



BIA TECHNOLOGY FOR ASSESSING MUSCLE MASS

An introductory guide

Andrew M. Prentice, PhD
Professor of International Nutrition

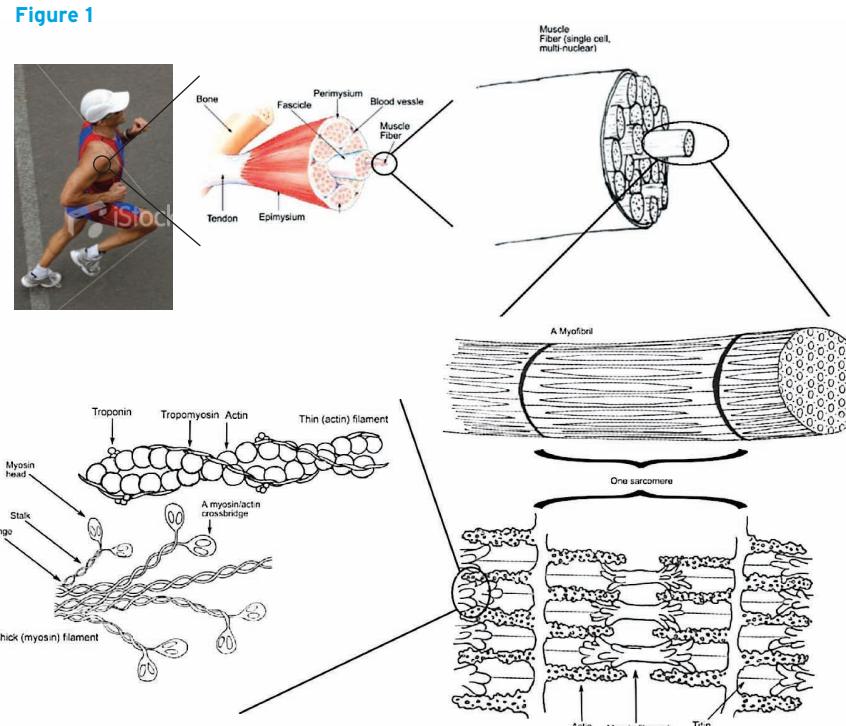
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Muscle - the body's powerhouse

Skeletal, cardiac and smooth muscles are responsible for all human movement - from the beating of a heart, and the drawing of a breath, to the running of a marathon. This booklet focuses solely on skeletal muscles.

There are approximately 695 skeletal muscles in a human body. Each contains contractile filaments that, under the control of efferent nerve signals, can slide over each other to create a force and hence cause movement.

Figure 1



Some of these involve fine control of the smallest action (the movement of an eye for instance) and others involve gross movements (such as the lifting of a leg by the quadriceps muscle). They can apply isometric force (gripping, squeezing, supporting a weight) or kinetic force (locomotion, movements).

Skeletal muscles contain a mixture of two broad fibre types: slow twitch and fast twitch. Slow twitch fibres generate less force but have good endurance; fast twitch fibres contract quickly and powerfully but fatigue rapidly.

Figure 2
Muscles Anterior

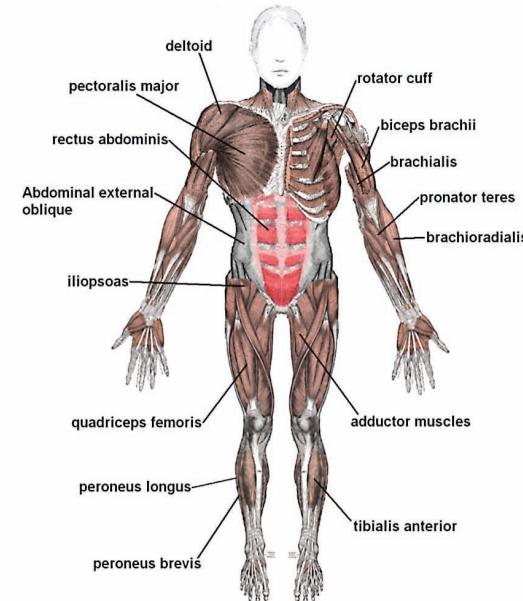
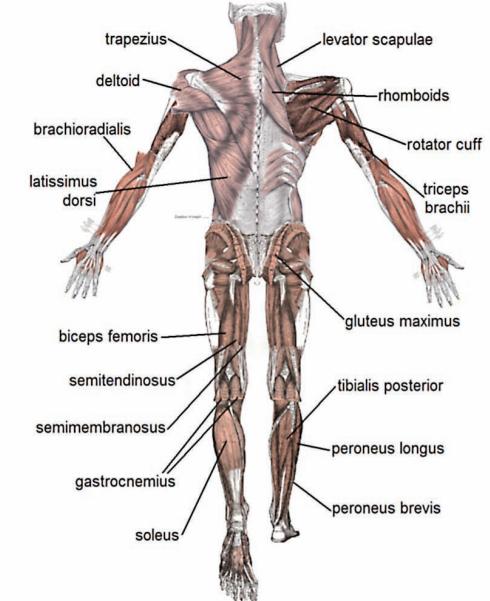


Figure 3
Muscles Posterior



Muscle through the lifecourse

All muscle cells arise from the mesodermal layer of embryonic germ cells and most are already formed by birth - ready to grow and be trained throughout life. Boys and girls have similar amounts of muscle until about the age of 10 years. During puberty testosterone drives a much greater expansion of skeletal muscle so that in adulthood an average man is 42% skeletal muscle and an average woman is 36%.

Muscle is a highly plastic tissue. In starvation it is 'consumed' to maintain a supply of amino acids and glucogenic precursors to ensure survival. With isometric training it can be greatly expanded and strengthened.

Anabolic steroids enhance this effect and can produce 'mass monsters' with muscle size and strength far greater than the natural genetic potential. Champion weightlifters can lift around 2.5 to 3 times their body weight.

Muscles are capable of prodigious feats of endurance. Recently, the Ironman Triathlon World Championship, consisting of a 2.4mile swim, a 112mile cycle and a 26.2mile run, was won in 8h10m (men's race) and 8h58m (women's race).

Muscle mass generally peaks in young adulthood and declines thereafter, with the rate of decline strongly influenced by the level of activity and physical work⁽¹⁾. However, even in old age muscles will respond well to training and important strength gains can be achieved⁽²⁾.



Muscle Metabolism

Muscle cells have varied and flexible requirements for fat and carbohydrate substrates. Switching between the two depends on the available supply and is governed by the Randle Cycle which ensures continued function – especially of the heart – under diverse nutritional circumstances. The efficiency with which human muscles can convert food energy to work ranges from about 20-25%.

In skeletal muscle, Type I (slow twitch) fibres are heavily perfused by capillaries and contain many mitochondria necessary for the oxidative conversion of food energy that allows the muscle to do physical work. Type II fibres are classified in several sub-types according to their speed of contraction. The fastest fibres contain few mitochondria and can sustain only short anaerobic bursts.

The major skeletal muscles contain mixtures of Type I and Type II fibres. The relative proportions are genetically regulated but can be altered by training. Training for endurance events increases the proportion of Type I slow twitch fibres and their ability to oxidise fat.

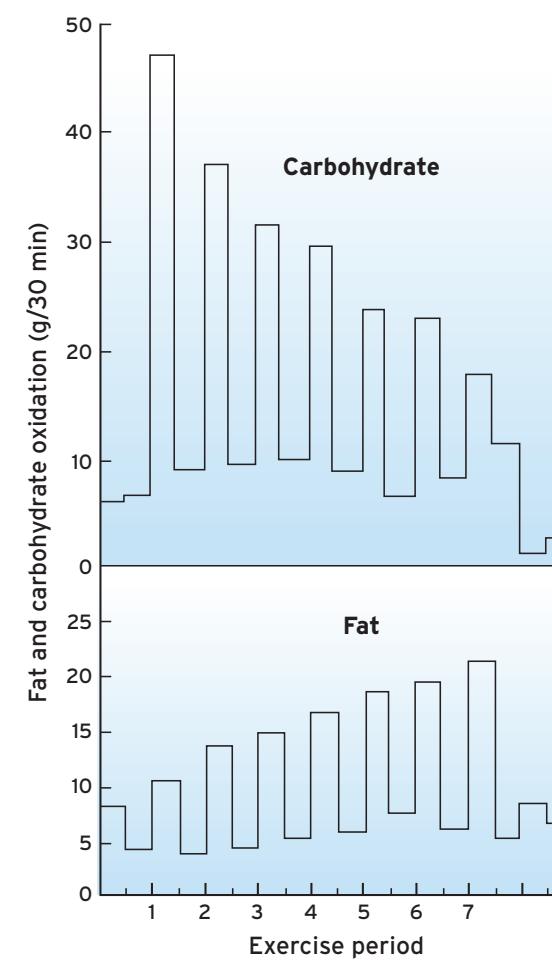
Glucose Uptake And Utilisation By Muscle

Due to their large size and high rates of energy expenditure when active, skeletal muscles represent a very important glucose 'sink' and together form the primary insulin-independent end organ. Skeletal muscle takes up glucose by energy-independent facilitated diffusion via the insulin-regulated GLUT 4 membrane transporter. It also utilizes glycogen stored within the muscle cells.

Figure 4 shows how the proportion of carbohydrate oxidized declines during exhaustive exercise as circulating glucose and stored glycogen reserves are depleted. As the carbohydrate supply becomes limited it is replaced by fat. The fat is derived both from circulating fatty acids derived from adipose tissue and from small intra-muscular depots of stored fat.

Figure 4

Fuel use during repeated 30min bouts of heavy exercise



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Murgatroyd PR et al (1994)
In J Obesity; 60:534-43.

Muscle Diseases

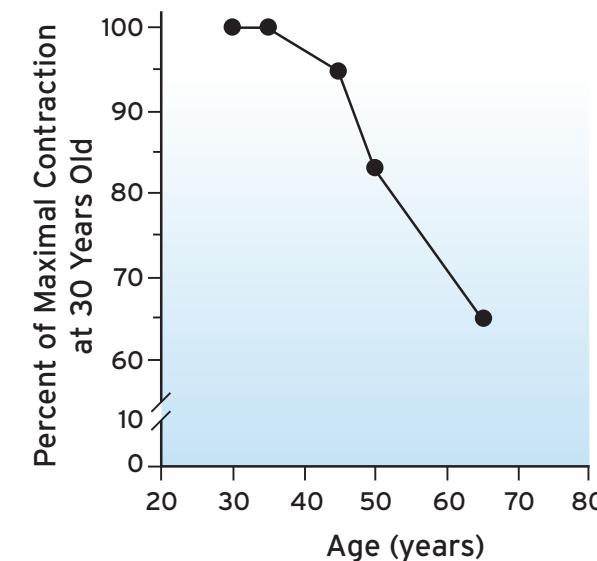
There is a wide range of clinical conditions that lead to muscle weakness and dysfunction. Muscular dystrophy is the generic term that covers dozens of hereditary diseases that lead to progressive muscle weakness through defects in muscle proteins and loss of muscle cells. Inherited metabolic defects in the ability to utilize glucose or fatty acids, or to store glycogen, can also contribute to muscle dysfunction. Additionally there are many neurological disorders that affect muscle function and may ultimately lead to muscle weakness (stroke, Parkinson's disease, multiple sclerosis, myasthenia gravis, etc).

Muscle atrophy (wasting) occurs as a side-effect of many clinical conditions that affect food intake and cause cachexia and tissue catabolism (such as cancers, AIDS, heart failure, lung and renal diseases, severe burns, and alcoholism).

Aging also results in a loss of muscle mass and strength (sarcopenia) caused by a combination of a gradual failure in the ability of satellite cells to regenerate new muscle cells and a decrease in the actions of the growth factors that normally maintain a healthy muscle mass. Between 50 and 80y of age there is approximately a 50% decline in muscle strength⁽¹⁾ (Fig 5). This can be slowed by training and a good diet, but it seems it cannot be wholly avoided. Sarcopenia is a very widespread problem in aging populations (see later).

Aging results in a loss of muscle mass and strength (sarcopenia) caused by a failure in the ability to regenerate new muscle cells and a decrease in the growth factors that normally maintain a healthy muscle mass.

Figure 5
Muscle Strength



Thompson LV. (1994) Effects of age and training on skeletal muscle physiology and performance. Phys Ther; 74: 71-81

The Importance of Maintaining a Healthy Muscle Mass

There is a broad range in muscle mass and function within any population group even excluding the extreme ends of the spectrum represented by muscle disease at one end and elite athletes at the other.

In young children a healthy muscle mass is critical to their motor development and participation in play and sports that can entrain a lifelong love of the recreational physical activity that is so important in maintaining metabolic health in the modern obesogenic environment.

In adulthood a gain in the proportion of fat mass to muscle mass reduces a person's power-to-weight ratio and makes everyday tasks, such as climbing stairs, more difficult. This creates a downward cycle in which a reluctance to take exercise (choosing to use escalators and elevators instead of stairs, for example) encourages a further gain in body fat and a deterioration in metabolic health.

In the elderly, a healthy muscle mass is essential to maintain mobility, everyday functions and quality of life⁽³⁾. It is especially important in maintaining good balance and hence avoiding the falls and fractures that contribute so greatly to ill-health and death among older people⁽⁴⁾.

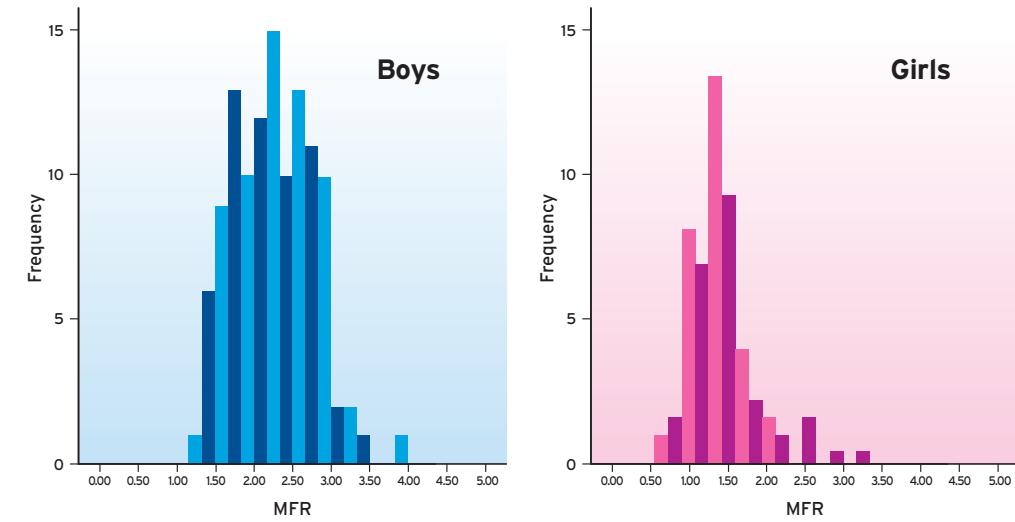
The ratio of muscle to fat is an important determinant of metabolic health.

The Yin and Yang of Muscle and Fat

Fat and muscle (and lean tissue more generally) have opposing effects on glucose sensitivity and hence the ratio of the two masses is an important determinant of metabolic health especially in relation to insulin resistance and the associated metabolic syndrome. Muscle utilizes glucose whereas the fatty acids derived from an excess adipose tissue mass inhibit the utilization of glucose. Hitherto there has been a major focus on the ill effects of a large fat mass without a full consideration of the compensatory value of a large, healthy and exercised muscle mass.

New research in children in which the skeletal muscle mass in arms and legs is compared to the total fat mass shows a 3-fold range in this ratio (see Figure 6). To date there has been no research comparing this ratio to measures of metabolic health, but theoretical reasoning based on prior evidence would suggest that those at the low end of the muscle mass: fat mass ratio would be at much greater risk than those at the high end.

Figure 6

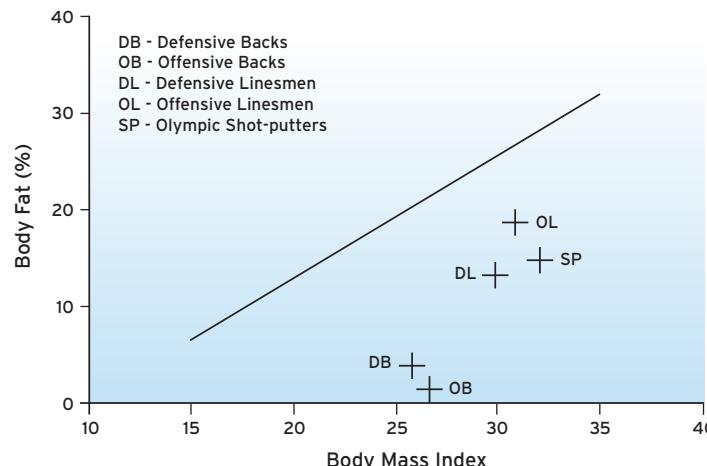


Fitness Versus Fatness

Fitness and fatness tend to be inversely related and both are related to metabolic health: fitness is beneficial, fatness is harmful. However, there are individuals in whom fatness, as assessed by the body mass index (BMI = weight (kg)/height²(m)) is highly misleading. An obvious example is among elite rugby players or American footballers (see Figure 7).

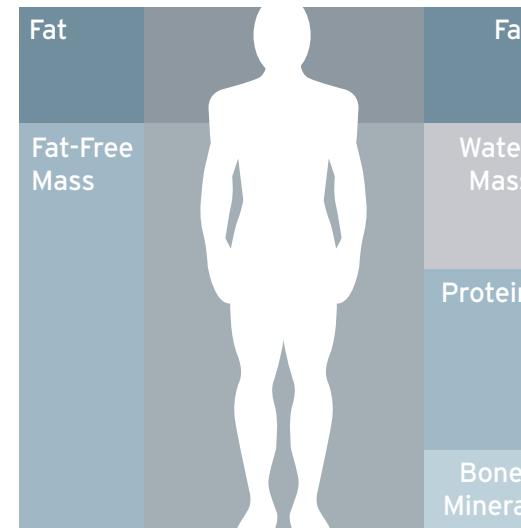
Even among those people with a high BMI who are genuinely fat there is a minority who are much fitter than their peers and evidence shows that their mortality risks are much lower⁽⁵⁾. Some scientists believe that fitness is much more important than fatness in predicting ill-health and early death and that the frequently demonstrated associations between obesity and mortality result from the fact that fatness generally correlates with fitness. Muscle, both skeletal and cardiac, is a critical component of fitness and hence is crucial to understanding the true causal pathways linking sedentariness, obesity and excess mortality.

Figure 7
Examples of mismatch between BMI and body fat in elite athletes



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What Methods are Available for Measuring Muscle Mass?



Human body composition is generally subdivided into the relative proportion of fat vs lean tissue.

The following basic definitions are useful:

- Fat mass (FM): the total amount of fat in a body including that in nerve tissues and the brain
- Fat-free mass (FFM): all the remaining tissues including fluids and the skeleton. Skeletal muscle forms the largest single component.
- Lean body mass (LBM): usually used interchangeably with FFM.
- Skeletal muscle mass (SMM): all skeletal muscle. Since it is impossible to quantify total SMM the term appendicular skeletal muscle-mass (ASMM) refers to the major muscles on the arms and legs, and provides a proxy for total SMM.



Bioelectrical impedance analysis (BIA)

BIA assesses body composition by passing a very small current through the body and assessing differences in impedance caused by the fact that fat and lean tissues have different electrical properties. Since all lean tissue in the limbs is either bone or muscle use of segmental BIA can provide a good proxy for skeletal muscle mass (SMM) by assessing the composition of limbs alone (see Box 2). As BIA is the focus of this report it is described in more detail later.

Anthropometry (skinfold thickness combined with limb circumferences) A formula exists whereby an estimate of the cross-sectional area of muscle in the upper arm can be computed by combining measures of the anterior and posterior skinfold thickness (to estimate subcutaneous fat) and the limb circumference. This is a highly approximate method developed for assessing malnutrition in developing countries and only estimates cross-sectional area at a single site. It is therefore of very limited value and rarely used.

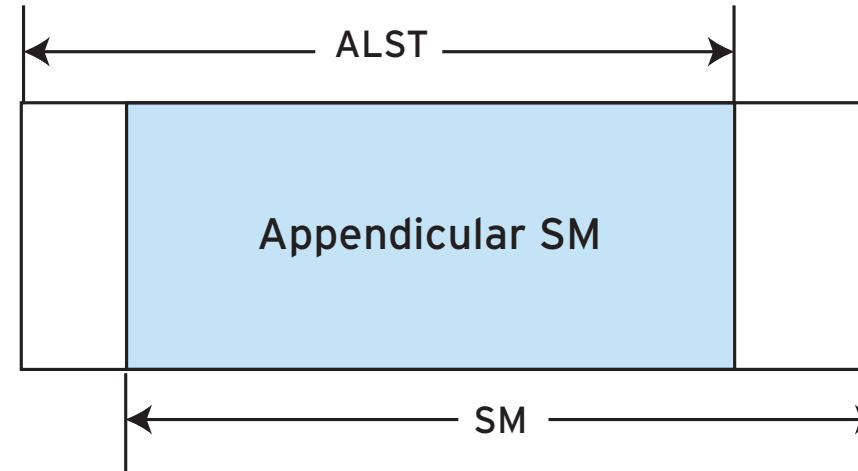
Dual-Xray absorptiometry (DXA) DXA body scanners used in clinical practice to measure bone density can also give an estimate of body composition. They use 'soft' X-rays that have a different level of attenuation as they pass through fat and lean tissue. The system can be calibrated using animal carcasses. DXA can give regional measures for the limbs and trunk, and - as with BIA - the limb lean tissue mass (appendicular) can be used as a good proxy for muscle mass⁽⁶⁾(see Box 2). However, the equipment is expensive, non-transportable and measurements are time consuming.

Peripheral quantitative computerized tomography (pQCT)

pQCT can be used to assess muscle density and the cross-sectional areas of muscle and fat in either the calf or forearm⁽⁷⁾. The equipment is expensive and semi-transportable.

Other highly technical methods There are a variety of other methods each of which has some significant advantages for assessing skeletal muscle, but each of these is highly technical and very expensive. These include: total-body potassium-40 counting (TBK); in vivo neutron activation analysis (NAA); computerized axial tomography (CAT scanning); magnetic resonance imaging (MRI) or spectroscopy (MRS); and total body electrical conductivity (TOBEC). These are used by a very small number of centres worldwide and only for detailed research studies. MRI and CAT scanners can be used to assess muscle mass of the heart also.

Box 2



ALST - appendicular lean soft tissue (ie excluding bone)
 SM - skeletal muscle

Why Measure Muscle Mass And Lean Tissue?

Weight management

Preserving muscle is a key component to successful weight loss, since even the most carefully devised weight loss regime will tend to cause some loss of lean-body mass and especially muscle. Monitoring such tissue loss and recommending exercise regimes and a high protein intake to overcome it may be valuable adjuncts to the treatment of obesity, and BIA offers a rapid and simple method for doing this.

Similarly building muscle is important for the long-term maintenance of a healthy body weight and composition. Studies in the US have shown that regular monitoring of body weight and adoption of regular exercise are the two features that identify successful long-term weight losers.

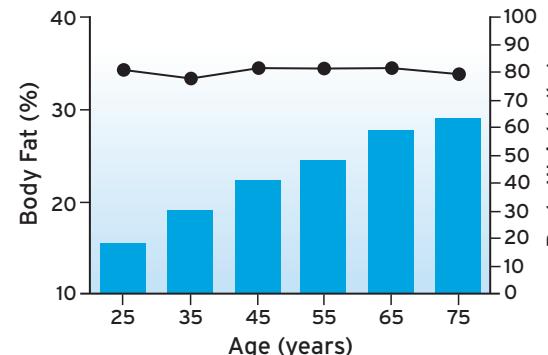
Limitations of BMI in community studies

Body mass index has been a very effective tool in epidemiological studies of obesity and in assessing population trends. In general it is a good predictor of adiposity and is strongly correlated with obesity-associated adverse health outcomes. However it has a number of limitations⁽⁸⁾. Misclassification of heavily muscled individuals has been described above (see Fig 7). The relationship between fat mass and BMI also differs quite substantially between different ethnic groups⁽⁸⁾.

A further important example is that BMI fails to register the progressive substitution of lean by fat tissue during aging. Many individuals will maintain a relatively constant body weight (and hence BMI) throughout their adult life, but this conceals the fact that lean tissue mass is gradually eroded and replaced by fat (Figure 8). Data from American men shows that average fat mass increases from about 15% body weight at 20y to almost 30% at 75 years⁽⁹⁾.

Figure 8

Age-related increase in body fat (solid bars) for normal men at constant BMI



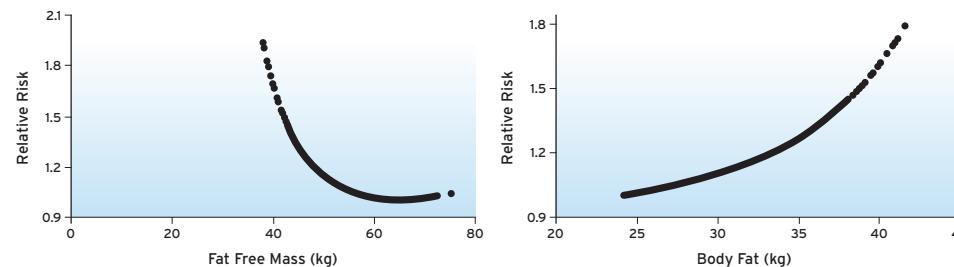
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Limitations of BMI in predicting mortality

Although most studies reveal strong associations between BMI and mortality the associations are complex and still not completely understood. U-shaped or reverse J-shaped curves are frequently observed indicating an elevated mortality at very low BMI. Figure 9⁽¹⁰⁾ shows that this may be explained by the fact that both low lean mass and high fat mass are risk factors for early death and that people with a very low BMI typically have a low lean and muscle mass⁽¹¹⁾.

Figure 9

Increased risk of mortality is predicted both by increased fat mass and by diminished fat free mass



Data from 60 year-old Swedish men. Reproduced with permission from Heitmann 2000.

Muscle-to-fat ratios in children

Assessing body composition in the paediatric setting can guide clinical decisions by identifying aberrant growth. Growth charts based on height, weight, BMI and head circumference have been available for many years. More recently waist and body fat charts⁽¹²⁾ have been added to the armoury. These will shortly be augmented by charts for (appendicular) skeletal muscle mass⁽¹³⁾ that will allow identification of children with abnormally low muscle mass (see Figure 10).

Assessment of muscle mass also allows the muscle-to-fat ratio (MFR) to be calculated. In boys of low-to-normal BMI this ratio averages about 2.3 (McCarthy, in preparation). These figures can be used to set the limit of normal at an MFR of 1.25 (defined as mean - 2SD which covers 97% of the population). Applying this figure to boys in the top quintile of BMI reveals that 40% have a low MFR but 60% have a normal MFR (Figure 11) suggesting that their high BMI is revealing a bulky, muscular build rather than obesity. Given the reciprocal effects of muscle and fat on insulin resistance it is likely that the MFR will prove a better index of future metabolic health than BMI - though this has yet to be tested.

Figure 10

Centile charts for skeletal muscle mass in children expressed as % of total fat-free mass.

Central line represents 50th centile. ASMM Appendicular skeletal muscle mass (ASMM). Fat free mass (FFM).

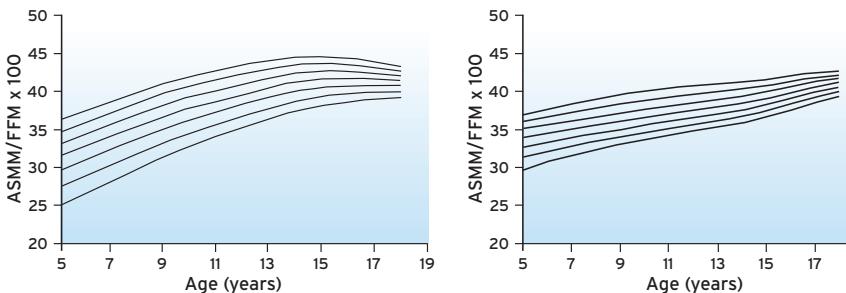
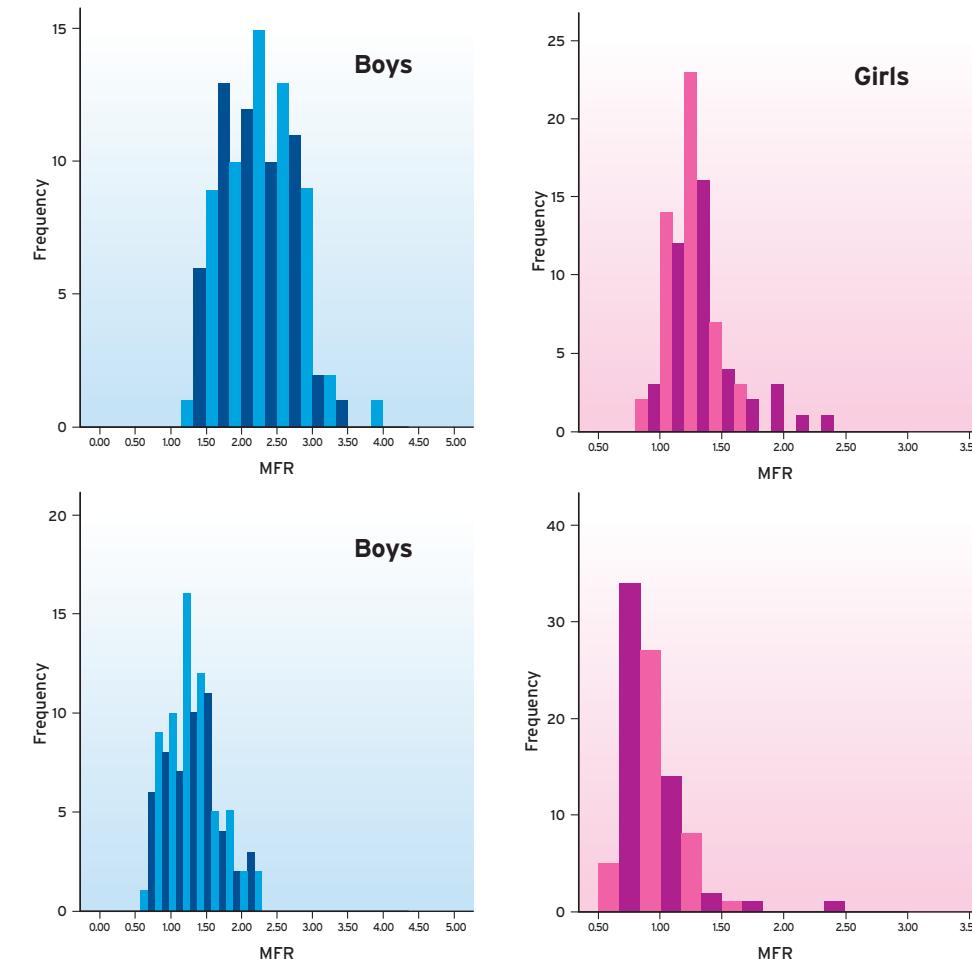


Figure 11

Muscle-fat ratios (MFR) from UK schoolchildren aged 10-18y.

Upper panels are from the middle fifth of the distribution based on BMI (kg/m^2) and the blue line is the mean minus 2 SDs used to define the limit of normal. Lower panels are the top fifth of the distribution based on BMI. Note the large numbers of children of high BMI who have an appropriately low MFR. (Unpublished data kindly provided by David McCarthy, London Metropolitan University).

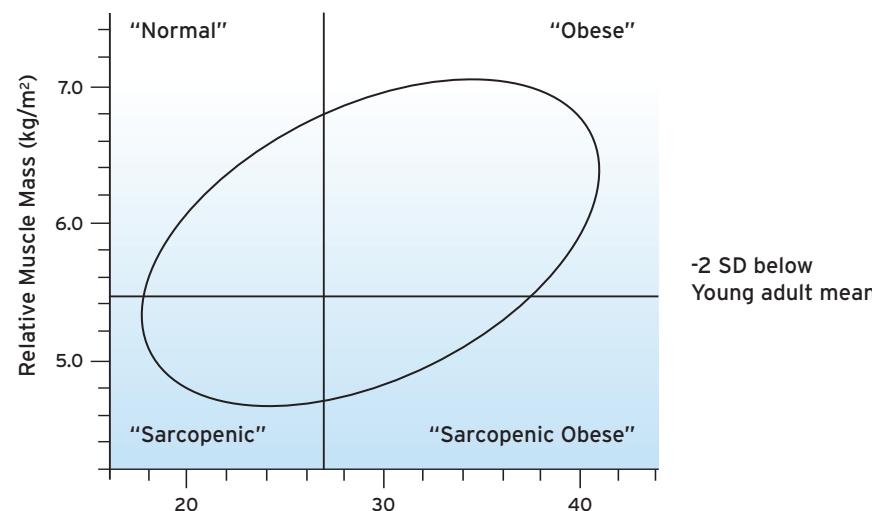


There is a greater than 3-fold range in the muscle-to-fat ratio among children.

Sarcopenic-obesity in adults

When adults gain weight it is usually gained in the proportion 75% fat to 25% lean tissue. Thus obese people tend to have a higher lean body mass than normal or underweight people. This extra lean tissue is required to carry around the extra weight (skeletal muscle and bone) and to service it (heart, liver, digestive tract). However, some obese people have an inappropriately low muscle and lean mass. The combination of a high fat mass with a low lean tissue and muscle mass is termed sarcopenic-obesity (Figure 12). Cutoffs defining sarcopenic-obesity together with the associated prevalence rates in the communities studied are now appearing in the literature.

Figure 12



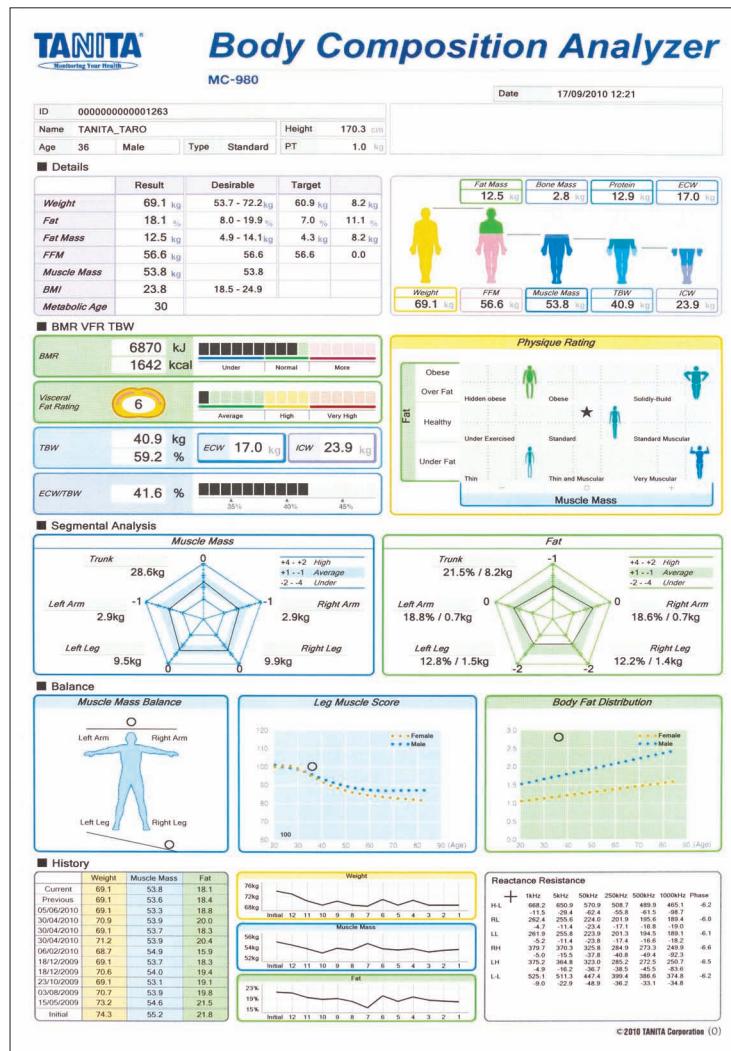
Although there are strong theoretical reasons to infer that sarcopenic-obesity will be predictive of poor metabolic health the relationships are complex and require further research. It is clear, however, that methods that can discriminate between fat, lean and muscle tissue will be required in order to elucidate the precise relationships between obesity, ageing and the major health outcomes⁽¹⁴⁾. Hitherto the technological difficulties in assessing muscle mass, especially in large-sample and field settings has hampered research. These have now been overcome by BIA technology and it will be possible to refine studies of the obesity phenotype in relation to health outcomes.

Measurement of muscle mass provides an additional useful tool that can be added to BMI within health monitoring systems and could be of high motivational value in encouraging the maintenance of healthy levels of physical activity. It will be helpful to promote a greater public understanding of the importance of maintaining a healthy skeletal muscle mass.



A high fat mass combined with low lean and muscle mass is termed 'sarcopenic-obesity'.

Figure 13



What is Novel about Tanita BIA Monitors?



Tanita pioneered the use of foot-to-foot BIA in which subjects simply have to remove their shoes and stand on a monitor that sends a minute current from one foot to the other. The measurement can be completed in 20 seconds, and is backed by a strong research programme over 20 years. There was initial scepticism as to whether a system just passing a current through the legs could be as accurate as previous 'tetrapolar' systems that attached stick-on electrodes to each ankle and each wrist. However, later research showed that (because they represent a very long thin conductor) arms actually introduce a disproportionate weighting to tetrapolar monitors and may hence reduce their accuracy if not adjusted for carefully.

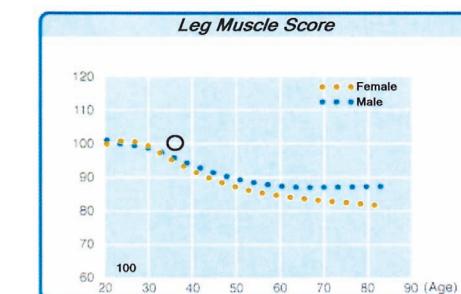
A New Generation of Tanita BIA Analyzers

The new Tanita Body Composition Analyser MC-980 uses 8-electrodes and require subjects to hold two hand-grips whilst standing on the monitor. This allows segmental analysis of the composition of arms, legs and trunk. Further analysis provides key indicators of the subject's muscle mass, body water and body fat status and can be shown on a Consultation Sheet (see Figure 13). With an in built Windows Operating System, automatic storage of measurements is possible, ensuring accurate trend analysis and database management.

Of particular interest is the 'Leg Muscle Score' plotted against reference data from healthy Americans (see Figure 14). This is based on the principle that leg muscle represents the largest fraction of muscle mass and hence comparisons of leg muscle give a good proxy indicator of overall muscle

mass. Similar scores could be derived for appendicular SMM (arms and legs).

Figure 14



Reference data were obtained from healthy individuals studied by St Luke's Hospital, New York. The black circle represents an example of how data appear on an individual's print out.

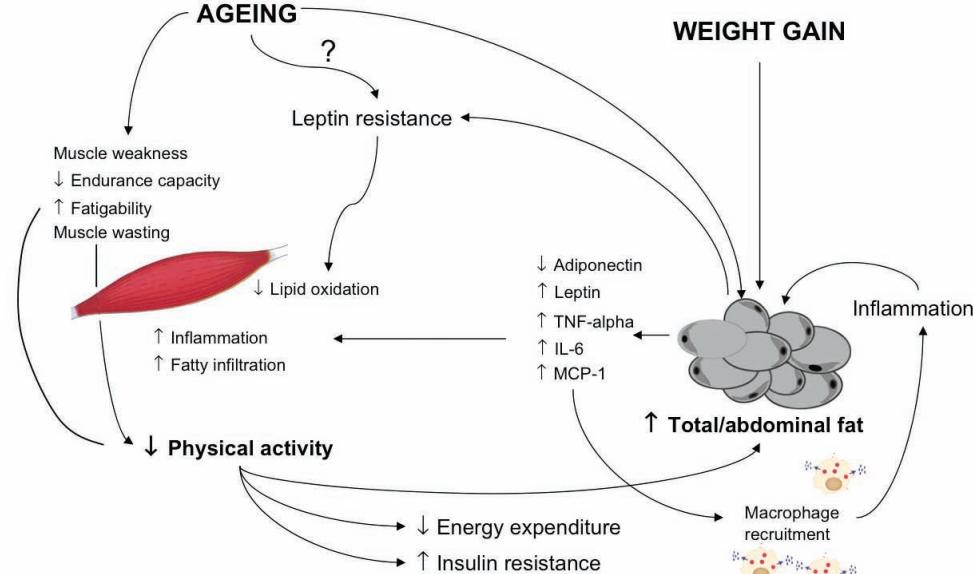
Sarcopenia in the elderly

The decrease in anabolic drive and in the muscle sensitivity to anabolic signals that occurs progressively with ageing, and the resultant decline in muscle mass (see Figure 5), is a major determinant of some of the morbidities associated with old age. Sarcopenic-obesity (SO) has been defined as a new category of obesity in the elderly and pathways for its etiology have been described (see Figure 15). Geriatric medicine now recognizes the key role of sarcopenia on the causal pathway to deteriorations in mobility and quality of life^(15,16), and in serious and life-threatening outcomes such as hip fractures^(eg 17,18). Muscle loss is associated with slowness, weakness and general frailty which in turn lead to early fatigue and low physical activity that then reinforce the cycle of muscle wasting. It remains controversial as to whether sarcopenic obesity is a predictor of mortality in the elderly with some studies showing that it is and others not^(eg 19,20).

There is a strong innate biological tendency towards progressive muscle loss that is driven by reductions in oestrogen and testosterone, in the sex hormone binding proteins (DHEAS) and in IGF-1. However, catabolism can be slowed by high levels of physical activity (eg by high work loads in poor subsistence-farming populations, or simply by personal choices to remain very physically active in affluent populations). They can be slowed and, to some extent reversed, by strength training even in the later decades of life⁽²⁾.

Given the critical importance of sarcopenia to health in later life there is a need to encourage measurements of muscle mass in a variety of settings: in epidemiological studies (where little attention has previously been focused on muscle), in health monitoring throughout adulthood, and in therapeutic programmes aimed at improving strength, mobility and quality of life in older people. BIA offers a simple and cost-effective method for such monitoring that could be widely used across many health settings from primary health care to hospital settings.

Figure 15



Inter-relationships between adipose tissue and muscle. A mechanism leading to sarcopenic obesity.

Reproduced with permission from: Zamboni et al (2008) Sarcopenic-obesity: a new category of obesity in the elderly. Nutr Metab Cardiovascular Dis; 18: 388-95.

Segmental BIA offers the most affordable and practical method for monitoring muscle mass.



Sarcopenic-obesity and cancer

A study has shown that sarcopenic-obesity was a strong independent predictor of survival in patients with solid tumours of the respiratory and gastrointestinal tracts⁽²¹⁾ and has suggested that failure to assess decrements in muscle and lean mass might lead to chemotoxicity through overdosing with cancer-therapeutic agents.

Sports performance and personal training

The value of assessing muscle mass in relation to athletic performance and the monitoring of strength-related training has long been recognised - but the available techniques for doing so have been limited. There are few training facilities that would possess whole-body CAT or MRI scanners, or any of the even more rarified methods. Segmental BIA therefore offers the most affordable and practical method. It can assess the muscle mass in each limb separately, or give a read out of a leg muscle index, or total appendicular skeletal muscle mass (ASMM). Measurements are rapid, non-invasive and repeatable.

Monitoring of limb muscle masses can be a valuable adjunct to training schemes ranging from the amateur to the ultra-elite. Applications include tracking the impact of training schedules, monitoring the advantages of different training schemes and/or dietary supplements, and investigating relationships between hydration status and muscle efficiency.

Summary

A healthy muscle mass is critical to metabolic health and optimal physical functioning for everyone throughout their lifespan. This has been known for decades, but the absence of appropriate measurement tools has limited the expansion and application of such knowledge. Segmental BIA now offers a route to over-coming these limitations by providing an affordable, robust and non-invasive means for monitoring appendicular skeletal muscle mass.

Future research in many fields (monitoring of normal growth; obesity and its metabolic sequelae; physical functioning in health, disease states and ageing; physical training; elite sports performance; etc) would now benefit from a more detailed and thorough assessment of body composition. As the knowledge base on the role of muscle in health expands, it is anticipated that significant new insights will emerge that can then be passed on to the general public as medical professionals strive to optimize quality of life and healthy longevity in the 21st century.

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This report was commissioned from Prof Andrew M. Prentice, PhD.

Professor Prentice is head of the MRC International Nutrition Group at the London School of Hygiene & Tropical Medicine and Director of the Nutrition Programme at MRC Laboratories, The Gambia. He is a member of the Tanita Medical Advisory Board.

The views presented are his own and do not imply endorsement by MRC or LSHTM.



TANITA Corporation
14-2, 1-Chome, Maeno-cho
Itabashi-ku, Tokyo, Japan 174-8630
Tel: +81-3-3968-7048
Fax: +81-3-3968-2661
Email: info@tanita.co.jp
Web: www.tanita.co.jp

TANITA Europe B.V.
Hoogoorddreef 56E
1101 BE Amsterdam
The Netherlands
Tel: +31-20-560-29-70
Fax: +31-20-560-29-88
Email: info@tanita.eu
Web: www.tanita.eu

TANITA Health Equipment H.K. Ltd
Unit 301-303 3/F Wing on Plaza,
62 Mody Road, Tsimshatsui East,
Kowloon, Hong Kong
Tel: +852-2838-7111
Fax: +852-2838-8667
Email: asia-pacific@tanita.co.jp
Web: www.tanita.com

TANITA Corporation of America, Inc.
2625 South Clearbrook Drive,
Arlington Heights, IL 60005 USA
Tel: +1-847-640-9241
Fax: +1-847-640-9261
Email: 4health@tanita.com
Web: www.tanita.com

TANITA (Shanghai) Trading Co. Ltd
Room 8005,
887 Huai Hai zhong Lu,
Shanghai,
The People's Republic Of China
Tel: +86-21-6474-6803
Fax: +86-21-6474-7901
Email: info@tanita.co.jp
Web: www.tanita.com.cn

TANITA India Private Limited
Level 8, Vibgyor Towers, C-62,
G Block, Bandra Kurla Complex,
Bandra (East), Mumbai 400 051
Tel: +91-22-4090-7174
Fax: +91-22-4090-7178
Email: info@tanita.co.in
Web: www.tanita.co.in