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REGULAR ARTICLE

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Abstract
Childhood and adolescence are decisive periods in human life. Body composition and psychological changes determine nutritional requirements as well as eating and physical activity behavior variability. Aims of the present paper are to discuss recent advances in measurements for quantifying total body and regional adiposity, and for mapping adipose tissue distribution in order to evaluate metabolic risk factors in children.

Among the new methods available for assessing pediatric body composition, magnetic resonance imaging (MRI) can serve as a reference method for measuring tissue and organ volumes because estimates is reliable independent of age. MRI is the method of choice for calibrating field methods designed to measure adipose tissue and skeletal muscle *in vivo* and is the only method available for measurement of internal tissues and organs.

MRI can be used to validate measures of important molecular level components such as fat measured by dual energy X-ray absorptiometry and bioimpedance analysis. Moreover, the large gap in available information for certain topics makes MRI measurement a dynamic and growing scientific area of body composition investigation.

INTRODUCTION

Pediatric obesity is a condition of excess body fat accumulation and a clinical diagnosis of obesity should based on an accurate direct or indirect measure of total body fat (1).

Independent of total adiposity, an upper body, central or visceral distribution of fat is believed to be a risk factor for poor health in both adults (2) and children (3). According to the NHLBI guidelines (4), excess in abdominal fat is associated with hyperlipidemia, cardiovascular risk factors, type 2 diabetes, and other morbidities. Accurate measurement of total and regional body fat is fundamental in order to detect as early as possible whether a given child is deviating from normal values or trends (1).

Childhood and adolescence are decisive periods in human life. Body composition and psychological changes determine nutritional requirements as well as eating and physical activity behavior variability (5). Several recent papers pointed out that breastfeeding or the delayed introduction of complementary foods (or both) could reduce the risk of later obesity (6–9). On the other hand, animal studies demonstrated that maternal protein restriction during pregnancy and lactation programmes susceptibility to visceral adiposity in the adult rat offspring, and that the coordinated upregulation of molecular pathways involved in adipogenesis and angiogenesis likely plays a key role in this process (10). However, beneficial effects of breastfeeding on avoiding excess infant weight gain, childhood obesity and high blood pressure have conflicting results (11,12). The lack of agreement among these studies (6–12) has concerned, in part, the appropriate measure of adiposity and/or obesity. Most studies used body mass index (BMI: kg/m^2) that could be defined a surrogate measure of adiposity (13,14). Differences in body weight are only in part related to differences in body fatness. In fact it is adiposity, rather than body weight per se, that may underlie the major health co-morbidities related with obesity (6) even in childhood (15). Allison and colleagues, using two perspective population-based cohort studies, showed among obese individuals, that weight loss is associated with increased mortality rate and fat loss with decreased mortality rate (16). Accurate measurement of adiposity in children is central to contemporary genetic and clinical research.

Aims of the remainder of the present paper are to discuss recent advances in measurements for quantifying total body and regional adiposity, and for mapping adipose tissue distribution in order to evaluate metabolic risk factors in children.

FAT MASS – TOTAL BODY FAT – FAT DISTRIBUTION

Fat mass increases from approximately 500 g at birth (14% of body weight) to more than 2000 g at 12 months of age (23% of body weight) (17). Estimated fat mass increases during the first 2–3 years of life, has little change through 5 or 6 years of age, at which time it increases rapidly in girls. Fat mass increases through adolescence in girls while in boys changes only a little, close in timing to the puberty spurt. Girls have, on average, approximately 1.5 times the fat mass of boys in late adolescents (18,19). Males gain almost twice as much fat free mass as females over adolescence, and females gain about twice as much fat mass as males (19,20).

Compared with adults, children have much variety in body composition due to growth and hormones related from infancy to adolescence (18). The traditional reference methods to assess body composition used in adults, could have serious model concerns when applied in children (1,18). These issues could create limitation in the accuracy of component prediction methods when predicting body fat. Some body composition methods (i.e. anthropometry, bioimpedance analysis and total body electrical conductivity) must be calibrated against a reference method (21). On the other hand, methods with minimal age-related assumption (i.e. magnetic resonance imaging, MRI) have an advantage over methods strictly derived from adult body composition.

The anatomical distribution of adipose tissue shows different patterns of changes with age and marked sexual dimorphism. Age, ethnic and racial differences in fat patterning have been previously described (18). In the newborn subcutaneous fat depots contribute to the vast majority of fat (80%) (22), but even in this age the visceral or central depots may be of greater metabolic importance and to our knowledge these fat store have not been quantified.

Baumgartner and colleagues described changes during adolescence related to stages of sexual maturity (23). In general, subcutaneous adipose tissue deposition increases on the trunk in boys during adolescence, and gluteal-femoral fat increases in girls (18–21,23). It is well known that metabolic disorders are more directly associated with abdominal adipose tissue than subcutaneous fat patterning. It has been shown using computed tomography (CT) that age influences visceral adipose tissue as well as gender and ethnicity (24,25), and Huang and colleagues estimated the rate of increase in visceral adipose tissue to be approximately 5.2 cm^2/year over a 3- to 5-year follow up period in children 8 years old at baseline (26).

Having estimates of body fat content are relevant to studies of performance, thermoregulation, physical activity, sports and ultimately risk factors for several diseases. Fat distribution is also fundamental, as variation in the distribution of fat is a risk factor in the development of several diseases later in life and in adults in particular, such as non-insulin-dependent diabetes mellitus and cardiovascular diseases.

IMAGING

Imaging methods such CT and MRI are considered the most accurate means available for *in vivo* quantification of body composition at the tissue–organ level (27). Both CT and MRI are the methods of choice for calibration of field methods designed to measure adipose tissue and skeletal muscle *in vivo* and are the only methods available for measurement of internal tissues and organ (28) MRI is increasing in use, particularly in children, because of radiation exposure associated with CT (29).

Adipose tissue can be divided into subcutaneous, visceral and intra-muscular adipose tissue (30). Organ volumes quantified included liver, kidney, spleen and brain, and in adults the mass of these organs predicts precisely resting energy expenditure (31); in children, however, the energy cost of growth requires a peculiar model to estimate energy expenditure (32).

MRI also is a well-suited method for evaluating infants, but because the tissue structure in such subjects is small, higher resolution is required than in adults for adequate accuracy (29). To avoid artifacts caused by motion, infants should ideally be measured when sleeping after being fed, with a pulse oximeter to monitor blood oxygen saturation during the scan. Another important issue is related to room temperature, which usually is low because of liquid helium or liquid nitrogen in the superconducting magnet. It is important to keep the subject warm with blankets or even a ball of warm water around the subject. In our unit, using this approach, we are able to scan also subjects below 3000 g and also between 34 and 40 weeks of gestational age (personal unpublished data). This opens the potential for studying the nutritional status of premature infants.

Recently we pooled data from various investigators to evaluate the relationship between anthropometry and MRI-derived abdominal fat in children and we evaluate the effect of puberty and ethnicity on the relationship between anthropometry and MRI. We concluded that waist circumference can be considered a good predictor of abdominal adiposity according to its relationship with visceral adipose tissue measured by MRI (33).

Intramyocellular lipid and intrahepatic lipid have been measured in children by non invasive proton (or 1-hydrogen) magnetic resonance spectroscopy (MRS) for the reason that these two lipid compartments are related to insulin resistance (29). This spectroscopic method requires pre-scan adjustments, such as selection of anatomic location and suppression of water signals. The intramyocellular lipid and intrahepatic lipid is quantified from corresponding spectral peaks and results are expressed as a ratio to creatinine or water content (29). Also cardiac MRI is now being used in relationship with adipose tissue in pediatrics, as cardiovascular disease is a major consequence of obesity (29).

Measurements by MRI are especially suitable for comparisons between individuals, and MRI can be used to evaluate body composition in longitudinal studies. The reproducibility of MRI measurements of subcutaneous adipose tissue in infants is 2.4–4.0% (1,34).

Potential problems and solutions

For children it is usually difficult to stay immobile during MRI measurements and even to follow instructions. This is particularly true for children between the ages of 6 months to 4 years. Recent advances in MRI technology provide a potential solution. In fact new acquisition data could reduce artifacts caused by movements (35). This technique reduces movement artifacts but remains a need to develop techniques that could compensate artifacts induced by muscle movements (35).

CONCLUSIONS

MRI produces **high-resolution** images of all major body composition **components** at the tissue-system level (28).

Although access and cost remain obstacles to routine use, these imaging approach are now used extensively in body composition research.

The acquired data in pediatric studies could provide unique nutritional and metabolic information not obtainable by other methods. No known health risks are associated with MRI measurements.

MRI can serve as a reference method for measuring tissue and organ volumes because estimates will be reliable independent of age. In fact, it is likely that MRI can be used to validate measures of important molecular level components such as fat measured by Dual energy X-ray absorptiometry and bioimpedance analysis. Moreover, the large gap in available information for some topic in pediatric makes MRI measurements a dynamic and growing scientific area of body composition investigation.

References

1. Sopher A, Shen W, Pietrobelli A. Pediatric body composition. In: Heymsfield SB, Lohman TG, Wang ZM, Going SB, editors. *Human body composition.*Human Kinetics, Champaign IL, 2005; 129–40.
2. Okosun IS, Liao Y, Rotimi CN, Prewitt TE, Cooper RS. Abdominal adiposity and clustering of multiple metabolic syndrome in White, Black and Hispanic Americans. *Ann Epidemiol* 2000; 10: 263–70.
3. Lurbe E, Alvarez V, Redon J. Obesity, body fat distribution, and ambulatory blood pressure in children and adolescents. *J Clin Hypertens (Greenwich)* 2001; 3: 362–7.
4. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults–the evidence report. National Institutes of Health. *Obes Res* 1998; 6(Suppl 2): 51S–209S.
5. Rodriguez G, Moreno LA, Blay MG, Blay VA, Garagorri JM, Sarria A, et al. Body composition in adolescence: measurements and metabolic aspects. *Int J Obes* 2004; 28: S54–8.
6. Burdette HL, Whitaker RC, Hall WC, Daniels SR. Breastfeeding, introduction of complementary foods, and adiposity at 5 y of age. *Am J Clin Nutr* 2006; 83: 550–8.
7. Arenz S, Ruckerl R, Koletzko B, von Kries R. Breastfeeding and childhood obesity – a systematic review. *Int J Obes* 2004; 28: 1247–56.
8. Dewey KG. Is breastfeeding protective against child obesity? *J Hum Lact* 2003; 19: 9–18.
9. Owen CG, Martin RM, Whincup PH, Smith GB, Cook DG. Effect of infant feeding on the risk o obesity across the life course. A quantitative review of published evidence. *Pediatrics* 2005; 115: 1367–77.
10. Guan H, Arany E, van Beek JP, Chamson-Reig A, Thyssen S, Hill AJ, Yang K. Adipose tissue gene expression profiling reveals distinct molecular pathways that define visceral adiposity in offspring of maternal protein-restricted rats. *Am J Physiol Endocrinol Metab* 2005; 288: E663–73.
11. Martin RM, Ness AR, Gunnell D, Emmett P, Davey Smith G. Does breast-feeding in infancy lower blood pressure in childhood? The Avon Longitudinal Study of Parents and Children (ALSPAG). *Circulation* 2004; 109: 1259–66.
12. Baker JL, Michaelsen KF, Rasmussen KM, Sorensen TIA. Maternal prepregant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *Am J Clin Nutr* 2004; 80: 1579–88.
13. Pietrobelli A, Faith MS, Allison DB, Gallagher D, Chiumello G, Heymsfield SB. Body mass index as a measure of adiposity among children and adolescents: a validation study. *J Pediatrics* 1998; 132: 204–10.
14. Pietrobelli A, Tatò L. Body composition measurements: from the past to the future. *Acta Paediatrica* 2005; 94: 8–13.
15. Reilly JJ, Armstrong J, Dorosty AR, et al. Early life risk factors for obesity in childhood: cohort study. *BMJ* 2005; 330: 1357–9.
16. Allison DB, Zannolli R, Faith MS, Heo M, Pietrobelli A, VanItallie TB, et al. Weight loss increases and fat loss decreases all-cause mortality rate: results from two independent cohort studies. *Int J Obes* 1999; 23: 603–11.
17. Fomon SJ, Nelson SE. Body composition of the male and female reference infants. *Ann Rev Nutr* 2002; 22: 1–17.
18. Forbes GB. *The human body composition: growth, aging, nutrition, and activity*. New York: Springer-Verlag, 1987.
19. Malina RM, Bouchard C, Bar-Or O. Growth, maturation, and physical activity. *Human Kinetics*, Champaign, IL, 2004.
20. Fomon SJ, Haschke F, Ziegler EE, Nelson SE. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr* 1982; 35: 1169–75.
21. Lohman TG. Applicability of body composition techniques and constants for children and youths. *Exerc Sport Sci Rev* 1986; 14: 325–57.
22. Bernstein I. Fetal body composition. *Curr Opin Clin Nutr Metab Care* 2005; 8: 613–7.
23. Baumgartner RN, Roche AF, Guo S, Lohman TG, Boileau R, Slaughter M. Adipose tissue distribution – the stability of principal components by sex, ethnicity, and maturation stage. *Hum Biol* 1986; 58: 719–35.
24. Figueroa-Colon R, Mayo MS, Treuth MS, Aldridge RA, Hunter GR, Berland L, et al. Variability in abdominal adipose tissue measurements using computed tomography in prepubertal girls. *Int J Obes* 1998; 22: 1019–23.
25. Gower BA, Nagy TR, Goran MI. Visceral fat, insulin sensitivity, and lipids in prepubertal children. *Diabetes* 1999; 48: 1515–21.
26. Huang TTK, Johnson MS, Figueroa-Colon R, Dwyer JH, Goran MI. Growth of visceral fat, subcutaneous abdominal fat and total body fat in children. *Obes Res* 2001; 9: 283–9.
27. Heymsfield SB, Ross R, Wang ZM, Frager D. Imaging techniques of body composition, advantages of measurement and new uses. In: Carlson-Newberry SJ, Costello RB, editors. *Emerging technologies for nutrition research*. New York: National Academic Press, 1997: 127–50.
28. Ross R, Janssen I. Computed tomography and magnetic resonance imaging. In: Heymsfield SB, Lohman TG, Wang ZM, Going SB, editors. *Human body composition*, Human kinetics, Champaign, IL, 2005; 89–108.
29. Shen W, Liu H, Punyanitya M, Chen J, Heymsfield SB. Pediatric obesity phenotyping by magnetic resonance methods. *Curr Opin Cli Nutr Metab Care* 2005; 8: 595–601.
30. Shen W, Wang ZM, Punyanitya M, et al. Adipose tissue quantification by imaging methods: a proposed classification. *Obes Res* 2003; 11: 5–16.
31. Gallagher DS, Belmonte D, Deurenberg P, et al. Organ tissue mass measurements allows modeling of REE and metabolically active tissue mass. *Am J Physiol* 1998; 275: E249–58.
32. Hsu A, Heshka S, Janumala I, et al. Larger mass of high-metabolic-rate organs does not explain higher resting energy expenditure in children. *Am J Clin Nutr* 2003; 77: 1506–11.
33. Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR, et al. Crossvalidation of anthropometry against magnetic resonance imaging for the measurement of visceral and

subcutaneous adipose tissue in children. *Int J Obes* 2006; 30: 23–30.

34. Harrington TA, Thomas EL, Modi N, Frost G, Coutts GA, Bell JD. Fast and reproducible method for the direct quantitation of adipose tissue in newborn infants. *Lipids* 2002; 37: 95–100.

35. Forbes KP, Pipe JG, Karis JP, Farthing V, Heiserman JE. Brain imaging in the unsedated pediatric patient. Comparison of periodically rotated overlapping parallel lines with enhanced reconstruction and single-shot fast spin-echo sequences. *Am J Neuroradiol* 2003; 24: 794–8.