근감소증의 진단

- 체성분측정 -

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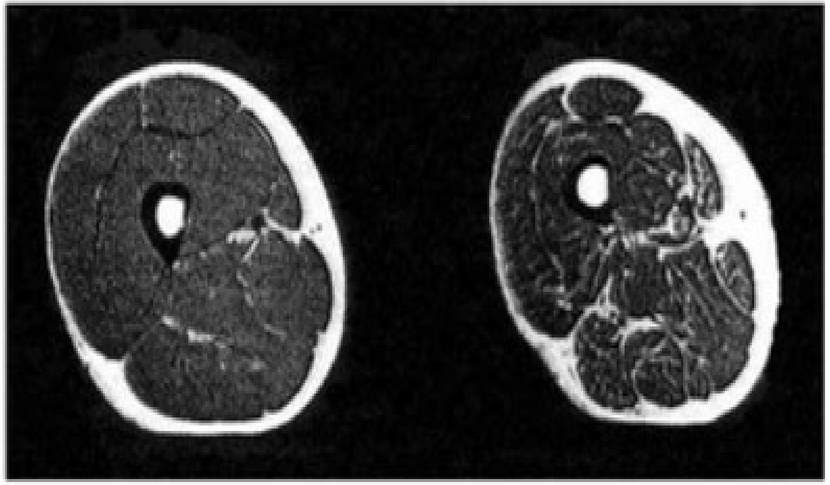

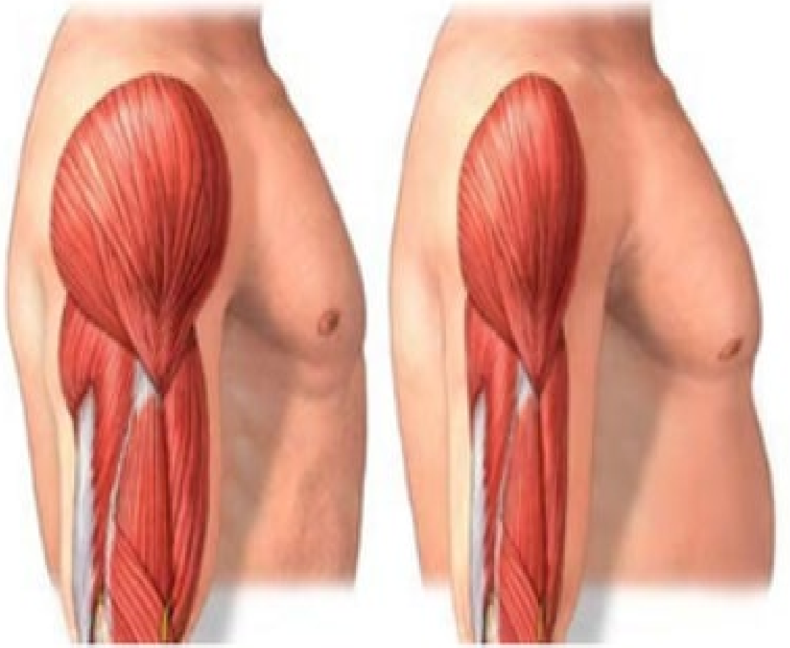

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Sarcopenia

- **Condition characterized** by **progressive** and **generalized reduction** in **skeletal muscle mass** and **muscle strength**

  → **Increased risk** of **adverse outcomes** (disability, hospitalization, death)

Muscle quantity

- **Total body Skeletal Muscle Mass (SMM)**
- **Appendicular Skeletal Muscle Mass (ASM)**
- **Appendicular Lean Mass (ALM)**
- **Skeletal Mass Index (SMI)**
  - ASM / height^2
- **Muscle cross-sectional area of specific muscle group**

Muscle mass cutoff points

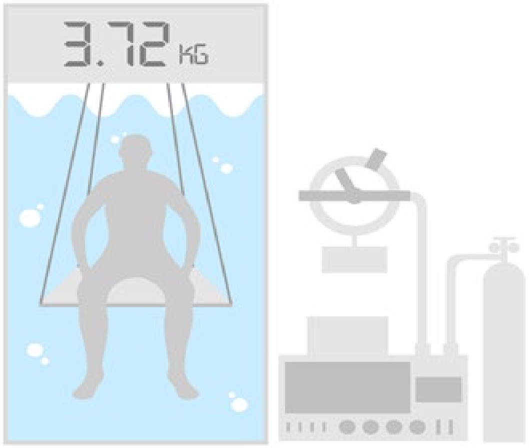
Study group	Cutoff points	
Asian Working Group for Sarcopenia (AWGS)	ASM / height^2 (DXA)	Men < 7.0 kg/m^2
		Women < 5.4 kg/m^2
	ASM / height^2 (BIA)	Men < 7.0 kg/m^2
		Women < 5.7 kg/m^2
International Working Group on Sarcopenia (IWGS)	ASM / height^2	Men ≤ 7.23 kg/m^2
		Women ≤ 5.67 kg/m^2
European Working Group on Sarcopenia in Older People (EWGSOP)	ASM / height^2	Men < 7.0 kg/m^2
		Women < 5.5 kg/m^2

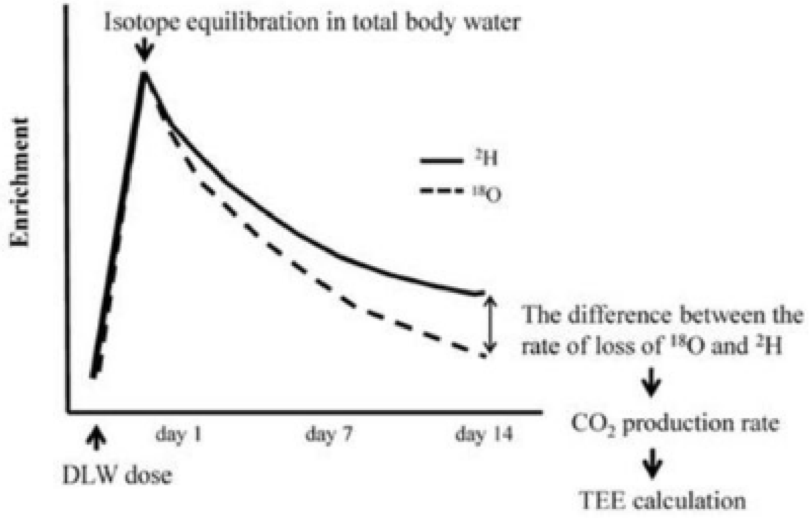
Accurate methods

- **Densitometry** (수중체밀도법)
  - Muscle > water > fat
  - Most valid and reliable method
- **Hydrometry** (deuterium dilution)
- **Echo-MRI**

However,

- ➢ Complex measurement protocols
- ➢ Require specialized expertise
- ➢ Costly equipment





Validated tests and tools

Variable	Clinical practice
Case finding	SARC-F questionnaire
	Ishii screening tool
Skeletal muscle strength	Grip strength
	Chair stand test (chair rise test)
Skeletal muscle mass or muscle quality	Dual-energy X-ray absorptiometry (**DXA**)
	Bioelectrical impedance analysis (**BIA**)
	Lumbar muscle cross-sectional area by **CT** or **MRI**
Physical performance	Gait speed
	Short physical performance battery (SPPB)
	Timed-up-and-go test (TUG)
	400-meter walk or long-distance corridor walk (400-m walk)

Tool selection

- **Patient**
  - Disability, Mobility
- **Access to technical resources**
  - Community, Clinic, Hospital, Research center
- **Purpose of testing**
  - Progression monitoring, Monitoring rehabilitation and recovery

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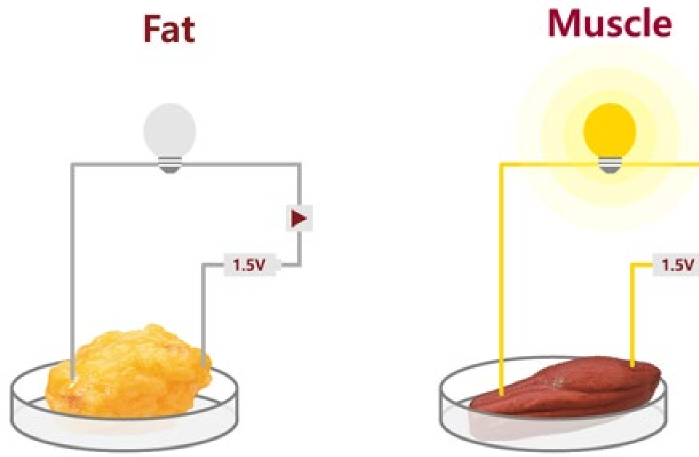
Historical background

- Since 1871, **Electrical properties** of **tissues** have been described
- By 1970s, the **foundations of BIA** were established
- By 1980s, **<u>single-frequency BIA</u>** analyzers were commercially available
- By 1990s, market included **<u>multi-frequency BIA</u>** analyzers, **<u>Segmental BIA</u>**
- In 2020, <u>3MHz high-frequency BIA</u>

Principles

- 인체는 전기가 잘 통하는 수분으로 이루어짐
- **수분량에 따라 저항이 달라진다는 원리**
- 인체에 미세한 교류전류를 흘려 보내 생겨나는 **Bioimpedance index (BI)**

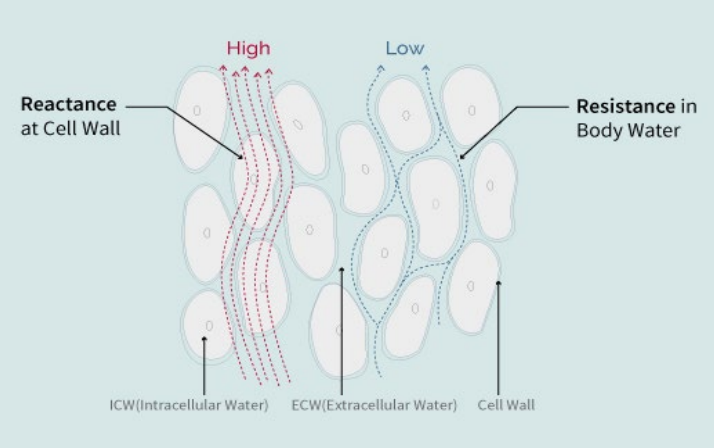
  → 체수분 측정



Principles

- **Resistance (저항)**
  - 전류의 흐름을 방해하는 정도. 수분 또는 근육이 많으면 저항이 작고, 수분이 적으면 저항이 높음
  - Arises from **extracellular fluid** and **intracellular fluid**

- **Reactance (유도저항)**
  - 전류가 세포막을 통과하여 세포 내 수분에 전류가 흐를 때 **세포막에 전류를 방해하는 전기저항**
  - Arises from **cell membranes**



- **Impedance (전기적 흐름을 방해하는 정도)**
  - 인체에 미세한 교류 전류 흘렸을 때 발생하는 인체저항
  - **저항과 유도저항**의 벡터 **합**

Principles

- **Cylinder model** for the relationship between **impedance** and **geometry**

- 체수분 부피

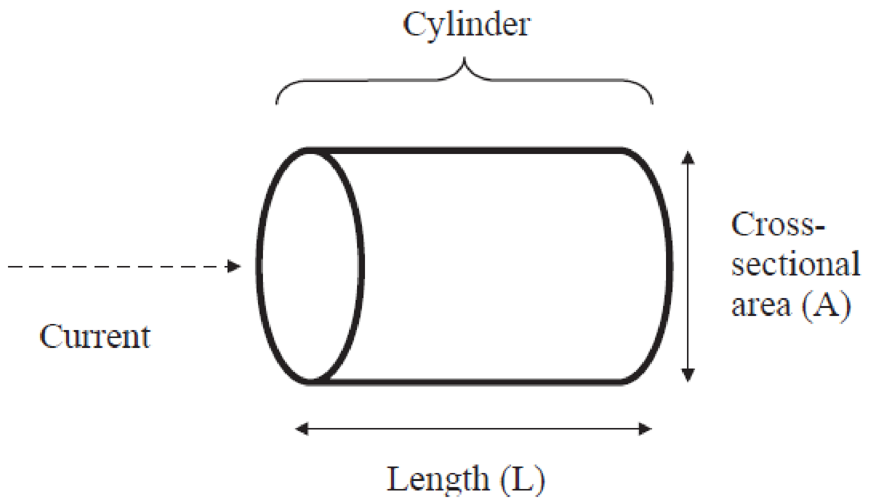
① 실린더 부피 계산 (부피 = 길이 x 면적)

② 임피던스의 특성 : 임피던스는 단면적에 반비례 하고, 길이에 비례

a. Resistance (R) = $\rho L/A = \rho L^2/V$

b. Volume (V) = $\rho L^2/R$ → bioimpedance index (BI)

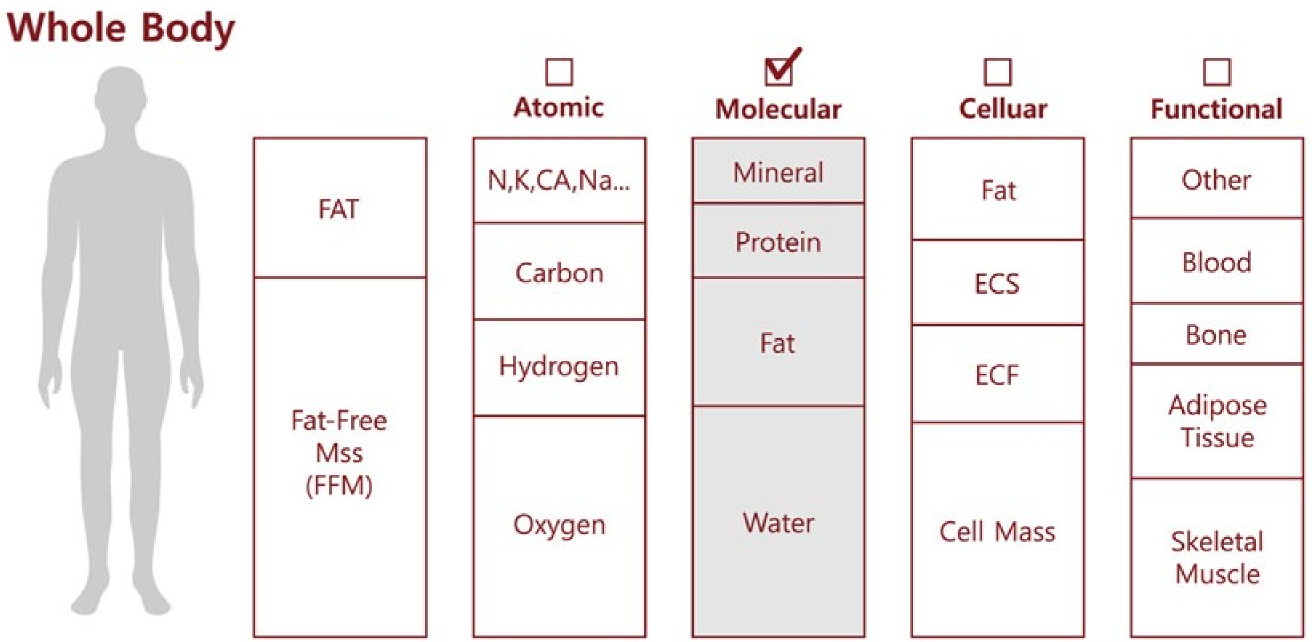
(ρ is resistivity of conducting material)



Principles

- **임피던스**와 **실린더 길이** (인체; 사람의 키) → **전체 체수분 부피**
- **임피던스 측정** → **체수분 부피 산출** → **<u>제지방</u> (Fat free mass)** 과 **지방 (Fat)**

  └ 단백질 (근육), 무기질 (뼈)

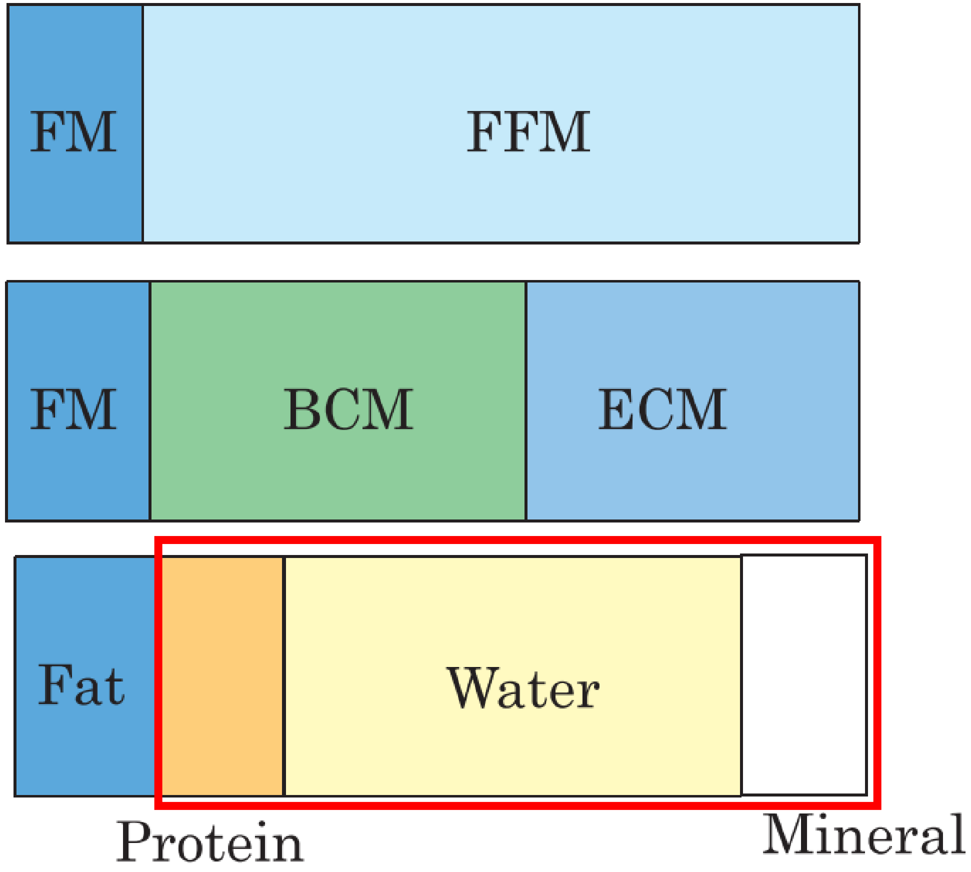


Body composition compartments

- **Fat mass (FM)**
  - Indicates the water-free body component
- **Fat-free mass (FFM)**
  - Skeletal muscle, internal organs, interstitial fat tissue
  - Total body water = ECW + ICW

Body Composition Analysis

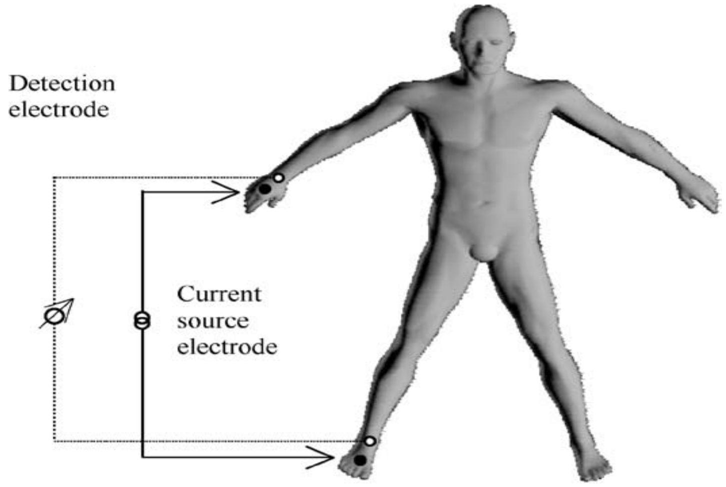
	Values	Total Body Water	Soft Lean Mass	Fat Free Mass	Weight
Total Body Water (L)	27.5 (26.3 ~ 32.1)	27.5	35.1 (33.3 ~ 40.7)	37.3 (35.8 ~ 43.7)	59.1 (43.9 ~ 59.5)
Protein (kg)	7.2 (7.0 ~ 8.6)				
Minerals (kg)	2.63 (2.44 ~ 2.98)	non-osseous			
Body Fat Mass (kg)	21.8 (10.3 ~ 16.5)				



Methods

Single frequency BIA (SF-BIA)

- **At 50 kHz, is passed between surface electrodes** placed on hand and foot
- **Not** measure **TBW**
- Measure **weighted sum** of **ECW + ICW resistivity**
- **Estimate FFM** and **TBW, but cannot** determine **differences** in **ICW**
- **Based on** a mixture **theories** and **empirical equations**



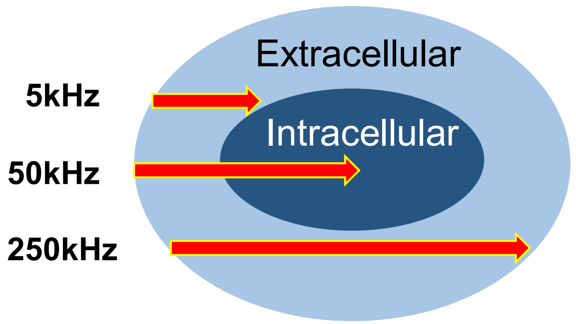
Methods

Multi-frequency BIA (MF-BIA)

- **Different frequencies** (0, 1, 5, 50, 100, 200-500 kHz) to evaluate **FFM, TBW, ICW, ECW**

- At **low frequency** (1–5 kHz), electric current **not** penetrate cell membrane
  → Current pass through extracellular fluid

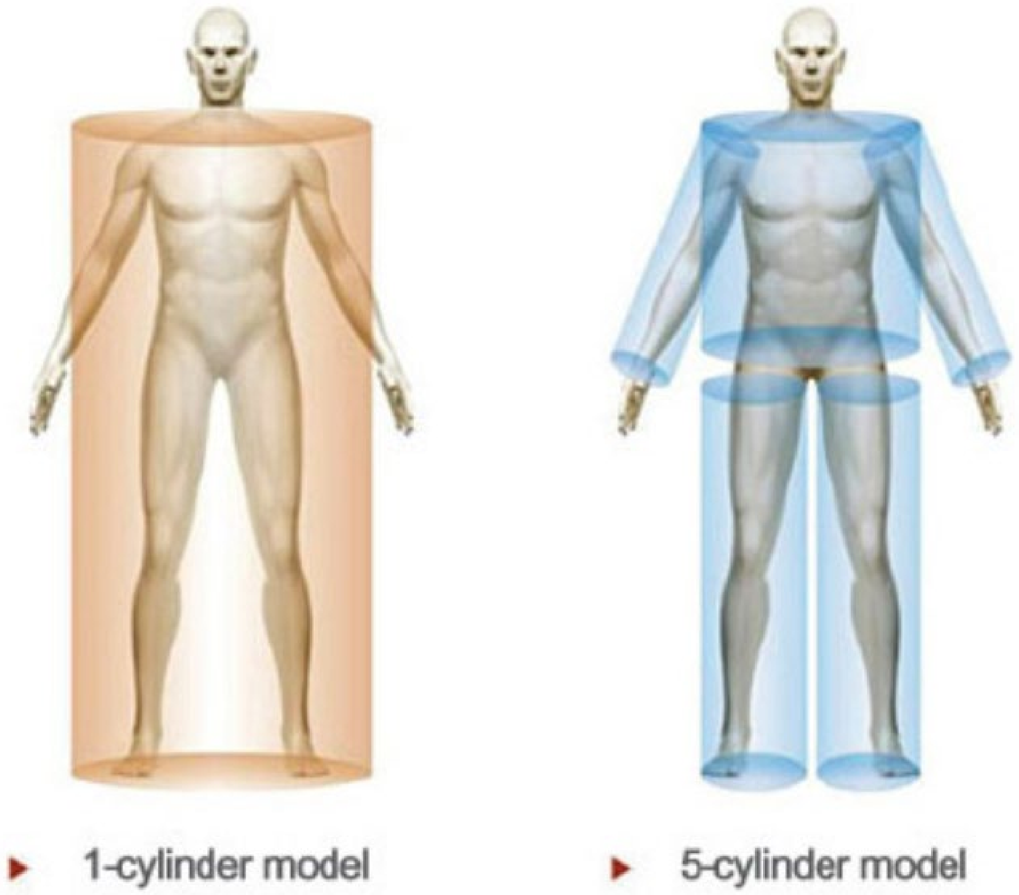
- At **higher frequency** (>50 kHz), current **pass** through cell membrane
  → Intracellular and extracellular fluid compartments



Methods

Direct Segmental Multi-frequency BIA (DSM-BIA)

- **Human body is made up of five cylinders**
  - Right arm, left arm, torso, right leg, left leg
- **8-point tactile electrode system** with **direct segmental analysis** to measure **impedance** in **five body cylinders** using **multiple frequencies**
- **No estimations** or **empirical equations**



Methods

- **The higher the frequency, the more difficult** it is to **control the frequency** in human body which results in **unstable impedance measurement**
- **3MHz frequency** penetrates through **cell membranes** even better
- **Enables differentiate ICW, ECW** and **more accurate measurement** of **TBW**

Assumptions

- **Human body is divides into <u>five cylinder</u> with a uniform electric conductivity**
  - Trunk, upper and lower extremities
- **FFM contain virtually all the water** and **conducting electrolytes in body**
- **FFM hydration is constant**
- **Conductive length is conventionally considered stature**

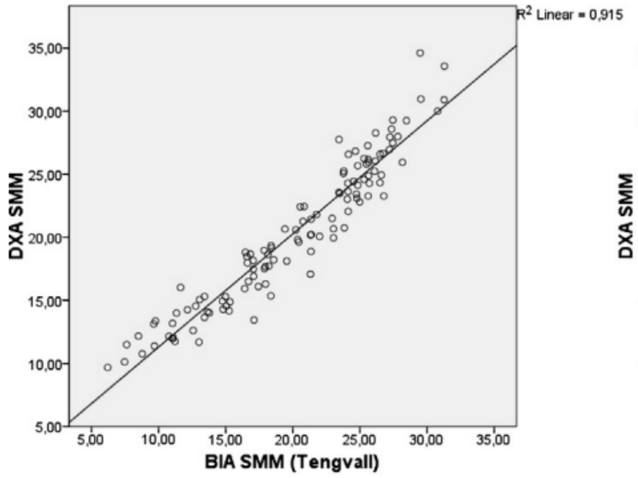
Assumptions

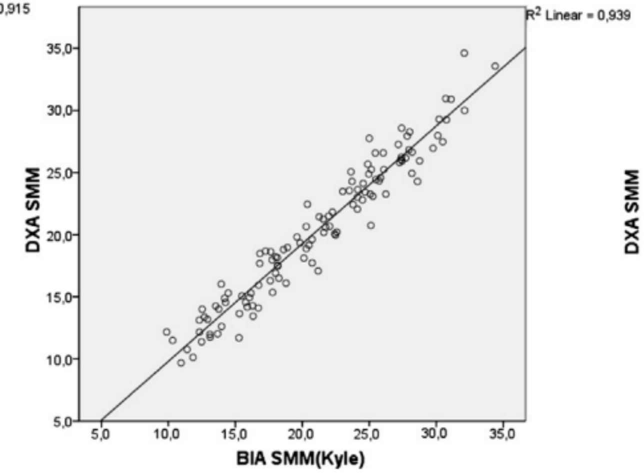
- Assess **total body water**
- By assuming **a constant hydration, predict** the amount of **FFM**
- **FFM** is **calculated** from **total body weight**

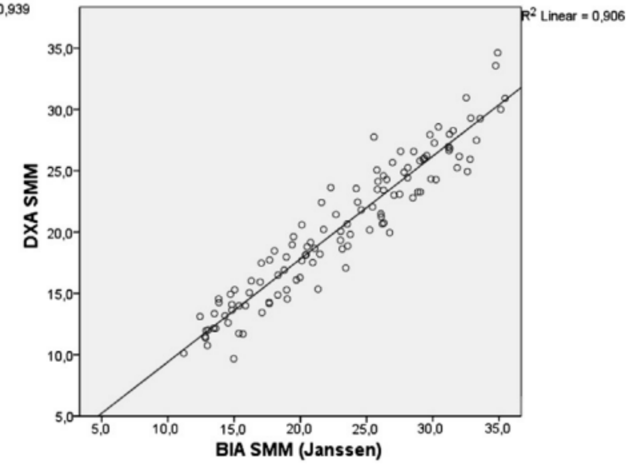
  using the assumption that **73% of FFM is water** in adults

Validity studies

- **Linear regression of skeletal muscle mass estimates**



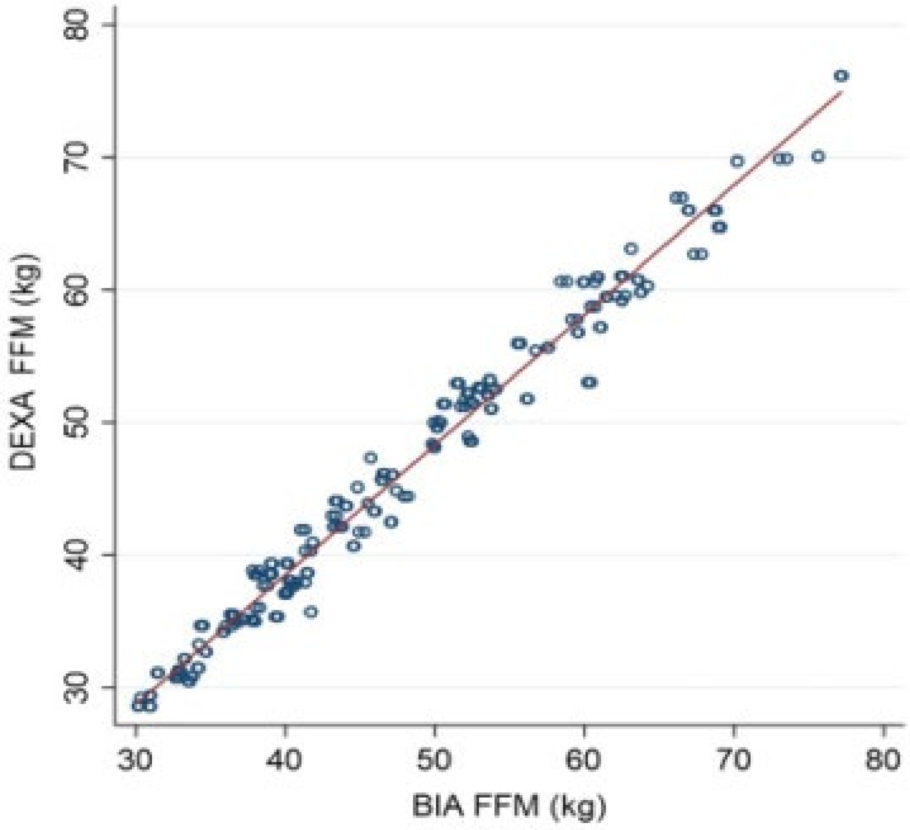




- **r 0.956, adjusted r^2 0.914**
- **r 0.969, adjusted r^2 0.939**
- **r 0.952, adjusted r^2 0.905**

Validity studies

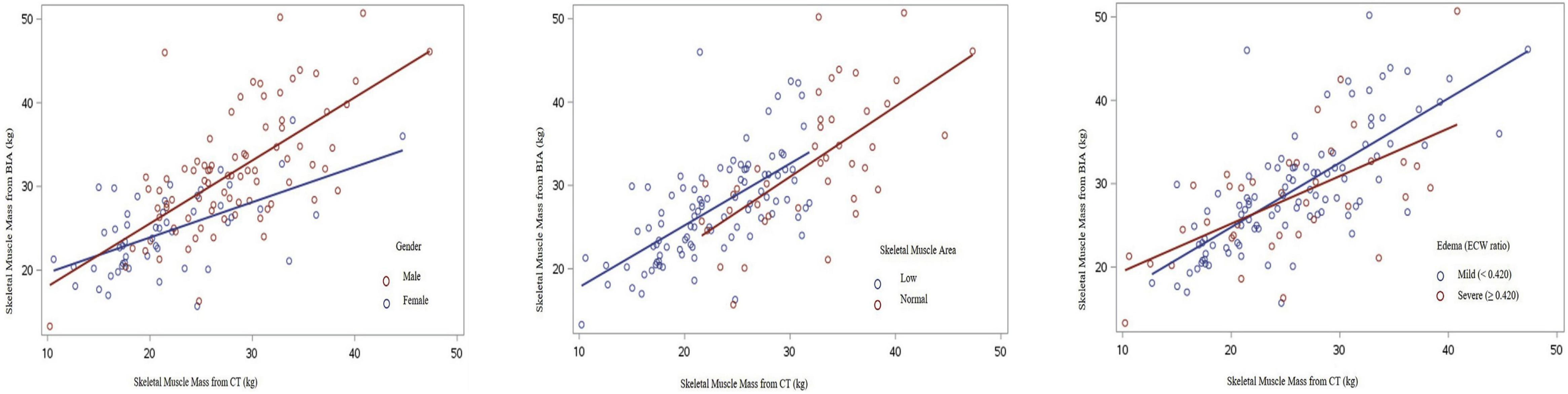
- **High correlation of FFM between DXA and BIA**



	ALM			Fat-Free Mass			Percent Body Fat		
	β	R^2	RMSE (kg)	β	R^2	RMSE (kg)	β	R^2	RMSE (%)
InBody 970									
Overall	0.971	0.943	1.567	0.989	0.979	1.663	0.964	0.929	2.448
Male	0.956	0.914	1.692	0.988	0.977	1.714	0.962	0.925	2.447
Female	0.960	0.923	1.139	0.988	0.976	1.621	0.964	0.929	2.465

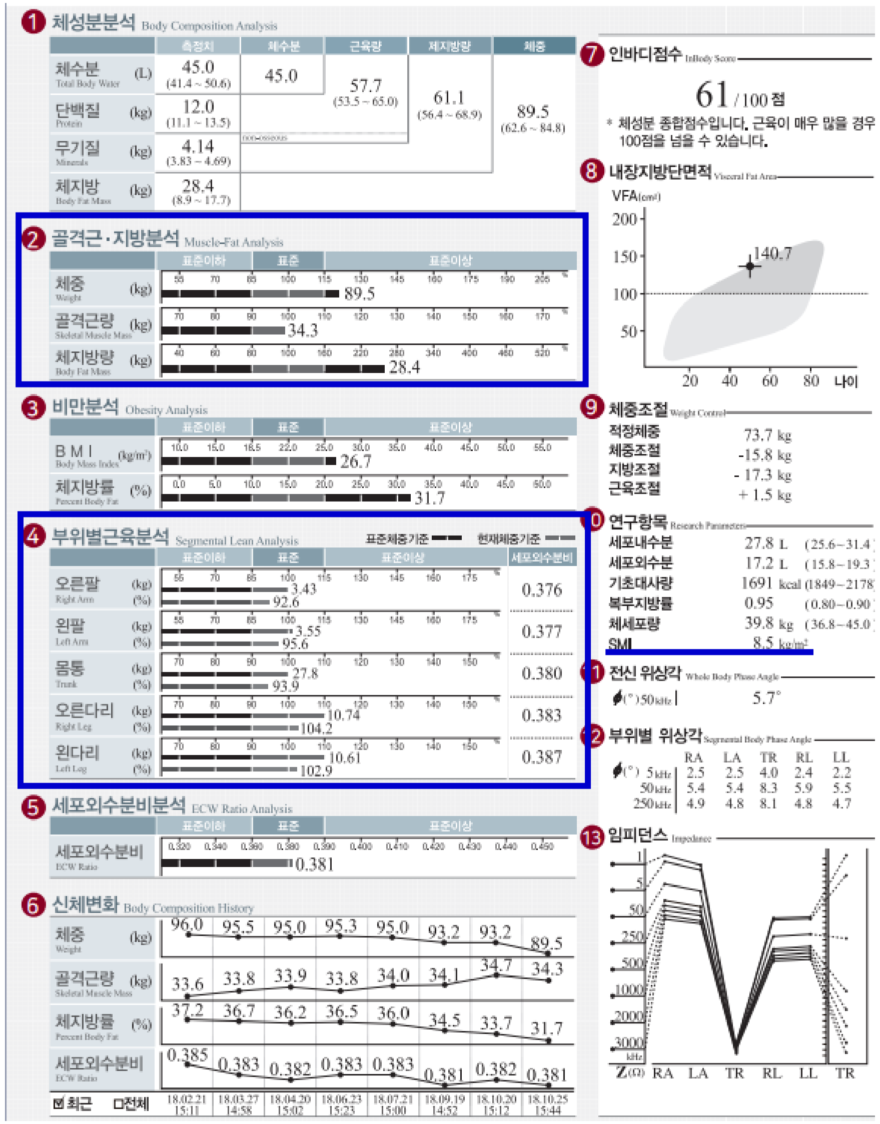
Validity studies

- **SMM measure by BIA showed high correlation with SMM calculation by CT**



- **Correlation** between **skeletal muscle mass** measured by **CT** and **BIA** based on Sex , Skeletal muscle area, Edema subgroups

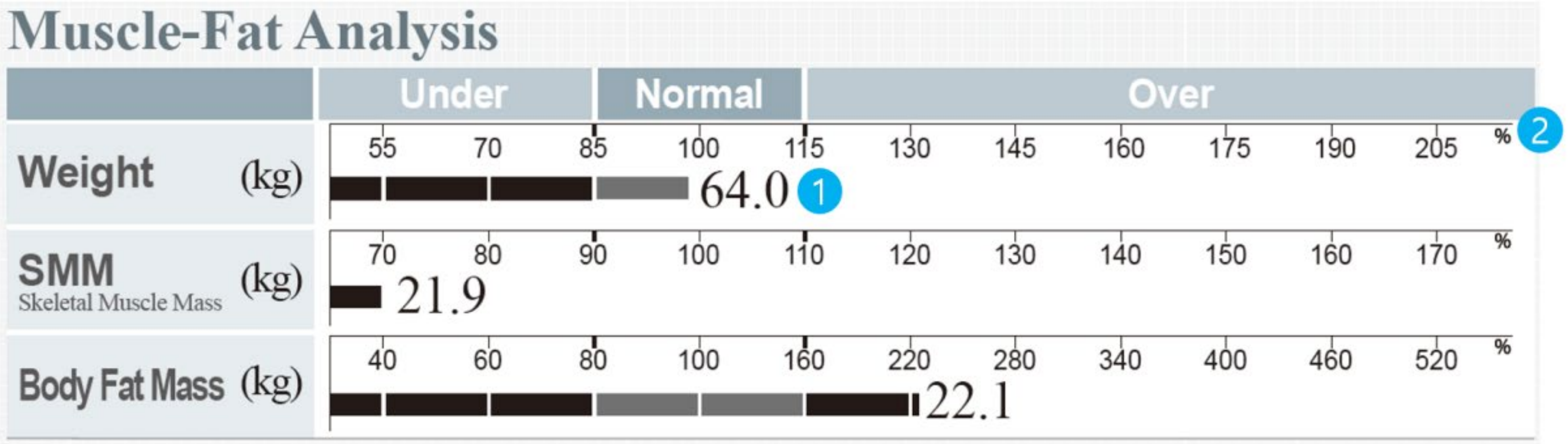
Body Composition Result Sheet



Body Composition Result

Sarcopenia Dx.

- **Skeletal Muscle Mass**



① Weight, Skeletal Muscle Mass and Body Fat Mass are displayed in kg

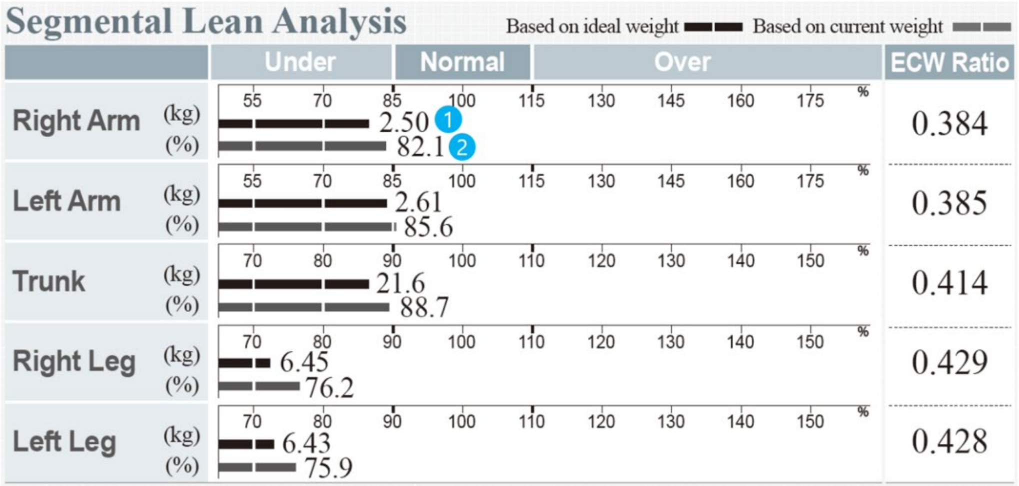
② Ratio of Weight, Skeletal Muscle Mass, Body Fat Mass is displayed based on the ideal weight

▪ If Skeletal Muscle Mass is at 100%, sufficient amount of muscle mass compared to your ideal weight

Body Composition Result

Sarcopenia Dx.

- **Segmental Lean Analysis**



① Amount of lean mass in kg

Length of bar shows how much muscle mass compared to ideal body weight

② Lean mass in percentage

Length of bar shows the percentage of lean mass compared to current weight

- Help to plan more specific exercises by analyzing the lean mass in each segments

Body Composition Result

- **SMI (Skeletal Muscle Mass Index)**

Research Parameters

Intracellular Water	18.3	L	(23.0~28.0)
Extracellular Water	13.0	L	(14.0~17.2)
Basal Metabolic Rate	1275	kcal	(1428~1663)
Waist-Hip Ratio	1.14		(0.80~0.90)
Body Cell Mass	26.2	kg	(32.8~40.2)
SMI	6.0	kg/m^2	

- Index can be used to diagnose sarcopenia (ASM / height^2)
- Asian assessment criteria for male is 7.0kg/m^2 and 5.7kg/m^2 for female

Advantages

- **Affordable**
- **Portable**
- **Quick** and **noninvasive**
- **No radiation exposure**
- **Ease of use**
- **Reproducible**

Disadvantages

- **Indirect method**
- **Precision and accuracy are influenced by several factors**
  - **Patient** factors : adiposity degree, fluid and electrolyte status, skin temperature
  - **Environmental** factors: ambient temperature, proximity to metal surfaces and electronic device
  - **Assumptions** underlying **prediction**: SF-BIA or MF-BIA
  - **Instrumentation** factors
  - **Variations** in measurement protocols

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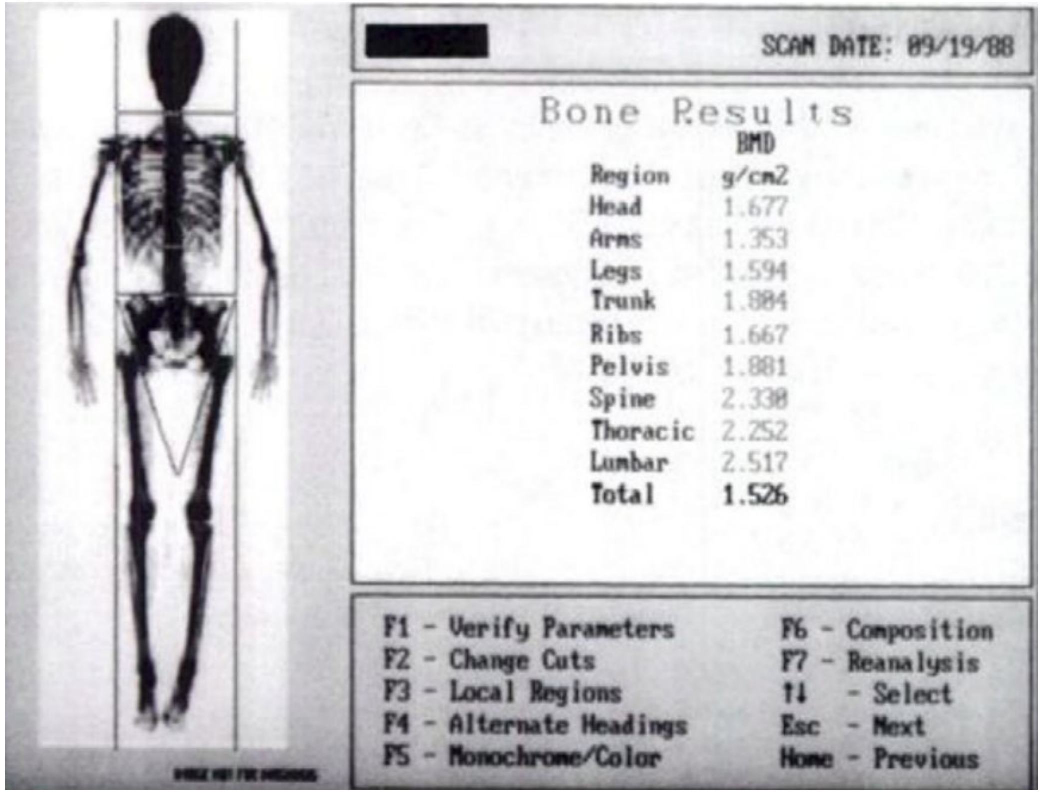
Early papers on body composition and DXA

- **Accurate to reference materials** of **lard** and **water** representing **fat** and **lean tissues**



Lunar DPX pencil beam system circa **1990**

DXA, Body composition at **molecular level**

- **Overall flexibility** to complete **DXA body composition assessments** on subjects of **different heights, widths, weights** has improved **in the past 30 years**

- **Quantification of <u>whole body</u>** <u>and</u> **<u>regional components</u>**
    - **FM**, lean mass (**LM**), bone mineral content (**BMC**)

Principles

- Measure **X-ray transmission** in crossing tissue of human body at **two different energy levels**
- **Radiation energies** are **variably attenuated** (absorbed or scattered) by **anatomical structures**
- **Low-density material** (soft tissue) allow **more photons** to pass through → **attenuate** X-ray beam **lesser** than material with **higher density** (bone)

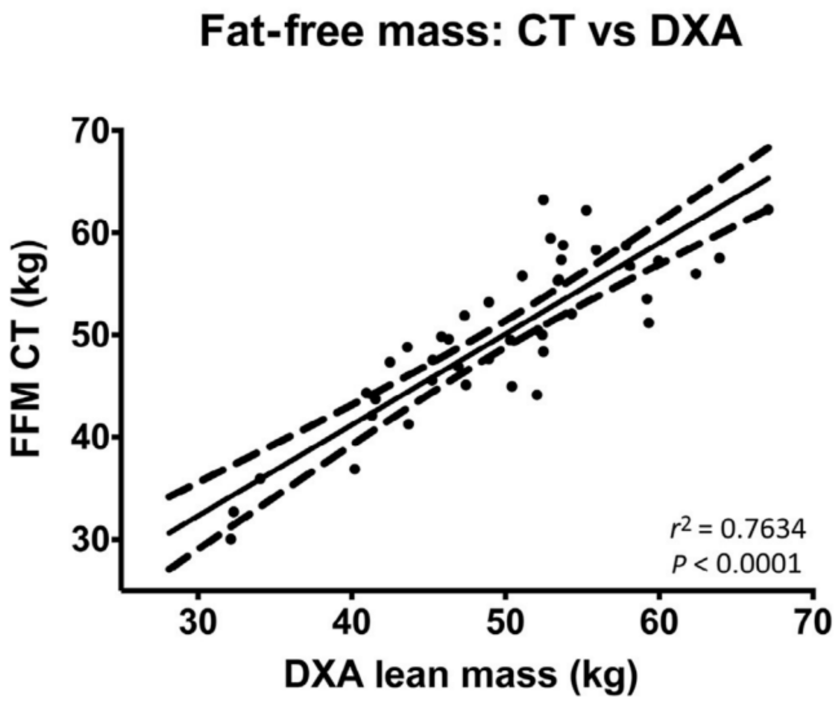
Principles

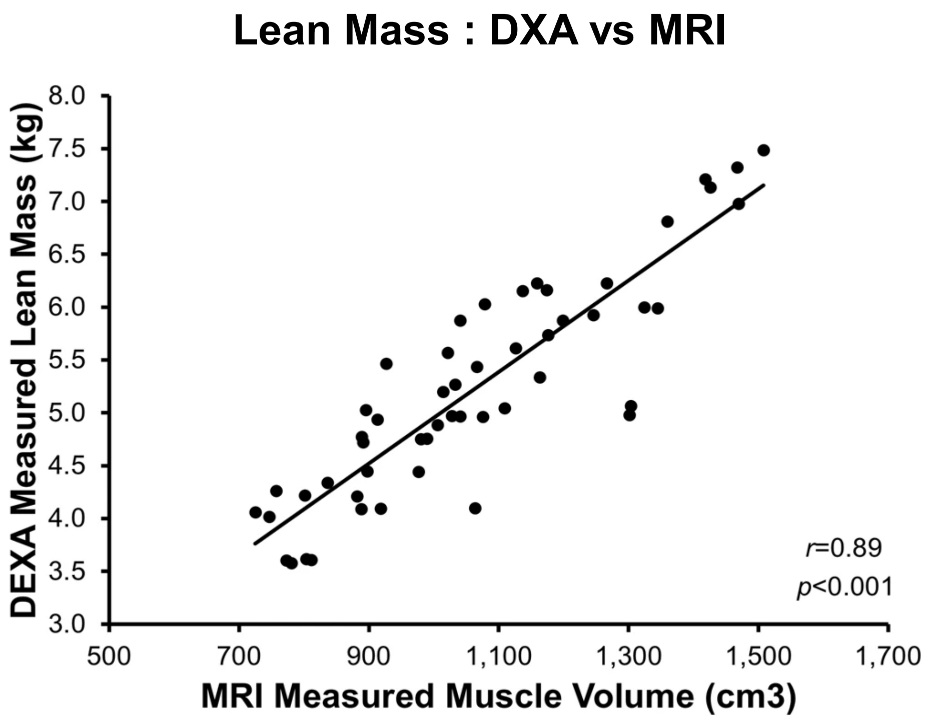
- **DXA estimate <u>R-value</u>**
  - Ratio of **attenuation coefficients** at two different energy levels
- **R-value**
  - Soft tissue vary depending on soft tissue composition
    - The lower are R-values, the higher is fat percentage
  - Constant for bone and fat in all patients

Principles

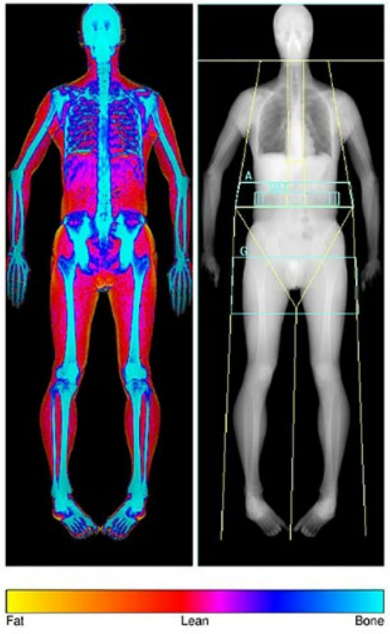
- **Not** measure **directly FM, LM, BMC**
- In pixels containing bone, **DXA distinguish bone from soft tissue (FM + LM)**
- **FM+LM calculated** in neighboring **bone-free pixels → Quantity of FM, LM**
  - **Assuming** amount of **fat over bone** is **same** as **fat over bone-free tissues**
- **The latest generation DXA**
  - Single whole-body scan
    - Low radiation exposure, Fast acquisition time
  - Providing high-resolution images, very accurate data

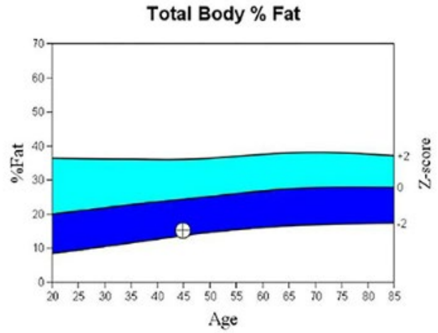
Validity studies





Body Composition Result Sheet





Source: NHANES Classic White Male.

World Health Organization Body Mass Index Classification
BMI = 21.1 WHO Classification Normal

BMI has some limitations and an actual diagnosis of overweight or obesity should be made by a health professional. Obesity is associated with heart disease, certain types of cancer, type 2 diabetes, and other health risks. The higher a person's BMI is above 25, the greater their weight-related risks.

Body Composition Results

Region	Fat Mass (g)	Lean + BMC (g)	Total Mass (g)	% Fat	%Fat Percentile YN	%Fat Percentile AM
L Arm	579	3461	4041	14.3	29	11
R Arm	618	3319	3937	15.7	35	15
Trunk	4563	29147	33710	13.5	17	4
L Leg	1961	9915	11876	16.5	19	11
R Leg	1909	10431	12341	15.5	14	7
Subtotal	9631	5627[illegible]	[illegible]5905	14.6	18	4
Head	1161	350[illegible]	4669	24.9		
Total	**10792**	**5978[illegible]**	**[illegible]0574**	**15.3**	**19**	**5**
Android (A)	777	4288	5065	15.3		
Gynoid (G)	2079	9774	11854	17.5		

Scan Date: 17 December 2018 ID: A1217180B
Scan Type: a Whole Body
Analysis: 06 August 2019 13:45 Version 13.6.0.5
Auto Whole Body Fan Beam
Operator: DA
Model: Horizon A (S/N 301197M)
Comment: Valutazione BCA

Adipose Indices

Measure	Result	Percentile YN	Percentile AM
Total Body % Fat	**15.3**	**19**	**5**
Fat Mass/Height² (kg/m²)	3.33	17	5
Android/Gynoid Ratio	0.87		
% Fat Trunk/% Fat Legs	0.85	37	12
Trunk/Limb Fat Mass Ratio	0.90	36	10
Est. VAT Mass (g)	312		
Est. VAT Volume (cm³)	338		
Est. VAT Area (cm²)	64.8		

Lean Indices

Measure	Result	Percentile YN	Percentile AM
Lean/Height² (kg/m²)	17.6	20	12
Appen. Lean/Height² (kg/m²)	7.91	20	16

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

Body Composition Result

Sarcopenia Dx.

Adipose Indices

Measure	Result	Percentile YN	Percentile AM
Total Body % Fat	**43.7**	**85**	**55**
Fat Mass/Height² (kg/m²)	13.2	80	61
Android/Gynoid Ratio	0.98		
% Fat Trunk/% Fat Legs	1.02	91	76
Trunk/Limb Fat Mass Ratio	1.38	99	90
Est. VAT Mass (g)	931		
Est. VAT Volume (cm³)	1006		
Est. VAT Area (cm²)	193		

Lean Indices

Measure	Result	Percentile YN	Percentile AM
Lean/Height² (kg/m²)	16.3	70	68
Appen. Lean/Height² (kg/m²)	→ 6.31	44	54

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

- Append. Lean/Height^2 = 6.31 kg/m^2

  → Upper limit
  (pathological values are < 5.4 kg/m^2 for women according to AWGS)

Advantages

- **High precision, accuracy, reproducibility**
- **Quick** and **noninvasive**
- **Good availability**
- **Low radiation exposure**
  - 1–7 μSv : normal background radiation received over 1 day at sea level
- **Able to differentiate FM, LM, BMC**
- **Obtaining regional measures** (e.g., ALM)

Disadvantages

- **Variability of instrument calibration procedures, hardware and software version between manufacturers**
- **Requires specific technical skills and operator experience**
- **Contraindicated in pregnancy**
- **Body thickness and hydration status may influence the measurements**
- **Inability to discriminate the different types of fat**
  - Visceral, subcutaneous, intramuscular

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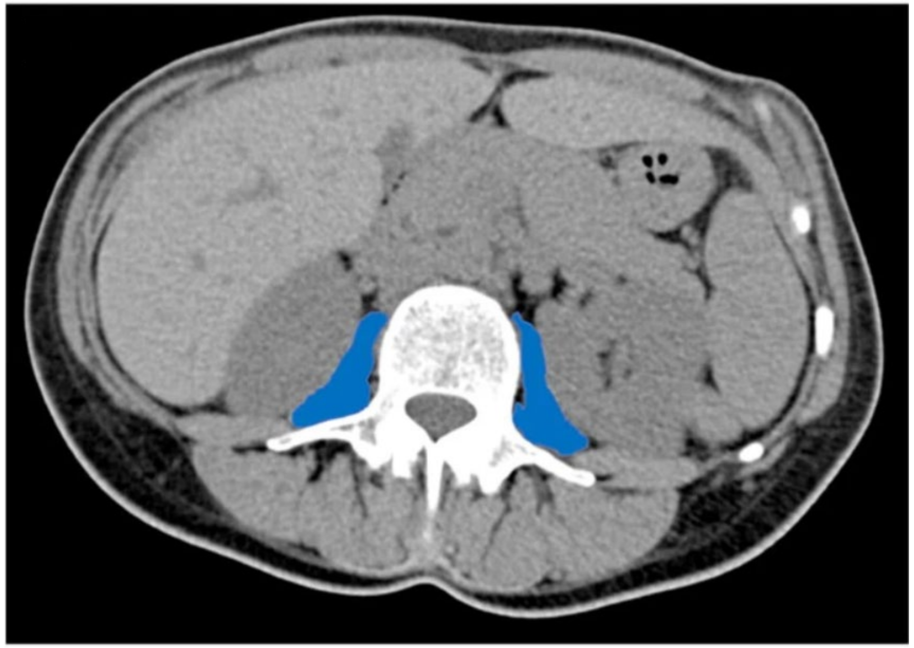
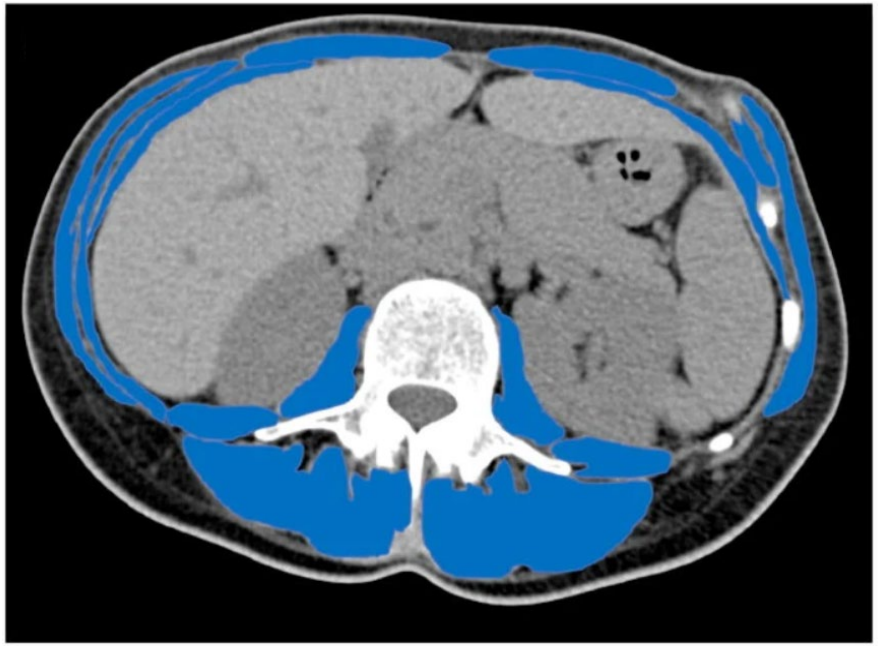
Computed tomography (CT)

- Assess both **muscle mass** and **quality**
- Measure **muscle size** and **attenuation** in **specific district**
- Measurements obtained from **single cross-sectional slice** are **highly accurate** to estimate **body composition**
- **Strong correlation** between **single-slice** and **skeletal muscle distribution**
- **SMI cutoff values to use for muscle mass assessment on CT**
  - **CSA** (Cross-sectional area) **/ height**^{2} : **52 - 55** cm^2/m^2 for men and **39 - 41** cm^2/m^2 for women
- **No consensus** on standardized **CT thresholds** of **sarcopenia**

Lumbar 3rd vertebra imaging by CT

- CT images of L3 correlate with whole-body muscle





- CSA of both psoas muscles (blue) at the L3 level can be used as imaging biomarker of **sarcopenia**
- CSA of all muscles (paraspinous, psoas, abdominal) included in axial CT image at L3 level (blue) can be used to assess **muscle status**

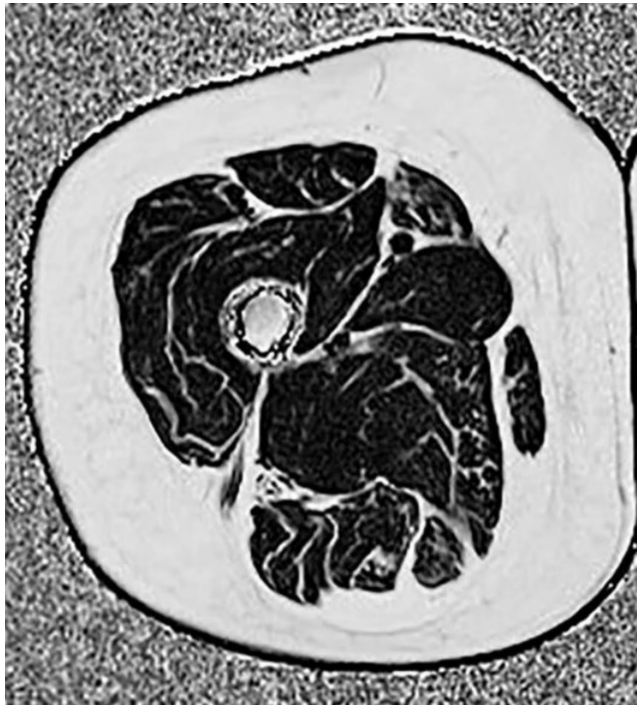
Magnetic resonance (MR)

- Measure the **amount of muscle** and **fat tissue** due to **high contrast resolution** and **multiparametricity**
- Accuracy in assessment of **muscle CSA/volume** is **very high**
- Studies have been performed on **different muscular districts, with no standardization** of imaging protocol
- Assess **muscle quality**
  - Muscular edema, fibrous infiltration, fiber contractility, elasticity

Magnetic resonance (MR)

- Dixon MR sequence of the right thigh

- Both fat and water components



- Fat fraction that can be used to quantify fatty infiltration of muscle

CT and MR

- **Pros**
  - Good predictor of whole-body skeletal muscle mass and sensitive to change
  - Strongly correlated with total body muscle volume

- **Cons**
  - High equipment costs
  - Lack of portability
  - Requirement for highly-trained personnel to use
  - Cut-off points for low muscle mass are not yet well defined
  - Not commonly used in primary care

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Conclusion

- **BIA** can be used **as prognostic** and **assessment** body composition tool
- **DXA** is the **most accepted** imaging modality with **clear cutoff points** to identify **sarcopenia** with close-to-zero radiation dose
- **CT** is the **most promising** with **clear cutoff values** for **muscle mass**
- These can be used to **diagnose sarcopenia** and to **monitor** during treatment