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DIPLOMA THESIS

HUMAN BODY COMPOSITION DURING ONTOGENESIS

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2. ABSTRACT

This diploma thesis refers to human body composition and its alterations by physiological and pathological processes that occur during different stages of life. Fat mass, fat free mass and total body water represent the major components of the human body which are modified during infancy, childhood, puberty, pregnancy and adulthood. Bioelectrical Impedance Analysis (BIA), Dual Energy Absorptiometry (DEXA), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are some methods which are utilized for the qualitative and quantitative assessment of the body composition according to nutritional and pathological state of each individual, targeting the optimal clinical outcome. During growth, the amount of total body water elevates through infancy but it gradually declines in the next stages of life. Fat mass or total body fat possesses higher values during infancy, pregnancy and aging whereas it increases preferentially in female population at puberty. Muscle mass is elevated significantly in males during puberty and declines gradually due to aging. Osteoporosis, obesity and wasting diseases such as anorexia, cachexia and sarcopenia provoke severe disturbances in body composition compartments resulting in high rates of morbidity and mortality of the population.

3. ABSTRAKT

Tato diplomová práce se zabývá složením těla člověka a jeho změnami způsobenými fyziologickými a patologickými procesy, které se vyskytují v různých fázích života. Tuková tkáň, tukuprostá tkáň a celková tělesná voda představují hlavní součásti lidského těla, které se mění v průběhu kojeneckého věku, dětství, dospívání, těhotenství a dospělosti. Bioelektrická impedanční analýza (BIA), duální rentgenová tělesná denzitometrie (DEXA), počítačová tomografie (CT) a magnetická rezonance (MRI) jsou vybrané metody, které jsou využívány pro klinické kvalitativní a kvantitativní stanovení tělesného složení podle nutričního a patologického stavu každého jednotlivce. Během růstu, množství celkové tělesné vody se zvyšuje v průběhu dětství, v dalších fázích života postupně klesá. Hmotnost tukové tkáně nebo celkového tělesného tuku má vyšší hodnoty během kojeneckého věku, těhotenství a stárnutí, přednostně se zvyšuje v ženské populaci v pubertě. Svalová hmota je významně zvýšena u mužů během puberty a postupně klesá v důsledku stárnutí. Osteoporóza, obezita a další nemoci vyvolávající odbourávání tělesné hmoty, jako je anorexie, kachexie a sarkopenie, mohou vyvolat vážné poruchy ve složení těla, přispívající ke zvýšení morbidity a mortality.

4. INTRODUCTION

Body composition reflects the level of the organism health and its changes. The monitoring of these changes is essential for the comprehension and the determination of the mechanisms in which environmental factors affect the composition of individual components of the body. It describes the quantity of the main body compartments such as water, muscle, fat and bone. The study of this field represents a reliable tool for the establishment of an appropriate and beneficial treatment in particular diseases and informs about the nutritional status of a person or a population at the level of health, aging or during the occurence of a disease.

Ontogenesis refers to the main stages of life such as infancy, childhood, puberty, adulthood, aging as well as pregnancy and breast-feeding. Throughout these stages, significant alterations occur in the composition of the human body depending on weight, height, race and sex differentiations. The amount of total body water, fat mass, fat free mass and bone mass differs in each stage, since the rate of development reduces with aging and hormonal alterations.

The body composition is also affected by the presence of pathological conditions such as obesity, cachexia and osteoporosis. The underlying conditions provoke abnormal changes in fat mass, lean tissue mass and bone mass resulting in a significant reduction of the quality of life, with an increased risk of deaths among the population. The assessment of these components can be accomplished in atomic, molecular, cellular, tissue and whole body level using various methodological techniques during ontogenesis as well as during the presence of such disease.

The aim of the current diploma thesis is to specify the body composition alterations that occur in human throughout ontogenesis and in certain diseases. For this to be accomplished, the elucidation of major tissues and components is necessary. In addition, some of the most widely used methods for the analysis of the body composition will be described, as well as, its levels and models that analysis is based on. The compartments in which greater focus will be given are fat mass, fat free mass, bone mass and total body water.

5. BODY COMPOSITION

Body composition represents a part of human biology; it refers to nutritional intake and expenses throughout time. It is a determinant of energy expenditure, particularly, at rest and describes percentages of fat, bone, water and muscle in human body. Due to continuous changes that occur in the human body during the life, body composition does not remain constant. These changes can be the result of physiological processes, such as aging but it can also be the result of pathological conditions and diseases. The measurement of body composition in clinical practice is a major tool for diagnosis, prevention and therapy of various diseases (Thibault et al, 2012).

5.1 Major components of human body composition

Human body consists of many components, the major one being the water. Total body water (TBW) constitutes 60% of body weight. The remaining 40% consists of fat mass (FM) and fat free mass (FFM).

Total body water (TBW) is composed of intracellular (40%) and extracellular fluid (20%). Intracellular fluid is present within the plasma membrane of body cells where chemical reactions take place. Instead, extracellular fluid is present outside the plasma membrane of living cells and consists of two compartments, interstitial and intravascular. The interstitial compartment is filled with interstitial fluid (15%) that allows the movement of ions, proteins and nutrients through the cell from the outside of the cell to the inside, while intravascular compartment is filled with the major intravascular fluid (5%), blood, together with blood cells, globulins, glucose and ions.

Watson et al study noted that the most appropriate linear regression equations for the measurement of total body volume related to age, height and weight in middle age women and men were:

Total body water = 2.447 - 0.09516 age + 0.1074 height + 0.3362 weight, for men

And total body water = -2.097 + 0.1069 height + 0.2466 weight, for women (Watson, 1980).

In general, height, the absolute volume of water in the body and the fraction of the body that is water, decrease with age, the fraction of the body that is fat increases with age,

while weight increases to a maximum level in middle age and then decreases (Watson, 1980).

Fat mass (FM): Fat mass is mainly presented in adipose tissue but it is also presented in other tissues. It contains the fundamental fat and the storage fat. The fundamental fat is necessary for the function of some parts of our body such as brain, bone marrow, nervous tissue and cellular membranes. It also consists of phospholipids of cellular membranes and other lipids mainly sphingomyelin. According to the theoretical model of Behnke (1959), the fundamental fat of a reference woman constitutes 9-12% of body weight and is higher than that of a reference man (3% of body weight). This happens because the fundamental fat presented in women contains the sex specific fat, found in special areas of their body such as breast, hips and thighs. The sex specific fat is also related to hormonal factors and reproductive procedures in the body of a reference woman (Norgan, 1997). On the contrary, the storage fat is composed of triglycerides and it is mainly distributed in subcutaneous, interior and visceral compartments and its amount reflects the surplus energy of the organism (Manios, 2006).

Fat-free mass (FFM) contains all fat-free chemical substances and tissues including water, muscle, connective tissue, bone minerals and it represents a basic part of internal organs.

BIA equation for the measurement of FFM is the following:

According to Ramirez et al: $FFM= 0.661*(H^2/ R_{50}) + 0.200\ W- 0.32$, where R_{50} is the resistance at 50kHz frequency, W- weight in kg and H- height in cm (Wan et al, 2014).

5.2 Main tissues related to body composition

Adipose tissue is the main fat storage region in healthy adults and it contains the highest amount of storage fat and sex specific fat. It represents a form of connective tissue consisting of adipocytes, veins and fibers and its chemical composition is comprised of 83% fat, 15% water, 2% protein. It is divided in two types of connective tissue, the white adipose tissue and the brown adipose tissue that differ in terms of functions in the body (Manios, 2006).

Muscle tissue is the largest in mass tissue of the human body. Specifically, it constitutes 45% of man body weight and 36% of woman body weight. There are 3 main categories

of muscle tissue: skeletal, smooth and cardiac muscle tissue. The skeletal muscle tissue contains skeletal muscle fibers that are controlled by central nervous system while smooth and cardiac muscles are under control of autonomic nervous system, therefore movement of muscles cannot be controlled. Generally, muscle tissue consists of 75% water, 20% protein, 5% of inorganic salts, sodium, potassium, chloride, calcium, magnesium and phosphorus ions, intramuscular triglycerides and glycogen (McArdle, 2002).

Bone tissue: Bones are comprised of the most rigid part of connective tissue in human body, the bone tissue. Bone tissue constitutes the skeleton. They cover 15% and 12% of body weight in men and women, respectively and their composition is approximately: 70% mineral salts, 22% protein, and about 8% water. The skeleton contains 99% of total body calcium, 35% sodium and approximately 60% of magnesium (Green and Kleeman, 1991). Bone tissue is formed by 3 types of cells osteoblasts, osteocytes and osteoclasts.

Bone matrix consists of the osteoid (organic part), crystalline mineral salts and calcium in the form of hydroxyapatite (inorganic part). Osteoclasts and osteoblasts participate in the formation and resorption of bone, a process called bone remodeling. Depending on the ordinance of bone matrix, the bone tissue is distinguished to trabecular (spongy) bone (25%), which is the inner meshwork and has trabecular structure, and cortical (compact) bone (75%) which is less metabolically active and represents the dense outer part of bone. The main functions of bones are the mechanical support of skeleton, protection of susceptible anatomical structures storage of calcium phosphate, participation in homeostasis regulation of calcium and phosphorus and in the regulation of acid-base balance of the organism (Rang et al, 2012).

5.3 Body composition levels and models

The comprehension and knowledge of the body composition models is of great importance in the selection of an appropriate body composition analysis method as well as for the proper evaluation of the results of that specific method.

Two-compartment model:

Two-compartment model represents a theoretical model in which many methods of analysis of body composition are based on. It distinguishes the body mass in FM and FFM compartments. FM consists of different lipids whereas FFM contains water, proteins, glycogen and minerals.

Five- compartment model:

Five-level model or Wang et al model consists of five distinct levels: atomic, molecular, cellular, tissue organ, whole body level.

- ***Atomic level*** consists of 11 elements among which, more than 96% of body mass, includes oxygen, hydrogen, nitrogen, carbon. Other important elements are calcium, phosphorus, potassium, sulfur, sodium, chlorine and magnesium. Most of these major elements are used to measure directly, in vivo, the whole body content mainly by neutron activation analysis or whole body counting. Moreover, some of the elements such as total body carbon, nitrogen and potassium are utilized to derive total body fat, protein and body cell mass in coordination with higher level models (Manios, 2006).

- In ***Molecular level,*** all the 11 elements found in the atomic level, are incorporated into molecules forming many chemical compounds that exist in human body, including water, lipids, proteins, carbohydrates, bone minerals and soft tissue minerals (Manios, 2006).

  - On the ***Cellular level***, the human body is composed of three main compartments: cells, extracellular fluid and extracellular solids. The cells such as fat, muscle and bone cells are supported by extracellular solids and surrounded by extracellular fluids. Extracellular fluids are used for the transport of nutrients as well as for the elimination of toxic substances. According to Moore et al, cells are subdivided into FFM (fat-free mass) and FM (fat mass) where FFM is referred as BCM (Body Cell Mass) and it is responsible for the most metabolic processes that occur in the body (Pietrobelli, 2000). So, Body Weight = lipids + BCM + Extracellular fluids + Extracellular solids. The researchers suggested the measurement of total body potassium (TBK) for the estimation of BCM. Specifically, potassium is present in the body as an intracellular cation and its concentration in intracellular fluids is 150 mmol /L. So, if we estimate total body potassium by ^{40}K or neutron activation

analysis method, it is possible to calculate indirectly the amount of intracellular fluids. Intracellular fluids are 80% of Body Cell Mass, so BCM = ICF/ 0.8 (Newton et al., 1999).

- ***Tissue –organ level:*** At this level, the main tissues related to body composition are skeletal muscle, adipose, and bone tissue. All tissues and organs are composed of many cells and all of them are metabolically active but they differ in their resting metabolic rates. Skeletal muscle and adipose tissue that are the most important and largest components in this level have low resting metabolic rates. On the other hand, organs such as liver, kidney and brain have higher metabolic rates (Elia, 2001). In experimental level, many investigators assumed that there is a linear relationship between REE and FFM in adults:

$$REE = a + b \cdot FFM$$

Where a represents the regression line intercept and b represents the slope (Wang et al, 2000).

Using progressive methods for the analysis of body composition such as CT and MRI is possible to determine quantitatively specific tissues and organs of human body. Based on the individual mass and the resting metabolic rates of tissues and organs, resting metabolic rate (RMR) of a human can be calculated by using appropriate equations (Müller et al, 2002).

- ***Whole-body level*** is divided into head, appendages and trunk. In this level, body shape and size are examined by some parameters:

    1. Circumferences (waist, thigh) that indicate body density, fat free mass, total protein body mass and energy stores.
    2. Skinfold thickness for the distribution of subcutaneous adipose tissue and fatness between adipose tissue and skin in some regions of body such as triceps, abdominal and calf.
    3. Body volume for the calculation of body density,
    4. Body weight (Bwt) for calculation of growth rate, obesity and under nutrition.

5. BMI (Body mass Index) that shows the total body fat by a formula which combines body weight in kg and height in meters (BMI=kg/m^2) (Manios, 2006).

5.4 Body Mass Index (BMI), Fat Mass Index (FMI), Fat Free Mass Index (FFMI).Determination and relationships.

Body surface area indicates basal metabolic rate and fat free mass. The use of BMI is generally accepted for the description of the fat content of body composition. However, an increase in BMI can happen due to an increase of fat mass or fat free mass, or both. The scientific approach has cited more specific indexes that are related to BMI, such as fat mass index (FMI) and fat free mass index (FFMI). So, if the total body weight of the human consists of FM and FFM, it can be written as:

$$BMI = \frac{TBW}{h^2}$$

Where, TBW is the total body water in kg and h is the height in m^2.

$$BMI = \frac{FM + FFM}{h^2}$$

Where, FM is the fat mass in kg, FFM is the fat free mass in kg and h is the height in m^2. According to the previous equation it can be assumed that:

$BFMI = \frac{FM}{h^2}$, where BFMI represents the body fat mass index, or

$BFFMI = \frac{FFM}{h^2}$, where BFFMI represents the body fat free mass index

In the study of VanItallie, factors such as age, sex and race were taken into consideration (VanItallie et al, 1990). FMI and FFMI are indexes for the determination of fat mass and fat-free mass in subjects of different heights related to age, sex and race. In contrast BMI does not provide information for these special features in a population.

The reference values of FFMI and FMI are better indicators for assessment of fatness in a population of a specific age and sex.

If BMI undergoes a change, this change is attributed to the changes in FMI or FFMI, or both. If BMI is constant, the relationship between FFMI and FMI is inversely proportional.

According to a cross-sectional study, the reference values of FFMI for healthy Caucasian young population of the same age but different sex are higher in young males than young females. Therefore, it can be assumed that males have increased muscle mass beyond height in comparison with women. On the contrary, FMI reference values in young women are 38% greater than the corresponding values of young men.

In the same study, it is noted that FMI of healthy Caucasian subjects increases during aging, whereas FFMI is constant. BMI is not fully related with these changes due to physiological alterations in body composition of elderly people (Schutz et al, 2002).

6. MEASUREMENT METHODS OF BODY COMPOSITION

For measuring the body composition, various techniques are employed in clinical practice for different conditions such as disease and nutritional status. There are indirect techniques, called in vivo techniques, and some direct techniques which refer to multicompartment models that are more recent and accurate (Wells et al, 2006). The direct techniques are the most useful nowadays in clinical practice for the assessment of body composition.

6.1 Bioelectrical impedance analysis (BIA)

BIA is a simple, quick and non-invasive procedure using computer analysis that estimates tissue and fluid compartments or generally TBW (total body water) by conducting electrical current to the human body. BIA also uses impedance at frequency of 50 kHz or different frequencies as the current flows. Impedance is expressed as Resistance (R) and Reactance (Xc) (Kyle et al., 2004).

The method of BIA is based on two compartment model and, by measurement of TBW, it permits to calculate FFM and FM. TBW is estimated using the constant relationship between FFM and TBW:

$$FFM = \frac{TBW}{0.73}$$

This means that hydration constant is 0.73 L/kg of FFM. However, hydration constant of FFM is changed by age, sex and race. (Lee et al, 2008). BIA is used in healthy subjects, in chronic diseases and also in patients with high BMI but it is not recommended in abnormal situations such as dehydration and over hydration of the subject, since the results for the measurement of body composition may be altered. (Thibault et al, 2012)

PRINCIPLES OF BIA

In human body, the impedance of biological tissue consists of the resistance and reactance. The resistance refers to the conductivity of body fluids to the electrical circuit, while reactance refers to cell membrane which acts as an insulator. Therefore, at high frequencies, impedance measurements are related with total body fluid volume

whereas at low frequencies, they are related with extracellular fluid volume. BIA measurements must be standardized in order to obtain reasonable results. Specifically, it is necessary to know that muscle contains a lot of water and electricity flows easily; that is why is called ‘’conductor’’ of electrical current. On the other hand, fat is called ’’insulator’’ and electricity does not flow. In case of muscle body water or FFM the impedance is low but in fat or FM the impedance is high (Kyle et al, 2004).

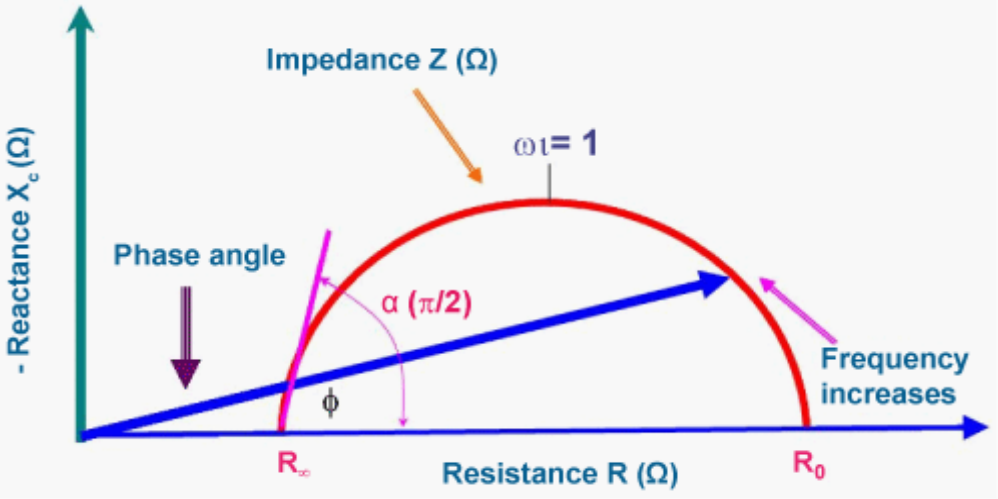

Figure 1: Cole-Cole model. Relationships between phase angle, resistance (R), reactance (Xc), impedance (Z) and frequency of the circuit. Resistance (R) refers to total body water (TBW) whereas reactance (Xc) refers to biological membranes. The sum of reactance and resistance is defined as impedance. R_0 reflects extracellular fluid when current frequency is zero. R∞ refers to the total body water in infinite frequencies applied current (Kyle et al, 2004).

Methods of BIA:

SF- BIA (single frequency BIA):

This method has a specific frequency, 50 kHz, and the electrodes are placed on hand and foot or in other devices the electrodes placed on hand-hand or foot-foot. In this frequency, it is possible to measure FFM and TBW in healthy subjects that are normal hydrated but this method cannot be used under abnormal hydration. In 50 kHz, it is possible to calculate TBW but it is impossible to differentiate the distribution of TBW in intracellular and extracellular compartment (Lee et al, 2008) (Kyle et al, 2004).

MF- BIA (Multi-frequency BIA):

MF-BIA uses impedances in different frequencies (from 1, 5, 50-500 kHz) for estimating FFM, TBW. By this method, the differentiation of intracellular and extracellular water in patients having fluid disturbances can be determined using empirical regression equations. In frequencies <5 kHz and >200 kHz, this method is not reproducible (Kyle et al, 2004).

Bioelectrical spectroscopy (BIS):

It measures the current resistance at frequencies 0 and ∞. At 0 frequency, the current passes through extracellular water whereas in ∞ frequencies the current passes through TBW. This method detects electrical properties of altered tissue. BIS permits the measurement of TBW and especially intracellular and extracellular volume measurement by mathematical equations such as Cole- Cole diagram (figure 1).

Multisegmental-BIA:

In these method, two more electrodes are placed into opposite side limbs or into the whole trunk in order to measure FFM as trunk due to its large cross-sectional area conduces to 10% of whole body impedance and 50% of whole body mass. The standardization of different devices and electrodes are required for desirable results. It is used for the assessment of fluid alterations in patients with chronic diseases such as liver and renal diseases as well as fluid changes in abdominal and pulmonary area.

As far as the validity of BIA concerned, the estimated error of various equations is about 2-3% and it can be defined as deviation range of 1.9- 4.0kg of FFM (Brodie, 1998). A reference method, such as multicompartment model, would be necessary used against BIA in order to limit these errors with better discrimination of ECW and ICW in population with various characteristics (Kyle et al, 2004).

Procedure:

More BIA devices are tetrapolar. They apply current of 500 μAmp at a single frequency of 50 kHz or more.

The four electrodes attached to the BIA Device, two for applying the current and two for sensing the current. The volunteer should be positioned on a non-conducting surface at least 50cm from any electrical device. He should lay on his back with his arms not touching the trunk. The thigh should not touch and the ankles should be at least 20cm apart. The head may be either on a thin pillow or level. The volunteer's skin should be cleaned with alcohol. The four electrodes are then attached to the hand, wrist, foot and ankle precisely where indicated. After, it is necessary to turn on the instrument and read the impedance .The test is completed within 5 minutes (Manios, 2006).

Conditions for proper BIA testing

The subject:

- should not exercise or drink alcohol for 8-12 hours before testing
- Should not eat or drink for at least 2 hours before testing (Evans et al, 1998).

Factors that affect impedance in human subjects:

- ***Hydration***-If the person is over-hydrated then the conductivity through tissues will be much higher and the impedance very low, giving them a low and inaccurate body fat percentage. If the volunteer is ill or recently exercised (dehydrated), then the impedance will be very high and the body fat percentage will be elevated.
- ***Water distribution***-The subject should lay on his back for not more that 5-10 minutes because otherwise their fluids tend to ''settle'' and the changes in impedance will be unpredictable
- ***Tissue orientation***-If tissues oriented perpendicular to the current's flow, the current is slowed by the increased number of membranes it must penetrate but if they are parallel to each other, impedance is reduced.

So, it is necessary to set carefully controlled conditions (Evans et al, 1998).

Data used to calculate TBW is:

- Resistance(R)
- Stature(S)=height
- Weight(w)
- Age (years)
- Sex (male=1,female=0)

By Lukaski and Bolonchuck formula, we can calculate TBW.

TBW= 0.372(S^2/R) +3.05 (sex) +0.142 (w)-0.069 (Age) (Lukaski et al, 1985)

Since the hydration constant of FFM is 0.73, it is possible to calculate FFM:

1. FFM=TBW/0,73
2. FM=weight-FFM
3. The percentage of body fat is calculated by: (fat mass/body weight)*100(Manios, 2006).

6.2 Dual energy X-ray absorptiometry (DEXA)

DEXA is a direct, non-invasive, relatively cheap method for the determination of areal densities of up to two components of an absorber. Especially, DEXA body composition analysis defines bone mineral mass, fat mass and lean soft tissue of human body by a ‘’dual –energy ‘’X-ray’’. It is the most useful tool for diagnosis of osteoporosis or osteopenia and assessment of fracture risk by measurement of vertebrae (spine), proximal femur (hip), distal forearm (wrist) and it constitutes the reference method for clinical practice. This method can be used in subjects of different ages and includes good accuracy and reproducibility in subjects with some disease or growth disorder (Laskey et al, 1996).

DEXA can analyze each ‘’two component’’ system separately. This is the reason why there is a division of Soft Tissue Pixel in which DEXA can analyze the area for fat mass and lean tissue mass in the portion of the body that does not contain bone. Bone Pixel in which DEXA analyzes the area for soft tissue mass (fat mass + lean tissue mass) and

bone mineral mass in the portion of the body that contains bone as x-ray beam pass through this pixel (Laskey et al, 1996).

Some definitions that are important to know are:

- Mass per unit area: when a human being that is a 3-dimensional absorber is analyzed by DEXA, it generates 2-dimensional flat image.
- Energy attenuation coefficient: as an energy x-ray beam passes through the bone mineral, some of the energy is lost due to Compton scattering and photoelectric effects. So, the intensity of x-ray beam is attenuated.
- R-value is the ratio of low energy attenuation coefficient to high energy attenuation coefficient.

Using R-values, we can determine the mass fraction of each component in a two component system. R-value for soft tissue (fat + lean tissue mass) is linearly related to the amount of fat in the tissue but generally in a real DEXA analysis, computer calculates it (Manios, 2006).

Procedure:

DEXA apparatus uses a low-energy x-ray beam of 40keV and a high-energy beam of 70keV. The detectors measure the energy of attenuated X-ray beams for each of the two energies, after passing through an absorbing material. If there is no absorbing material, there are no attenuation energies.

- The technician operates DEXA instrument from a computer. The scan of whole body is analyzed from the computer, as well.
- During the scanning procedure the X-ray is positioned below the subject and it is coordinated with the detector that is located above the subject by a rectilinear pattern movement.
- On the table of DEXA, there are ‘’blue lines’’ that helps the subject to be located in the right position within the scanning area.

Depending on the scan model, the time required for the procedure is about 15-45 minutes.

The lines present on DEXA table, divide the scanned image into segments of the whole body that we are interested. Then, the software analyzes each of these segments and makes up a report of each segment as well as the whole body composition on a table with R-values, areal densities(in terms of g/cm^2 scanned) and percentages of fat content of soft tissue and bone in each analyzed region (Manios, 2006).

Limitations:

it is not recommended to use DEXA in pregnant women because X-ray beams are used for the whole body analysis.

The composition of soft tissue is given by the R-value. When the bone mineral content is high then proportionally lean tissue mass is high, as well.

Example: Older women with osteopenic conditions will have an overestimated body fat because bone mineral is reduced as a percentage of the lean body mass (Laskey et al, 1996).

6.3 Computed Tomography (CT)

CT is an imaging method based on X-rays radiation and provides high quality images and resolutions of cross-sectional regions of the human body for the assessment of FFM. Even if its use is determined for diagnostic reasons in medicine, it has been proved that it is a useful tool for the assessment of body composition and nutritional status of the patient. This method is based on the principle of X-rays attenuation, as X-rays pass through different tissues of the human body. The X-rays detection from specific sensors provides information tissue density in each pixel. This information is used in combination with the anatomical site of each pixel which has been analyzed used for the division of tissues in fat, bone, muscle. Except from the total body fat percentage, CT assesses the distribution of body fat, quantitatively, in visceral and subcutaneous. Another advantage of this method is the evaluation of bone mass, shape and microarchitecture resulting in the differentiation of bone to cortical and trabecular

in each anatomical site. This property of CT is significantly useful in clinical research for patients with osteoporotic diseases (Manios, 2006). In conclusion, this method is accurate and valid but the high cost and the high levels of radiation in comparison with DEXA are major disadvantages (Lee et al, 2008).

6.4 Magnetic Resonance Imaging (MRI)

MRI is an in vivo method that uses electromagnetic waves and microwaves for the tissue imaging of the body. This method is very useful for the quantitative determination of organs and distribution of adipose tissue into visceral (intra-abdominal) and subcutaneous. MRI as well as CT examines patients with CV diseases, cancer and it also permits the assessment of energy expenditure at chronic diseases. The limitation errors of MRI is that encounters a highly cost method and the scanner field is not suitable for patients with extremely high BMI (Manios, 2006), (Lee et al, 2008).

7. CHANGES IN BODY COMPOSITION DURING ONTOGENESIS

7.1 Body composition in newborns

In the first year of newborn's life, progressive changes happen. Those changes occur mainly in length and weight, as well as in the development of the skeleton of the body accompanied with changes in body composition (Zampelas, 2003).

Water: The total body water of normal infant's body corresponds to 70%- 75% of body weight at birth. The volume of extracellular water during the first months of life exceeds the volume of intracellular water, while during growth this ratio decreases. In the end of the first year, total body water decreases to 60% of body weight and this decrement responds exclusively to extracellular water which reduces from 42% to 32%. Meanwhile, the intracellular water increases. The alterations of adipose and especially of muscle tissue is the main reason of these changes, since the amount of adipose tissue as well as the amount of muscle tissue increases (Zampelas, 2003) (Duggan,2008).

According Ellis et al., the mean percentage of total body water is 81.7 ± 1.7 (%) by using the PEA POD method and 77.6 % – 85.8 % using four- compartment model method in newborns, whose body mass ranges from 2.7- 7.1kg. By four-compartment model method analysis, the percentage of FFM can be also calculated by the formula:

$$\%TBW = 100 \cdot \frac{TBW}{FFM_{4-C\ Model}}$$ (Ellis, 2007)

Fat free mass: Fat free mass matures with the rate of increase of protein content, as the content of body water decreases. The content of fat free mass in protein is augmented in the first month from 12.5% to 17% at boys and 16.7% at girls. In a recent study, it was noticed that, fat free mass in absolute values (kg), increases considerably between first week and 12th week after birth (3.22kg to 8.50kg). By the age of 1.5 years, a negligible increase was noted (Eriksson et al, 2012).

Fat mass: Prenatally, the growth of fat body content is slow. The content of fat mass is calculated at 0.5% of body weight in the 5th month of pregnancy and at 16% in the end of pregnancy. After birth, the concentration of fat mass in newborn's body increases

rapidly until the 9th month of life. Between the 2nd and 6th month of life, growth of fat is twice the growth of muscle tissue (Zampellas, 2003). According to Eriksson et al.,during the first week after birth, total body fat is 13.5% and it is elevated significantly at 12th week of age (25.9%). However, in the period between 12th week and 1.5 years of age, total body fat increases only about 2% (Eriksson et al, 2012). Another research, comparing PEA POD method of air displacement plethysmography with a reference four-compartment model in healthy infants of 1.7- 23 weeks of age, found that the mean percentage of their body fat is about 16.9% with PEA POD method and 16.3% with four- compartment method (Ellis et al, 2007)

Newborns develop a reduction of weight after birth. This occurs especially in the premature newborns due to a higher percentage of extracellular water in their body (Zampelas, 2003).

Generally, in infants, the growth rate mainly the differentiation of bones and the maturation of different systems of organism performed rapidly. However, the tolerance of a baby in normal food is limited because digestive system, liver and kidneys are not mature enough. This is the reason why, newborns are feeded exclusively by breast milk, especially in the first six months of their lives (Zampelas, 2003).

7.2 Body composition in childhood

The period between infancy and puberty is called childhood and it is divided in three distinct periods:

- Babyhood (1-3 years),
- Preschool age (4-6 years), and
- School age (7-10 years).

The extremely fast rate of growth during infancy turns slow during childhood. For example, the weight and height gain are slower than that at the first year of life. The weight of a child is increased by 2-2.5kg per year, while height is increased by 7.5cm until the age of 7 years and 5cm until the beginning of puberty. In addition, growth alterations are observed between the two sexes. Despite the fact that waist

circumference values of boys and girls are similar, boys tend to accumulate more fat in the abdomen region and it is obvious especially during puberty (Zampellas, 2003).

Fat percentage tends to reduce considerably until the age of 6 years, reaching its minimum value. After the 6th year, fat percentage is increased because the organism is prepared for the beginning of puberty (Zampellas, 2003).

A great part of brain development is accomplished until the age of 2, so the number of brain cells is fulfilled. Contrariwise, the biggest part of the body is developed until the 2nd year. This is the reason why the head seems smaller and legs bigger than the rest of the body.

In childhood, the increased fat mass is attributed to the increasing number of adipocytes and not to the size of adipocytes, since the weight is normal. The increasing number of adipocytes refers to hyperplasia while the increased size of adipocytes refers to hypertrophy (Manios, 2006).

7.3 Body composition in puberty

The stable, but slow, development during childhood accelerates and differentiates between the two genders during puberty. It is the second stage after infancy that the rate of development is quick and intense with consecutive changes in sexual maturation, weight, height and body composition.

7.3.1 Somatic and sexual development

Definitions:

Puberty- is the period of human life where sexual maturation and ability of reproduction is observed. The definition of adolescence is identical; however, the adolescence is a broader term which includes the psychosocial development of teens, as well. The beginning of puberty corresponds to 11th year of life for girls and 13th year of life for boys (Zampelas, 2003).

Adolescence- the beginning of adolescence is determined by puberty. Adolescence starts gradually during the latent period, 10 ½ - 11 years, and ends gradually with the

beginning of adulthood (18 years until 21 years). It is divided in 3 stages: early adolescence (10 ½ -11 until 14 years), middle adolescence (14 until 16-17 years old) and late adolescence (16-17 until 20-21 years).

Menarche: period in which first menstruation is present. It is often manifested at the age between 10-16 years with average age of 13 years.

Menstruation: normal blood flow present in women almost every 28 days during a reproductive cycle. The beginning of menstruation has major influence on development, nutritional requirements and psychological status of teenage girls.

Amenorrhea: the retardation of menstruation, called primary amenorrhea, while interruption of menstruation that has already started, for more than three months is called secondary amenorrhea (Zampelas, 2003).

Sexual development:

The alterations which occur in the body of teenagers during puberty are attributed to hormonal factors. During puberty, changes in the brain and hypothalamus cause the release of a hormone that triggers the secretion of gonadotropins by hypothalamus. The secretion of gonadotropins provokes hormonal secretion for the development of the most of the secondary characteristics in both sexes; estrogens and progesterone for girls and testosterone for boys. In girls, the first sign that indicates the beginning of puberty is the development of ovaries, development of breast and growth of hair at the area of pudenda. Respectively, in boys, is noticed maturity of their genitals while the changes in voice, skin and allocation of hair are present later (Siervogel, 2003).

Changes in height and weight:

During puberty, the muscles, volume of blood and generally many organs of the body become doubled in size. The height of a teenager is increased by 20% in comparison with his final height and his weight by 50%. The growth spurt, which refers to the rapid rate of development during puberty, often represents the index of somatic development. In addition, the peak growth velocity is achieved at the age of 10 or 11 years by girls and at the age of 12 or 13 years by boys (Marshall, 1975). This is the reason why in the period of the early adolescence, girls are taller than boys for 4-5cm, while in late adolescence, boys end up much taller than girls. In boys, the peak growth velocity

coincides with the peak growth height, so the growth is 9 kg/ year. However, the height growth velocity is preceded by six months of weight growth velocity in the case of teenage girls, so their growth reaches 8,3kg/year in the age of 12.5 years. At the late stages of adolescence, the growth velocity of weight decreases in a same manner as growth velocity of height (Zampelas, 2003).

Body composition:

During early adolescence, the percent of body fat is elevated in boys in a greater amount than in girls but, in the period of late adolescence, girls acquire more fat whereas boys show an increase in muscle mass (Duggan et al, 2008). In late adolescence, the percent body fat of a teenager represents 23% and 12% of body weight in girls and boys, respectively. The distribution of fat in the body of teenage girls induces alterations in the shape of the body, since it is stored basically in specific regions such as buttocks and mammary glands. Moreover, the skeletal development is extremely rapid, since 40% of total bone mass is acquired during this period, approximately (Rizzoli, 1999) (Zampelas, 2003).

The skeleton increases in mass, the dimensions of bones change but the changes, especially of shoulders and pelvis, are predominantly apparent in both sexes. The trunk circumference increases more than that of pelvis in boy, while in girls the opposite occurs (Rodríguez et al, 2004). Significant differences are noticed in the development of bone mass and bone mineral density according to age, sex and skeletal region. For example, the bone mass of males constantly grows in different parts of the body, whereas the rate of skeletal development in females decreases dramatically from the age of 15-16 years in the spine and hip. Generally, the acquirement of high bone mass during puberty is an important protective factor against the occurrence of osteoporosis after menopause (Duggan, 2008).

7.3.2 Evaluation of physiological development

Different anthropometric parameters are used for the evaluation of physiological development of a teen. Traditionally, the weight and height represent the key measurements which can be used directly, but measurements of skinfold thickness and circumferences are useful, too (Siervogel, 2003).

The height is an important indicator of the nutritional status, whereas weight measurement provides incomplete information for body composition especially when the height is not involved (Zampelas, 2003). Specific indicators including height and weight in their formula, such as BMI, are practical and useful tools for the assessment of growth and body composition in children and teenagers. BMI can be applied in teenagers for the distinction of the population in low-weight, normal and overweight by using the so called cut-off points. A simple way for this evaluation is the use of growth charts based on the development of population standards. By using different time points on a growth chart, the complete estimation of special characteristics in the teenager development is enabled, since an individual teenager is in the same stage of growth comparatively with a group of people in the same age. For this reason, growth charts of BMI are notably practical (Weber, 2012).

The skinfold thicknesses measurement can be used directly or indirectly for the assessment of body fat percentage. It represents a reliable method for the estimation of subcutaneous fat if a good correlation with total fat of the body is considered. However, it is known that the relationship between subcutaneous and total fat alters during development of the subject so, the method of skinfold thicknesses for the assessment of body composition is necessary to set appropriate formulas specifically developed in adolescents or formulas that their reliability has been checked in adolescents (Weststrate, 1989).

The general principle is that the more skinfold thickness measured, if measurements are made at regular intervals, the more reliable results arising both for body composition at a given time, but mainly for the changes with the passage of time. However, between skinfold, the triceps skinfold shows an optimal correlation with total body fat in teens, in comparison with suprailiac and subscapular skinfold. So, the triceps skinfold together with BMI are recommended for the assessment of body composition and severe obesity at this age (Zampelas, 2003).

Different ratios of skinfold thicknesses or circumferences have been used, concerning the distribution of body fat. Among them, it seems that the ratio of trunk skinfold to extremities is more representative than waist to hip ratio for the assessment of body fat distribution. Unlike adults, the waist to hip ratio is not so reliable in adolescents because adolescents do not have high storage of body fat in abdominal region and there is no big

correlation between this ratio and total body fat in adolescents. This ratio becomes a reliable indicator of body fat distribution, the last years of adolescence (Zampelas, 2003).

7.4 Body composition in middle age

In adults, the physical development has been totally completed; the fat free mass reduces about 2-3% per decade with subsequent increase of fat mass and proportional reduction of the basal metabolic rate with fat free mass. This condition causes an increase in body weight if physical activity is not increased or energy intake is not reduced (Zampelas, 2003). In a previous study, it was noted that physical exercise reduces the levels of total body fat and body weight in male population but in female population, it enhances fat free mass values. By measurement of body composition with the method of hydrodensitometry, it was also noted that total body fat in healthy men and women at the age of 40-60 years increases about 0.37kg and 0.41kg per year while fat free mass decreases approximately about 0.07kg and 0.11kg per year, respectively (Guo et al, 1999). A cross sectional study examined by DEXA the changes in body composition in healthy Italian males and females during aging; age groups ranged from 18-30 years to 61-70 years. It was observed a small increase in fat mass (FM) in 31-40 years old female group and a stable rate of fat mass values in the following decade. In men those values continuously increased in all age groups. As far as total lean body mass is concerned in this study, the point where lean body mass started decline was at 40 years in male population, while in females the progression of this value remained stable in all ages after 18 years (Bazzocchi et al, 2013).

Between the age of 40 and 58 years old, menopause appears in women (Guo et al, 1999), although some genetic, environmental, lifestyle and race factors alter the age that menopause occurs (Gold, 2011). Menopause is defined as the end of reproductive age and it is characterized mainly by reduced production of estrogens. The hormonal alterations cause reduction of bone metabolism having as a consequence the reduction of bone density and the possible occurrence of osteoporosis. At this age, the loss of weight becomes more difficult, since there is a tendency for fat deposition with

simultaneous reduction of muscle tissue (Zampelas, 2003). From the cross sectional analysis of Sornay-Rendu et al, which examined women of age 31- 89 years old according to their menopausal status in the baseline of ninth monitoring annually, it was indicated that women after menopause irrespective to their age and without receiving estrogen therapy had approximately 23.9kg of fat body mass and 41.0kg fat free body mass, while these values in premenopausal women were about 20.8kg and 43.4kg, respectively. However, after adaptation of age in postmenopausal women receiving estrogen therapy and postmenopausal women without treatment, it was noticed that estrogen therapy enhances the total bone content and hip bone density but it does not affect BMI (Sornay-Rendu et al, 2012). The longitudinal analysis of this study concluded that age is a crucial factor of body composition alterations in comparison with interruption of menstruation- induce these changes (Sornay-Rendu et al, 2012) (Roubenoff, 2000). Middle age men and women show a preferential deposition of fat in the central part of the body (visceral fat), with this deposition to be more selective for male adults due to higher trunk to lower body fat ratio (Horber et al, 1996) (Bazzocchi et al, 2013).

7.5 Body composition in pregnancy

Pregnancy is a physiological situation in a woman's life. It lasts 40 weeks or about 280 days beginning from the first day of the last menstruation (Duggan et al., 2008). Many alterations happen in the body of a pregnant woman related to systems of the organism. These changes aim to regulate the metabolism of a pregnant woman, the development of fetus and the preparation of mother for childbirth and breastfeeding (Zampelas, 2003).

Body weight in pregnancy is increased due to anatomical and hormonal alterations which occur in woman's body for the appropriate development of fetus. Body weight is correlated with BMI. Based on a systematic review, normal weight gain in pregnant women with normal BMI (19.8-26kg/m^2) before conception ranges from 11.5-16kg (Manios, 2006).

Weight gain during gestation is related to the main components for fetal growth (amniotic fluid, placenta and uterus), the changes of body composition (increase of FM and TBW) and the development of body tissues (breast and uterus development)

(Hornstra et al, 2005). Due to these changes, the energy requirements of the pregnant body are increased, thus, basal metabolic rate (BMR) is increased by time, especially in the third trimester of gestation. However, pregnant women with low BMI perform lower BMR in comparison with BMR of women with high BMI in 3^{rd}, 6^{th} and 9^{th} month of gestation. This happens due to fat mass and fat free mass alterations as BMI is defined as the sum of fat mass and fat free mass (Prentice et al, 1996) (Butte et al, 2004).

Measurement of FM and FFM during reproductive period is valid using four-compartment model. It is composed of total body water (TBW), body volume, body weight and bone mineral content (Butte et al, 2004).

Total body water(TBW):

In the period of gestation, an increased water retention in body tissues and mainly in the extracellular space of the pregnant woman is noticed. However, in the end of gestation, the intracellular fluid increases about 550 mL,whereas extracellular fluid about 2700 mL. The amount of extracellular fluid is distributed in intravascular and extracellular space (Zampelas, 2003). During gestation it is considered that plasma volume expansion is about 45% of total body volume, since plasma volume is elevated to supply with oxygen the maternal tissues (Faupel-Badger, 2007). Forsem et al, by using BIA (Bioelectrical Impedance Analysis) method concluded that TBW increases during pregnancy and it declines after parturition. They also observed that BMI is the most valid and reproducible method for this purpose in comparison with anthropomeric methods (Lukaski et al, 1988).

By using dilution method for measurement of TBW in normal and diabetic pregnant women with H^2 [18O] tracer, the results showed that TBW and amniotic fluid were contiguous to diabetic and normal pregnant women (Denne et al, 1990).

Many studies observed that fat free mass is increased gradually during gestation. The four compartment model, is responsible, in a high degree, for the resting energy expenditure (REE). Due to high total energy expenditure correlating to weight gain and elevated levels of water in the body of pregnant woman, fat free mass is also elevated.Women with high BMI have a greater FFM than those with low BMI. The highest value is performed at the late stage of pregnancy whereas during postpartum period is decreased (Butte et al, 1998).

The deposition of fat distributed in shoulders, buttocks and thighs of woman due to high estrogen levels during pregnancy is an important factor for weight gain (Zampelas, 2003). The fat mass reserves the highest amount of energy and it increases by 3.7kg in the group of well-nourished women. In the third trimester of the reproductive cycle, the amount of fat mass is greater (21±5.6kg in women with normal BMI) than in the first and second trimester, whereas after childbirth is slowly reduced. Comparing the pre-pregnancy and postpartum period, a part of fat mass is conserved into the body of woman during postpartum period in order to cover energy requirements during breastfeeding (Butte et al, 1998).

7.6 Body composition during breastfeeding

During lactation, prolactin, a hormone which is secreted by hypophysis, stimulates the production of breast milk by mammary glands. After parturition, the levels of prolactin are significantly elevated and metabolic requirements are increased during lactation. Due to these requirements, women have to acquire more energy by food. WHO (World Health Organization) recommended that the breastfeeding is necessary for at least 6 months after parturition because it provides many beneficial effects to health of both, mother and child (Zampelas, 2003).

Breastfeeding favors the reduction of weight gain during pregnancy. It is believed that the high energy needs during the period of breastfeeding cause the activation of storage fat. A recent research showed that mothers who breastfeeded their babies for the first six months reduced more their body weight in comparison with those who did not breastfeeded (Dewey et al, 2001) (Dewey et al, 1993).

According to Motil et.al. and other studies, fat- free mass is maintained in lactating mothers with good nutritional status, as protein needs of breastfeeding milk are covered by a rich in protein food supplementation of mother (Motil et al, 1998). Other studies which examined the fat free mass alterations between lactating and non-lactating mothers, reached to the conclusion that there are no differences in fat free mass between them (Butte et al, 1998) (Sohlstrom et al, 1995).

During breastfeeding, fat mass distribution and deposition differs among populations. This is the reason why the conclusions of many studies are controversial. Butte et al. study support that during pregnancy the deposition of body fat is higher in the central parts of the body (trunk, thigh) and during lactation a high amount of body fat is mobilized from these parts for the production of energy needed for milk synthesis (Butte et al, 1998). However, it was reported that energy requirements for milk synthesis are covered, at a higher extent by nutrition of lactating mother (66%) than mobilization of body fat (34%) (Zampelas, 2003).

7.7 Body composition in elderly

Aging is accompanied by limited physiological reserves in all organs. That is why, when an elder has a disease, all other systems aggravate his situation even if they are not directly related to his illness. This exposes the elderly at risk by multiple concurrent disease states.

Physical changes in elderly

Continuous changes occur in body composition, function of tissues and metabolism throughout aging. The fat free mass is reduced gradually by age, while fat is increased. Deurenberg et al calculated the fat body content in different ages and performed the formula below:

$$\%body\ fat = 1.20 \cdot BMI + 0.23 \cdot age - 10.8 \cdot sex - 5.4$$

BMI= Body Mass Index

Sex (1=man, 0=woman)

This indicates that a young man with BMI=30 kg/m^2 has body fat 24,4% ,while a 80 years old man with the same BMI has 38% body fat (Zampelas, 2003).

According Bazzocchi et al, by assessment of body composition with BIA, total body fat in healthy elderly individuals (61-70 years), especially in women, was higher than in

smaller age groups. In addition android fat mass in relation to android lean mass was elevated in male group of age 61-70 years, while at ages 18- 60 years this relation was greater in female group. Jackson et al supported that BMI in elderly is increased in a same manner as fat mass, especially after 80 years (Bazzocchi et al, 2013). The loss of muscle mass comes mainly from skeletal muscles. In 1972, Novak et al. used the content of total body potassium as fat free mass indicator and found that the total body potassium was rapidly reduced at age of 41 - 60 years for men and after 60 years old in women. Muscle strength is reduced, as well. The research of Framingham indicated that 45% of women population at 65 to 74 years old and the rest 65% of age 75 to 84 years could not lift 4.5kg weight. Larsson et al, studied 114 men of age 11 to 70 and they found that the ability of isometric and isotonic activity is reduced after the age of 50 years about 24% to 36%. Therefore, they concluded that the strength loss is caused by atrophy of muscle fibers type 2 which have a 36% smaller diameter than muscle fibers at the age of 40 (Zampelas, 2003).

Fat free mass loss is an important contributor of disability and functional impairment in elderly. Body cell mass, which is the metabolically active component of FFM, decreases with aging and it is calculated by total body potassium with the formula:

$$BCM = 0.00833 \cdot TBK$$

Where BCM is the body cell mass in kg and TBK is the total body potassium in mmol (Genton, 2011).

With aging, the secretion of growth hormone as well as steroid hormones (androgens, estrogens) decreases. Many changes are observed in the central nervous system, including loss of neurons and alterations in their activation. In the immune system, there is an increase in production of inflammatory cytokines (IL-1, TNF-a, IL-6) leading to the loss of amino acids from muscles (Zampelas, 2003). Generally, elderly face problems in coordination of physiological functions in comparison with younger ones. Initially, the changes are obvious in cells. As the years pass, the continuous division of some cells in different stages of life becomes slower. Other cells such as brain, kidney and muscle cells do not continue dividing, but develop structural changes and many of them die. This, results in the functional reduction of important organs of the organism, thus, organs and tissues of the body are less able to correspond to environmental stimuli (St- Onge et al, 2010). According to Gerdon, who examined elderly of age $\geq$ 65 years at

9 years follow up, the body cell mass (BCM), appendicular skeletal muscle and fat free mass of men and women decline with age. Moreover, after 75 years, the values of fat free mass decreased by 3.7 ± 5.4kg in men and 3.6± 5.5kg in women. He also observed that lean tissue loss is reduced by enhanced physical exercise in males rather than females (Genton, 2011). The energy needs decrease about 3% per decade due to reduced physical activity, fat free mass and deceleration of basal metabolic rate. In 30-40 years, the lean tissue mass is about 60kg in men and 40kg in women but in 60 years, these values become 48kg and 36kg, respectively (Zampelas, 2003).

Every ten years, the total energy metabolism is limited by 7.5% in males and 6% in females, respectively (St- Onge, 2010). The protein metabolism is considered to be the 15-25% of BMR. The BMR is dependent on levels of thyroid hormones. Skeletal muscles are responsible for protein loss in a great degree, while, in lesser degree, liver and heart muscle. This is the reason why muscle mass represents 45% of body weight in young adult and 27% in elderly. Young studied protein synthesis in infants, adults and elderly providing them with N-glycine. By this way, he defined the concentration of isotope in the urine of participants. The results regarding total protein synthesis in young men with body weight 71±15kg were 3.0±0.2grams per 1kg of body weight per day, while in elderly with body weight 56±10kg was 1.9±0.2grams per 1kg of body weight per day. So, the protein synthesis at the age of 60 years seems to be 40% lower than this at the age of 30 years and decreases at about 8% at the age of 80 years (Zampelas, 2003).

Elderly tend to acquire higher percentage of body fat than younger ones for a given body weight or BMI and the distribution of body fat accumulates especially in intrabdominal part of the body (Manios, 2006). According to a cross- sectional study for male aging, the elevation of percent body fat is attributed to the reduction of lean mass (St- Onge, 2010).

7.8 Aging and sarcopenia

Sarcopenia is a condition associated with loss of muscle mass and strength due to aging. (Morley, 2001), (Muscaritoli, 2010).The term is derived from the Greek words ‘sarx’, which means flesh and ‘penia’, which means poverty (Morley, 2001). It is an age-related problem and its prevalence seems to be 13-24% in people under the age of 70

years, whereas it reaches over 50% in people older than 80 years old (Muscaritoli et al, 2010). Some researchers mention the loss of fat free mass with aging. This loss is referred in a large extent to muscle mass reduction (Elia, 2001). It has been calculated that from the age of 20 until the age of 80 years, the loss of muscle tissue mass is about 20-30% (Manios, 2006). This happens due to a reduction in size and number of skeletal muscle fibers of type I and II with aging (Muscaritoli et al, 2010). Muscle strength, basal metabolic rate, resting energy expenditure and aerobic capacity are simultaneously reduced due to the progressive loss of muscle, leading to metabolic and functional alterations in elderly. These changes are often related to FM gain in elderly resulting in sarcopenic obesity (Jacquelin- Ravel et al, 2012).

Typical features of sarcopenia are the reduced ability of muscle contraction and perfusion, as well as, the reduced ability of energy substrates and quick fatigue (Morley, 2001). This condition leads to immobility, reduced adaptation to stressful situations caused by diseases and generally the increased morbidity (Carmeli et al, 2002). Sarcopenia is also related with an increased loss of bone mass and greater fall frequency because of minimal muscle strength and balance (Muscaritoli et al, 2010). Causes can be also attributed to environmental factors such as inadequate nutrient intake from the diet and physical inactivity often observed in the elderly (Carmeli et al, 2002).

Generally, the muscle constitutes 60% of protein deposits in the body. It is considered that the loss of muscle tissue is the result of various functional mechanisms alterations. Alterations in hormonal profile, such as the reduction of growth hormone levels as well as of steroid hormones (estrogens, androgens), the non- physiological enzymatic activity, the changes in protein synthesis and metabolism due to increased anabolism, the high oxidative stress due to insufficient anti-oxidative immunity that can cause abnormalities of muscle cells are some changes considered responsible for the appearance of sarcopenia. The ion homeostasis turnover and especially the turnover of calcium is another cause that has been introduced to explain the loss of muscle tissue mass (Tudoraşcu et al, 2014) (Manios, 2006). Calcium is an essential element for the contraction and generally for the function of muscle (Tudoraşcu et al, 2014).

In the Central Nervous System, there are changes related to loss of alpha motor neurons and transformation of their activation. In the immune system, there is an increase in the production of catabolic inflammatory cytokines (IL-6, TNFα, IL-1) resulting in loss of

amino acids from the muscle. Due to this loss, the immunity cannot be supplied with an adequate amount of amino acids in order to successfully cope with metabolic stress situations (Roubenoff, 2000) (Muscaritoli et al, 2010).

DEXA method, by estimating the sum of lean soft tissue mass of upper and lower extremities, it is possible to evaluate the appendicular skeletal muscle mass (Bazzocchi et al, 2013). If appendicular skeletal muscle mass index (ASMM/h2) is two standard deviations below the mean values for a young adult reference population (7.26 kg/m2 and 5.45 kg/m^2 for males and females, respectively) and the pace of walking is lower than 0.8 m/s in a distance of 4m , the subject is considered as sarcopenic (Muscaritoli et al, 2010) (Kovarik, 2014).

8. BODY COMPOSITION UNDER PATHOLOGICAL CONDITIONS

8.1 Obesity

In the last decades, obesity represents one of the most serious health problems in about 310 million patients in the world. It is considered as a chronic disease and an important risk factor for developing chronic metabolic illnesses, whereas its main cause is that energy intake is higher than energy expenditure, predisposing to excess storage of body fat. Factors lead to obesity are over nutrition, lack of physical activity but can also be genetic, social and psychogenic (Todd et al, 2015). Major determinant of obesity is BMI. Obese person is considered an individual with BMI equal or higher than 30 kg/m^2 (Mitchell et al, 2011).

In hormonal level, white adipose tissue is an organ where fat is stored and it is responsible for the secretion of adipokines and proinflammatory cytokines (leptin, adiponectin, TNF-a and IL-6). Adinopectin and leptin are helpful adipokines for the regulatory function of body weight. In case of obesity, leptin, TNF-a and IL-6 are overproduced and adinopectin levels are reduced, evoking inflammation of adipose tissue. By this dysregulation, other organs such as muscle and liver become abnormal in function with continuous secretion of glucose and fatty acids in plasma, leading to hyperinsulinaemia. By this way, inflammatory conditions such as insulin resistance, cardiovascular diseases and diabetes mellitus occur (Bastard et al, 2006) (Piya et al, 2013).

A percent of obese older subjects of American population,possessincreased muscle mass as well as fat mass. However, compared to body weight, the muscle mass is low. The data concerning the prevalence of obesity in children is extremely worrying. It is presumed that a significant consequence of childhood and adolescent obesity is the occurence of obesity in adulthood. Actually, there is 37% probability, a 6-9 years old obese child to be an obese adult even if his parents have normal body weight. In the case of one obese parent the above percentage rises to 73%. Moreover,obese children are at higher risk of developing chronic diseases both in childhood and adulthood (Whitaker et al, 1997).

As far as the distribution of body fat in overweight (BMI = 25-30 kg/m²) and obese individuals (BMI>30kg/m²) are concerned, two most common types of obesity exist; the android type of obesity, characterized by excessive distribution of fat especially in abdominal area and gynoid type with higher deposition of fat in the lower part of the body (thighs, hips) (Patidar, 2013). The android type of obesity is present mostly in male population and people with this characteristic are more sensitive to appear cardiovascular problems due to secretion of damaging metabolites, called adipocytokines. The gynoid type affects mostly female population (Kihara et al, 2015).

Generally, population with high BMI prevails to cardiovascular and diabetic events in comparison with population with low BMI. A recent study showed that obese and overweight subjects, with central adiposity, are more susceptible to cardiovascular diseases than subjects with other types of obesity beyond BMI (Patidar, 2013). Moreover, the results of a cross-sectional study showed that Trinandian males with elevated intra- abdominal fat have higher glucose levels than Trinandian females with higher adiposity in thighs and hips. It is also found that patients with diabetes have high BMI than healthy ones (Nayak et al, 2015). Waist circumference and waist to hip ratio are the major determinants of central obesity-related diseases (Patidar, 2013), (Nayak et al, 2015).

8.2 Anorexia

Anorexia is defined as the loss of appetite andit can be established by the presence of a particular disease or a series of psychological symptoms related to alterations of hypothalamic mechanisms for food regulation. According to Functional Assessment ofAnorexia/Cachexia therapy (FAACT) and North Central Cancer Treatment Group Anorexia/Cachexia(NCCTG) questionnaire, a person is defined as anorectic if he has one of the following symptoms: quick feeling of satiety, changes in taste and smell and feeling of nausea and vomiting (Muscaritoli et al, 2010).

Anorexia nervosa is a debilitating disease with elevated percentages of mortality generating from excessive weight decline due to poor nourishment. In Western region, the frequency of deaths is estimated by 5.9- 18 % related predominantly due to heart problems (Nakai, 2015). Most frequently it appears in young population and exclusively in female population due to a psychological aspect to improve their somatic appearance

with harmful events arising in various parts of the body (Mehler et al, 2015) (Nakai et al, 2015). The fat mass and fat free mass loss due to low energy intake lead to protein loss and wasting. BMI and body weight are finally reduced due to these changes (Kerruish et al, 2002).

Anorexia related- disease represents a risk factor which is attributed to hormonal and immunological alterations due to the specific disease, resulting in deterioration of the condition (Muscaritoli et al, 2010). According to a cross sectional study of National Institute of cancer in Mexico, the highest percentage (61%) of individuals suffer from advanced cancer are anorectic and cachectic. Most of them are women and they develop the underlying symptoms of anorexia impairing their social, emotional and somatic level (Pèrez Camargo et al, 2014).

8.3 Cachexia

Cachexia is a syndrome with high rate of mortality characterised by excessive loss of muscle mass and fat mass or exclusively by reduction of muscle mass and increased protein catabolism due to a specific disease (Muscaritoli et al, 2010), (Jacquelin- Ravel et al, 2012). An unexplained weight loss in a six-month period indicates the presence of cachexia (Muscaritoli et al, 2010).

The separation of cachexia in precachexia, cachexia and refractory cachexia is very important for the early diagnosis of this condition in order to prevent complications related to chronic diseases (Muscaritoli et al, 2010) (Op den Kamp et al, 2013), (Jacquelin- Ravel, 2012). The pre-cachexia is characterized by an unwilling small weight loss <5% of body weight in a period of 6 months and the presence of chronic inflammatory diseases and anorexia as in the case of advanced cachexia. Metabolic alterations such as insulin sensitivity and systemic inflammation, revealed by increased levels of CRP (C - reactive protein), may also happen in pre-cachexia without considerable changes in body composition. In late stage cachexia-related disease such as lung cancer cachexia, there is a remarkable disintegration of skeletal muscle fibres whereas in precachectic patients, the loss is without significant loss of muscle strength (Op den Kamp et al, 2013) (Muscaritoli et al, 2010).

Refractory cachexia arises from the presence of chronic disorders such as cancer, Chronic Obstructive Pulmonary Disorder and heart failure and it is characterized by

anorexia and inflammatory processes. Inflammation plays an important role to the occurrence of cachexia. The overproduction of proinflammatory cytokines and the reduced production of anti-inflammatory cytokines are related to cachexia (Muscaritoli et al, 2010).

Cancer-related cachexia can be caused by inflammatory process, due to extended secretion of proinflammatory cytokines (IL-1, IL-6, TNF-a, INF-γ, LIF) by malignant cells or immune cells. Another factor that can induce cachexia is the secretion of serotonin from hypothalamus triggered by cytokines. Both factors lead to anorexia. In spite of anorexia, cancer cachectic patients reveal an increased basal metabolic rate with an elevated energy expenditure. This happens due to tumour needs for glucose with hyperactivation of Cori cycle (lactic acid is transformed to glucose), glucose and TGA-fatty acids cycle and gluconeogenesis for achieving it. As far as protein catabolism is concerned, excessive protein catabolism and reduced protein synthesis occur, resulting in a great loss of skeletal muscle and weight, which cannot be reversed with calorie intake. The gross protein catabolism is attributed to ubiquitin-proteasome pathway and significant amino acids are released and transported to the liver. Hypermetabolism of liver is observed due to overproduction of proteins in response to inflammation(Acute Phase Protein Synthesis). An extended period of this condition can be fatal(Muscaritoli et al, 2010) (Laviano et al, 2003)(Tisdale, 1997).

The definition of cachexia, from body composition point of view, is different from that of cachexia-related disease. Cachexia, without being causedby a specific disease, is characterized by weight reduction at about 5% during the last six months or with BMI of an individual lower than 20 kg/m² with subsequent weight decline about 2% for the last six months. It is also originated by the presence of sarcopenia when appendicular skeletal muscle index, measured by DEXA, is lower than 7.26 kg/m² for men and 5.45kg/m² in women with subsequent weight loss of 2% for the last six months (Kovarik et al, 2014).

Body composition knowledge is useful for diagnosis of the changes in muscle mass during cachexia and sarcopenia. Generally, skeletal muscle is the active part of FFM (consists of 44% FFM with resting energy expenditure 15 kcal per kilogram) and the indicators which are used for its assessment are those of lumbar skeletal muscle mass and median FFM. The methods for the assignment of these indexes are CT, for lumbar

skeletal muscle mass index, and BIA, for the assessment of FFMI. FFMI values,obtained by BIA, lower than 18.9 kg/m2 for young male population and 15.4 kg/m2 for young female population indicate muscle decline,whereas the values of skeletal muscle mass index, by CT, are 52.4 cm2/ m2 for males and 38.5 cm^2/m^2 for females. (Jacquelin- Ravel et al, 2012).

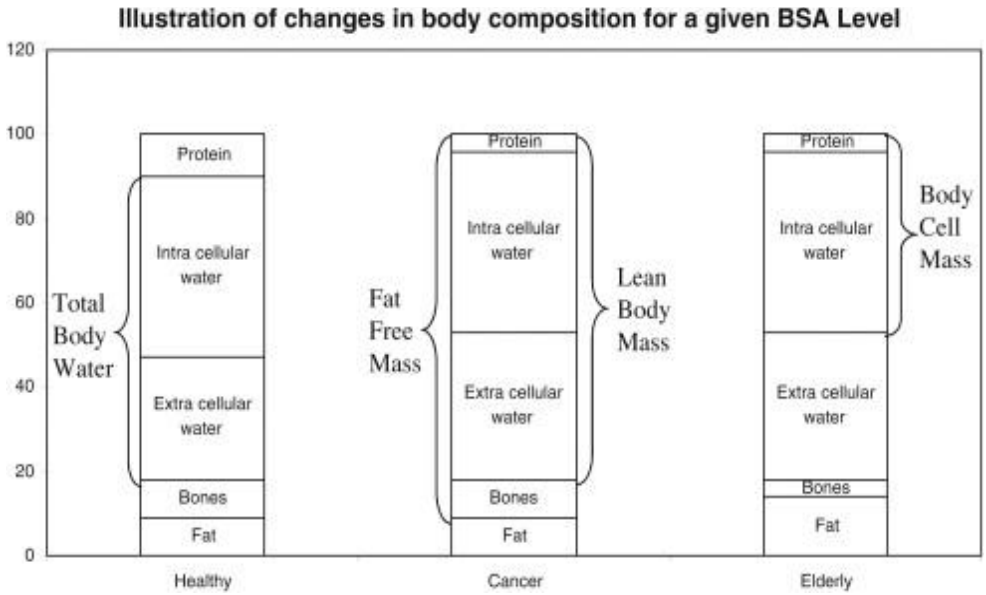

Figure 2. Illustration of changes in body composition for a given body surface area (BSA) level (Jacquelin-Ravel et al, 2012).

8.4 Osteoporosis

Osteoporosis is a progressive disease which is caused by loss of bone mass and bone density. It is determined by the deformation of bone microarchitectute resulting in a high frequency of fractures and falls which are the main factors of morbidity and mortality in Europe (Faje, 2012) (Kanis, 2013). Osteoporosis is most frequently present in elderly. The diagnosis of osteoporosis and the evaluation of related fractures,especially in hips and vertebrae by DEXA method, represent significant tools for the prevention of the disease and the subsequent increase in the quality of life of osteoporotic patients. According World Health Organization, an individual is defined as osteoporotic if T- score, which characterizes bone mineral density, is ≤ - 2. 5 standard deviations of that of a young well-being female reference population while Z-score characterizes the risk of hip fractures by standard deviations in which bone mineral density of a person varies from the reference population of the same age and gender (Kanis, 2013).

8.4.1 Effect of fat mass, muscle mass and body weight on bone

Bone resists different mechanical forces from the skeleton. The forces applied to the bone are affected by total body mass, muscle mass and fat mass by supporting bone remodelling and strength. Body mass exerts momentous static forces to the bone, supporting its strength, while muscle mass applies a dynamic load which is closely correlated with total bone mineral content and surpasses the static load that body weight supplies to the bone. Fat mass exerts a static strain on the bone mass and alleviates bone impact forces (Faje, 2012).

Body weight consists of fat, muscle and bone mass. Bone mass is directly correlated with muscle mass and body weight, due to mechanical processes that explained above. However, fat mass is related proportionally with body weight but its relationship with bone mass is controversial. Hsu et al indicated that individuals with high relative values of body fat mass (in %) irrespective of age , body weight and physical exercise are more susceptible to osteoporosis and fragility of bones so, absolute values of fat mass (kg) influence bone mass in a negative way (Hsu et al, 2006).

9. CONCLUSION

Fat mass, fat free mass, bone mass and total body water are the major compartments of human body and they are affected dramatically in different stages of life. In the first years of life, the changes in these components are attributed to the increase in body weight and height. During infancy, the rate of development is rapid and the content of total body water and, especially, extracellular water is extremely high as well as the percentage of body fat at birth. During childhood the growth rate decreases, in comparison with the infant period, and the percentage of body fat declines significantly in the 6^{th} year of age, while, after this period, it increases in order to support the changes which take place during puberty. Moreover, the extracellular water is reduced, while the intracellular water increases due to production of new cells. The differentiation of both genders is significant in puberty, since the quantity and distribution of body fat is much higher in females than in males. Males acquire more muscle mass, while girls acquire more fat mass, which is mainly distributed in breast and hips. During adulthood, the somatic development is stabilized and fat free mass gradually decreases about 2-3% per decade, while fat mass increases with increasing age. In elderly, due to the physiological processes of aging, the fat mass is elevated and it is stored particularly in the abdominal area, while fat free mass decreases significantly resulting in the presence of a devastating disease such as sarcopenia. During pregnancy and breastfeeding, the fat mass, plasma volume and especially total body water increase due to hormonal alterations and the requirements of the fetus.

Apart from the physiological processes that occur at different stages of age, pathological conditions such as obesity, cachexia, anorexia and osteoporosis also modify the body components. Anorexia provokes reduction in body weight and BMI due to loss of fat mass and fat free mass caused by protein loss. However, the low energy intake for a long time period, due to anorexia, leads to a progressive disease, cachexia, which is characterized by excessive reduction of muscle mass with or without loss of fat mass, with subsequent reduction of body weight about 5% at a six month period. Osteoporosis evokes a rapid loss of bone mass, while obesity causes storage of excessive amount of body fat due to high food consumption. The manifestation of those diseases is associated with chronic disabilities and their prevalence is considered extremely high.

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11. LIST OF FIGURES

12. LIST OF ABBREVIATIONS

TBW : Total Body Water

FM : Fat Mass

FFM : Fat Free Mass

ECF : Extracellular Fluid

ICF : Intracellular Fluid

BCM : Body Cell Mass

REE : Resting Energy Expenditure

BMI : Body Mass Index

FFMI : Fat Free Mass Index

FMI : Fat Mass Index

BIA : Bioelectrical Impedance Analysis

MRI : Magnetic Resonance Imaging

CT : Computed Tomography

DEXA : Dual Energy X-ray Absorptiometry

BMR : Basal Metabolic Rate

ASMM : Appendicular Skeletal Muscle Mass

ASMMI : Appendicular Skeletal Muscle Mass Index

IL-6 : Interleukin- 6

IL-1 : Interleukin-1

TNF-α : Tumor Necrosis Factor alpha

INF-γ: Interferon gamma

LIF: Leukemia Inhibitory Factor

CRP: C - reactive protein

TBK : Total Body potassium