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Optimal Clinical use of DXA in Children and Adolescents

Kate A Ward, PhD and Nicola J Crabtree, PhD

Key learning points

- Dual energy X-ray absorptiometry (DXA) is the recommended assessment modality for the assessment of fracture risk
- It is important to adjust a lumbar spine bone density scan result for short or tall stature by calculating bone mineral apparent density (BMAD)
- Vertebral fracture assessment can be used to screen for moderate and severe vertebral fractures
- A diagnosis of osteoporosis in children requires a history of fracture, a either pathological vertebral fracture or multiple long bone fractures with a history of reduced bone density for age and size. It cannot be defined by an abnormal bone density alone
- DXA is also a useful tool to assess skeletal development and body composition abnormalities, including the measurement of visceral and adipose fat

Why do we measure bone mineral density?

During childhood and puberty adolescents acquire approximately 50% of their bone mass. If this acquisition is incomplete or disturbed due to a chronic condition or disease the resulting deficit in bone mass accrual may persist into adulthood.

The rationale for using DXA in childhood is multi-factorial but can be broadly grouped into the following areas:[1]

- Assessing the impact of chronic disease and its treatment in children and adolescents
- Evaluating current and future risk of fragility fracture
- Monitoring the effect of modifiable factors on skeletal growth and development (e.g. physical activity, diet, pubertal dysfunction and growth delay)

DXA has been shown to predict fracture in healthy children[2], in fracture-prone children[3] and in those with chronic disease[4]. The 2013 ISCD guidelines were produced to aid the clinical use and interpretation of DXA measurements in children[5]. There are five individual position statements and simple user guide[6]; briefly for clinical assessment of bone mineral density the recommendations are to scan the lumbar spine and total body less head, at no more than 6-12 monthly intervals, adjusting for short/tall stature where required.

In 2019 the guidelines were updated to include scanning additional skeletal sites namely; the forearm, proximal femur, and the lateral distal femur. The new guidelines also recommended vertebral fracture assessment by DXA for the identification of moderate and severe vertebral fractures[7].

Clinically, the lumbar spine is the most robust and useful site for diagnostic use and for monitoring. The total body less-head measures are most appropriate when looking at bone mass acquisition and skeletal development, particularly in the clinical research setting.

It is extremely important to note that ISCD guidance gives a definition of osteoporosis in children based on low-trauma fracture with and without a BMD measurement, and in the context of the clinical history of the child. The DXA measurement is intended to assist the clinician and should not be used as a standalone diagnostic tool.

The aim of this paper is to provide clinical guidance for the use of current outputs offered using the Advanced Paediatric Report, available with Hologic Apex 4.6 or 5.6.

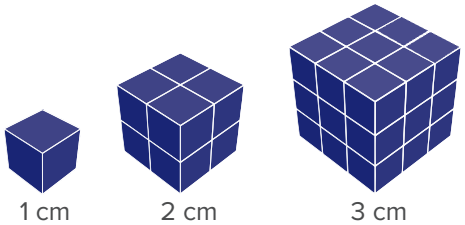
Clinical indications for bone mineral density assessment

There are many medical conditions in which DXA may be useful (see below)[8], other referrals come when a child has recurrent fractures in the absence of an obvious underlying predisposition.

- Primary bone disorders – e.g. osteogenesis imperfecta, idiopathic juvenile osteoporosis
- Neuromuscular diseases – e.g. immobilisation, cerebral palsy, muscular dystrophies, spinal cord injury
- Inflammatory conditions – e.g. inflammatory bowel disease, cystic fibrosis
- Juvenile rheumatic disorders – e.g. idiopathic arthritis, vasculitis, dermatomyositis, systemic lupus erythematosus
- Nutritional and/or Endocrine disorders – e.g. coeliac disease, anorexia nervosa, Cushing Syndrome, hyperparathyroidism
- Others – e.g. Haematological conditions (acute lymphoblastic leukaemia, thalassaemia and sickle cell anaemia), inherited metabolic diseases (galactosaemia, glycogen storage disease), solid organ transplantation, Ehlers-Danlos syndrome
- Monitoring effect of bone-targeted treatment – e.g. bisphosphonates
- Monitoring the effects of medium and long term glucocorticoid therapy

What are the technical considerations for using DXA in children?

Low BMD as measured by DXA is not necessarily synonymous with fracture risk due to the technical limitations of the measurement technique. This is because it provides a two-dimensional or areal bone mineral density (aBMD) measured in g/cm^2 rather than a true volumetric bone mineral density measured in g/cm^3 [9,10]. The result of this is that DXA BMD measurements are size-dependent and are affected by growth. Consequently, BMD may be underestimated in children who are short for their age and overestimated in children who are tall for their age **(See Figure 1)**.



	1 cm	2 cm	3 cm
BMC (g)	1	8	27
Area (cm^2)	1	4	9
A-BMD (g/cm^2)	1	2	3
Volumetric BMD (g/cm^3)	1	1	1

Figure 1. The difference between volumetric and areal bone mineral density in differently sized bones, is assessed by dual-energy x-ray absorptiometry.

Failure to account for delayed growth and/or skeletal maturation is a common cause of misinterpretation of paediatric DXA results[11,12]. As a consequence, ISCD recommend that results should be size adjusted in children. There are several ways to adjust for size:

1. **Volume:** Estimating a volumetric BMD from the two-dimensional BMD
2. **Body size:** Relating aBMD or bone mineral content to bone and body size
3. **Function:** Relating aBMD or BMC to muscle mass

Our recommended size-adjustment techniques are provided below in italics for the purpose indicated in bold type.

Fracture risk assessment

Lumbar spine bone mineral apparent density (BMAD)

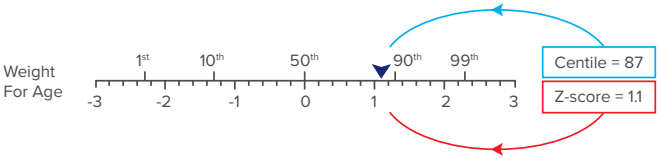
The most frequently used method of size adjustment in paediatric DXA is the calculation of bone mineral apparent density (BMAD) which is an estimated volumetric bone density[9]. At the lumbar spine, BMAD is calculated by Apex software using the projected bone area to calculate the volume of the bone, and from this BMAD calculated (g/cm^3). The relative size independence of this parameter makes BMAD a useful surrogate marker for bone strength and has also been shown to be related to fracture risk in children[13,14] **(See Figure 2)**.

Region	Area (cm^2)	BMC (g)	BMAD (g/cm^3)	BMAD Z-score	AM (%ile)	BMD (g/cm^2)	BMD Z-score	AM (%ile)
L1-L4	**41.9**	**41.9**	**0.305**	**-0.5**	**30**	**1.000**	**-1.4**	**10**

Figure 2. Clinical example of BMAD.

Understanding the Z-Scale

As both Z- score and percentiles are clinically used, they are displayed on a single graph



In the case above, the results demonstrate that a Z-score of +1.1 equates to a value on the 87th centile. The underlying practical implication is a mathematical relationship between Z-scores and percentiles; some clinicians find percentiles easier to use and understand while Z-scores may be more helpful for diagnostic use or for evaluating extreme results beyond the 1st and 99th percentiles.

Bone acquisition and development

Total body less head

Whilst recommended by ISCD, total body less-head measures have limited clinical applicability for fracture risk assessment in children with chronic disease. Total body measurements are more a reflection of skeletal growth and mineralisation than of fracture risk prediction. A geometric approach, such as BMAD (as above) cannot be used to reduce the size dependence of total body (or total body less head) of DXA aBMD and BMC measurements. Therefore, a different approach is required. To evaluate these measurements, we recommend assessing total body less head BMC in relation to the child's size or their bone area. This means that the measurements, once taking size into account, help to give a more global picture of skeletal development.

There are several approaches available within the Hologic Apex software. These are:

The functional approach:

A recommended functional approach is based on the close relationship between bone strength and muscle strength[15]. In DXA terms, this means using total body less head BMC together with lean mass. The two stages of assessment are: (i) whether the child has sufficient muscle for their height, and (ii) whether they have sufficient bone for that muscle. This leads to four outcomes:

(i) Appropriate muscle mass for their height and appropriate bone mass for their muscle mass;

(ii) Primary bone defect, where the child has sufficient muscle for their height but insufficient bone mass for their muscle;

(iii) Primary muscle defect where the child has reduced muscle for their height but sufficient bone for their muscle mass;

(iv) A mixed muscle and bone defect where muscle and bone are both reduced.

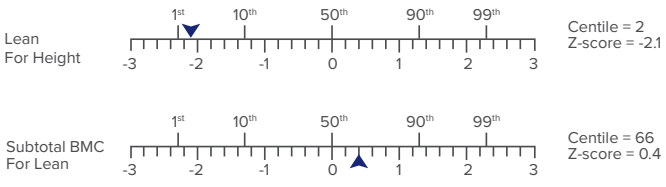


Figure 3. These show low **Lean Mass for Height** and normal **Sub Total BMC for Lean Mass**, i.e primary muscle deficit.

The other available techniques within the software are:

Height-for-age Z-score (HAZ) adjusted BMD:

The HAZ method is also a two-stage approach, first calculating the child's height relative to their age using Centre for Disease Control and Prevention (CDC) growth charts. The second stage is to mathematically adjusting the total body-less head aBMD with this value[16].

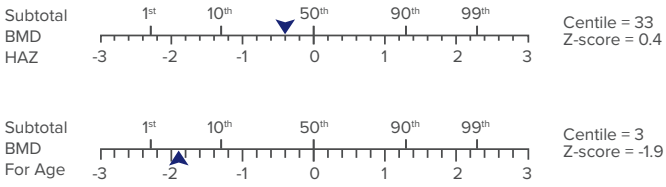


Figure 4. Example of HAZ output.
This example shows normal Subtotal BMD when adjusted for height Z-score. (Subtotal BMD vs Age for this sunject, who is short of stature, was low (Z-score of -1.9; Centile = 3rd)

The "Mølgaard" model

This is a three stage approach to explain reduced aBMD. The three-stage model assesses height for age (short bones), bone area for height (narrow bones), and BMC for bone area (light bones)[17].

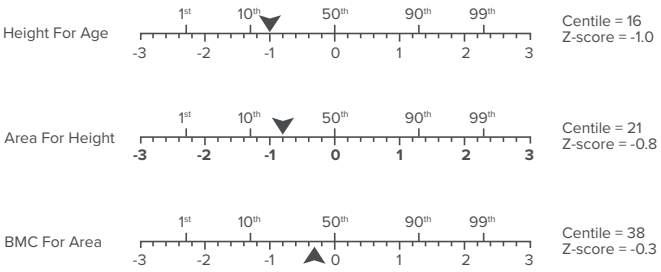


Figure 5. Example of Mølgaard output.

Provision of body size Z-scores or percentiles

Z-scores and percentiles are also available for weight, height and body mass index. It is very important to recognise that reference data used is currently the CDC Growth Charts from the USA and therefore may not be applicable in other countries.

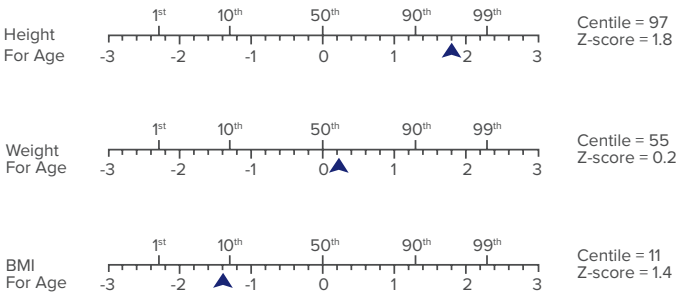


Figure 6. Example of growth output.

Apparent age adjustments

Within the software it is possible to adjust the aBMD for an apparent age such as height for age, or bone age as opposed to chronological age. These functions are not recommended without a clear understanding of the implication of what these apparent ages reflect with respect to skeletal and pubertal development. For example, a child who has the height of a 10-year old but the age and maturation of an 18-year old is an inappropriate comparison because it is not taking into consideration their stage of development.

If bone age is used the aBMD value will be more appropriate for their developmental stage but may still not give an appropriate correction for their skeletal size and height.

Vertebral fracture assessment

There is increasing recognition of the importance of the identification of vertebral fractures in children, particularly in those taking long-term corticosteroids[18-20]. These fractures are often occult (present without pain/symptoms) but can be highly predictive of further risk of fracture. Until recently diagnosis of these fractures was with lateral spine radiographs, however with the introduction of better quality images from the Hologic Horizon® scanner, it is now feasible to screen for vertebral fracture and vertebral deformities in children using the vertebral assessment tool at the same time as a routine DXA. The use of DXA for the identification of vertebral fractures has been endorsed in the latest ISCD guidelines[7].

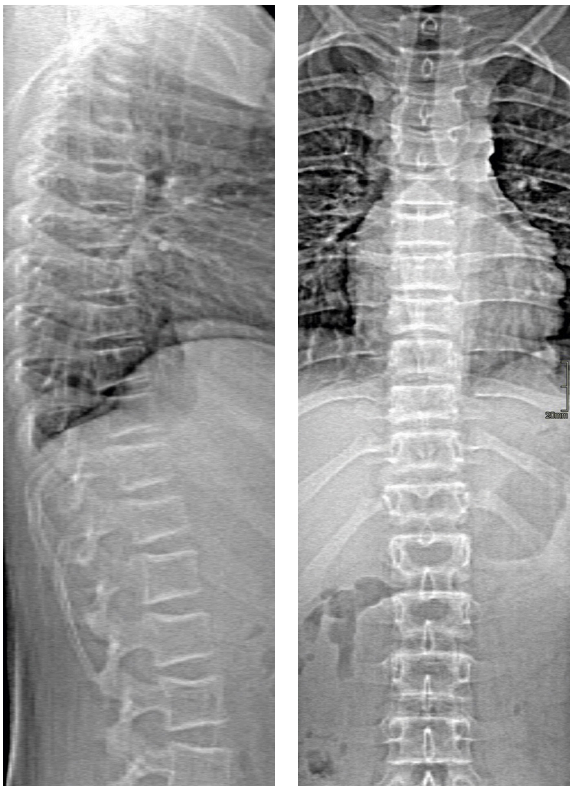


Figure 7. Pediatric IVA (lateral and AP view of the spine).

Body composition

The additional benefit of measuring total body by DXA is that alongside the bone assessment it is possible to obtain a measurement of body composition. Body composition evaluation consists of an estimation of bone, fat and lean mass. These parameters can be presented as total or regional values and as with bone density assessments can be presented in relation to age, height or body size. The current suggested outputs are:

- **Total Body %Fat (Adiposity):** The ratio of fat mass to total mass for age
- **Fat Mass Index (FMI):** FMI = Fat Mass/Height^2. It is a more accurate measure of obesity than Body Mass Index (BMI) because it calculates the amount of fat a child has in relation to their height instead of total weight relative to height. The higher this number, the more fat they have
- **Fat Free mass index (FMI):** FFMI = Lean/Height^2. It is the amount of lean mass relative to a child's height. The higher this number, the more muscle they have

Supplementary measures available are estimated visceral adipose tissue (VAT), mass, volume, and area. These are measurement of visceral fat, the pathogenic or "bad fat" around the insides of organs. In adolescents these measurements have been shown to be associated with an increased risk of metabolic syndrome and coronary heart disease[21-23].

Adipose and Lean Indices

Measure	Result	Percentile	
		YN	AM
Total Body % Fat	**27.1**		**22**
Fat Mass/Height² (kg/m²)	5.53		28
Android/Gynoid Ratio	0.63		
% Fat Trunk/% Fat Legs	0.71		45
Trunk/Limb Fat Mass Ratio	0.67		38
Est. VAT Mass (g)	149		
Est. VAT Volume (cm³)	161		
Est. VAT Area (cm²)	30.9		

Lean Indices

Measure	Result	Percentile	
		YN	AM
Lean/Height² (kg/m²)	14.0		50
Appen. Lean/Height² (kg/m²)	6.16		54

Est. VAT = Estimated Visceral Adipose Tissue
YN = Young Normal
AM = Age Matched

About the authors

Kate is Professor of Global Musculoskeletal Health at MRC Lifecourse Epidemiology and is Director of the NIHR Southampton Global Nutrition Research Group. Kate co-leads the Sub-Saharan Africa Musculoskeletal Network.

Her current and future research aims to gain a better understanding of how to achieve and maintain potential to ensure healthy musculoskeletal system throughout life. She is an Honorary Senior Research Fellow at MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine, and Honorary Associate Professor at the University of The Witwatersrand, South Africa.

Kate is President-Elect of the Bone Research Society and serves on several Royal Osteoporosis Society committees. Kate is Associate Editor of the Journal of Bone and Mineral Research. Kate was a member of American Society for Bone and Mineral Research Council (2017-2020) and is the UK Ambassador for ASBMR Member Engagement. Kate is also a member of the International Osteoporosis Foundation Committee for Scientific Advisors. Kate was Secretary of the Bone Research Society (2015-2018), serving as a committee member from 2011. She represents University of Southampton on World Universities Network Public Health and Global Africa Group.

Dr. Crabtree is a Principal Clinical Scientist at Birmingham Children's Hospital, U.K.

Her research concentrates predominately on bone development in the healthy child and in children with chronic diseases. In 2007 she completed her PhD thesis "Interpretation of Paediatric Bone Evaluation by DXA". In 2010 she was awarded a NIHR Research fellowship to prospectively evaluate fracture risk in children with chronic inflammatory and/or disabling conditions. In addition to this study Dr. Crabtree was also awarded an Arthritis Research-UK grant to collate bone density data in 3,500 healthy children from across the UK. She has an active interest in the development of imaging techniques which can improve the diagnosis of bone health and increased fracture risk in chronically sick children. She has a special interest the muscle-bone relationship and how disruption of this relationship affects bone development in both a paediatric and aging populations. Dr. Crabtree is an internationally recognised expert in DXA, bone and mineral metabolism, bone biology, muscle and bone interaction, the interpretation of bone density in children, and the effects of chronic disease on paediatric bone health. She has published more than 100 original research manuscripts and book chapters on these topics and maintains a leadership role in the field of paediatric densitometry.

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Example of reports

Lumbar spine report

Patient biography

Main BMD results

Evolution graph

User selected Z-scales

Hologic Radiology
35 Crosby Dr
Bedford, MA 01730

Telephone: 781-999-7300

Name: Horizon Peds 7 yrs	Sex: Female	Height: 49.5 in
Patient ID: Removed	Ethnicity: White	Weight: 55.1 lb
DOB: November 01, 2006		Age: 7

Referring Physician:

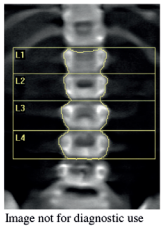
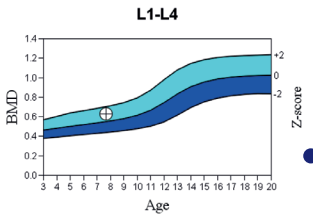


Image not for diagnostic use



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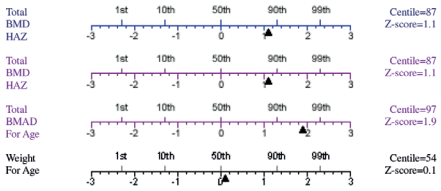
Exam Date: July 01, 2014



DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMAD g/cm³	BMD (g/cm²)	Z-score	AM (%ile)
L1	5.93	3.41	0.236	0.575		
L2	7.05	4.32	0.231	0.612		
L3	8.23	5.39	0.228	0.655		
L4	8.50	5.67	0.229	0.667		
L1-L4	**29.70**	**18.79**	**0.230**	**0.632**	**1.2**	**88**

Total BMD CV 1.0%

Scan ID: A1008140Q
Scan Type: f Lumbar Spine
Analysis: October 08, 2014 17:19 Version 13.5.3
Lumbar Spine
Operator:
Model: Horizon A (S/N 200042)
Comment: Removed

HOLOGIC®

Example of reports

Hip report

Patient biography

Main BMD results

Evolution graph

User selected Z-scales

Hologic Radiology
35 Crosby Dr
Bedford, MA 01730

Telephone: 781-999-7300

Name: Horizon Ped Hip	Sex: Female	Height: 55.0 in
Patient ID:	Ethnicity: White	Weight: 112.0 lb
DOB: February 14, 2000	Height Age: 12.00	Age: 15

Referring Physician: Bones, M MD

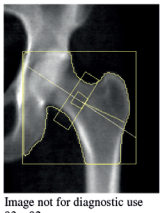
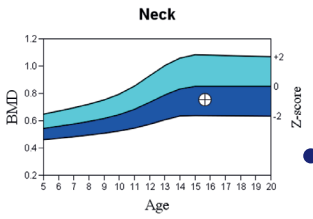


Image not for diagnostic use
93 x 92
NECK: 48 x 15
HAL: 96 mm



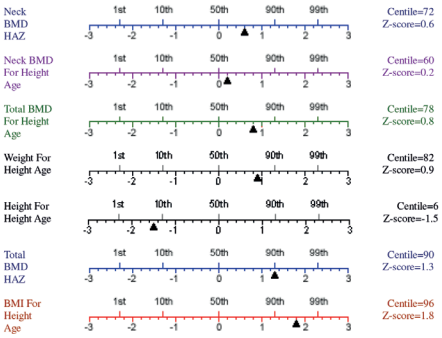
Source: 2012 BMDCS/NHANES White Female.

DXA Results Summary:

Region	Area (cm²)	BMC (g)	BMAD g/cm³	BMD (g/cm²)	Z - score	AM (%Ile)
Neck	4.68	3.53	0.308	0.754	-0.9	20
Total	29.06	25.24		0.868	-0.6	27

Total BMD CV 1.0%

Exam Date: October 13, 2015



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Example of reports

Whole body report

Patient biography

Main BMD and Body Composition results

Evolution graph

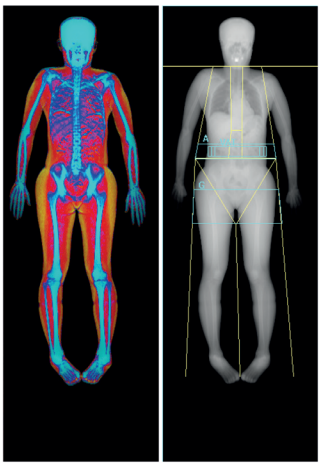
User selected Z-scales

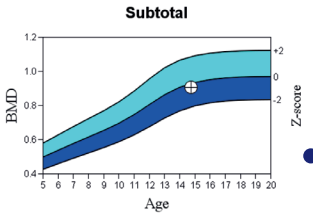
Name: Peds WB, 14 YRS
Patient ID:
DOB: 06 June 1996

Sex: Female
Ethnicity: White

Height: 149.9 cm
Weight: 47.6 kg
Age: 14

Referring Physician:





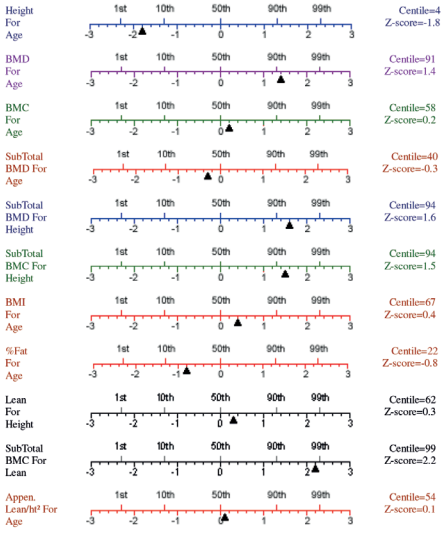
Source: 2012 BMDCS

DXA Results Summary:

Region	Fat Mass (g)	Lean Mass (g)	% Fat	BMC (g)	BMD (g/cm²)
L Arm	761	1604.7	30.7	114.67	0.696
R Arm	752	1572.9	30.8	116.77	0.694
Trunk	4584	15014.3	22.8	471.32	
L Leg	2702	5291.5	32.6	306.08	1.081
R Leg	2666	5369.2	32.0	305.03	1.126
Subtotal	11465	28852.6	27.5	1313.87	0.907
Head	963	2639.8	22.8	627.85	2.584
Total	**12427**	**31492.4**	**27.1**	**1941.72**	**1.148**
Android (A)	585		22.7		
Gynoid (G)	2499		35.8		

Scan ID: A03091104
Scan Type: a Whole Body
Analysis: 08 December 2016 12:14 Version 13.6.0.4
Auto Whole Body Fan Beam
Operator:
Model:
Comment:

Exam Date: 09 March 2011



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Example of reports

Body composition report

Patient biography

Evolution graph

Whole body and segmental body composition results

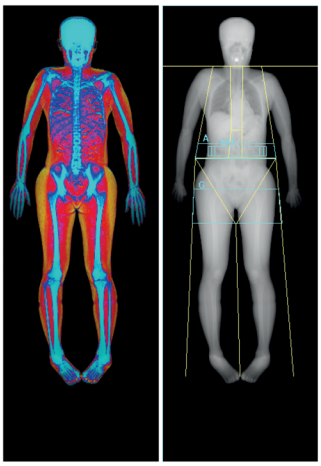
Adipose Indices including VAT results

Lean Indices

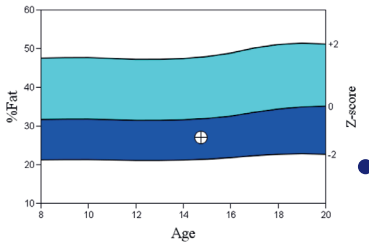
Name: Peds WB, 14 YRS
Patient ID:
DOB: XXXXX

Sex: Female
Ethnicity: White

Height: 149.9 cm
Weight: 47.6 kg
Age: 14



Total Body % Fat



Source: 2008 NHANES White Female

Body Composition Results

Region	Fat Mass (g)	Lean + BMC (g)	Total Mass (g)	% Fat	%Fat Percentile YN	%Fat Percentile AM
L Arm	761	1719	2480	30.7		31
R Arm	752	1690	2441	30.8		33
Trunk	4584	15486	20070	22.8		27
L Leg	2702	5598	8299	32.6		19
R Leg	2666	5674	8340	32.0		16
Subtotal	11465	30167	41631	27.5		23
Head	963	3268	4230	22.8		
Total	**12427**	**33434**	**45862**	**27.1**		**22**
Android (A)	585	1998	2584	22.7		
Gynoid (G)	2499	4489	6987	35.8		

Adipose Indices

Measure	Result	Percentile YN	Percentile AM
Total Body % Fat	**27.1**		**22**
Fat Mass/Height² (kg/m²)	5.53		28
Android/Gynoid Ratio	0.63		
% Fat Trunk/% Fat Legs	0.71		45
Trunk/Limb Fat Mass Ratio	0.67		38
Est. VAT Mass (g)	149		
Est. VAT Volume (cm³)	161		
Est. VAT Area (cm²)	30.9		

Lean Indices

Measure	Result	Percentile YN	Percentile AM
Lean/Height² (kg/m²)	14.0		50
Appen. Lean/Height² (kg/m²)	6.16		54

Est. VAT = Estimated Visceral Adipose Tissue
YN = Young Normal
AM = Age Matched

TBAR1209 - NHANES BCA calibration

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