMD CV 1.0%, ACF = 1.026, BCF = 1.004, TH = 4.305

Revised 2018 (Resolution 9)*

ACR–SPR–SSR PRACTICE PARAMETER FOR THE PERFORMANCE OF MUSCULOSKELETAL QUANTITATIVE COMPUTED TOMOGRAPHY (QCT)

https://www.acr.org/-/media/ACR/Files/Practice-Parameters/QCT.pdf

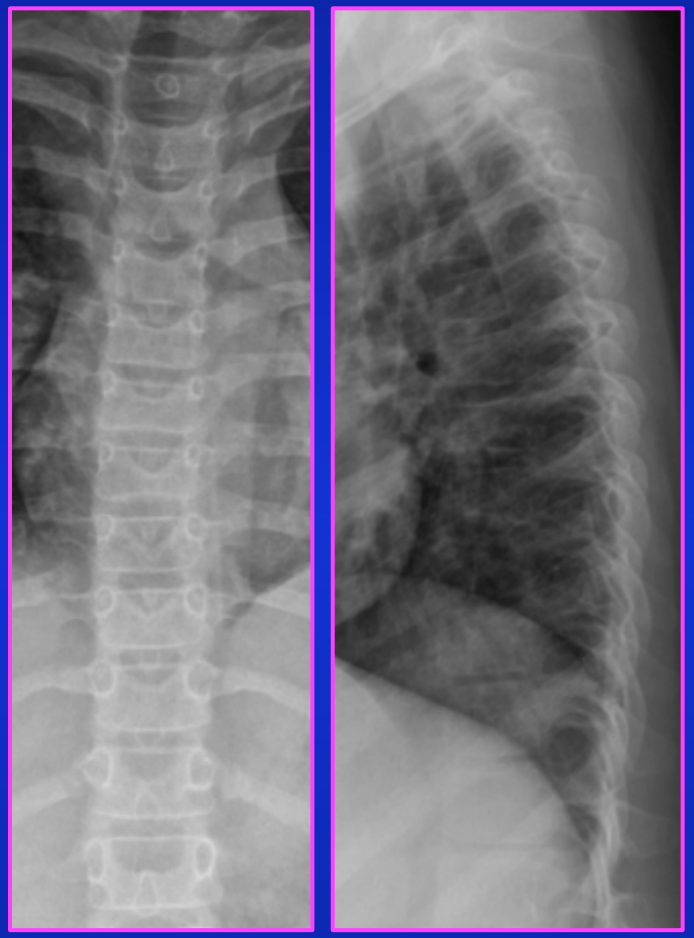
- Z-scores < 2.0 = "low bone mineral density"
- "Because QCT can assess both volume and density of bone in the axial and appendicular skeleton, it may be more useful than DXA in children"



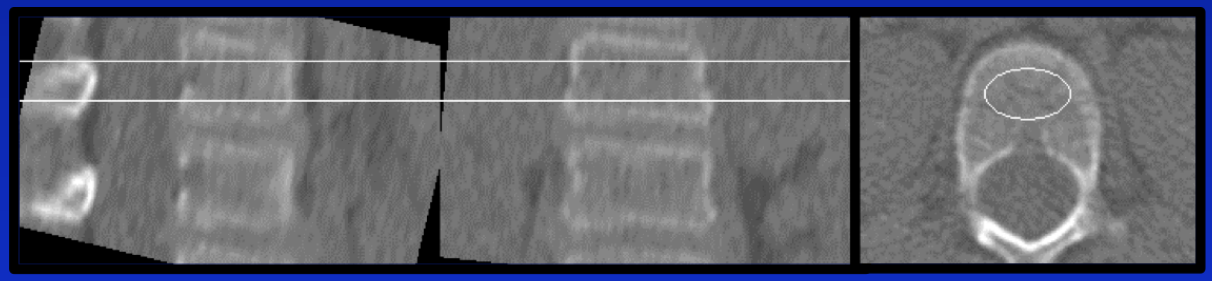
Gilsanz et al. Radiology 2009;250:222
Engelke. J Clin Densit 2017;20:309

SPR
S. Kaste, MD, MS
J. Perez-Rossello, MD

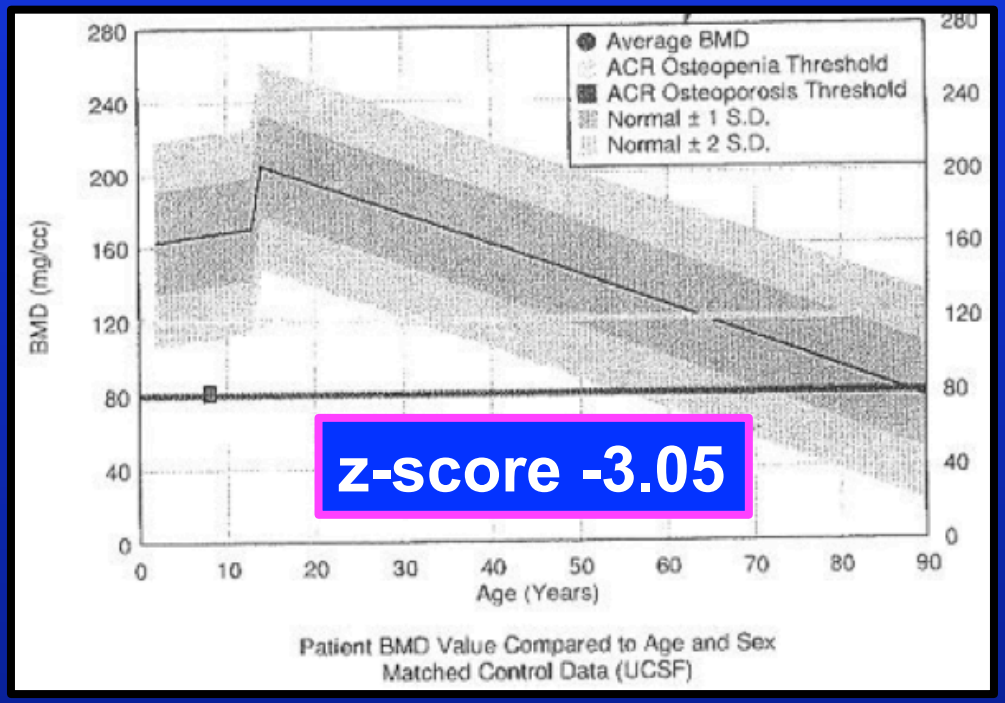
QCT – Vertebral Trabecular Compartment



8 yo M slipped in ice
multiple compression fractures
"subjectively osteopenic"

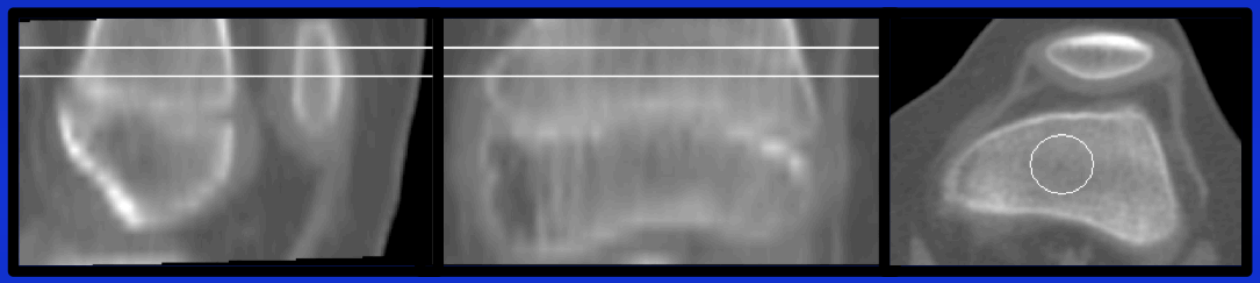


QCT at L1 an L2
Average Trabecular BMD: 81.2 mg/cm3
Age/sex matched normal UCSF: 166.7+/-28

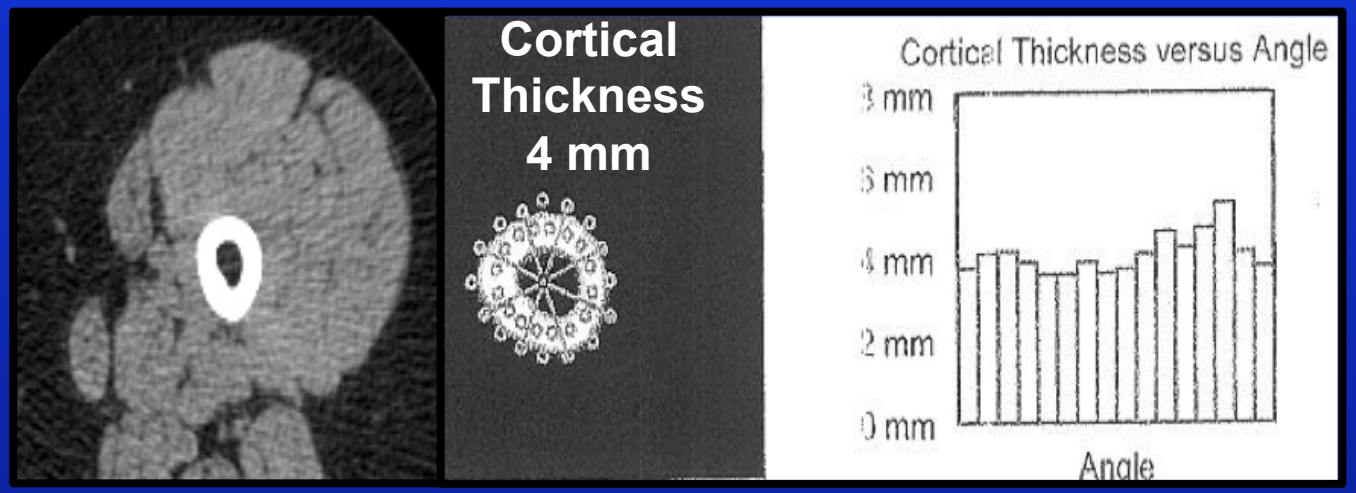


QCT - Trabecular and Cortical Compartments

- Relative lack of normative data for appendicular sites
  - Gilsanz: Femur cortical bone density
  - Leonard: Tibia cortical and trabecular bone density
- Measurements as baseline for longitudinal evaluation
- Mid and distal femur to identify early density changes



Distal Femur Metaphysis
Trabecular BMD
120 mg/cm3



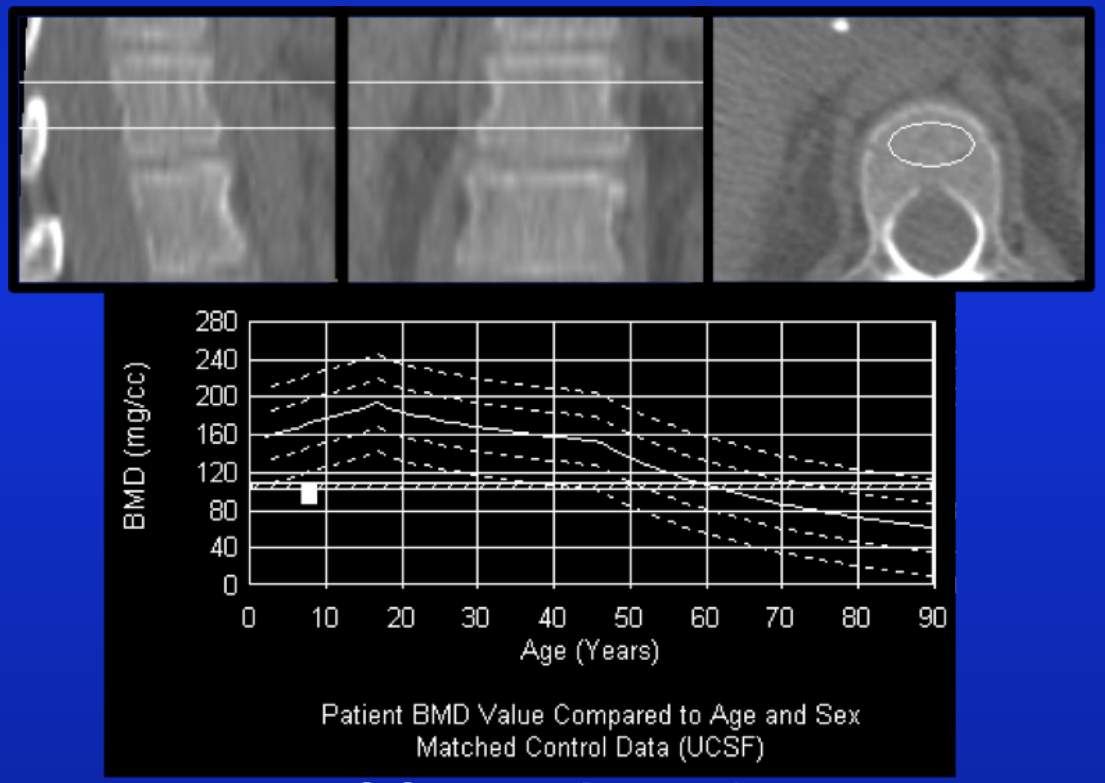
Mid Femur
Cortical BMD
978 mg/cm3

Gilsanz (2009) Radiology 250:222
Gilsanz (1998) J Clin Endocrinol Metab 83:1420

Children that would benefit from QCT

- Complex chronic diseases
- Disability and/or deformity
- Patients that may move
- Patients with hardware/tubes

8 yo Jeune Syndrome

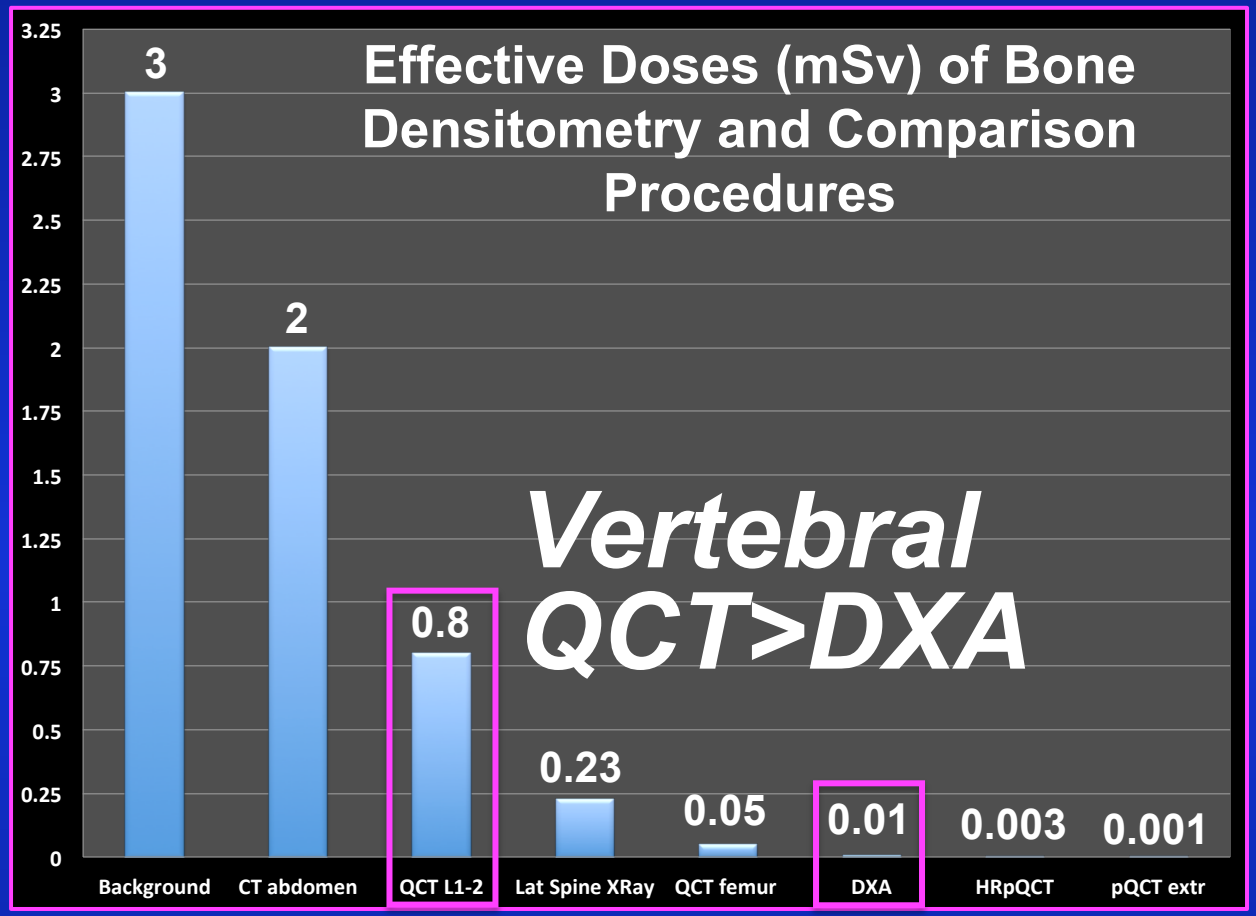


QCT at L1 an L2

Average Trabecular BMD: 96.5 mg/cm3

Age/sex matched UCSF: 172.3; z-score -2.91

Vertebral Bone Density

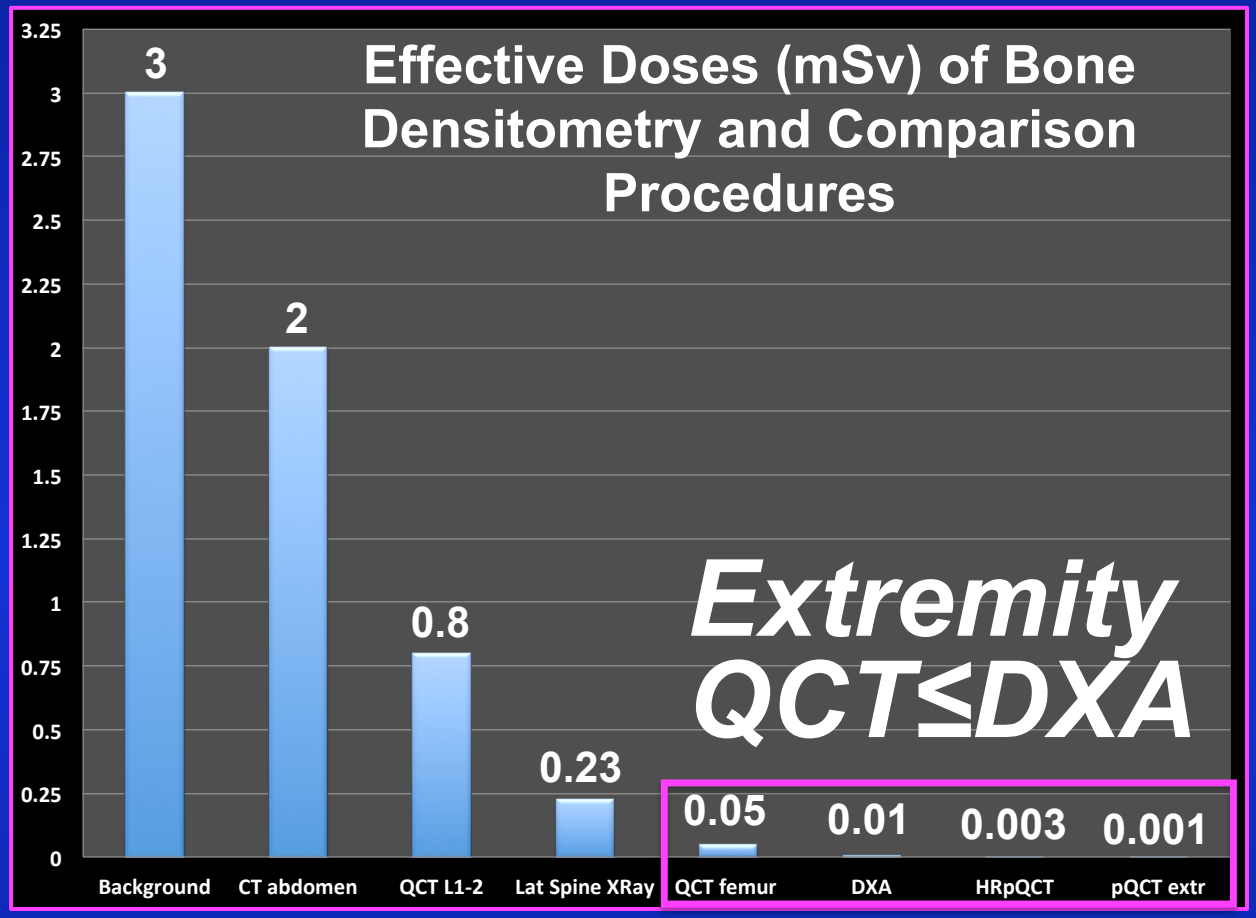


QCT dose higher than DXA but in diseased children dose is acceptable

Burrows (2010) Osteoporos Int 21:515
Engelke (2008) J Clin Densit 11:123

Adiotomre (2017) Eur Radiol 27:2188
Adams (2014) J Clin Densit 17:258
Huda (2007) AJR 188:540

Extremity Bone Density



pQCT dose acceptable for obtaining normative data in the extremities of healthy subjects

Dose (mSv) Dual-Energy QCT

Central QCT; Effective Dose Values (Calculated for a Helical 64-Detector Row Siemens Definition Flash Scanner Using the Pediatric Body Scan Mode Using 80 kV X-ray Tube Voltage and 100 mAs With a Slice Thickness of 0.6 mm and a Pitch of 1)

Age (yr)	Scan length (cm)	Sex	Effective dose (mSv)
15	10	M	0.59
		F	0.61
10	8	M	0.80
		F	0.84
5	6	M	1.02
		F	1.09

Dual energy scanning may account for changes in fat composition of the trabecular compartment and give more accurate measurements

Adams (2014) J Clin Densit 17:258

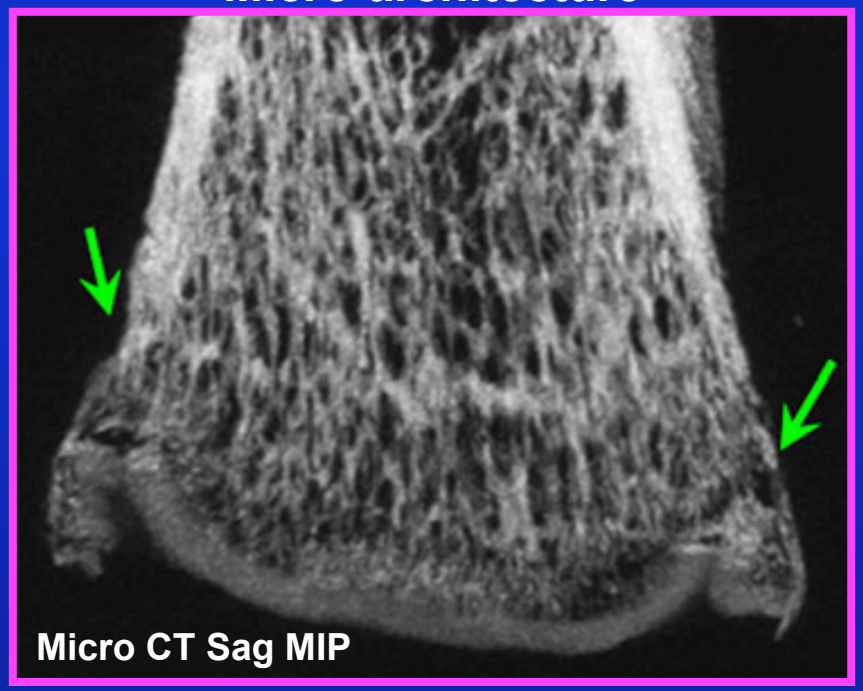
Pediatric Challenges

- Limitations of normative databases
  - Model specific, software analysis variability
  - Ethnic normative data
- Validation of ‘correction’ methods
  - Height, bone age, Tanner stage
  - Body composition
- Optimize protocols
  - Identify measurement sites
  - Phantom vs asynchronous techniques

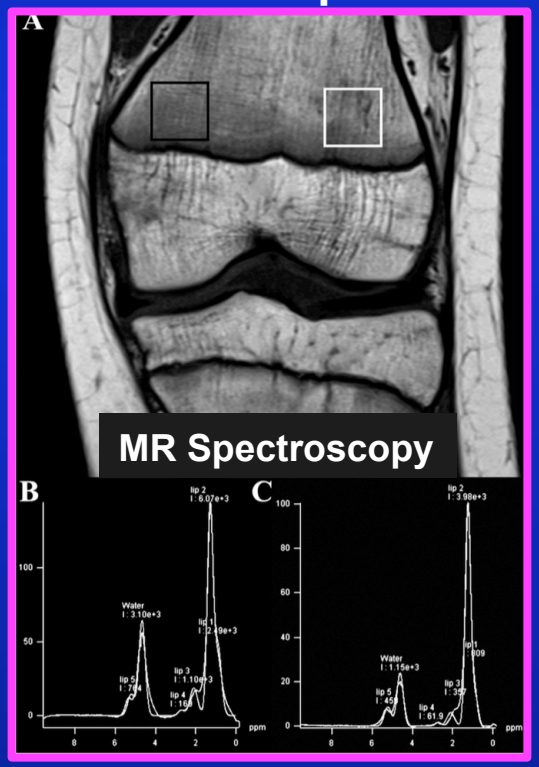
Future Research – Fracture Risk

- Microarchitecture
- Marrow and body composition
- Biomechanical properties of bone (FEA)

Micro-architecture



Marrow composition



Tsai (2014) Pediatr Radiol 44:124

Vajapeyam, Ecklund et al (2018) Bone 110:335

Take Home Points

- Wide variability in the assessment of demineralization with digital radiography
  - The radiologist may be the first to identify “decrease bone density” or asymptomatic fractures
- Optimal evaluation with quantitative techniques
  - DXA
  - QCT (high resolution, dual energy techniques)