Mini-review

Evaluation of bone density in infancy and adolescence. Review of medical literature and personal experience

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Summary

The evolution of medical and surgical therapies allows the increased survival rate of a growing number of children affected by rare pathologies. In this light osteoporotic disease is also of orthopaedic interest as it is sometimes the outward manifestation of serious pathologies (i.e. osteogenesis imperfecta). Sometimes, even in infancy and adolescence, osteoporosis is associated with complications due to fractures; in other cases it seems to have no immediate consequence. Nevertheless it must be considered as a fracture risk factor in adulthood as it negatively affects the achievement of peak bone mass. The evaluation of variations in bone mass that take place during growth is thus of particular importance in order to guarantee a level of bone health suitable for the next phase.
These remarks compose the premise of a study on bone resistance carried out on a study population of between 6 and 18 years of age in the city of Pavia. To determine the resistance of the bone an ultrasound device was employed (Omnisense™, Sunlight Medical Ltd, Tel Aviv, Israel) in two skeletal sites, distal radius and midshaft of tibia.
The analysis of our results and a review of the relevant literature indicate that the median values of normality, against which we compare the measurements of the patients under examination, depend not only on age, sex, skeletal sites, race, and even ethnic group. The introduction of this new parameter, to be kept in mind when interpreting the results, invites us to be very prudent in determining the diagnostic threshold values in paediatric age. As with anthropometric data (weight, height, cranial circumference) it is possible to suggest an interpretation of the patient's SOS values comparing them with the 'centile curves' typical to the region the child belongs to.
Of course, further studies are required to understand what are the variables involved and to determine the extension of the geographical area to be examined to obtain suitable reference curves.

KEY WORDS: osteoporosis, children, QUS.

Introduction

Numerous techniques of bone mineral density (BMD) measurement in the various skeletal segments have been developed over the years.
X-Ray examination is of little use in diagnosing precociously an osteoporotic state and radiometry, which allows us to make semi quantitative measurements, is barely precise enough. To overcome these limits research has been directed towards different and ever more sophisticated systems able to provide a clinical understanding of even slight variations in bone density. The most common methods for the evaluation of bone density are based on the different absorption of ionising radiations by bone and soft tissues. Absorptiometry was the first quantitative procedure for the evaluation of bone mass to be used extensively; this technique was based on the photonic attenuation phenomenon which as a consequence provided the opportunity to analyse the characteristics of the material traversed.
Single photon ray absorptiometry (SPA) used I^{125} isotopes, which could emit photons with an energy of 28 Kev.
Since SPA could only be used on peripheral bones, its importance has waned in the past few years. The densitometric exam of the spine and the femur is now possible thanks to the introduction of methods which employ two spectra, such as dual photon absorptiometry (DPA).
Nevertheless, even DPA has been heavily criticised for its insufficient reproducibility, due to the variability of photon intensity which is limited and dependent on the entity of the isotopic source.
Dual-energy spectrum densitometry has undergone gradual technical improvements passing from isotopic sources to X-ray sources, a technique which was perfected in 1987.Dual-energy X-ray absorption (DXA) seems suited to follow up studies although this does not limit its systematic errors, caused mainly by superimposition effects that reduce the value of the single measurement; in this area DXA is affected by the same issues described for DPA (13).
Since mineral bone density measured with DXA seems to be the best means for predicting the risk of fracture it is currently regarded as the 'gold standard' for osteoporosis diagnosis (14, 15, 16).
In truth the greater part of reference literature on this subject refers to studies carried out on the adult population; for the evaluation of bone mass in paediatric age certain considerations are necessary.
For patients in infancy and adolescence the ideal method for measuring bone mass should be innocuous, fast and easily carried out on patients of every age.
DXA presents only some of the necessary requirements, nevertheless also revealing some limitations (17, 18, 19).
In paediatric subjects it is necessary to consider that the process of bone remodelling and the variations in size of the skeleton have indeed a great influence on bone mass values; it follows that, although DXA is the most commonly used technique for its evaluation, both the accuracy and the precision of the equipment seem inferior in paediatric age compared with adulthood (21, 22, 23).
For this reason numerous attempts at normalising BMD values to the variations of body size have been made (17, 24).
Regarding the site to be examined, the International Society of Cli-

nical Densitometry has established that in paediatric patients the ideal measurement sites are the spine and the total body. Some Authors, however, disagree and have suggested that the examination of multiple 'regions of interest' (ROI) is more useful from a practical point of view as it allows a better interpretation of the clinical profile of each patient (21, 26).

From what has emerged it would seem that the evaluation of bone mass in paediatric age with DXA is vulnerable to criticism, or, in any case, needs to be interpreted with great care.

One system for obtaining more accurate information regarding real bone volume is represented by QTC which can be carried out in any skeletal site. Studies with QTC in healthy children have shown that cortical bone in the appendicular skeleton remains fairly constant and is not influenced by age, by anthropometric parameters, by puberty, sex or race (27).

Nevertheless, the equipment is expensive and involves maintenance and specific staff training costs; in addition to this, being exposed to ionising radiation, however minimally, makes it inadvisable for use in screening surveys.

These limitations have been partially overcome by the introduction of equipment for peripheral QTC which is less expensive, but only able to take measurements of the appendicular skeleton (28). The main advantage of this technique is that it measures mineral density per volume unit (mg/cc), thus proving independent of size, and that it can measure parameters such as total area, cortical width and muscular area in cross section, also providing information on muscular geometry and evaluating the functioning of the muscle-bone unit (29).

Peripheral QTC (pQCT) could thus represent an advantageous evolution of QTC; however lack of precision remains a limitation along with the small number of reference values obtained and the impossibility of measuring the axial skeleton (21).

A growing interest in bone ultrasonography has been developing over the past years. This technique permits the study of bone mass without subjecting the patient to radiations and also provides information on qualitative and structural characteristics which are equally important in determining risk of osteoporotic fractures. In 1998 in the United States the F.D.A. approved the employment of an ultrasound screening device and this certainly provoked a rapid expansion of ultrasound techniques in clinical deployment (31).

Ultrasound devices (QUS) have thus been suggested as an alternative to other diagnostic techniques, particularly as they do not involve the use of radiations, are relatively inexpensive and easy to use (28, 32 ,33, 34, 31, 35).

Ultrasound bone measurements can be carried out in various peripheral sites. Certain Authors regard ultrasonometry as less accurate than DXA, and only employable as a pre-screening solution (37, 38, 15, 10, 39, 40, 41).

Other comparison studies between the two techniques, on the other hand, conclude that the results are virtually identical both in adults (42, 43, 44) and in growing subjects (18, 34, 45).

It is however, necessary to take extreme care with the interpretation of the numerical results obtained with ultrasound techniques. Threshold values set by the OMS for the diagnosis of osteopenia-osteoporosis (16) do not seem to be appropriate when measure in skeletal sites different from the spine, radius or femur and with different measurement methods, like QUS (46, 47).

The interpretation of such values may also vary depending on the type of device used (48, 49).

Materials and methods

The survey was carried out on a study population of children and adolescents (boys and girls) of ages between 6 and 18 years, covering a total of 652 healthy subjects.

The measurements were carried out using the Omnisense™ device (Sunlight Medical Ltd, Tel Aviv, Israel) at the middle-third of the tibia and at the distal third of the radius on the nondominant side (as recommended by the International Society for Clinical Densitometry) (51).

The analysis of the data was carried out calculating the averages and standard deviations of the SOS for each age group and creating the curves of normal distribution.

Simple linear regression was used to find the relationships between SOS values and anthropometric data.

To localise the independent SOS predictors between age, weight, height and pubertal status multiple linear regression was used. The normal distribution curves obtained were also compared with the device database and those provided by other Authors who employed Omnisense™ to measure SOS in a population of paediatric subjects. For methodology and preliminary results please refer to the bibliography (13, 55).

Discussion

From the analysis of our results it emerged that the indicative SOS values of bone resistance vary depending on sex, age and site, as described in the relevant literature, in subjects from whom measurements were taken with both ultrasound and DXA devices (45, 51, 54, 56, 57, 58, 59) (Figures 1, 2).

The comparison between the SOS values found in our study population and those of the devices database allowed us to highlight a different variation of median values both for males and females (Figures 3,4) From here important clinical consequences can be drawn as the variation in normality values occasions a different diagnostic classification. We then carried out a comparison between our data, the device's data and the reference curves traced by other Authors using Omnisense™, in the same skeletal sites in an Israeli study population (55).

The data obtained by Zadik et al. (55) is basically identical to the reference data provided by the construction company (Sunlight Technologies, Tel Aviv, Israel) with the exception of the values found in the female tibia after puberty. Vice versa, our values differ in multiple instances (Figure 5).

This can realistically be justified by the uniformity of 'environmental factors' common to the population resident in the territory of the Hebrew state; this in spite of the fact that the composition of society is quite heterogeneous both in origin and place of provenance. The difference with our values, although referring to a Caucasian population, indicates that it is necessary to consider not only the reference curves specific to each race, but also certain sub-groupings probably identifiable on the basis of geographic distribution.

In the reference literature there exist certain studies on the influence of race or ethnicity on bone mass measurement carried out with DXA (61-68). We did'nt find any data on the comparison between the normal distribution curves in different ethnic groups obtained with the US method.

Conclusion

Although DXA is the most commonly used method for the diagnosis of osteoporosis in adults, in children the interpretation of the data requires a lot of care. The use of US in a paediatric study population appears to be of interest as, on the one hand, it provides information on the quality of the bone which cannot be obtained with DXA and, on the other, it presents itself as the ideal technique for screening investigation.

From the analysis of our curves it emerges that the median normality values depend not only on age, sex, skeletal site examined and race but also ethnic group (intending by the latter a group of individuals sharing historical-religious cultural characteristics).

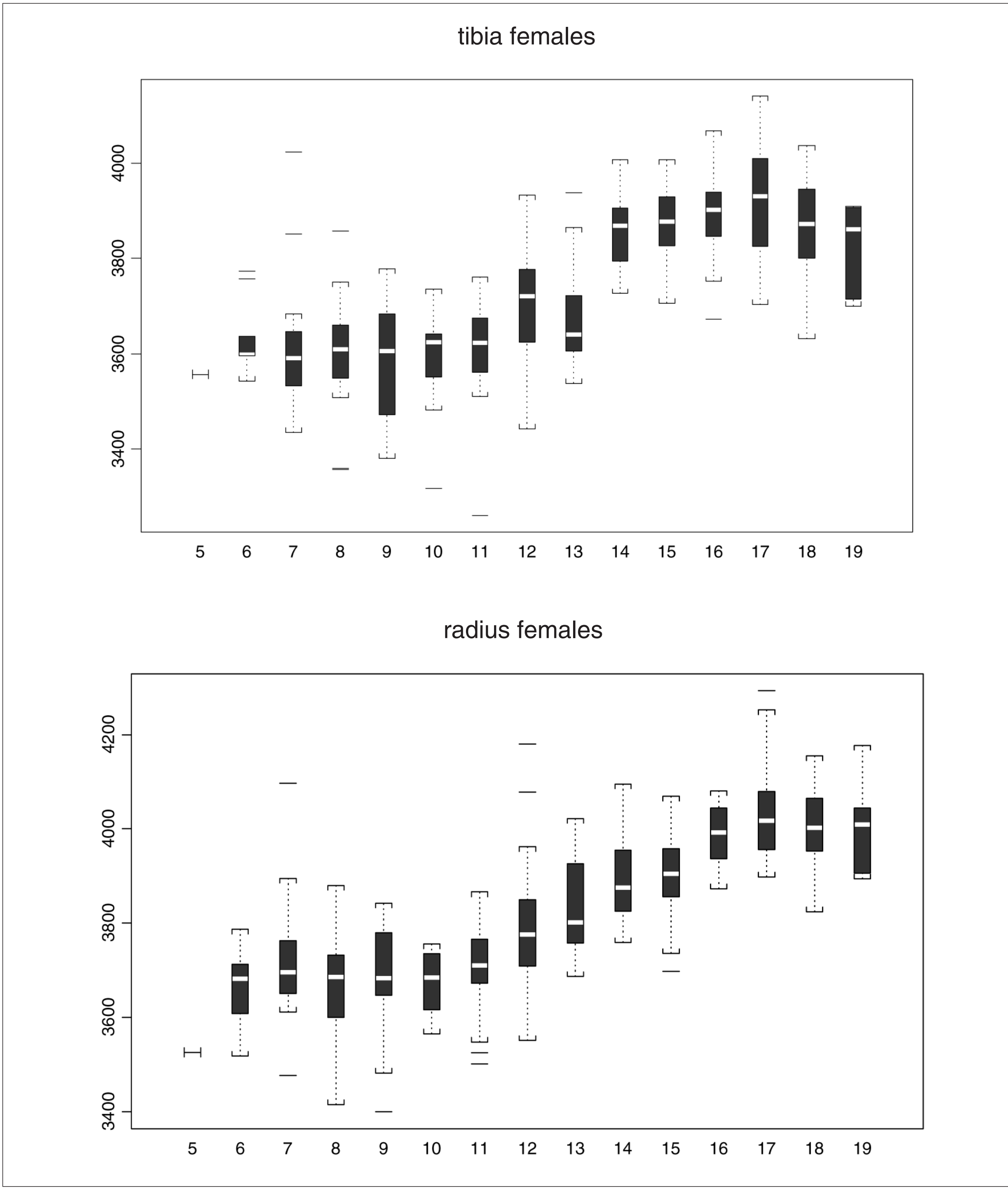

Figure 1 - SOS values in females (tibia and radius).

In order to correctly interpret the results the data should be compared with reference paediatric curves, divided by site, age, sex, race. Bearing in mind the influence of environmental factors, it is possible to also advance an interpretation of patient's SOS values comparing them with the 'centile curves' of the region to which the child belongs (in the same way that weight and height are evaluated in paediatric care). Naturally, further research is necessary to understand which variables are involved and to determine the extension of the geographical area to be examined in order to obtain suitable reference curves.

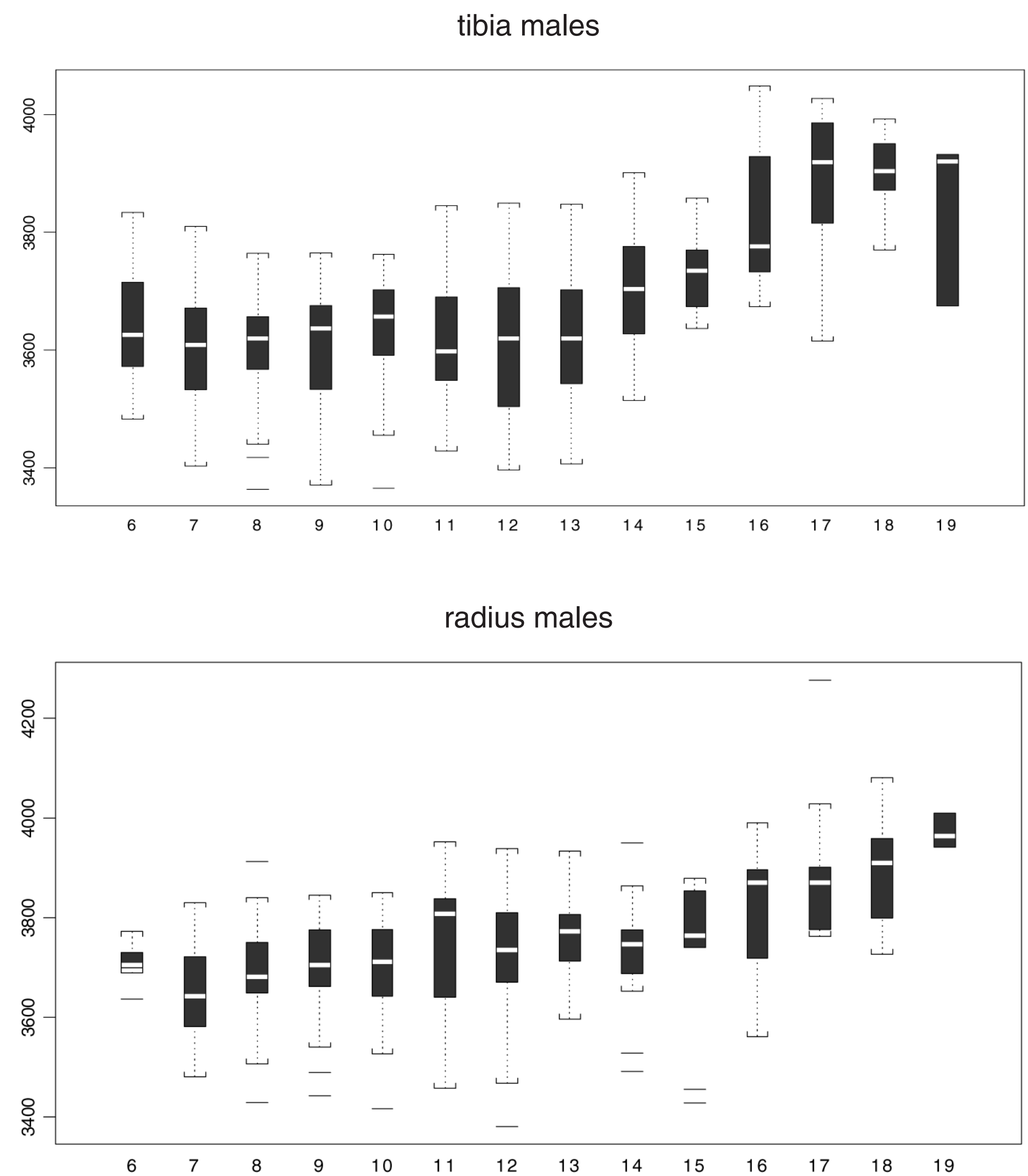

Figure 2 - SOS values in males (tibia and radius)

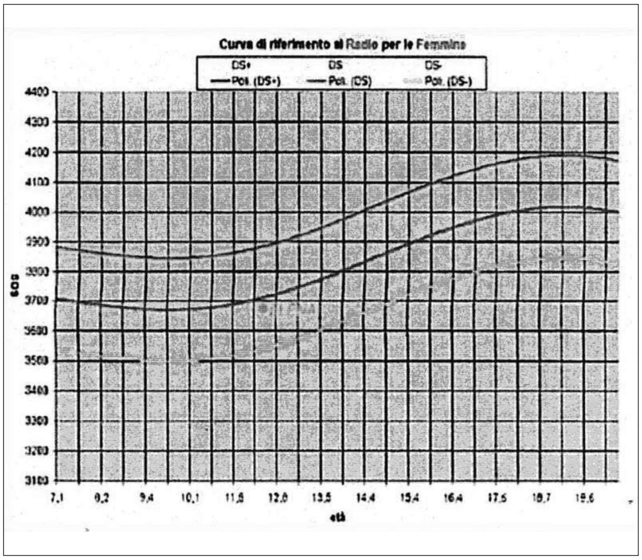

Figure 3 - Elena is placed under the average line on the reference curve for radius in females.

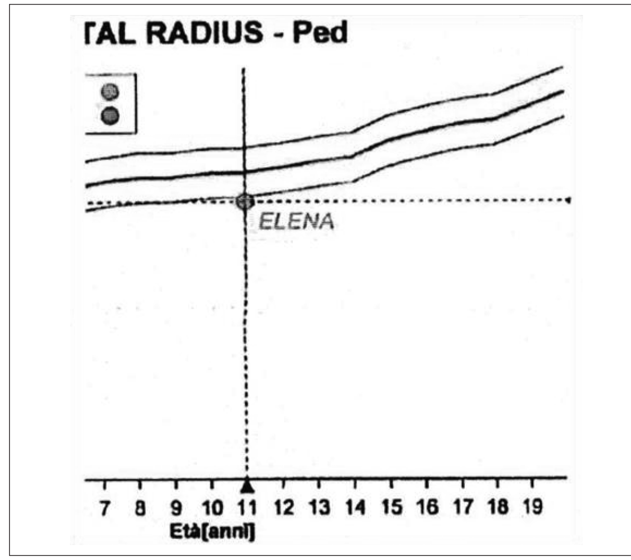

Figure 4 - Elena is placed under the line representing -1DS (Z- score < - 1) in the pediatric reference curve for radius in females.

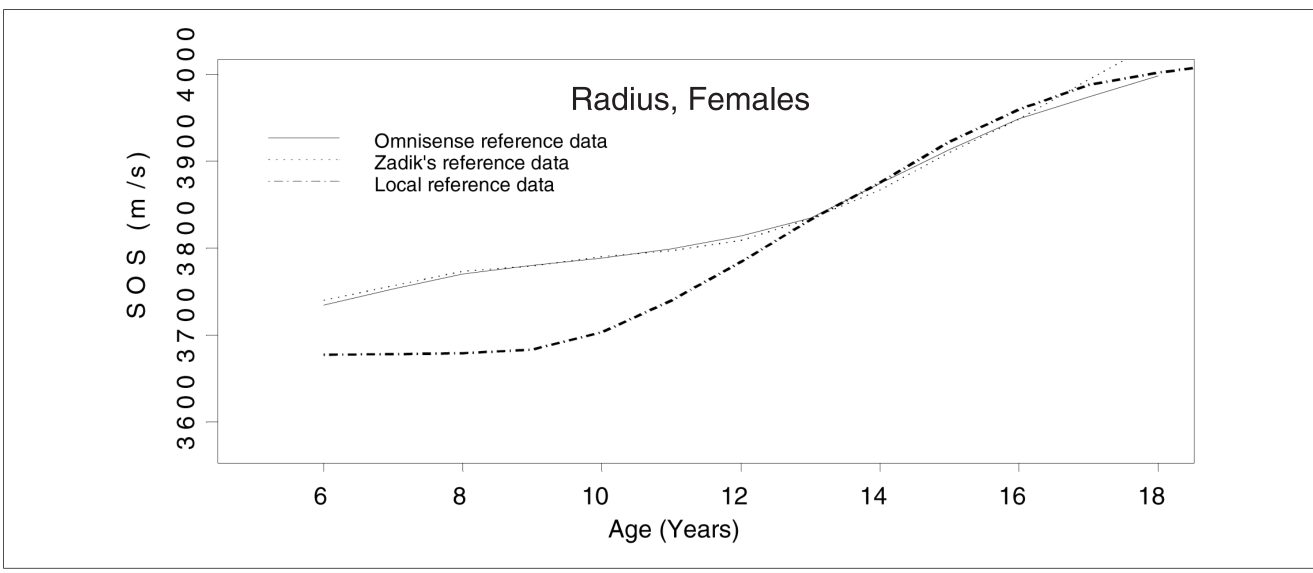

Figure 5 - Reference values in different populations (females).

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