Incontro Società Medico Chirurgica di Ferrara

La sarcopenia: definizioni, patogenesi e trattamento

Metodiche strumentali per la valutazione della massa muscolare

Dott Andrea Rossi

Clinica Geriatrica

Azienda Ospedaliera Universitaria Integrata di Verona

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"Sarcopenia is a term that denotes the
decline in muscle mass *and*
strength that occurs with healthy aging."

Rosenberg, Am J Clin Nutr 1989

"Sarcopenia is part of normal aging
and does not require a disease to occur,
although it is accellerated by chronic diseases."

Roubenoff et al, J Gerontol 2000

REPORT

Sarcopenia: European consensus on definition and diagnosis

Report of the European Working Group on Sarcopenia in Older People

ALFONSO J. CRUZ-JENTOFT[1], JEAN PIERRE BAEYENS[2], JÜRGEN M. BAUER[3], YVES BOIRIE[4], TOMMY CEDERHOLM[5], FRANCESCO LANDI[6], FINBARR C. MARTIN[7], JEAN-PIERRE MICHEL[8], YVES ROLLAND[9], STÉPHANE M. SCHNEIDER[10], EVA TOPINKOVÁ[11], MAURITS VANDEWOUDE[12], MAURO ZAMBONI[13]

[1]Servicio de Geriatría, Hospital Universitario Ramón y Cajal, Madrid, Spain
[2]AZ Damiaan Hospital, Oostende, Belgium
[3]Department of Geriatric Medicine, University of Erlangen-Nürnberg, Nürnberg, Germany
[4]Clermont Université, UFR Médecine, UMR 1019, F-63001 Clermont-Ferrand, France
[5]Institutionen för Folkhälso- och Vårdvetenskap/Klinisk Nutrition och Metabolism, Uppsala Universitet, Uppsala, Sweden
[6]Istituto di Medicina Interna e Geriatria, Università Cattolica del Sacro Cuore, Roma, Italy
[7]Department of Ageing and Health, Guys and St Thomas' NHS Foundation Trust, London, UK
[8]Département de Réhabilitation et Gériatrie, Hôpitaux Universitaires de Genève, Geneva, Switzerland
[9]Gérontopôle de Toulouse, Hospital La Grave-Casselardit, Toulouse, France
[10]Gastroentérologie et Nutrition Clinique, CHU de Nice, Université de Nice Sophia-Antipolis, Nice, France
[11]Geriatrická Klinika I Lékařská Fakulta, Univerzita Karlova v Praze, Prague, Czech Republic
[12]Department of Geriatrics, University of Antwerp, Ziekenhuisnetwerk Antwerpen (ZNA), Antwerp, Belgium
[13]Department of Biomedical and Surgical Sciences, Division of Geriatrics, University of Verona, Verona, Italy

Age and Ageing 2010; 39: 412–423

Criteria for the diagnosis of sarcopenia

Diagnosis is based on documentation of criterion 1 plus (criterion 2 or criterion 3).

1- Low muscle mass

2-Low muscle strength

3- Low physical performance

Cruz-Jentoft Alfonso J et al Sarcopenia: European Consensus on Definition and Diagnosis. Report of the European Working Group on Sarcopenia in Older People- Age and Ageing,2010 ; 1-12

OBJECTIVES:

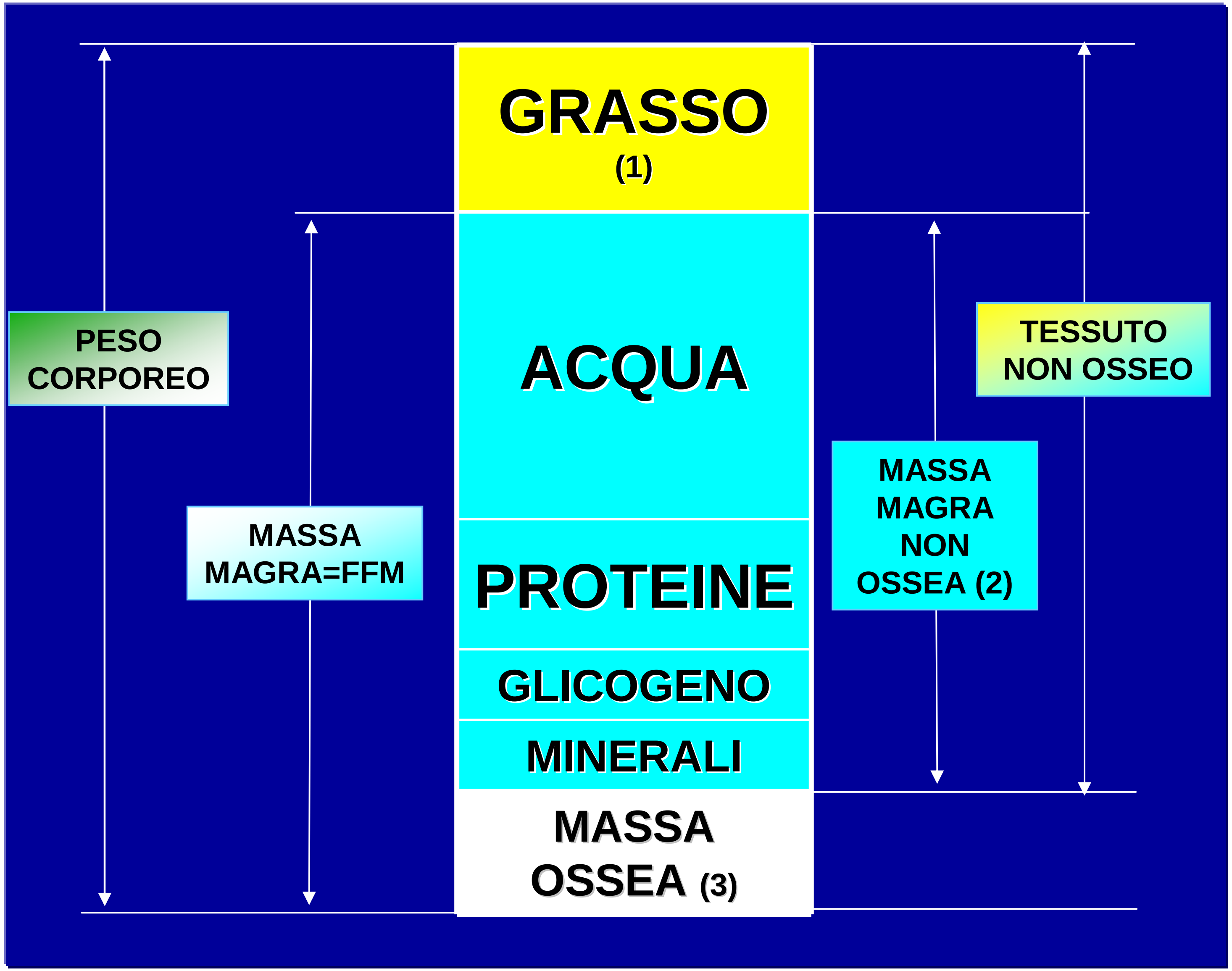
- Methods for muscle mass in vivo with muscle metabolites

- Nuclear techniques for quantifyng muscle mass in vivo

- Bioelettrical Impedance analysis and Air-displacement plethysmography system

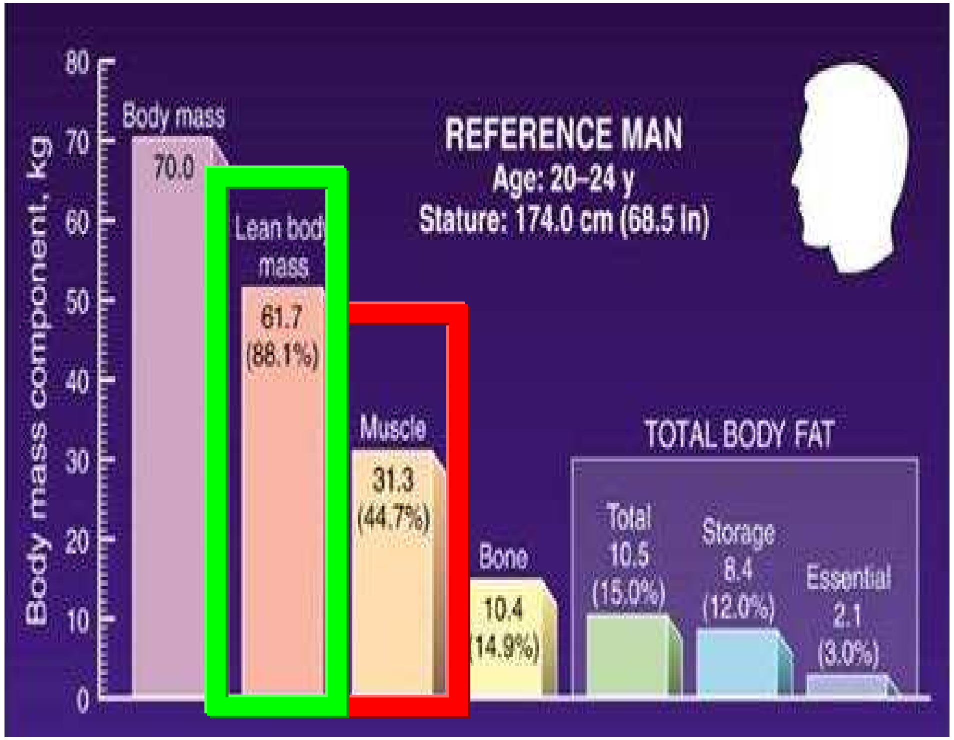
- Most used Radiographic methods for quantifyng muscle mass in vivo

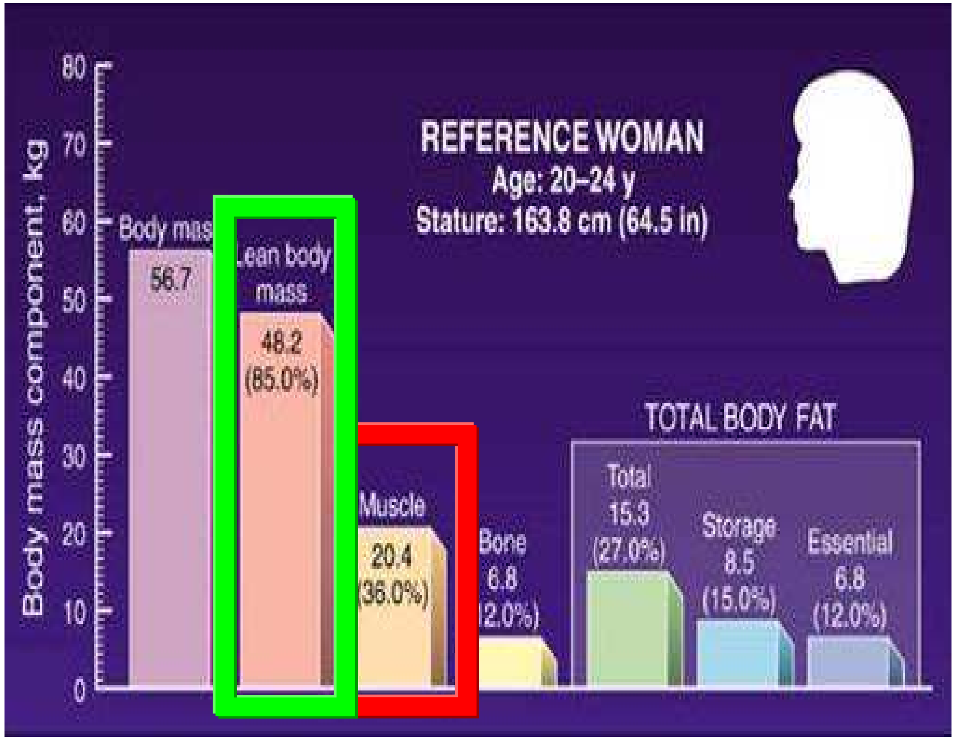
Modello a tre compartimenti, massa magra non ossea (2), massa grassa (1), massa ossea (3)



Adapted from Hoffman DJ et al. In press

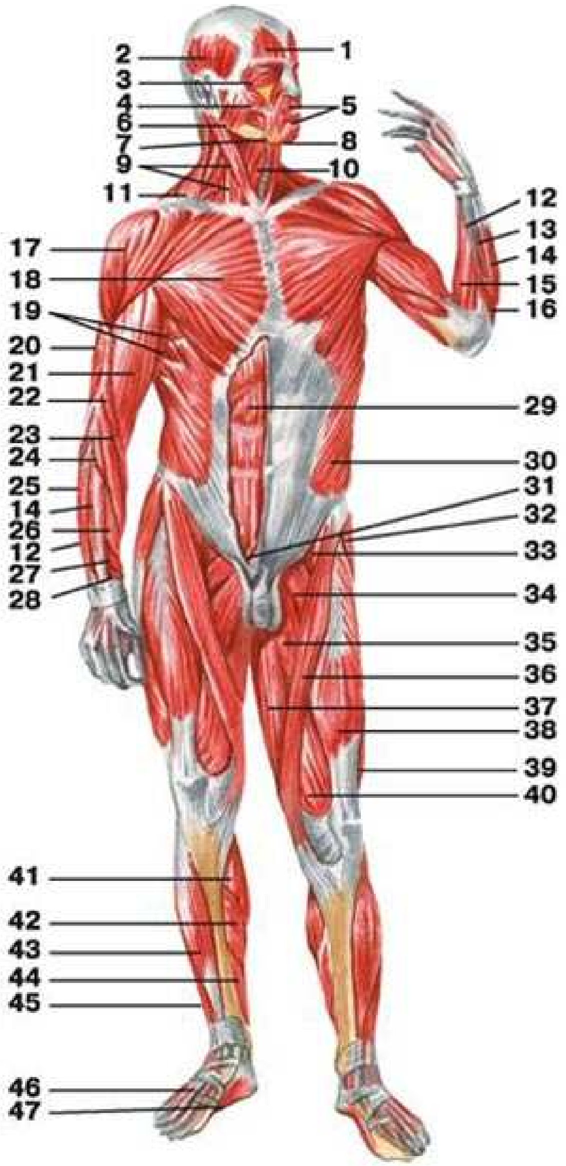
The reference man and woman





International Commision on Radiological protection (IRCP);
Report of the task group on reference man. Oxford Pergamon Press

Massa Muscolare

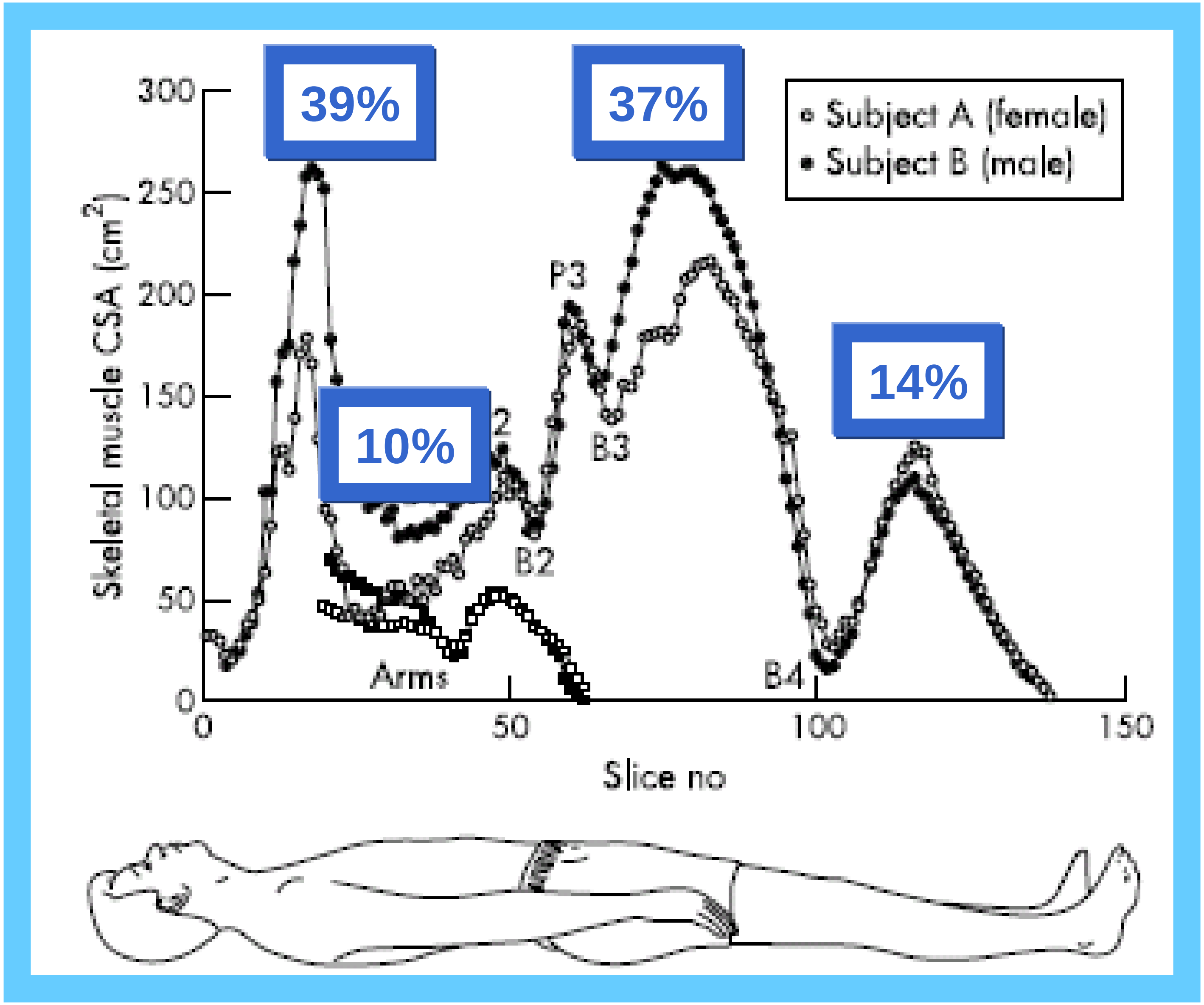


•comprende massa muscolare scheletrica (400 muscoli) + liscia + cardiaca

•soprattutto nelle gambe, meno in braccia, tronco e testa

Heymsfield SB; Human body composition, II edition Cap 14; 2005

Distribution of skeletal muscle cross sectional area (MRI CSA) measurements per slice (10 men and 10 women)



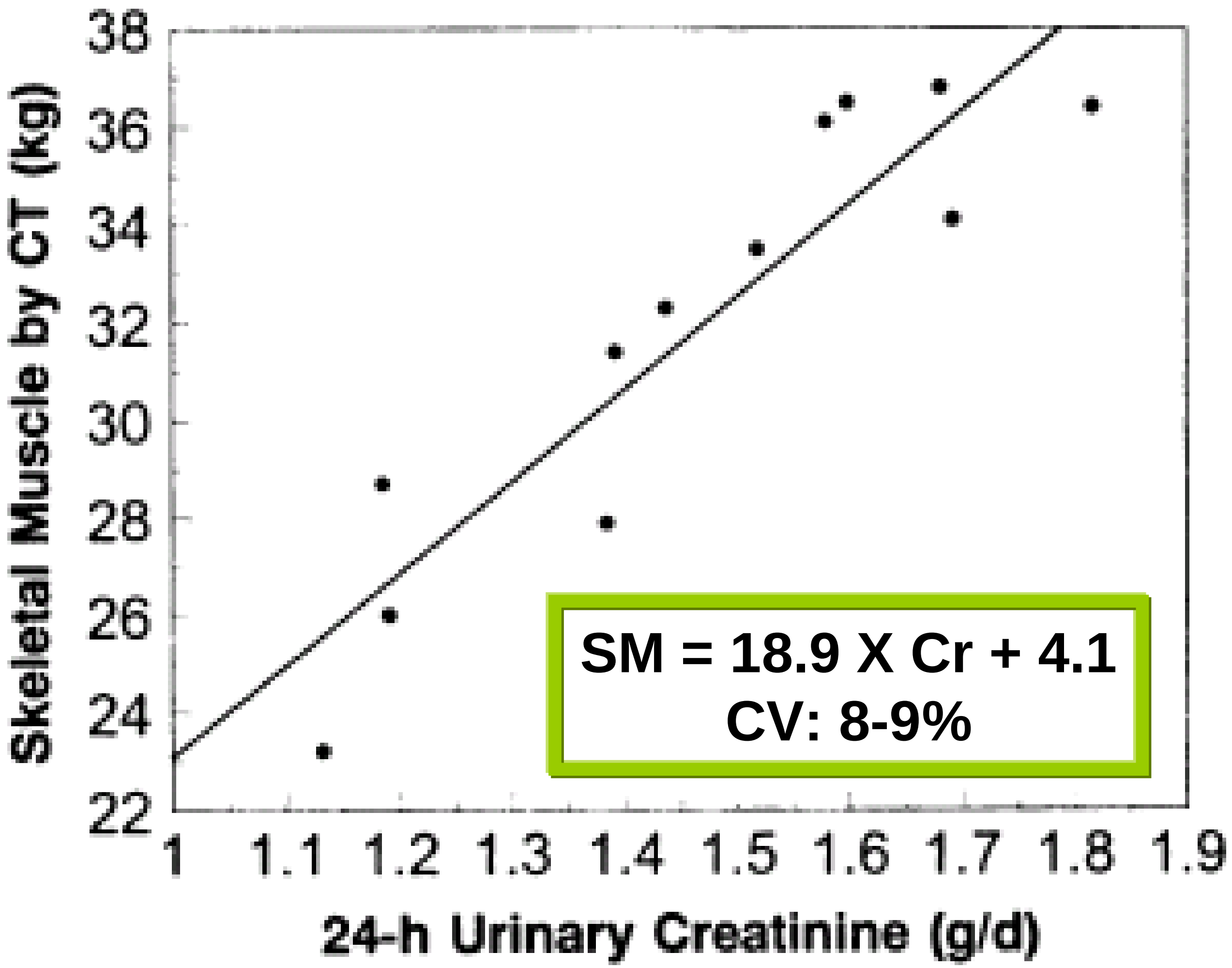
Abe T. Br J Sports Med 2003;37:436–440

methods for muscle mass in vivo with muscle metabolites

- Creatinina
- 3-Metilistidina

Relation between total-body skeletal muscle mass (SM) measured by computerized axial tomography (CT) and 24-h creatinine

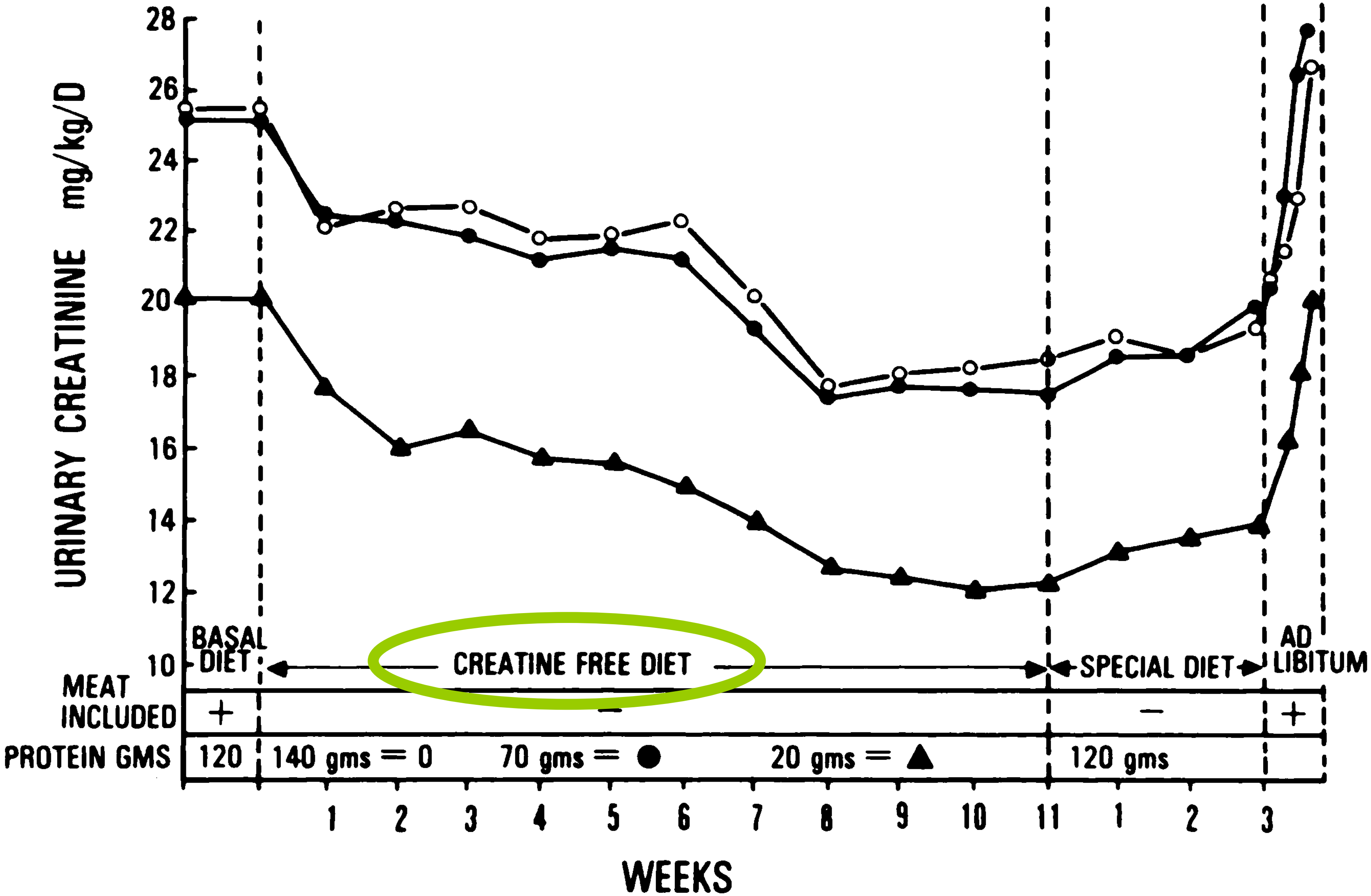
The American Journal of Clinical Nutrition



Wang Z et al. Am J Clin Nutr 1996;63:863-9

Influence of dietary protein and creatine on urinary creatinine excretion (n = 6).

The American Journal of Clinical Nutrition



Heymsfield et al. Am J Clin Nutr 1983;37:478-494

Creatinina

- È un precursore della creatina a livello epatico e renale (Borsook and Dubnoff 1947).
- 1 grammo di creatinina escreta corrisponde a 18-20 kg massa muscolare (Talbot 1938; Cheek 1968)

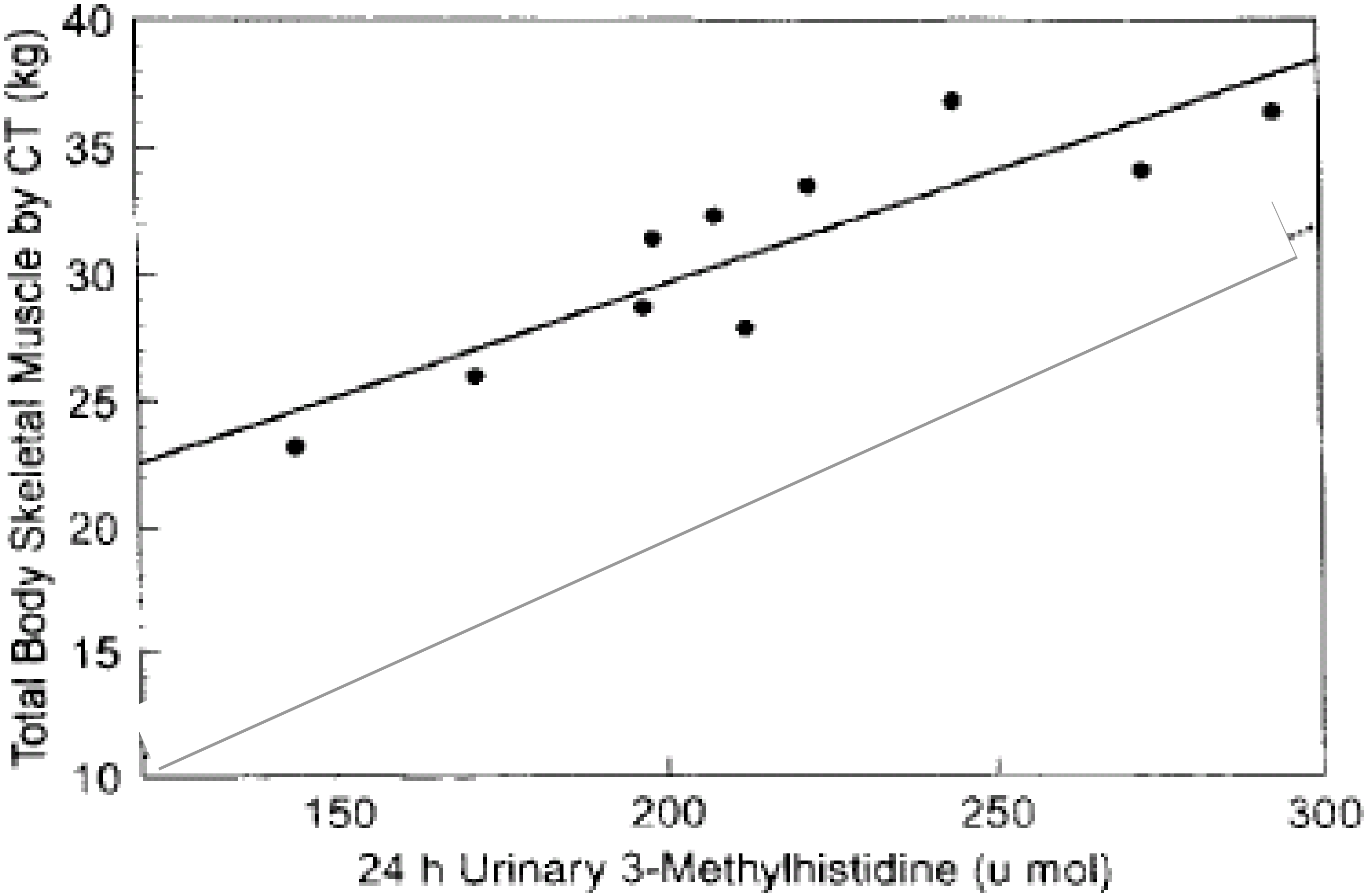
Limitationi:

- C'è un ampia variabilità individuale di escrezione di creatinina giornaliera in relazione in particolare all'introito alimentare.
- Altri fattori posso alterare la misurazione: età, sesso, livello di attività fisica e profilo metabolico.

3-Metilistidina

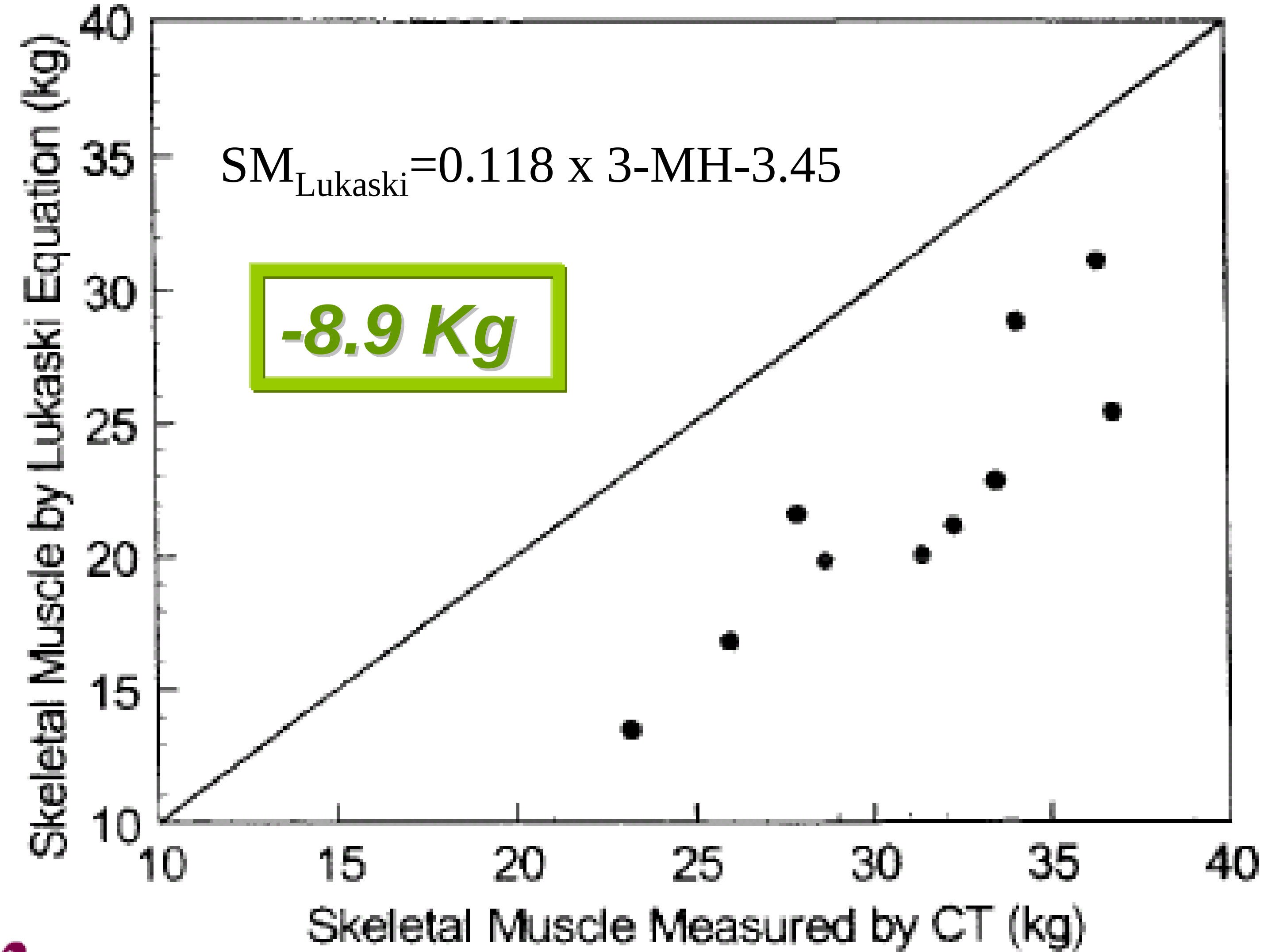
- 3-Metilistidina (3-MH) è un aminoacido che è misura del catabolismo delle proteine muscolari. La sua concentrazione nel muscolo umano è relativamente costante tra i 4 e i 65 anni, ma cala con la riduzione dell’escrezione urinaria legata all’età.

Total body skeletal muscle mass (SM. in kilograms) measured by computerized axial tomography (CT) (ordinate) vs 24-hour urinary 3-methylhistidine excretion (3-MH, W micromoles)(n = 10)



Wang Z et al. JPEN J Parenter Enteral Nutr 1998 22: 82

Total body skeletal muscle mass measured by the Lukaski equation (SM , in kilograms) on the ordinate vs total body skeletal muscle mass measured by multiscan computerized axial tomography (CT) method



Wang Z et al. JPEN J Parenter Enteral Nutr 1998 22: 82

aspen
American Society for Parenteral and Enteral Nutrition

3-MH

Limitazioni:

- L’uso di 3-MH come marker di massa muscolare è stata criticata in considerazione della potenziale influenza del turnover di proteine non muscolari (Rennie and Millward 1983).
- È stato evidenziato contributo di proteine provenienti da cute e tratto gastrointestinale rispetto all’escrezione urinaria di 3MH.
- La misurazione richiede dieta priva di carne per permettere l’eliminazione di quota endogena di 3-MH.

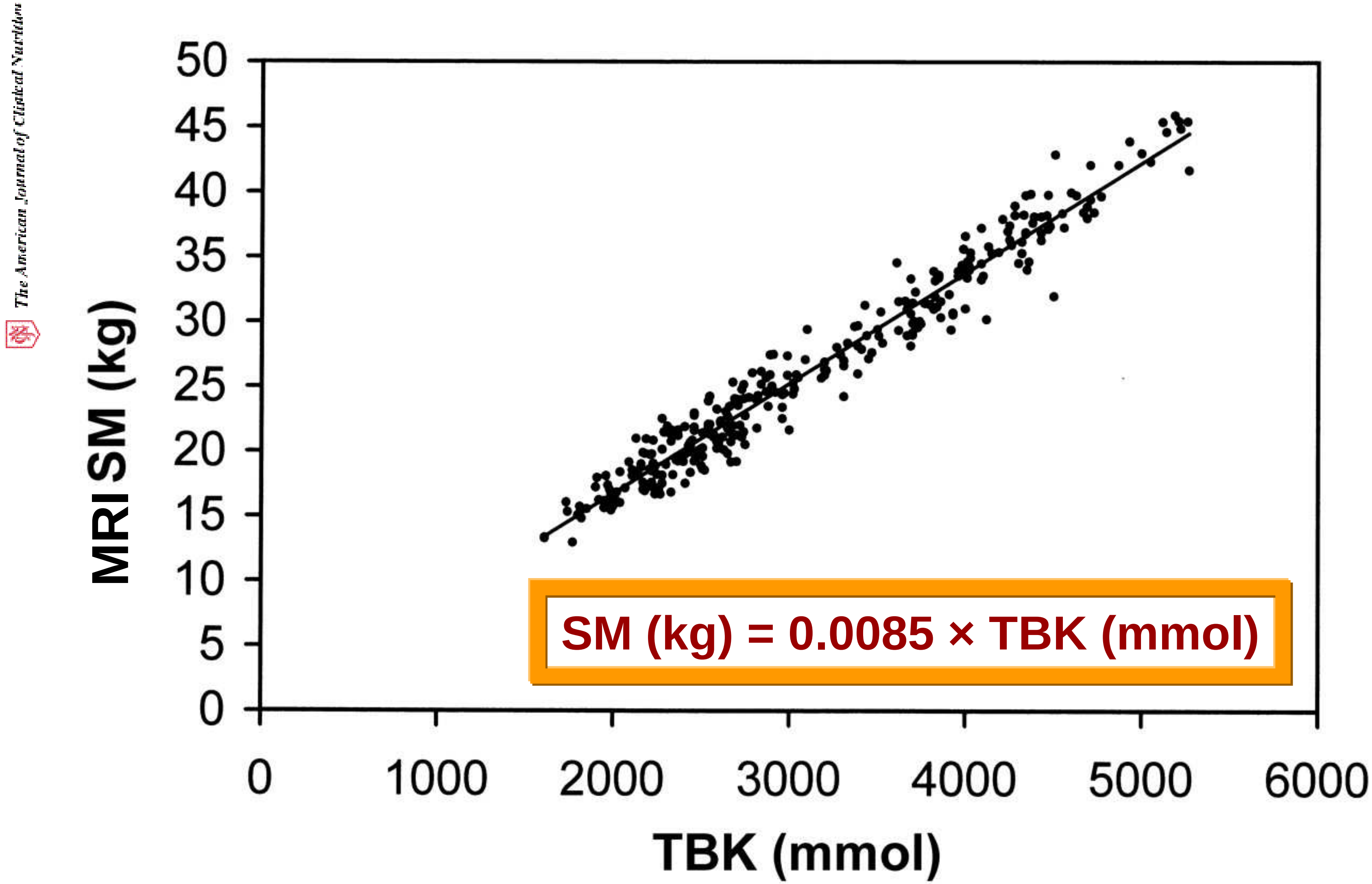
Nuclear techniques for quantifyng muscle mass in vivo

- Total body potassium

K^{40} - Whole Body Counting

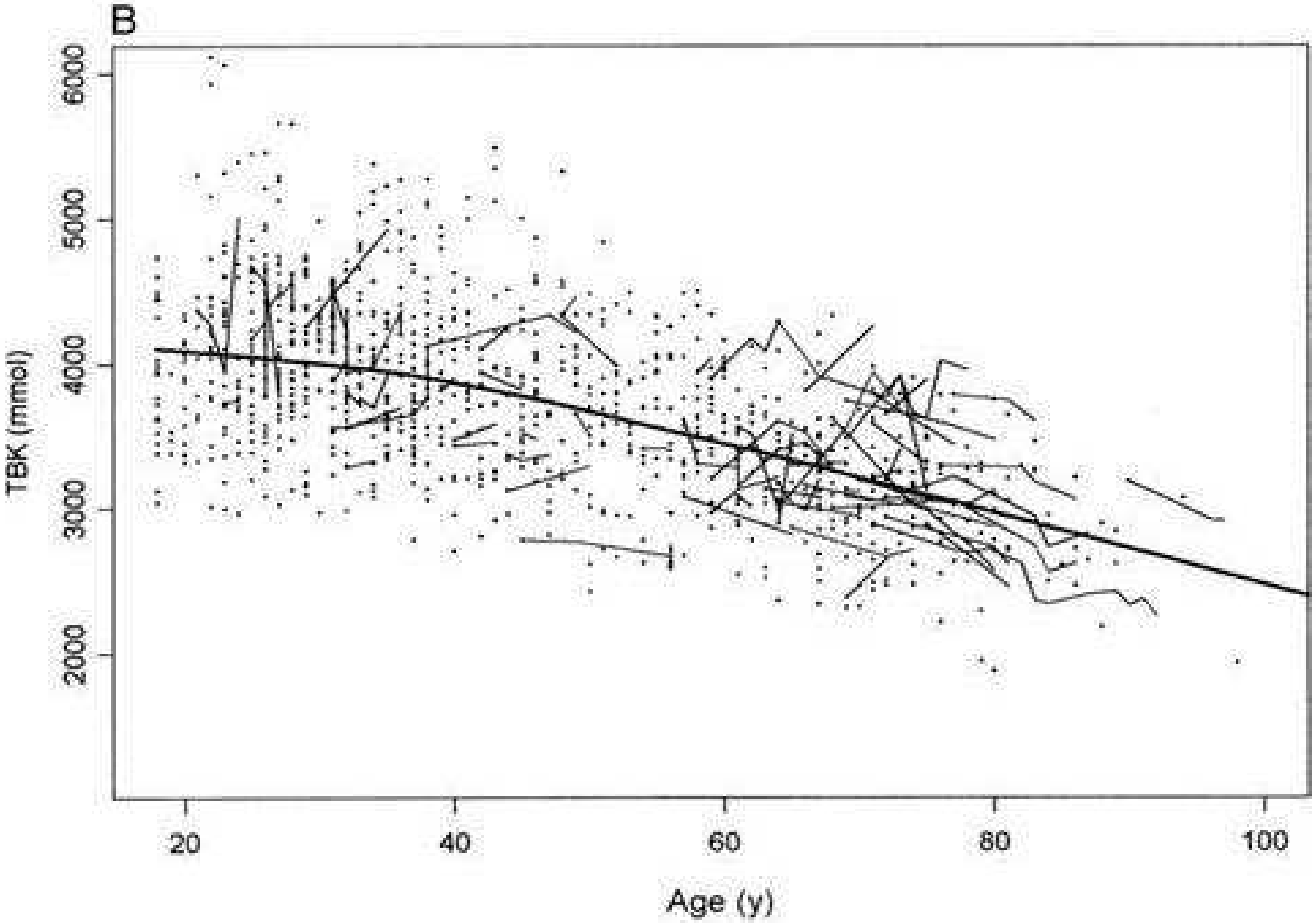
- K^{40} emette radiazione gamma
- Usando contatori total body la quantità di radiazioni emesse può essere determinata
- Assunzioni:
  - frazione constante di K^{40} nel potassio corporeo (0.0118%)
  - frazione costante di potassio nella massa non grassa

Total-body skeletal muscle (SM) measured by magnetic resonance imaging plotted against total body potassium (TBK) measured by whole-body 40K counting.



Wang Z et al. Am J Clin Nutr 2003;77:76-82

Changes in total body potassium (TBK) with age in 973 men (1200 observations).



He Q et al. Am J Clin Nutr 2003;78:72-77

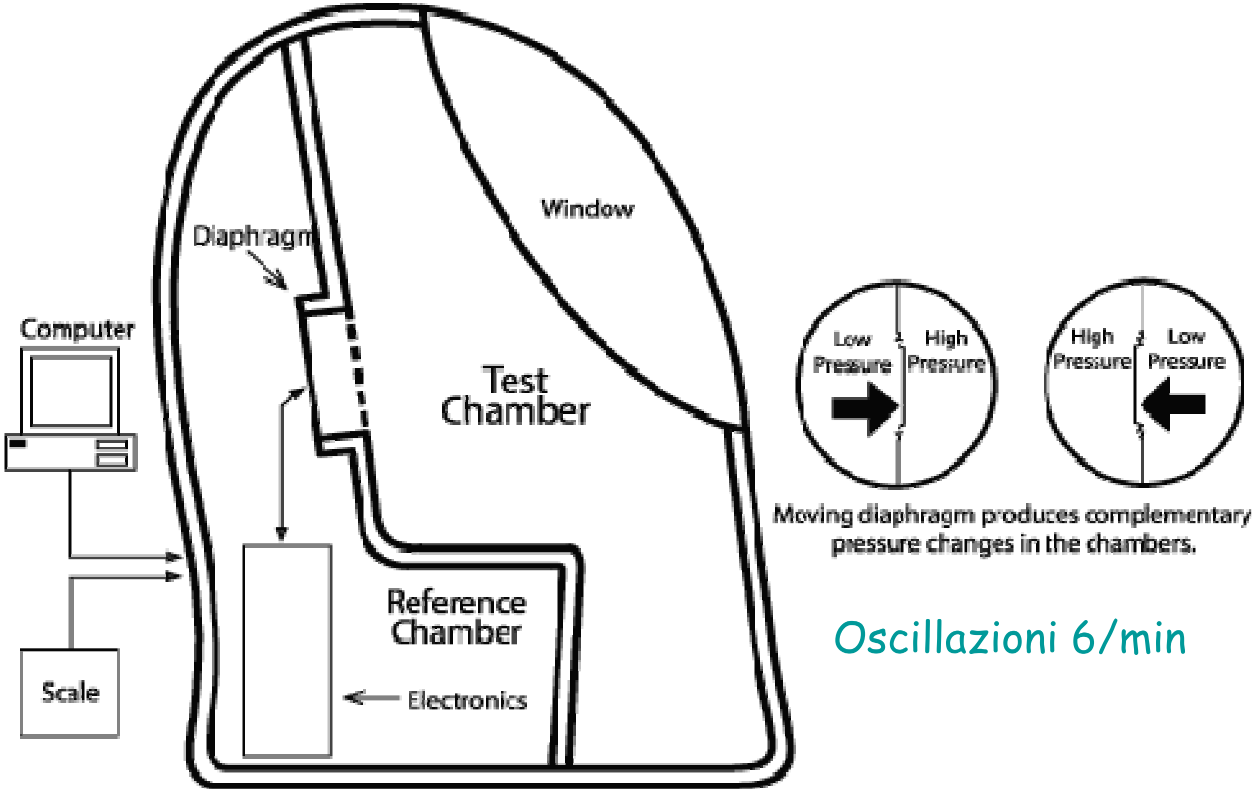
K^{40} - Whole Body Counting

- Tecnica non invasiva non richiede digiuno
- Dai 20 ai 40 minuti ad esame.
- Precisione:5% per gli adulti. 8-12% nei bambini.
- 180 centri al mondo (la metà negli USA).
- Costo dipende da età della popolazione esaminata
- Costo dell'esame nell'adulto $10,000-15,000.
- Costo di camera schermata dove eseguire l'esame è di $80,000.

Most used methods for quantifyng muscle mass in vivo

- Air-displacement plethysmography system
- Bioelettrical Impedance analysis

Air-Displacement Plethysmography (BOD POD)



Oscillazioni 6/min

Pricipio fisico: legge dei gas di Boyle e Mariotte
A temperatura costante il volume (V) occupato da una determinata massa è inversamente proporzionale alla pressione cui quella massa è sottoposta

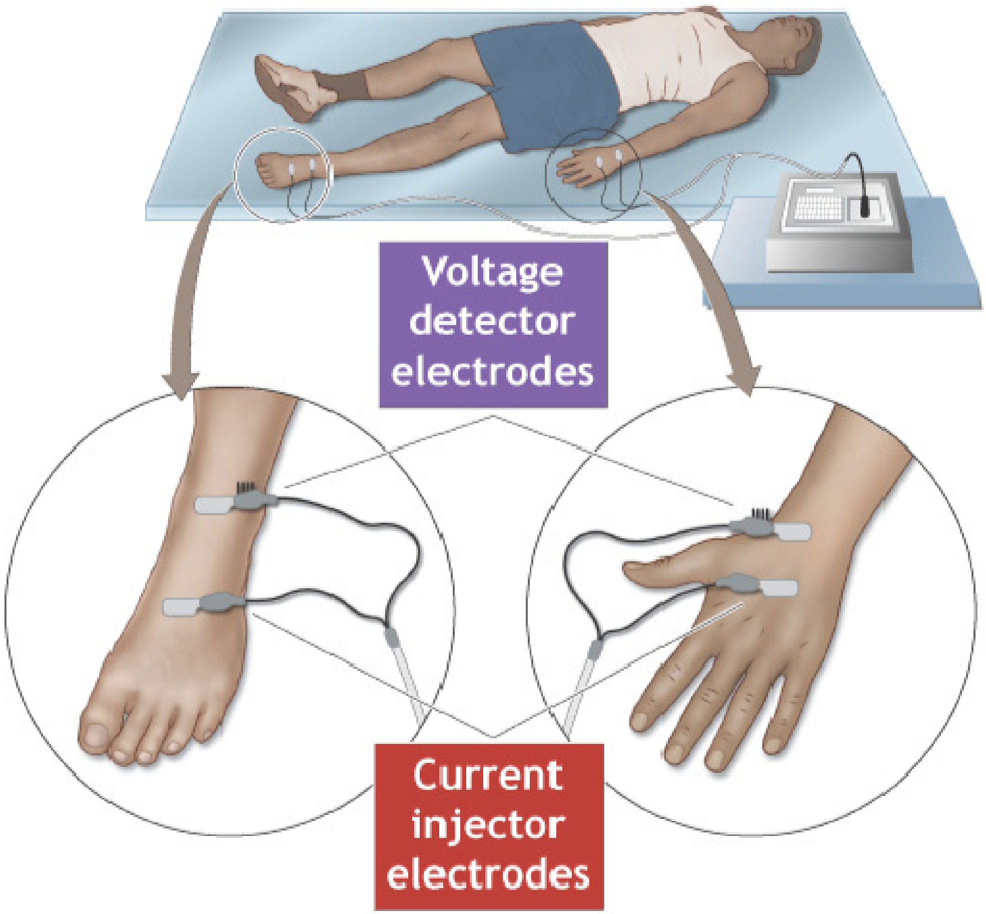
Calcola il volume, quindi il PS; per ottenere la massa adiposa si usa la Formula di SIRI: Massa adiposa% = (4950/densità-4,5)100
Dove: densità FM = 900 kg/m^3; densità FFM= 1100 kg/m^3

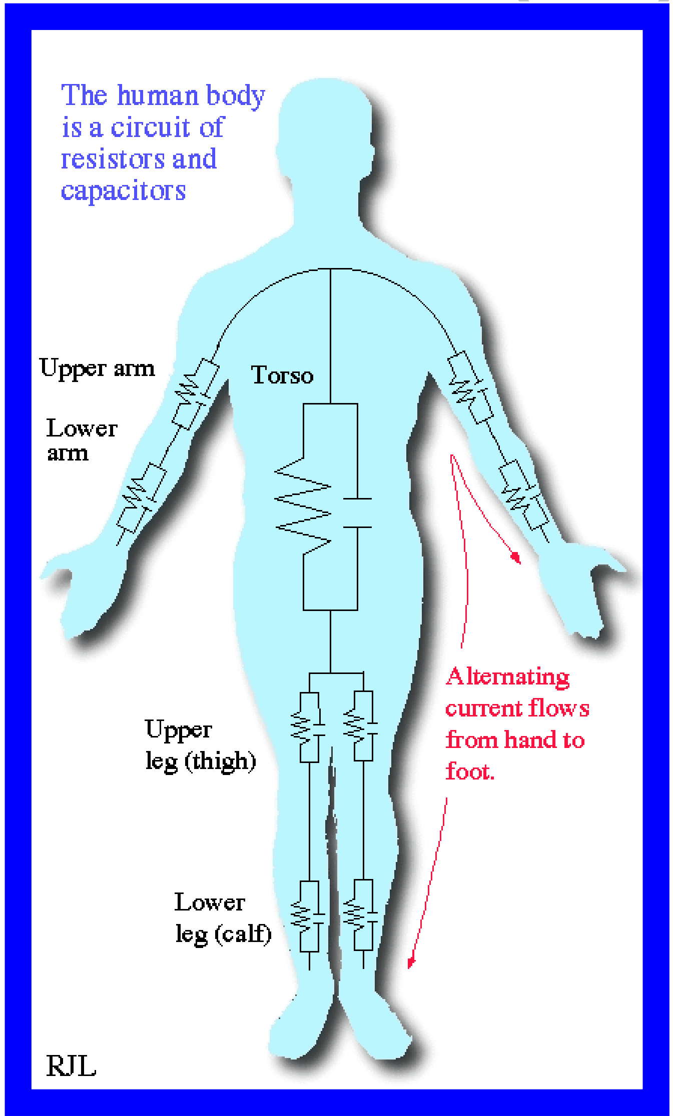
Air-Displacement Plethysmography (BOD POD)

Vantaggi e svantaggi

- Range di errore è dell' 2% simile alla bilancia idrostatica
- Richiede 5 minuti
- Può ospitare soggetti fino ai 400 kg
- È formula dipendente
- Scarsa trasportabilità ed estremamente costosa

Bioelectrical impedance assessment (BIA)





- Sviluppato negli anni 60
- Una corrente a basso voltaggio (50 kHz 800 µA max) viene fatta passare attraverso il corpo del paziente

Janssen I,
J Appl Physiol 2001

BIOIMPEDENZIOMETRIA: modello bicompartimentale

Consente di stimare l' Acqua Corporea Totale

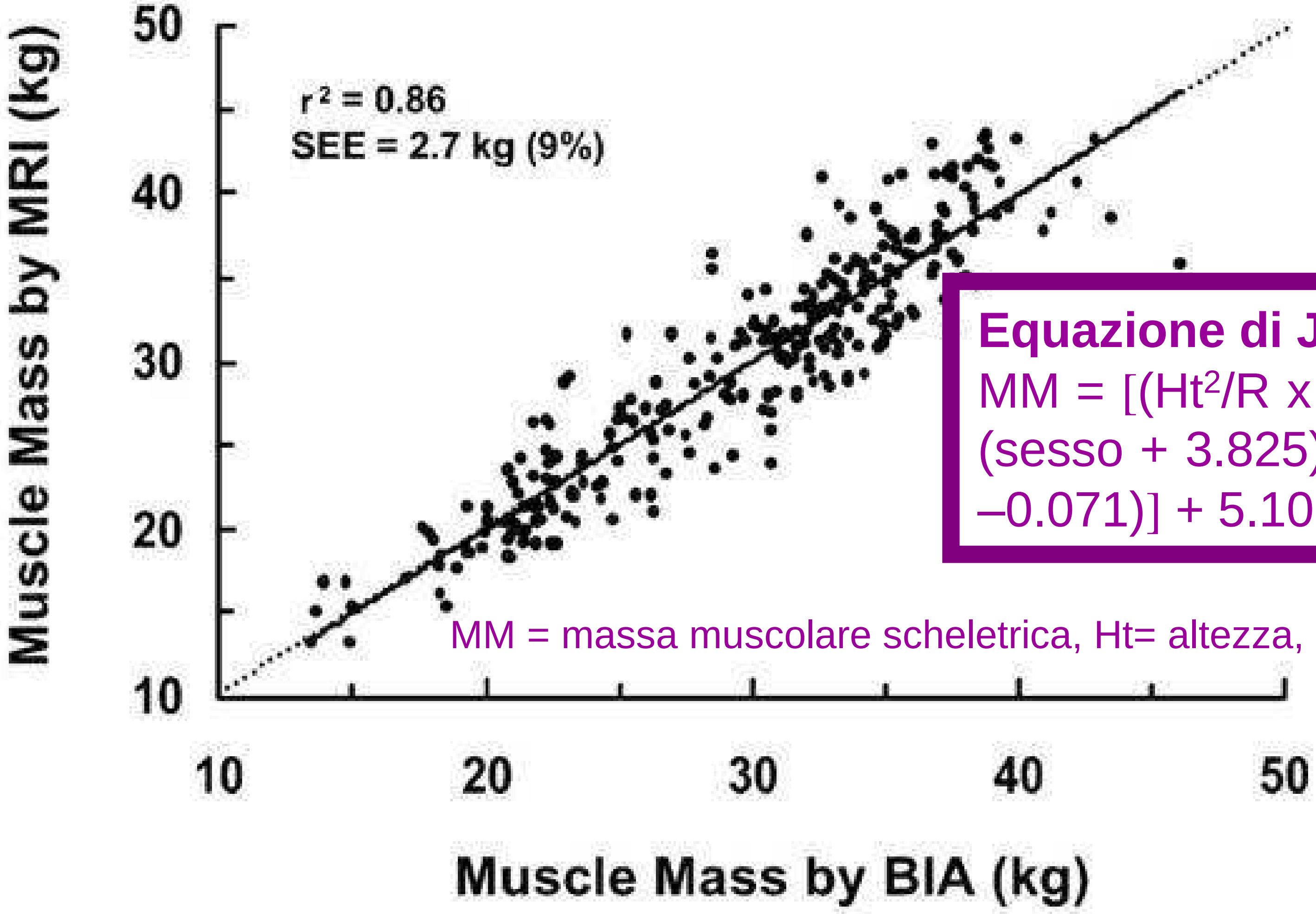
Corrente → Organismo vivente

Fluidi extra-cellulari = Conduttori	Membrane cellulari = Condensatori
↓	↓
Attraversandoli la corrente incontra una:	La forza con cui si oppongono al passaggio della corrente:
↓	↓
Resistenza	**Reattanza**

Resistenza è maggiore nel tessuto grasso (14-22% acqua)

Conduttanza è maggiore nel tessuto magro (73% acqua) che quindi offrirà minore resistenza

Correlation of skeletal muscle mass as evaluted on the basis of the regression equation derived and measured with MRI (388 men and women, aged 18–86 yr)



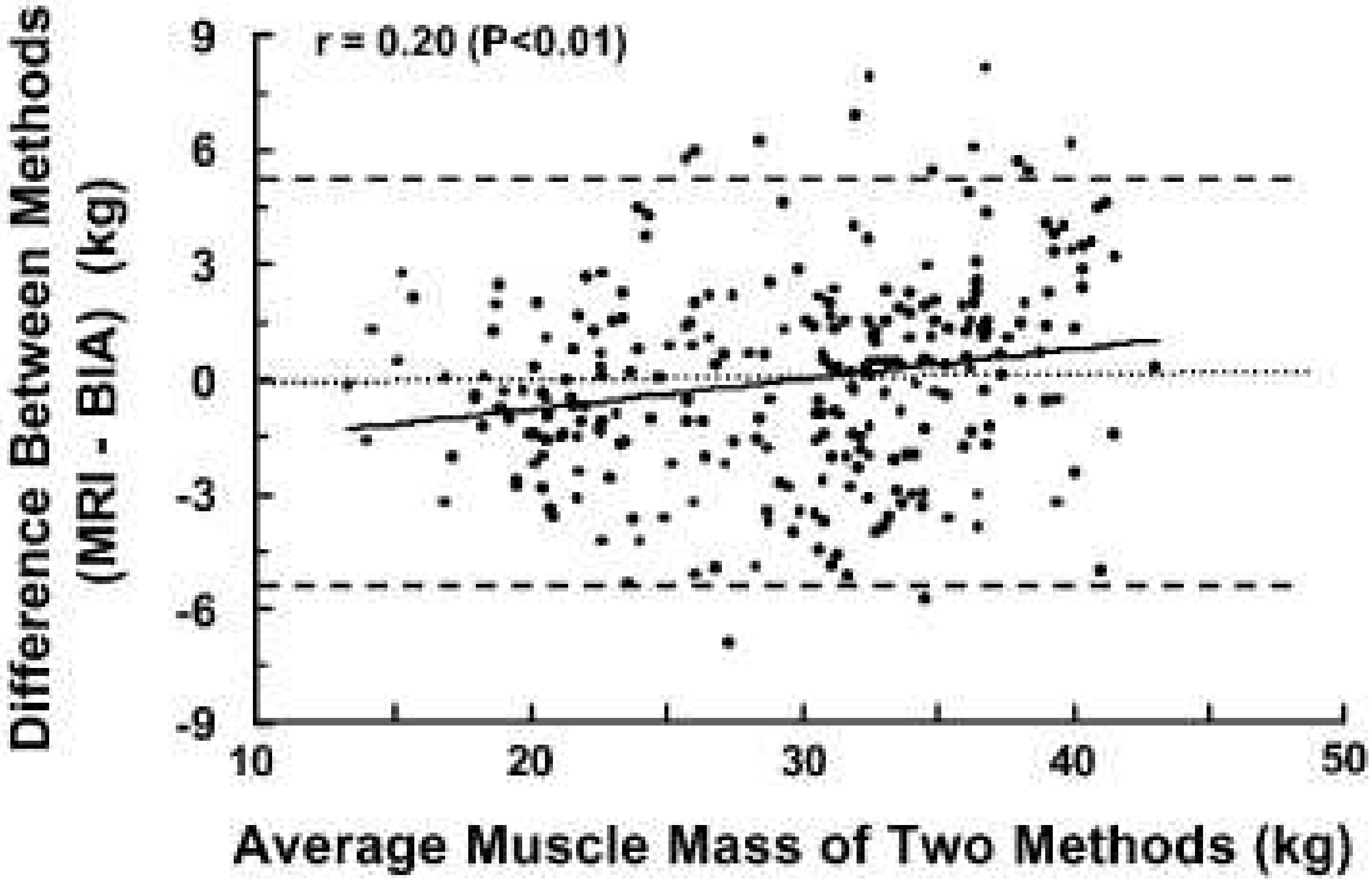
Equazione di Janssen:
$MM = [(Ht^2/R \times 0.401) + (sesso + 3.825) + (età \times -0.071)] + 5.102$

MM = massa muscolare scheletrica, Ht= altezza, R= resistenza

Janssen I et al. J Appl Physiol 2000;89:465-471

Journal of Applied Physiology

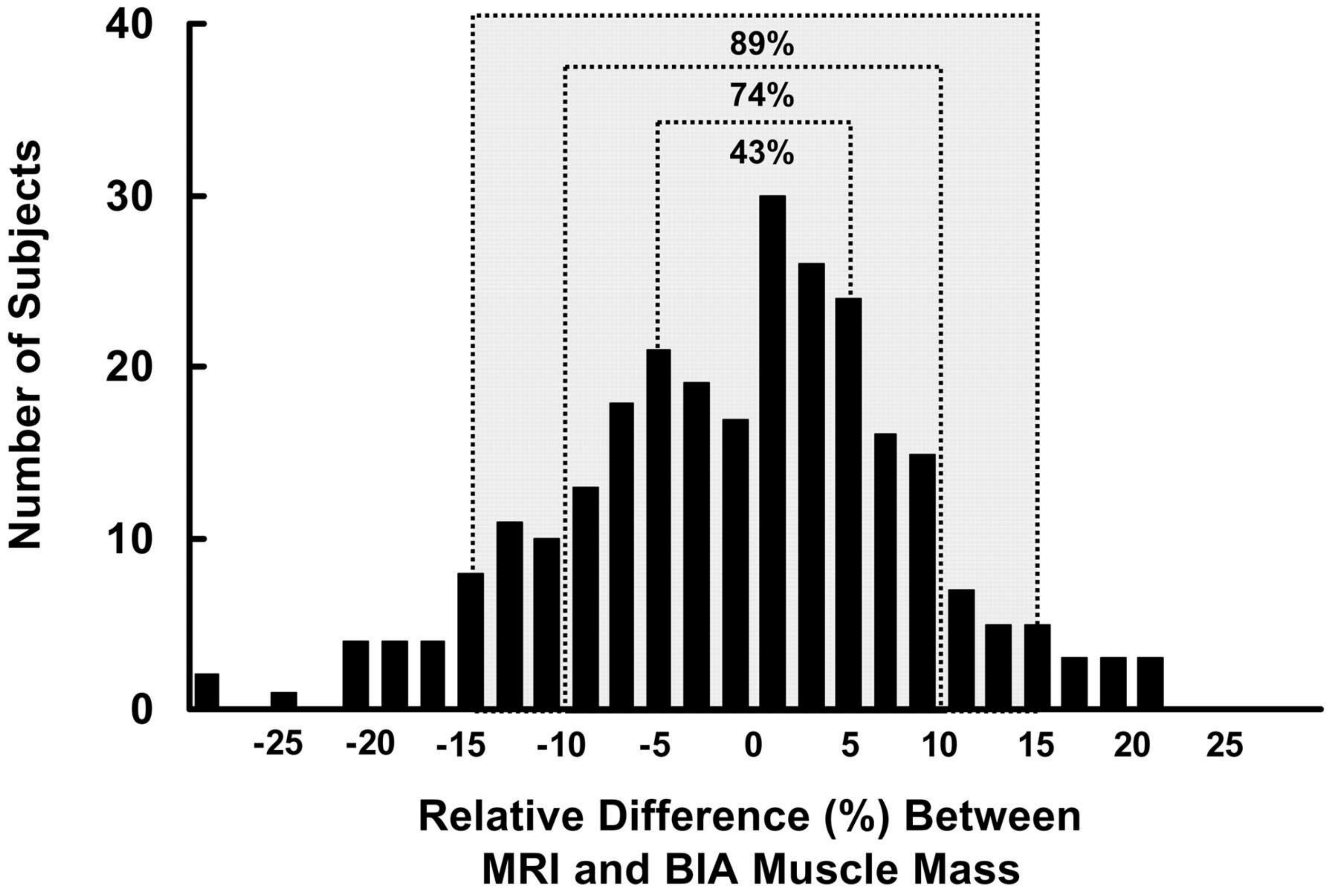
Difference between skeletal muscle mass measured by MRI and BIA vs. average skeletal muscle mass measured by the 2 methods for the Caucasian subjects.



Janssen I et al. J Appl Physiol 2000;89:465-471

Journal of Applied Physiology

Distribution of relative differences between MRI-measured and BIA-predicted skeletal muscle mass within the Caucasian subjects.



Janssen I et al. J Appl Physiol 2000;89:465-471

Journal of Applied Physiology

Vantaggi della BIA

- non è richiede molta esperienza ed abilità
- strumentazione è portatile
- investimento e spese di manutenzione relativamente basse
- misurazione sul paziente è indolore e rapida

Svantaggi della BIA

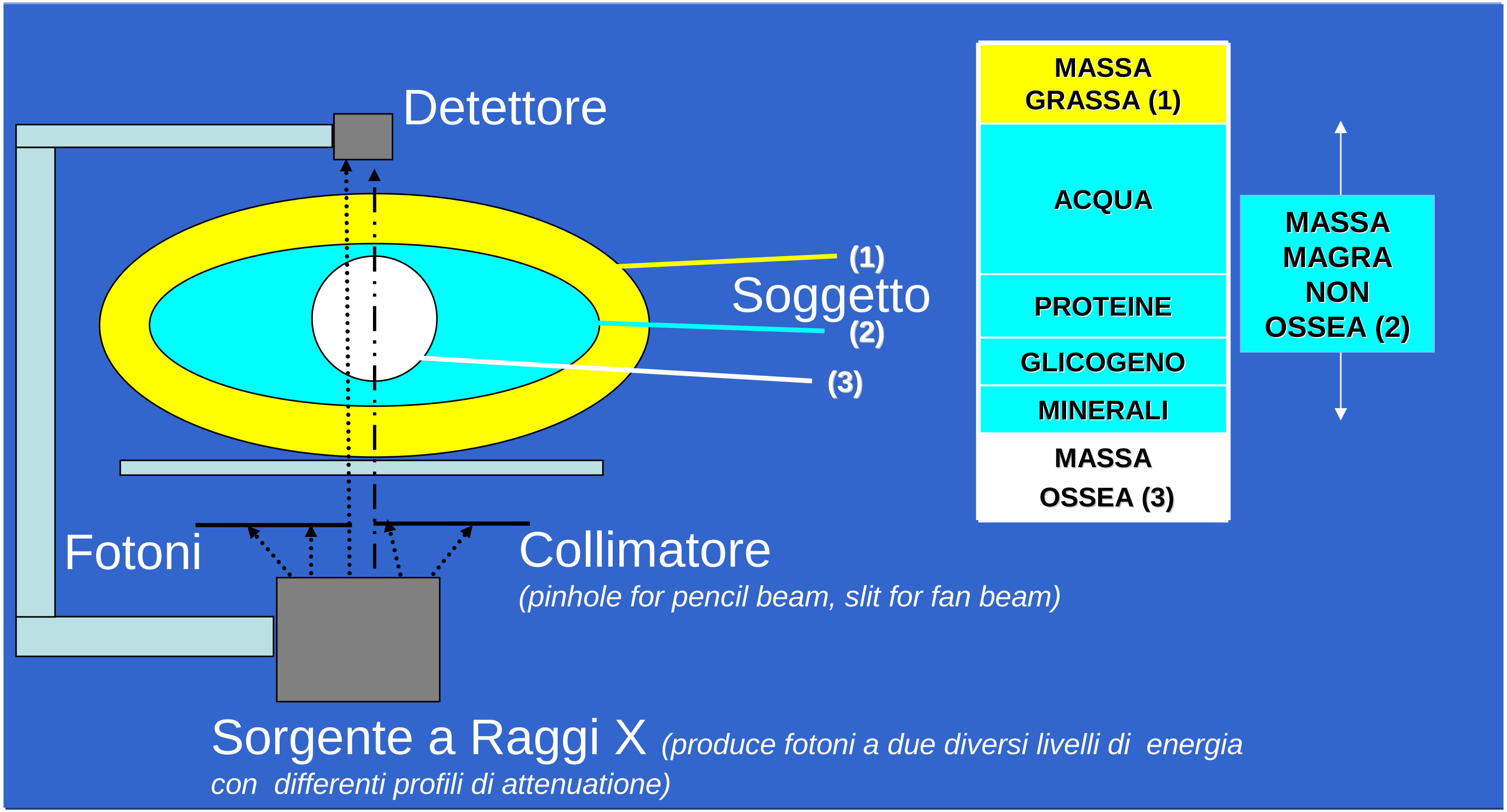
- altamente influenzata dallo stato di idratazione del soggetto
- influenzata da temperatura ambientale
- Non permette di distinguere massa magra appendicolare
- **è formula dipendente**

Most used Radiographic methods for quantifyng muscle mass in vivo

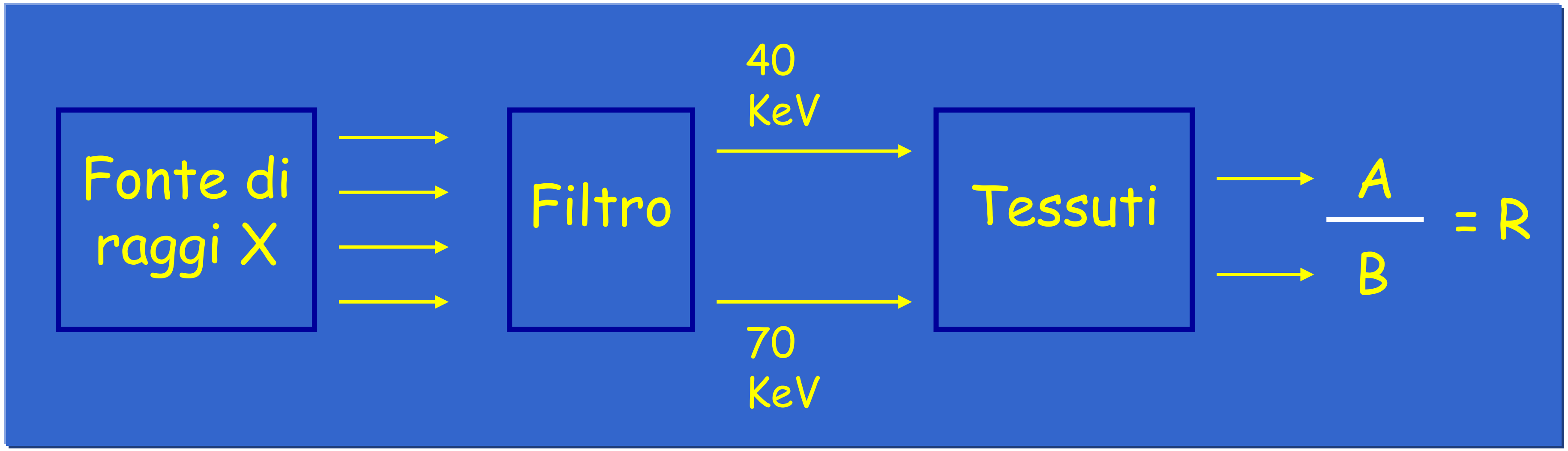
- Dual Energy X-ray absorptiometry
- Computed Tomography
- Magnetic Resonance

Dual energy X-Ray absorptiometry DXA

Dual Energy X-ray Absorptiometry

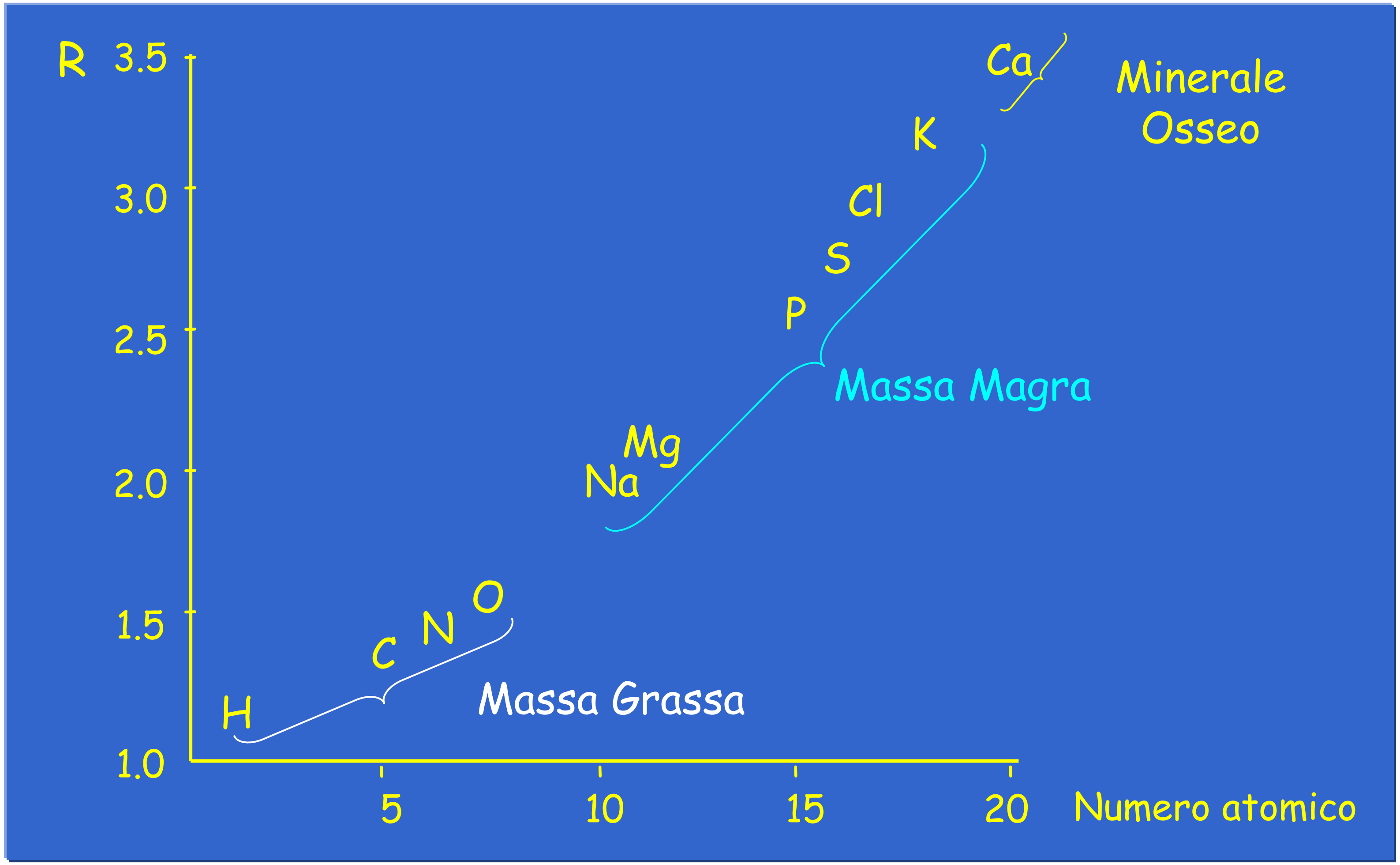


Dual-energy X-ray Absorpiometry (DXA)



dove R rapporto fra il valore di attenuazione subito dal raggio a più bassa energia (A) e quello subito dal raggio a energia più elevata (B). Tale rapporto risulta tanto più elevato quanto più alto è il numero atomico della sostanza attraversata.

Dual-energy X-ray Absorpiometry (DXA)

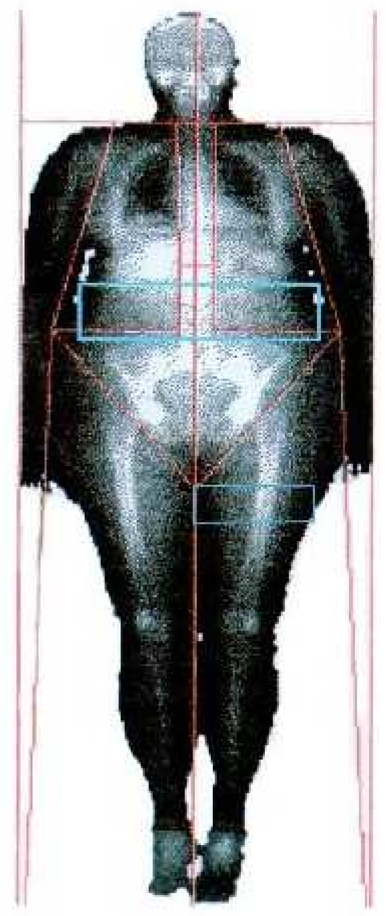


I trigliceridi (= massa grassa), essendo costituiti da H, C e O, hanno il minimo valore di R; i liquidi intra ed extra-cellulari (=massa magra), contenenti Na, K e Cl, hanno valori di R intermedi. L'osso minerale e i cristalli di idrossiapatite hanno i valori più elevati di R.

TOTAL BODY Dual-energy X-ray Absorpiometry (DXA)

Total body. Women
59 kg, BMI 22.6

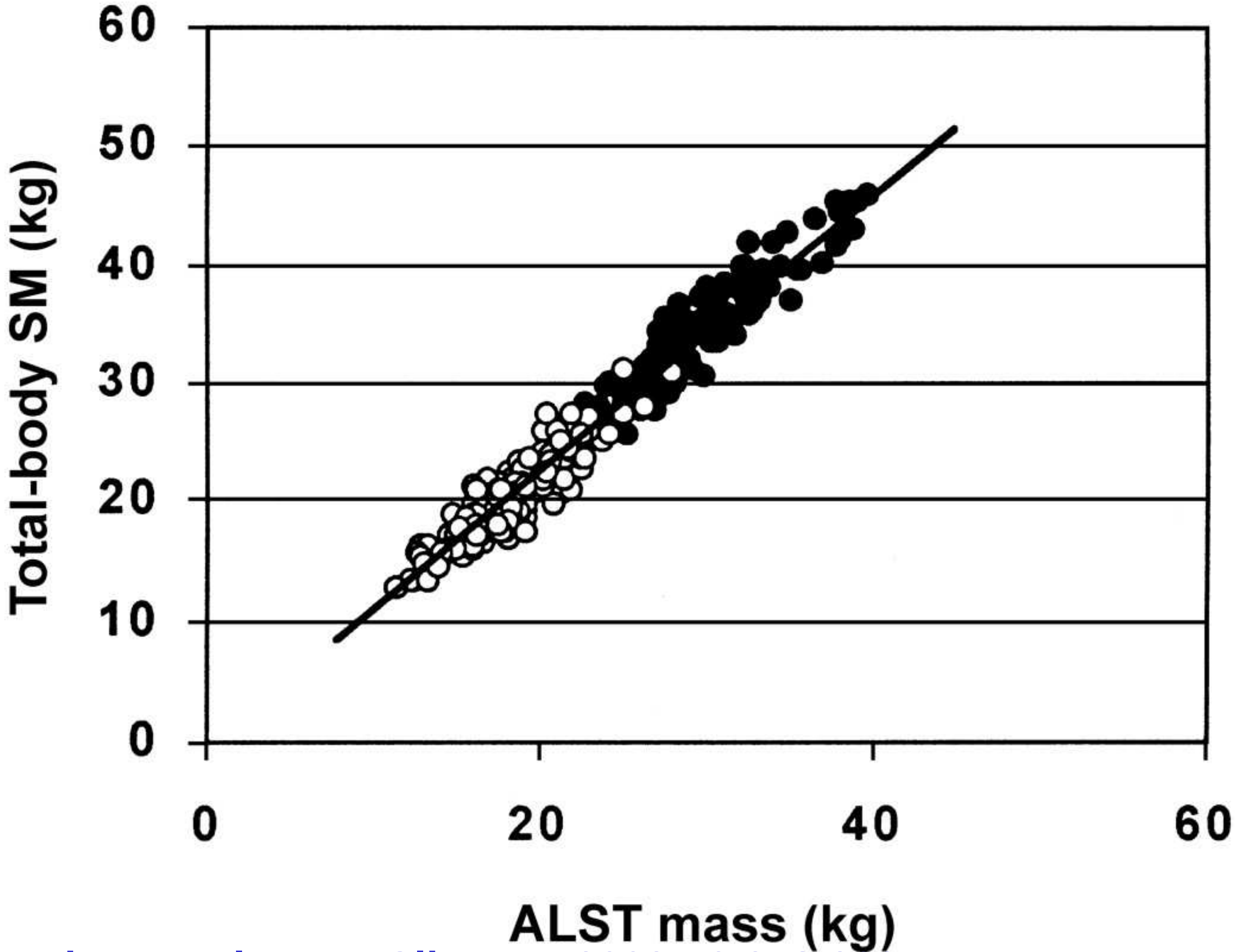
Total body. Women
kg 104, BMI 34



Brownbill RA and Ilich JZ, 2004

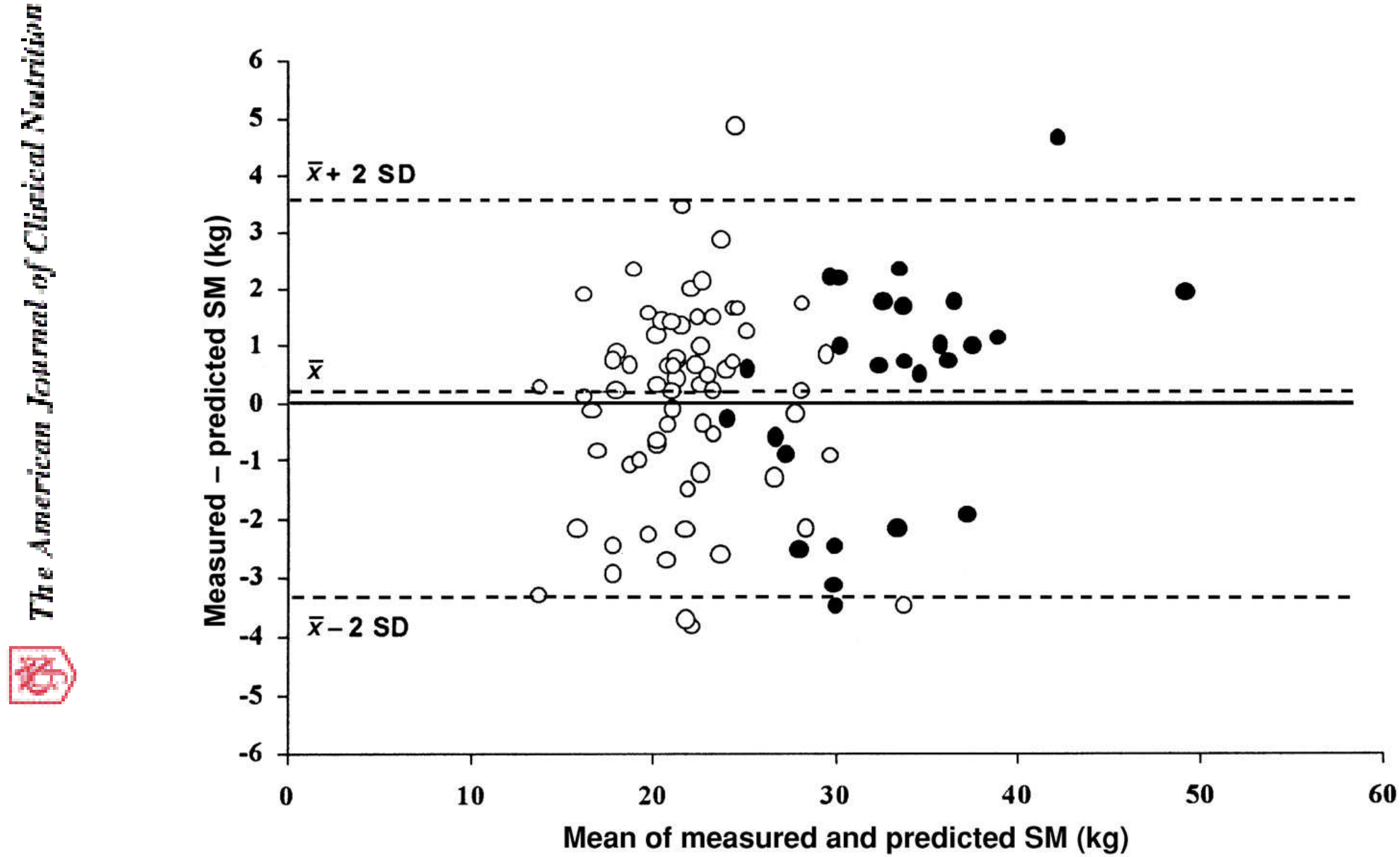
Correlation between total-body skeletal muscle (SM) mass estimated by *magnetic resonance imaging* and appendicular lean soft tissue (ALST) mass estimated by *dual-energy X-ray absorptiometry* in men (•) and women (○) in the model-development group.

The American Journal of Clinical Nutrition



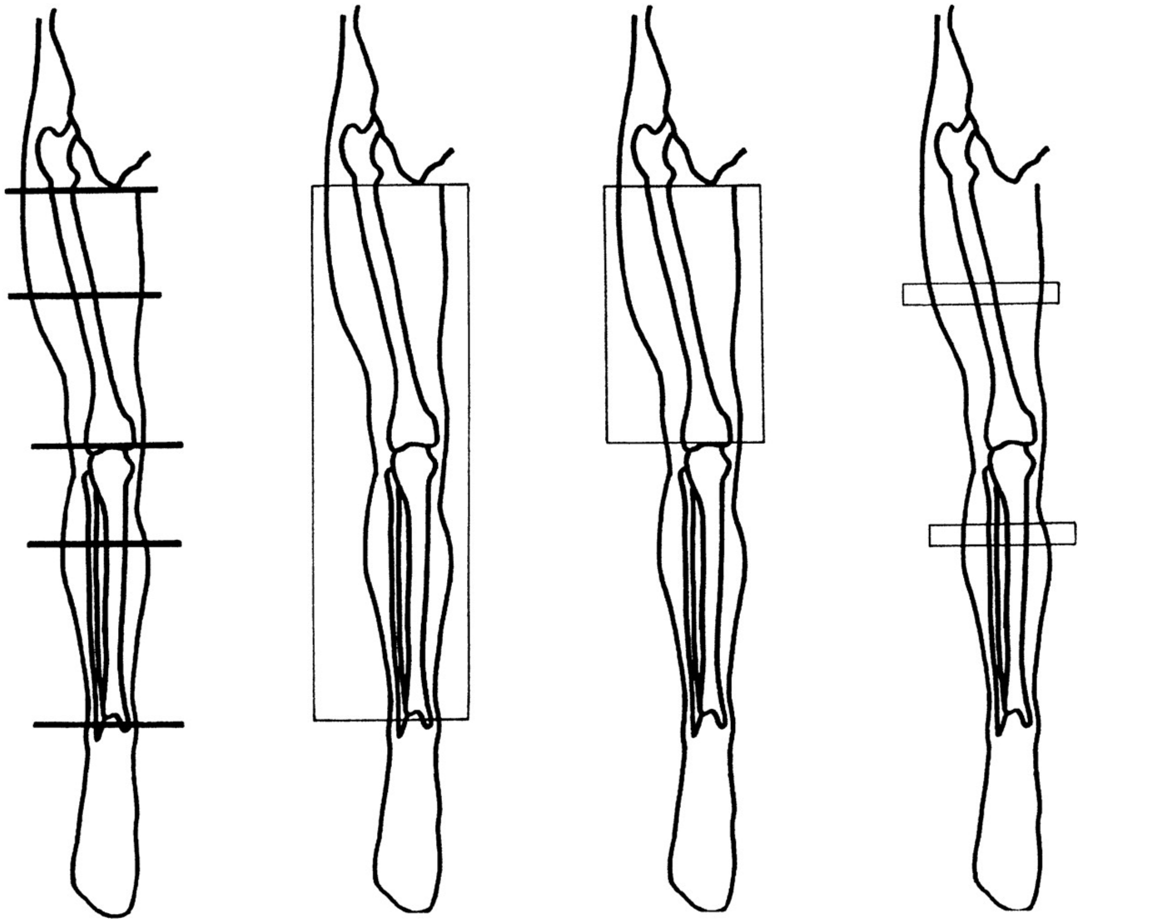
Kim J et al. Am J Clin Nutr 2002;76:378-383

Correlation between the difference in measured and predicted total-body skeletal muscle (SM) mass and the mean of measured and predicted SM mass in men (•) and women (○) in the model-validation group.



Kim J et al. Am J Clin Nutr 2002;76:378-383

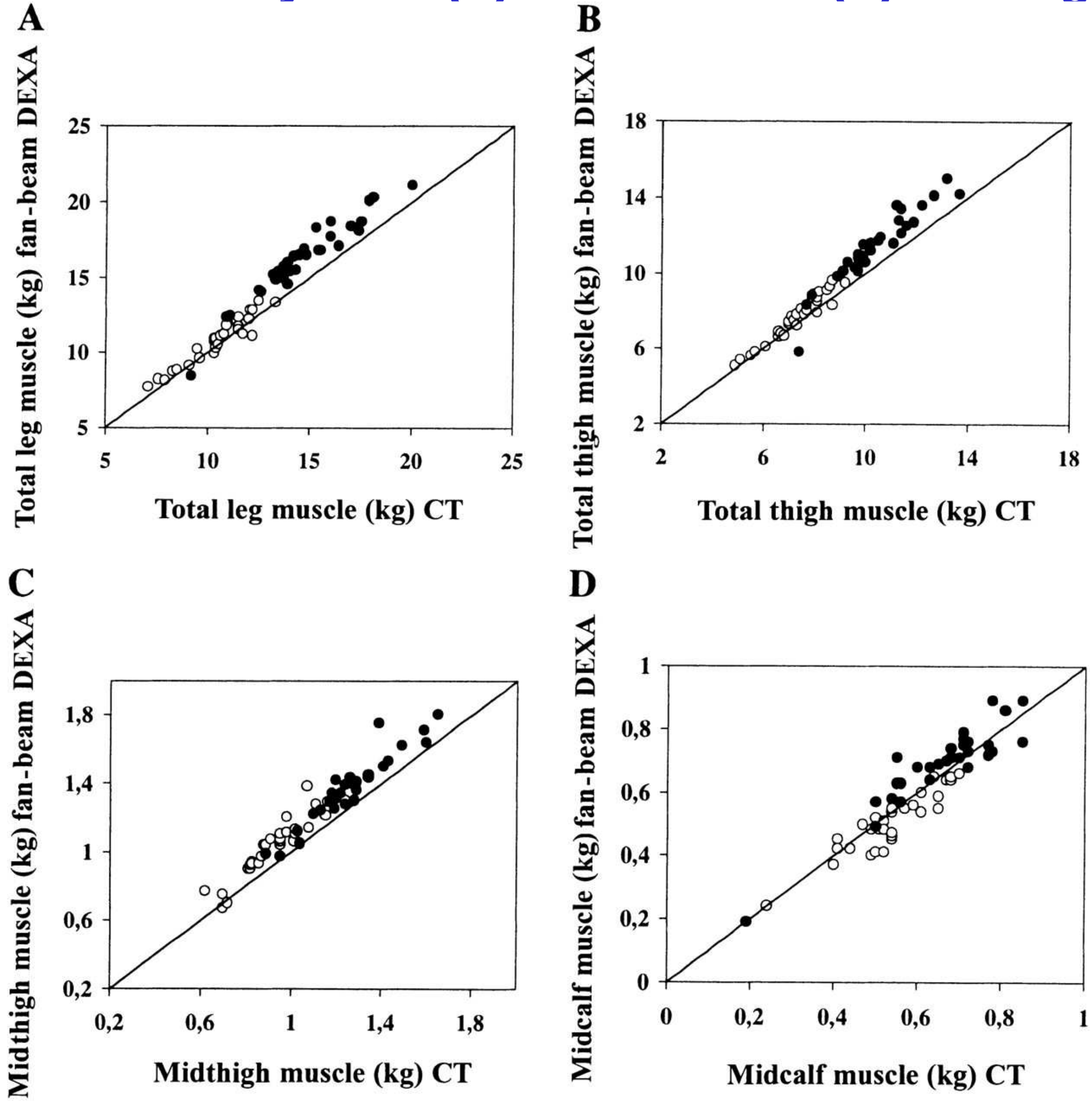
Location of computed tomography (CT) slices and areas used in dual-energy X-ray absorptiometry (DEXA) scan analysis to measure leg skeletal muscle mass.



Visser M et al. J Appl Physiol 1999;87:1513-1520

Journal of Applied Physiology

A–D: relationship between muscle mass by fan-beam DEXA and by multislice CT in elderly men (●) and women (○) at 4 leg regions.



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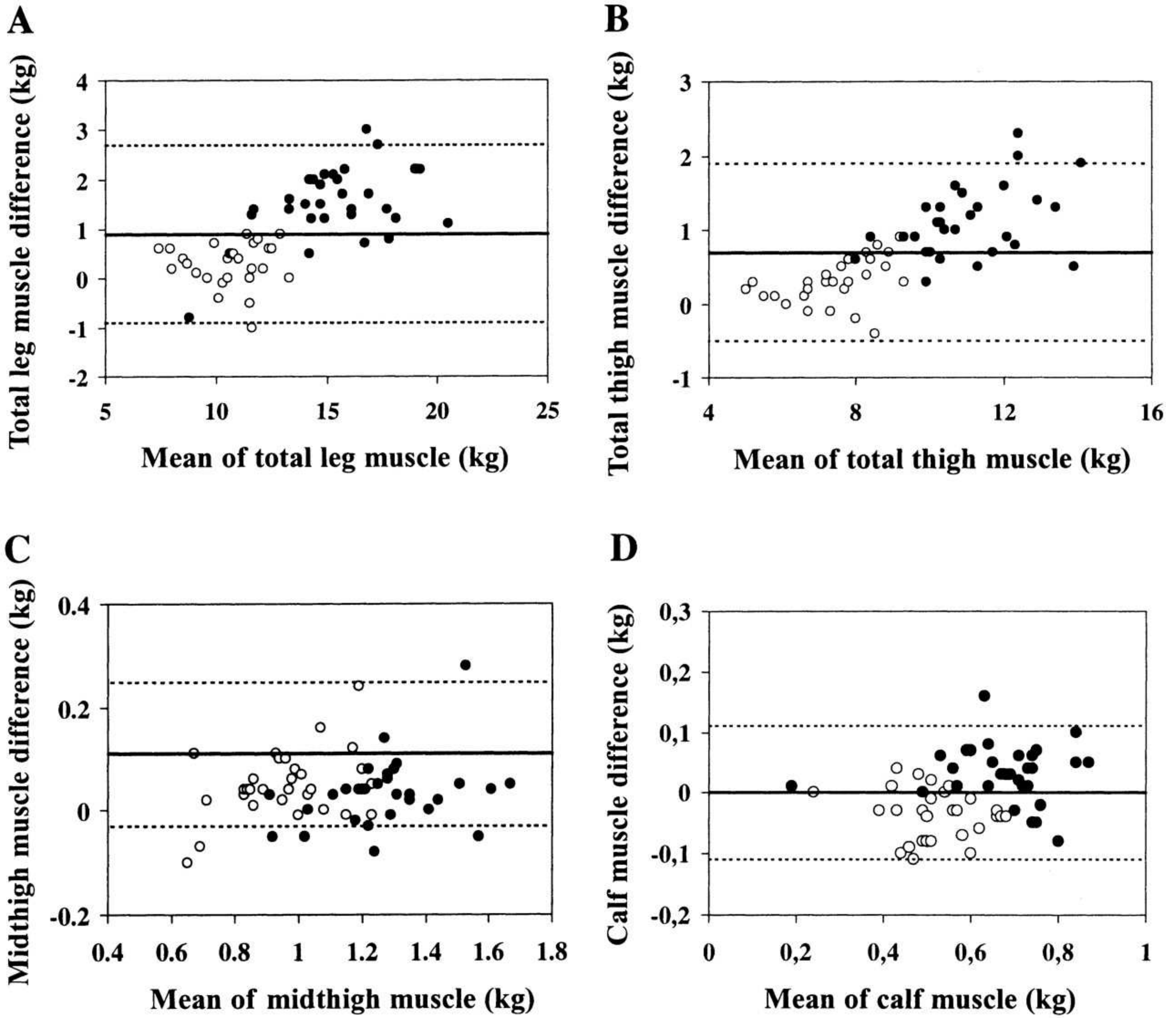
Visser M et al. J Appl Physiol 1999;87:1513-1520

A–D: difference in muscle mass between fan-beam DEXA and by multislice CT plotted against the mean at 4 leg regions.



Visser M et al. J Appl Physiol 1999;87:1513-1520

Weight and dimensions limits of different DXA models

Manufacturer/ Densitometer	Weight Limit kg (lb)	Table Dimensions cm
GE Lunar iDXA (2010)	182 Kg	287 × 132
GE Lunar Prodigy	136 (300)	197.5 × 60
GE Lunar DPX-MD	136 (300)	196.8 × 57.6
Hologic QDR series	136 (300)	195.6 × 65- 67
Hologic Discovery Series (2010)	204 Kg	195 × 65
Norland XR-46	114 (250)	193 × 64
Norland XR-36	114 (250)	193 × 64

Comparison between Dexa Hologic QDR 2000 and 4500

TABLE 1. TOTAL BODY COMPOSITION RESULTS USING PENCIL-BEAM AND FAN-BEAM HOLOGIC DXA INSTRUMENTS

Scan mode	*BMD* *(g/cm²)*	*BMC* *(g)*	*Fat* *(kg)*	*Lean* *(kg)*	*%fat*	Wt_{DXA} *(kg)*
Pencil-beam*						
mean	0.942	1549.5	13.9	32.4	26.4	47.9
SD	0.191	838.5	11.0	14.7	9.4	24.7
min.	0.619	384.8	1.8	10.4	8.9	16.0
max.	1.284	3425.6	48.0	67.6	46.9	119.0
Fan-Beam*						
mean†	0.949	1556.9	13.1[b]	33.5[c]	25.5[a]	48.2[c]
SD	0.173	781.0	9.5	15.8	7.1	24.8
min.	0.678	407.4	2.5	10.9	11.7	16.3
max.	1.263	3149.4	41.8	75.1	41.1	120.0

n = 47 (21 males, 26 females); body weight = 48.4 ± 24.8 kg; range = 16.3–120.0 kg.

* Pencil-beam = Hologic QDR-2000W, enhanced whole-body V5.71 analysis; fan-beam = Hologic QDR-4500A, whole-body V8.21a analysis.

† Paired *t*-test results for pencil-beam vs. fan-beam: ([a]$p < 0.02$, [b]$p < 0.0001$, [c]$p < 0.00001$.

Advantages and disadvantages of DXA

- **Advantages**
  x-ray exposure is minimal (< 1 mrem for 1 scan)
  subregion evaluation is allowed
  quick: total body scan
    - Pencil beam DXA (20-25 min)
    - Fan beam DXA (< 4-4.5 min)

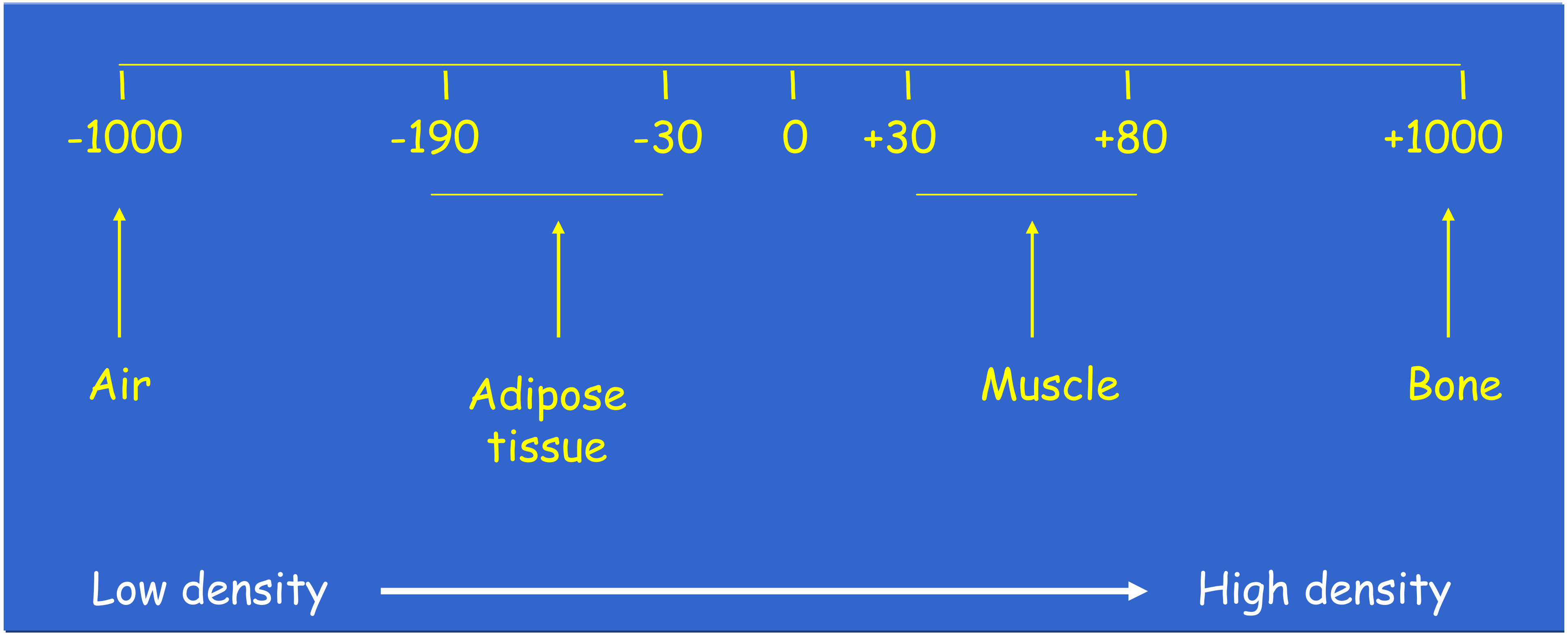
  used in large clinical trials
  Highly precise and reproducible technique (CV for fat mass 1-1.7% and for FFM 0.7-1.0%)

- **Disadvantages**
  costs (machine and technicians)
  not transportable
  lose accuracy with incresing body thickness, than lose precision and accuracy in thicker obese subjects
  radiation exposure (as a day of sunbathing)
  weight and dimensions limits

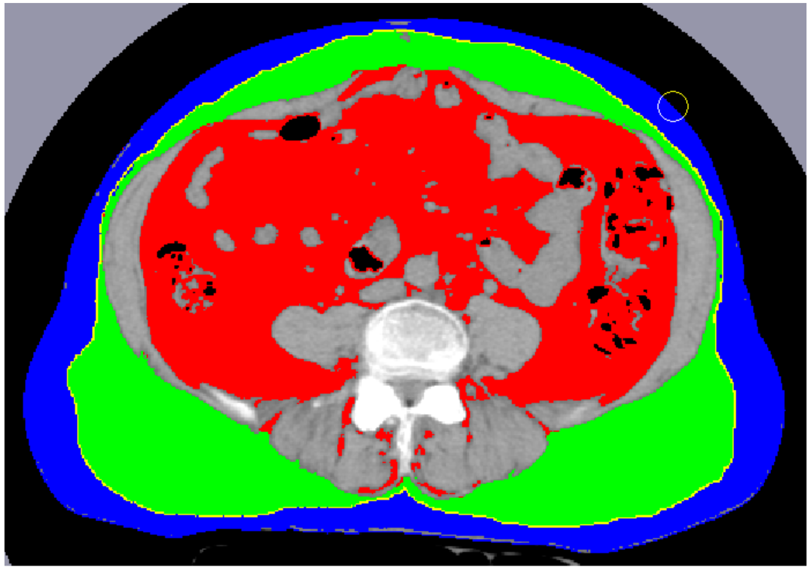
CT scan

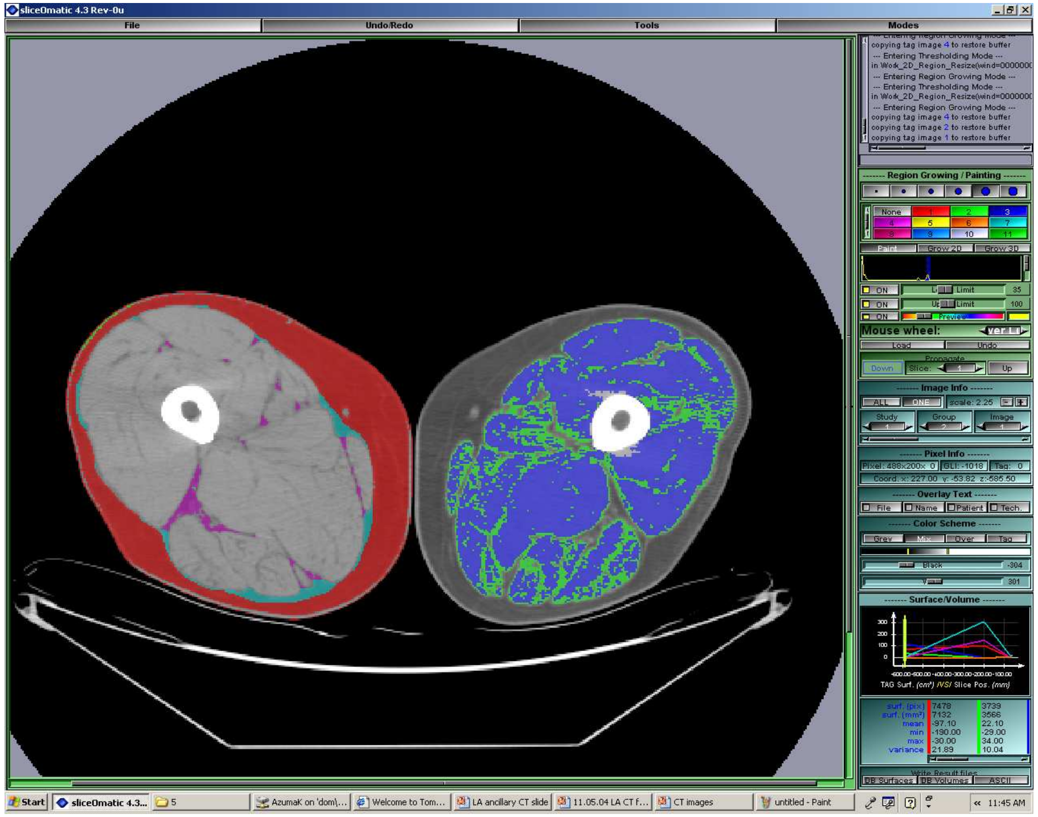
CT can differentiate tissues based on their attenuation characteristics, which depend on their density.

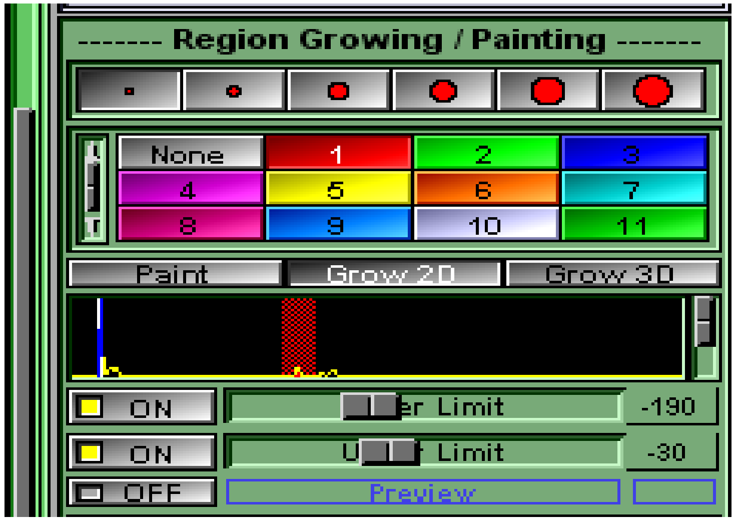
X-ray attenuation is quantified as Hounsfield Units (HU).



CT analysis with Sliceomatic Region Growing Mode Abdomen and Thigh







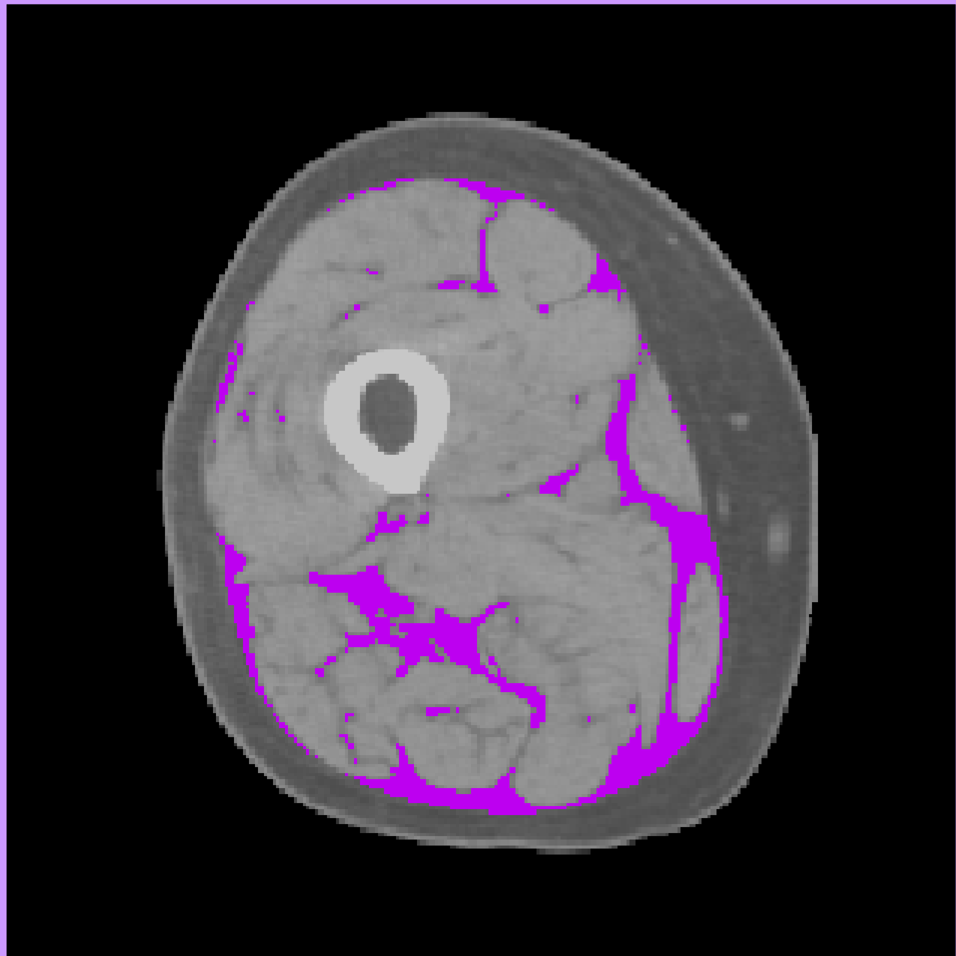
Hounsfield units:

>200 HU for bone

-30 to -190 HU for AT

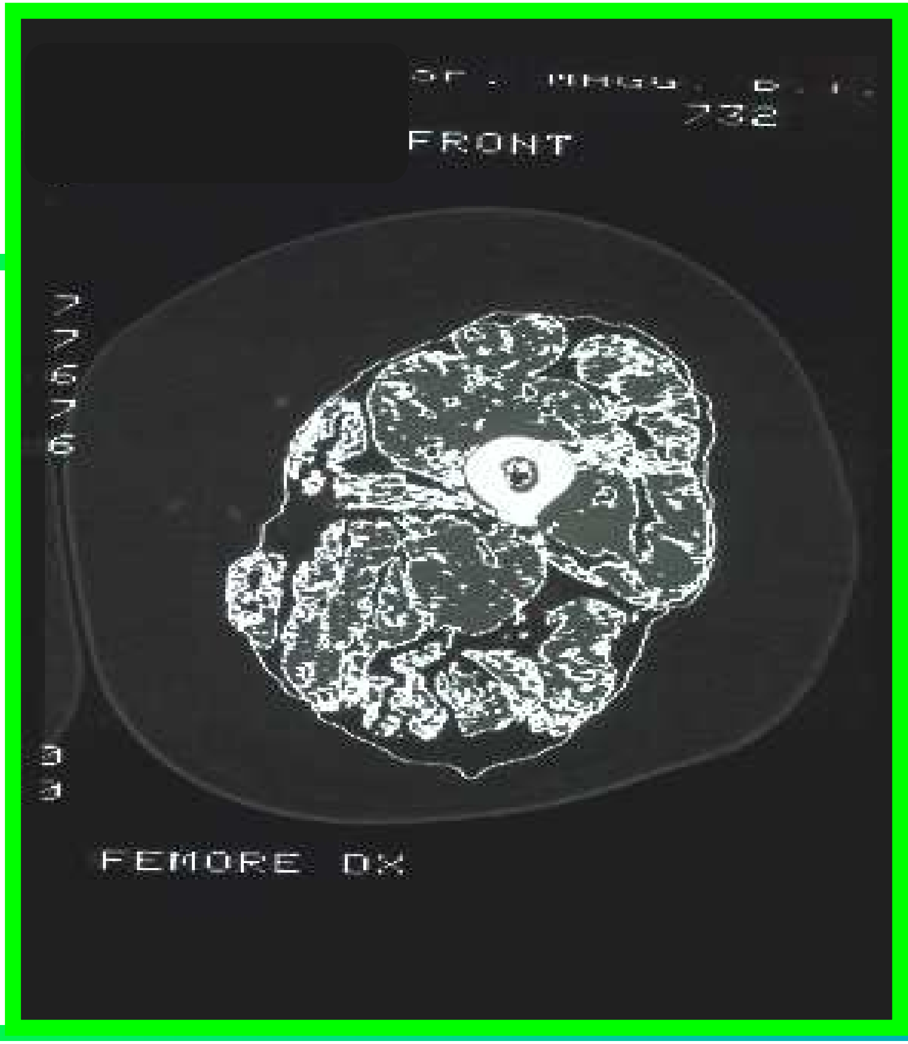
0 to 100 HU for muscle

Intermuscular Fat (CT)



Goodpaster et al., 2006

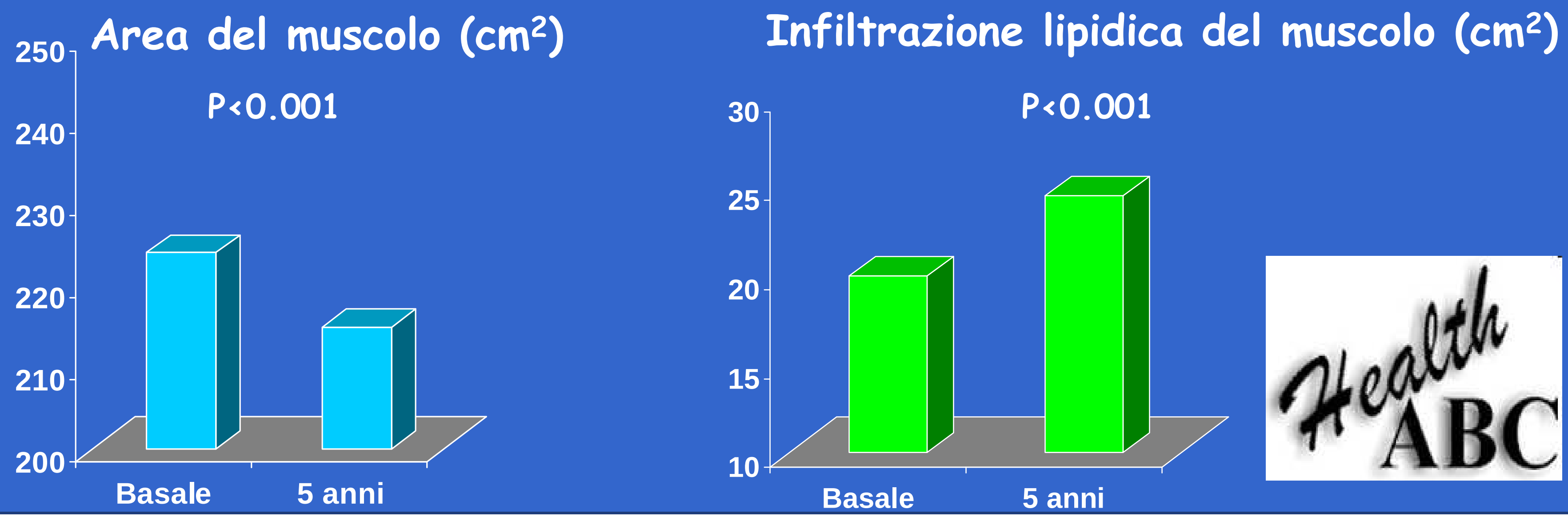
LDLT women, 69 year, BMI 49, W 121 cm, diabetes

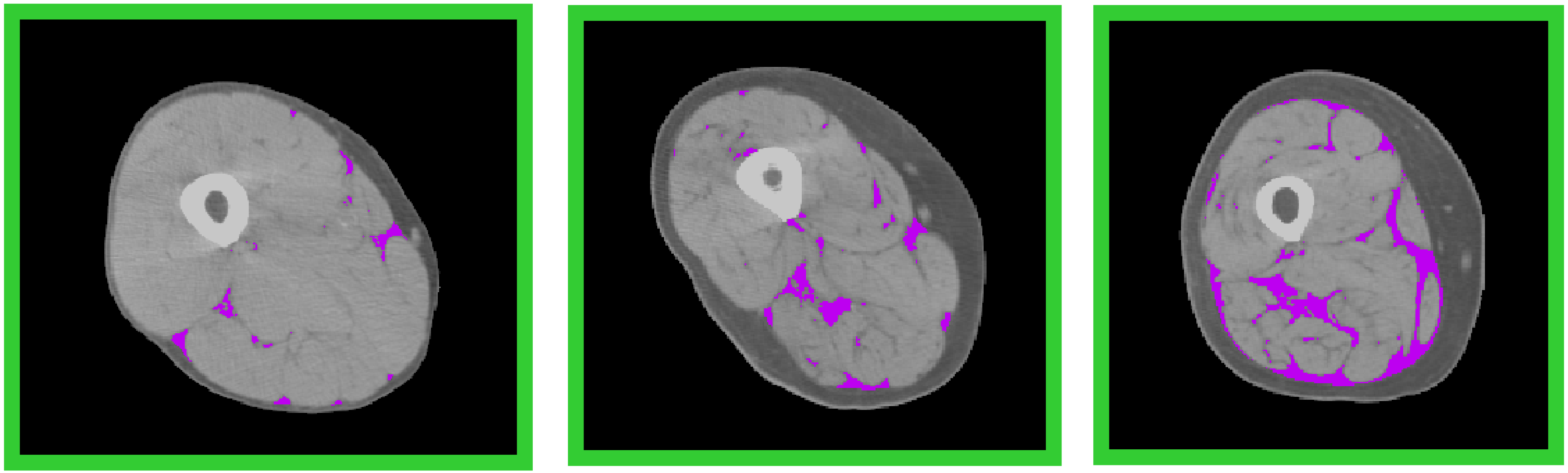


<u>Muscle density</u> (Hounsfield unit) - average value of muscle = lean, fat, collagen, blood vessels– <u>lower density</u> means <u>more fat</u>

<u>Myosteatosis</u> – muscle density and/or intramuscular fat

Modificazione della composizione corporea della coscia valutate mediante TAC (n=1981) in 5 anni di follow-up





Rossi AP et al. J Geront 2011

Computer Tomography (CT)

Advantages

Cross-sectional measurement of lean and fat areas in a specific part of the body

Evaluation of muscle quality parameters (intermuscular fat)

Relatively rapid (approx 30 min for whole body scan)

Can be used for longitudinal studies

Low frequency of artifacts compared to MRI

Disadvantages

Exposure to radiation

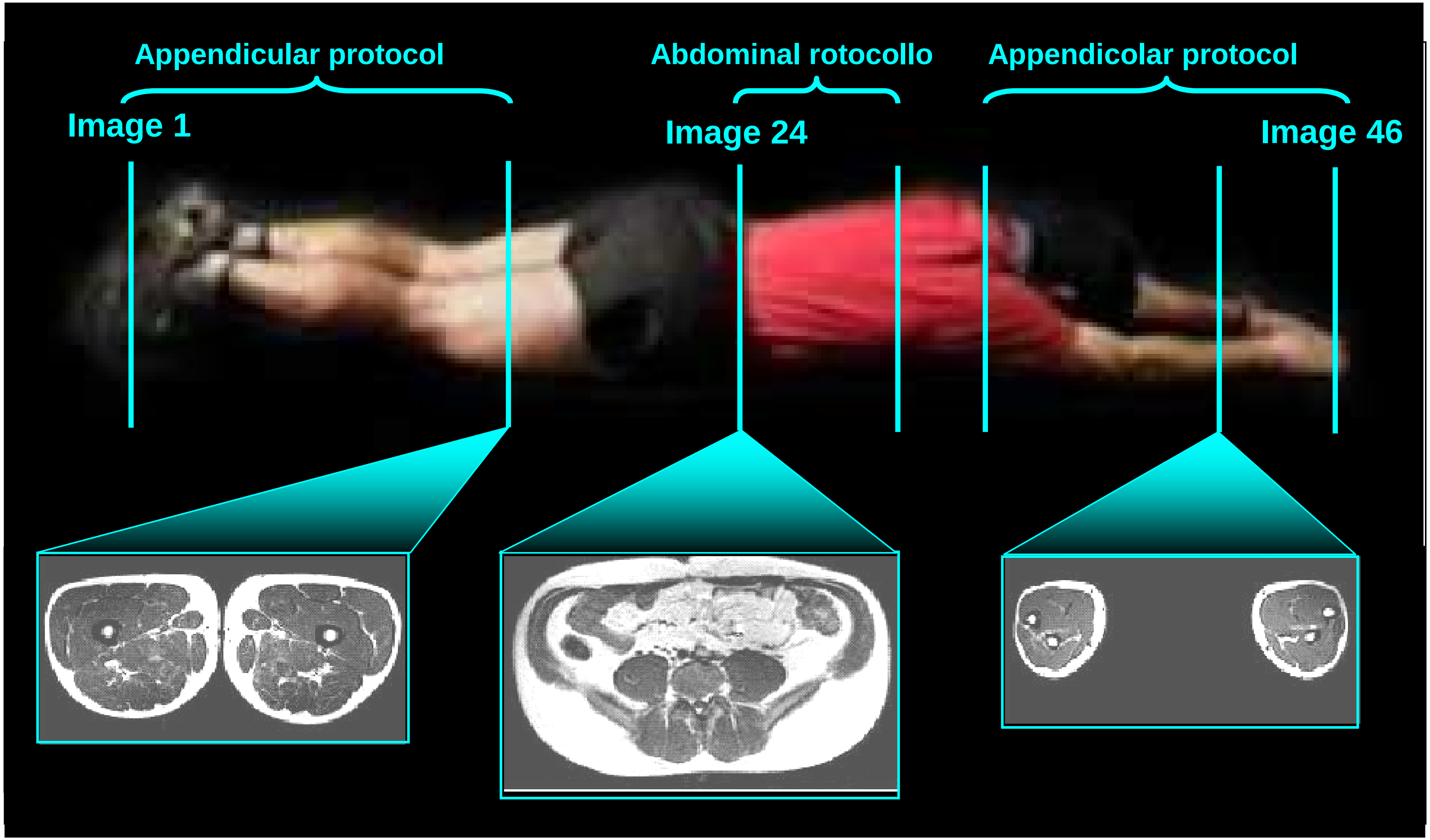
Time- consuming

High space to requirements

Technically difficult to perform

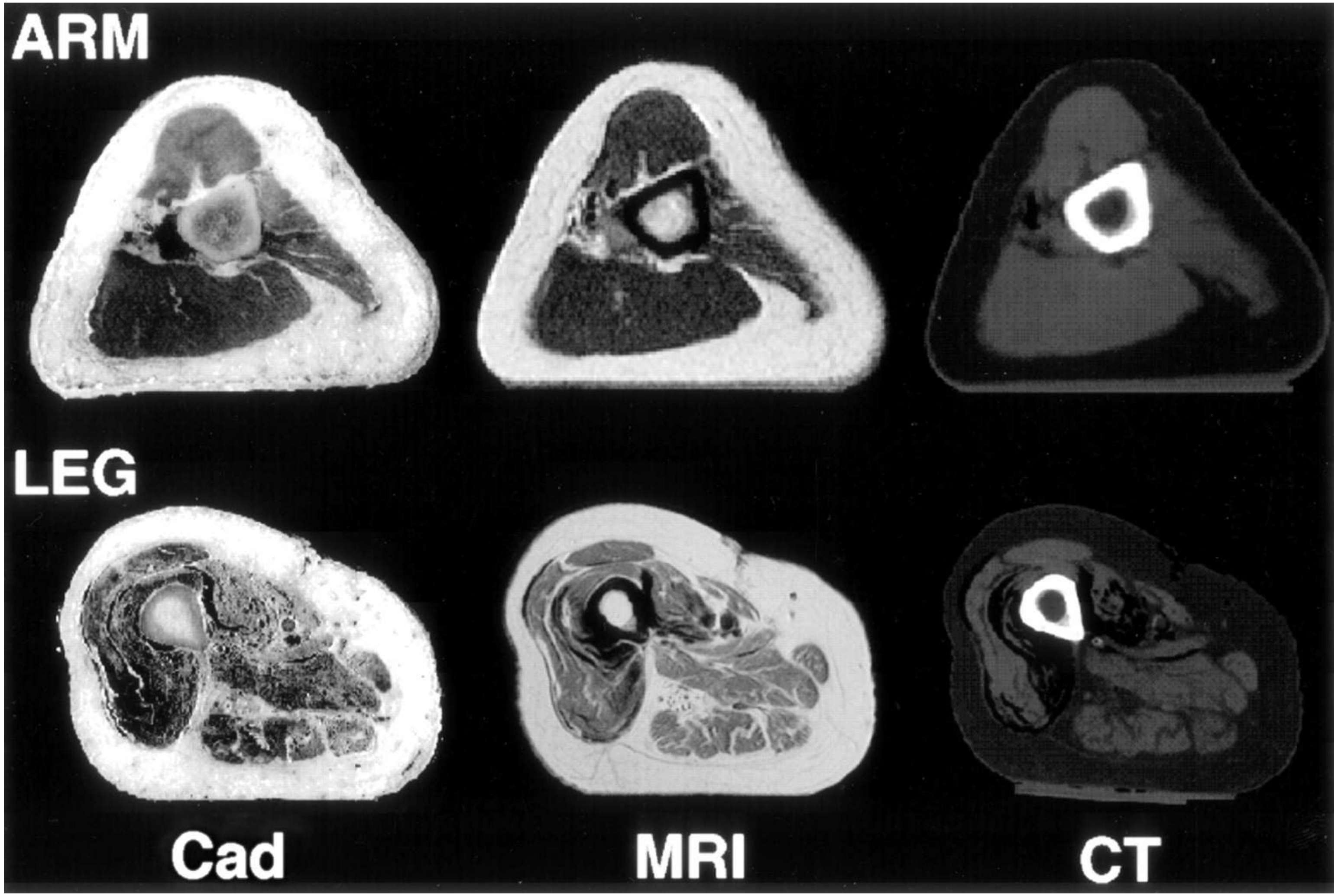
Expensive

Magnetic Resonance Imaging (MRI)



Heymsfield S, Ross R, Wang Z Handbook of Obesity; 2000

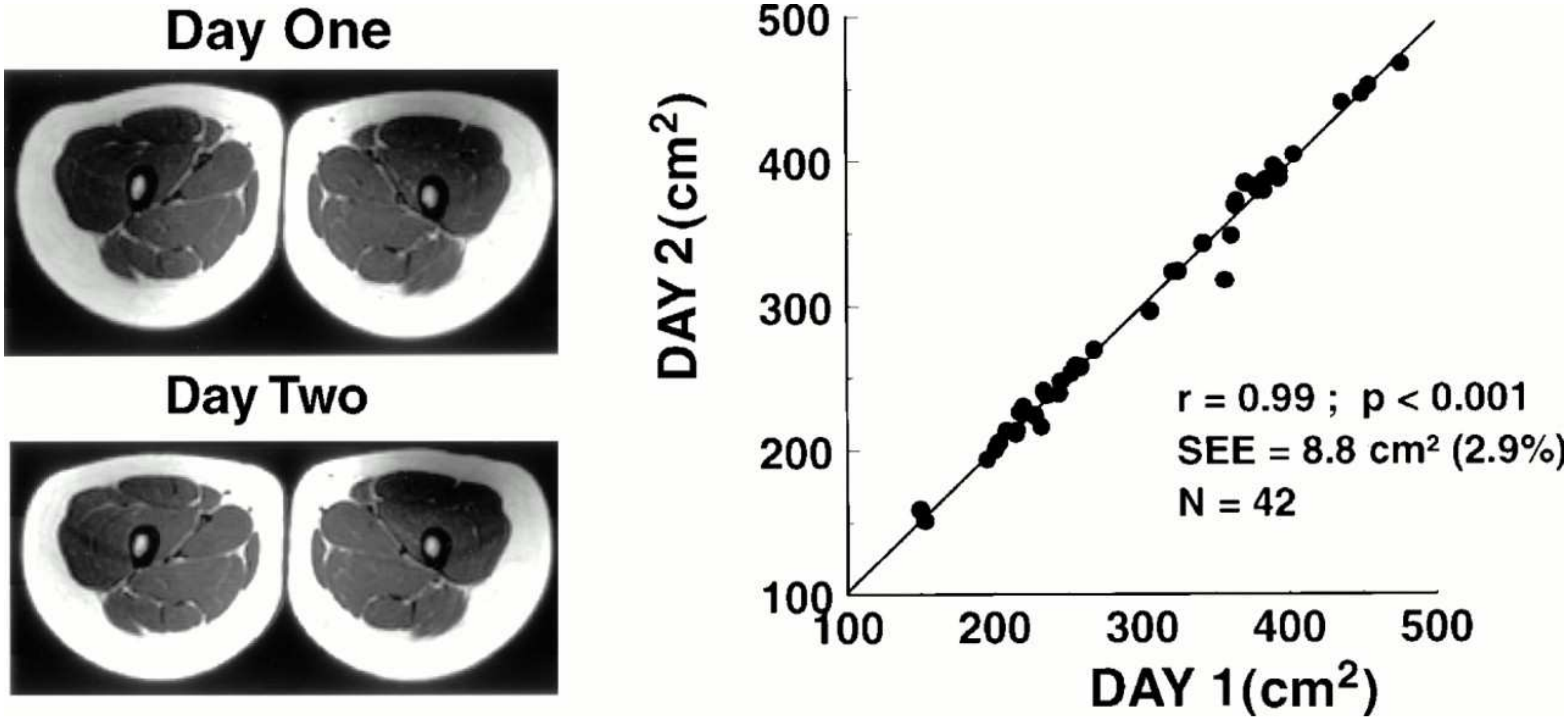
Illustration of typical images of arm and leg as obtained by magnetic resonance imaging (MRI), computerized tomography (CT), and cadaver (Cad).



Journal of Applied Physiology

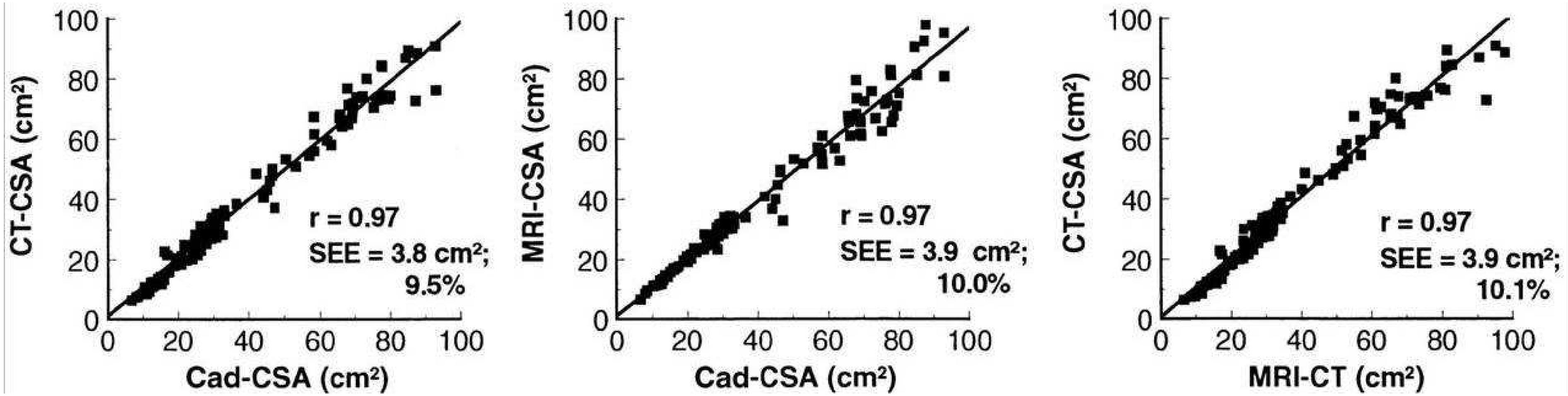
Mitsiopoulos N et al. J Appl Physiol 1998;85:115-122

Comparison of typical in vivo magnetic resonance images obtained on 2 separate days from the same subject at the level of the midthigh.



Mitsiopoulos N et al. J Appl Physiol 1998;85:115-122

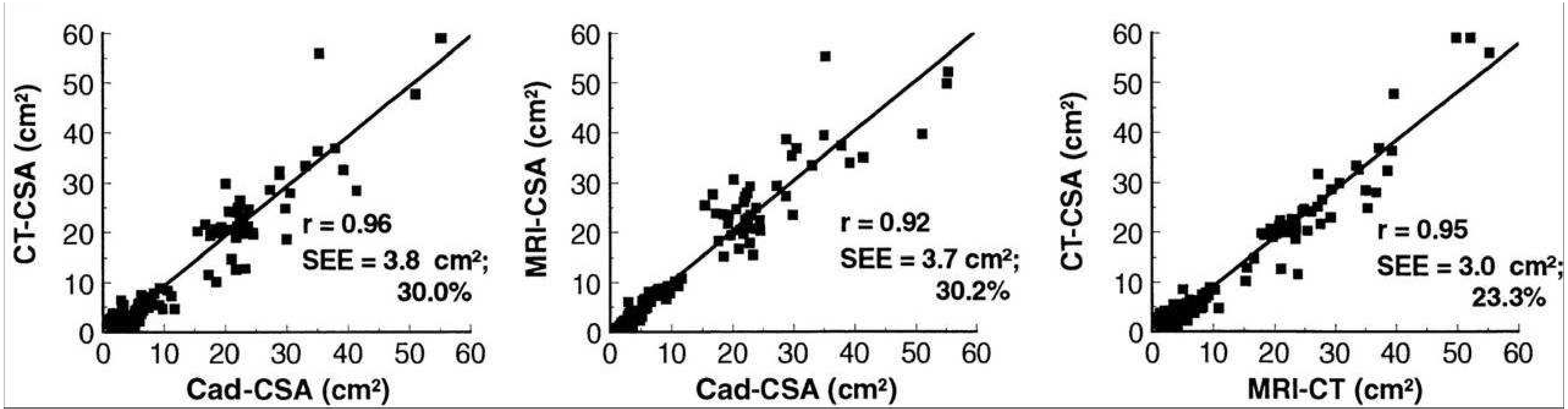
Regression analyses among MRI, CT, and Cad for Skeletal muscle



Journal of Applied Physiology

Mitsiopoulos N et al. J Appl Physiol 1998;85:115-122

Regression analyses among MRI, CT, and Cad for interstitial adipose tissue



Journal of Applied Physiology

Mitsiopoulos N et al. J Appl Physiol 1998;85:115-122

Magnetic Resonance Imaging (MRI)

Advantages

Does not use ionizing radiation

High quality image and can accurately quantify both subcutaneous & visceral fat

Relatively rapid (approx 30 min for whole body scan)

Can be used for longitudinal studies

Disadvantages

Not available appropriate image analysis software

Less precise for intermuscular fat quantification

Some exclusions (e.g. pacemakers)

Expensive

High frequency of artifacts ("shading" at the peripheries of images due to inhomogeneity in the magnetic field)

Comparison of methods for assessing skeletal muscle mass

	Creatinine /3-MH	TBK-TBN	DXA	MRI	CT	ANTH	BIA
Accurate?	●●●	●●	●●●	●●●●	●●●●	●	●●
Reproducible?	●●	●●●	●●●●	●●●	●●●	●	●●●
Cost to purchase?	●●●	●●●●	●●●	●●●●	●●●●	●	●
Cost to operate?	●●●●	●●●	●●	●●●	●●●	●	●
Technician training?	●●●●	●●●	●●	●●●●	●●●	●●	●
Radiation exposure?	●	●	●●	●	●●●●	●	●
Site	WB	WB	R,WB	R,WB	R,WB	R,WB	R(?),WB
Trasportable?	●	●●	●●	●	●	●●●●	●●●●

Lukaski H; Human body composition, II edition Cap 14; 2005