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Adaptation of the human tibia to physiological load measured using quantitative computed tomography on men practising marathon. Transversal investigation: How does ultradistal bone density vary with training?

Summary

The adaptation of the skeleton to the dynamic mechanical stresses is known since the middle of the XIXth century. In contrast to the bone degradation related to pathological conditions (e.g. osteoporosis), no reliable data are known for healthy young or mature people practising a physiological sport with varying intensity. This triggered us to carry out a transversal and longitudinal investigation on men practising marathon, using a high precision appendicular quantitative computed tomograph for the assessment of the morphological and densitometric characteristics of the proximal and distal tibia. This paper relates the transversal aspect of this investigation on the distal part of the tibia.
In a prospective cohort study, healthy volunteers were distributed on three groups: A control group 1 non practising marathon, a group 2 practising moderate training (30–50 km/week) and a group 3 practising intensive training (80 km/week). 10 tomograms were obtained at the ultradistal part of the tibia and 6 tomograms at the junction between the metaphysis and the diaphysis. The measured values were the total ultradistal bone density D100, the ultradistal trabecular density D50 (i.e. of the internal part of the tomograms) and the bone density P100 at the dia-metaphyseal junction. *Transversal study:* The comparison is made between subjects of the different groups of training, but with similar morphology (same body mass index).
96 subjects (1: 20, 2: 45, 3: 31) have been measured. The control subjects are heavier, higher and show a larger BMI than the subjects with moderate training; in contrast, the subjects with intense training are lighter, smaller and show a smaller BMI. The difference between the groups, smaller at 20 years old, increases with the age. All the three values of density (D100, D50 and P100) are in average higher for group 2 than for group 1, and for group 3 than for group 2. The trabecular bone density D50 slightly decreases with the age, and the density P50 at a level whereby the bone is mainly cortical slightly increases with the age.
Wolff's law is corroborated by our measurements. However, subjects with denser or less dense bone might indicate a pathological behaviour or an inadequate training.

Key words:
Marathon, training, tibia, bone adaptation, quantitative computed tomography, densitometry

Résumé

Adaptation du tibia humain aux charges physiologiques, mesurée par tomodensitométrie quantitative chez des marathoniens. Partie I : Investigation transversale: Comment la densité osseuse ultradistale varie-t-elle avec l'intensité de l'entraînement?
L'adaptation de l'os aux contraintes fonctionnelles est établie depuis le milieu du XIX^{e} siècle. Au contraire des dégradations osseuses d'origine pathologique, comme par exemple l'ostéoporose, il n'y a pratiquement pas de données fiables pour les gens jeunes ou adultes pratiquant un sport avec une intensité variable. Cela nous a incité à évaluer des marathoniens à l'aide d'un tomodensitomètre quantitatif pour les membres appendiculaires, afin d'obtenir des données morphologiques et densitométriques du tibia proximal et distal. Ce papier rapporte l'étude transversale de cette investigation sur le tibia distal.
Dans une étude prospective, une cohorte de volontaires sains a été répartie en trois groupes: un groupe de contrôle 1 ne pratiquant pas le marathon, un groupe 2 de marathoniens pratiquant un entraînement modéré (30–50 km par semaine), et un groupe 3 de marathoniens pratiquant un entraînement intense (80 km par semaine). 10 tomogrammes ont été obtenus dans la partie ultradistale du tibia, et 6 tomogrammes à la jonction entre la diaphyse et la métaphyse. Les grandeurs mesurées ont été la densité osseuse de la section totale D100, la densité trabéculaire D50 (dans la partie centrale des tomogrammes) et la densité osseuse P100 à la jonction dia-métaphysaire. *Analyse transversale:* La comparaison a été faite entre les différents groupes, pour une morphologie semblable (c.-à-d. le même indice de Quételet).
96 sujets (1: 20, 2: 45, 3: 31) ont été évalués. Les sujets du groupe de contrôle sont plus lourds, plus grands et plus corpulents que les sujets pratiquant un entraînement modéré; au contraire, les sujets pratiquant un entraînement intense sont plus petits, plus minces et moins corpulents. Les trois mesures de densité (D100, D50, P100) ont été en moyenne plus élevées pour le groupe 2 que pour le groupe 1, et pour le groupe 3 que pour le groupe 2. La densité osseuse trabécullaire D50 diminue légèrement avec l'âge, et la densité dans une région plus corticale P100 augmente avec l'âge. La loi de Wolff est corroborée par nos mesures. Toutefois, des individus présentant une densité osseuse trop basse ou trop élevée indiquent un comportement osseux pathologique ou entraînement inadéquat.

Introduction

Sport is known to prevent bone degradation due to ageing. However, inadequate training and particularly overload might lead to complications. These complications are due to either indirect effect, e.g. amenorrhoea in young women, which leads to bone loss (osteopenia), or direct skeletal injury like stress fractures (for the engineer: fatigue fractures). The former perturbation (perturbation of the sexual hormones activity) has also been observed in men (De Souza et al. [1]), which leads to higher bone turnover (remodelling). For both these effects, the bone remodelling plays an important role, whereby an apparent bone atrophy due to the resorption of old bone must take place before new bone formation, in the microscopical aspect of bone adaptation to the mechanical stress.

The adaptation of the skeleton to the mechanical stress has been established from the morphology of the cancellous bones since more than 130 years [2–5]. This adaptation, which consists in both an architectural modelling of the spongy bone (orientation and mineral mass of the trabeculae) and of the cancellous bone (cortex thickness), appears to relate to dynamic stresses, in order to sustain the load with the minimum of bone. This behaviour is strongly suggested by the morphology of the metaphysis of long bones.

Animal investigations have been made in order to understand this phenomenon since the end of the ’40s [6–8]. These early experiments which were initiated by Rütishauser and continued up to the early ’70s were carried out using non-physiological loading models, whereby a local overload resulted from a diaphyseal segment resection (e.g. radius, the ulna being overloaded), without loading control. They had however the merit to show a dramatic ulnar hypertrophy. Hert et al. [9–11] developed an external fixator in order to apply a monitorised bending moment, and found a bone production at the tensile and the compressive aspect of sheep tibiae; this investigation was stopped, being a political victim of the «Praha spring» in 1968 (Hert, personal communication). Rubin and Lanyon [12–16] improved this technique by using a motorised external fixator at a stress protected long bone, and were able to show that bone apposition was produced by a load which generates a strain larger than 1000 $\mu\varepsilon$, and that bone atrophy appears when the load is smaller than this value of 1000 $\mu\varepsilon$ – 1000 $\mu\varepsilon$ being the usual strain amplitude sustained by the bones during physiological weight bearing. In the experiments of Rubin and Lanyon, the apposition or the atrophy was linearly proportional to the deviation to this equilibrium value. An astonishing finding of Lanyon and Rubin was that the bone reaction was apparently not related to a long duration training, but only few cycles of bone loading was enough to enhance the bony adaptation.

In *humans* the first assessment (to our knowledge) has been made by Jones et al. [17] using X-ray on professional tennis players, comparing the humerus of the active arm to the contralateral humerus, which was taken as control. An active hypertrophy has been established for the active bone; however, it might be argued that this adaptation was not due to «normal» adaptation (to physiological loads), but a reaction to microtrauma generated by the shocks or impacts.

In the past decade, many measurements have been made in men and women practising different sports, using the newly introduced precise methods of assessima osteoporosis, e.g. DEXA (Dual Energy X-ray Absorptiometry). Platen et al. [18] measured the bone mineral density on 104 male subjects, practising different sport activities. They found relevant increase in bone density at either the spine or the proximal femur *(fig. 1).* Higher bone density was correlated with higher skeletal activity. Running activity resulted in higher density within the proximal femur than within the spine.

Most of the investigators found an increase in bone density with training. However, contradictory findings have been reported. E.g. Hetland et al. [19] found a slight tendency of the bone mineral content to decrease with intense training (runners, weekly distance of running from 0 to 150 km/week). Although the data presented by these authors show that this decrease is strongly influenced by outliers, the tendency cannot be rejected from the values whereby outliers are excluded. A possible explanation is that too intense training results in increased remodelling, with temporary bone loss (bone resorption takes place before the bone apposition).

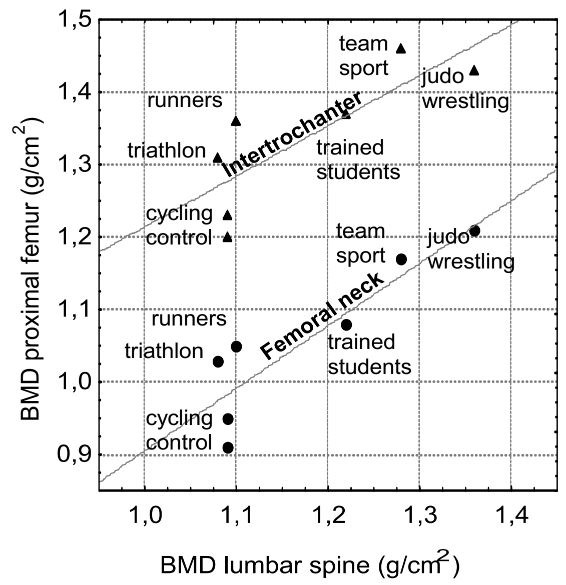

Figure 1: Bone mineral density found using DEXA at the lumbar spine and at the proximal femur from data of Platen et al. [18] for different sport activities on male athletes. Running activity (runners, triathlon, team sports like soccer) leads to higher BMD within the femur than within the spine.

Whalen et al. [20] published on the Internet a comparison of bone density of female marathon runners, using biphotonic densitometry. They found that runners are significantly lighter than non-runners. Calcanear bone density measured by single-energy absorptiometry and normalised by body weight was significantly higher in runners. Gary Beaupré advised QCT (quantitative computed tomography) as better tool for assessing densitometrical and geometrical bony adaptation; this is the current research project of Whalen et al. [21]. The same idea was also the purpose of our ongoing project.

To our knowledge, no investigation upon the bone adaptation to load in sport activity using quantitative computed tomography has been reported. Investigations on humans in conditions of microgravity have been carried out in space. The appendicular computed tomographs Isotom and Densiscan were developed by Rüegsegger [22, 23] for this purpose. However, the investigations were conducted either on too small a number of subjects or with a poor follow-up. This incited us to use this high-precision quantitative computed tomography for assessing the adaptation of proximal and distal tibia in relationship to the time on men (whereby the bone adaptation is less prone to be due to hormonal osteoporosis). This longitudinal and transversal investigation is currently carried out on young and mature men practising the marathon.

The goal and the purpose of the present paper is to show the bone adaptation within the distal part of the tibia, for young and mature male marathon runners practising moderate or intensive training, with a control group of non-marathon runners.

Method

Research subjects. Volunteers were non-smoking men practising the marathon, and a control group, 25–45 years old. Three groups have been made:

1. Control group: Non-obese and non-smoking men, without training for running.

2. Group with moderate training (30–50 km of training during the week).
3. Group with intensive training (>80 km of training during the week).

The *subject characteristics* were their age, weight and height, and the body mass index BMI of Quételet: BMI = weight / $height^2$ in $[kg/m^2]$. The subjects are slender for BMI < 18 and obese for BMI > 30.

Tomograph: The peripheral quantitative computed tomograph (pQCT) Densiscan 1000 (Scanco Medical, Bassersdorf/Zürich) is a high-precision and low-irradiation instrument specially designed for long bone densitometry.

Measurements were made at the distal part of the tibia using the standard scanning program (developed for assessing the osteoporosis), which obtains 10 ultradistal tomograms (whereby the cross-sections contain trabecular and cortical bone), and 6 tomograms more proximally (whereby the cross-sections contain mainly only cortical bone). The position is determined using a *scout view*, the first scout view being taken as reference, with a *reference line* chosen by the investigator at the horizontal surface of the distal extremity of the tibia. The precision of this reference line is ±1 mm. When a series of consecutive sessions is analysed, elaborated analysis software allows for exact comparison of the same volume of bone assessed in each session. The precision and accuracy of the values are better than 0,3%. Typical tomograms are shown in *figure 2*.

The mineral bone density (in $[mg/cm^3]$)[1] was calculated from the total cross-sectional area of the tibia including cortical and cancellous bone (D100) within an ultradistal volume, from the 50% of the internal area including only cancellous bone (D50) within the same ultradistal volume, and the total cross-sectional area (P100) at the junction between the metaphysis and the diaphysis, whereby the bone is nearly only cortical.

Data analysis. A visual examination of possible differences between the groups was first made on boxplots *(fig. 3)*, which show the median ± upper and lower quartiles, the maximum and the minimum values and the outliers (whereby the difference to the median is larger than + or –1.5 interquartile range) and extreme values (whereby the difference to the median is larger than + or –1.5 interquartile range).

Density values (D100, D50 and P100) were displayed in relationship to the age or to the body mass index, whereby confidence limits were displayed as mean values of the pooled measurements ± 1 time the standard deviation (dotted line) and ± 2.5 times the standard deviation (continuous line).

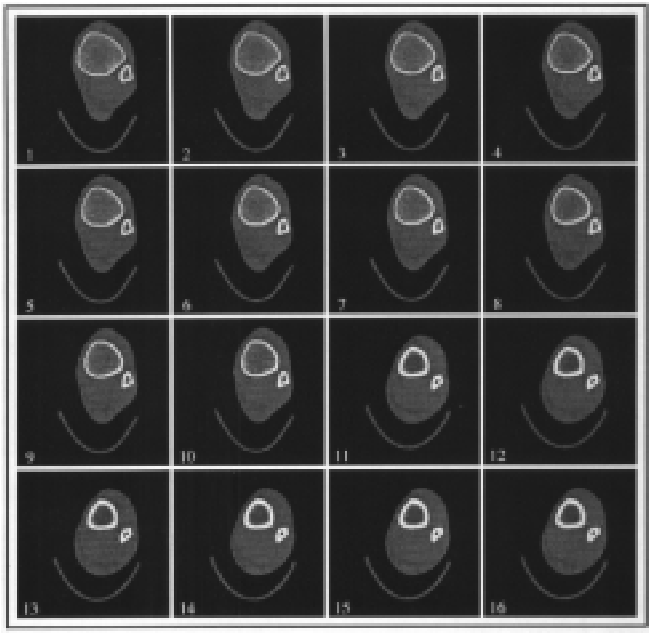

Figure 2: 16 tomograms obtained at the distal tibia: 10 of them every mm at the ultra distal part, whereby the bone within the medullary cavity is mainly trabecular, and 6 at the junction between the diaphysis and the metaphysis.

A trend of increase or decrease with the age is shown by the linear regression.

A principal component analysis has been made in order to discriminate the confounding factors (i.e. the effect of the morphology of the subjects upon the measured bone density, in contrast to the effect of the training upon the bone density).

Our *working hypothesis* is that higher training will result in more dense bone, either cortical or trabecular: Density in group 1 < density in group 2 < density in group 3.

Ethical condition: An ethical commission has accepted this investigation. The subjects were clearly informed by an oral explanation of the experimental conditions, completed by a written explanation, and they signed a disclosure.

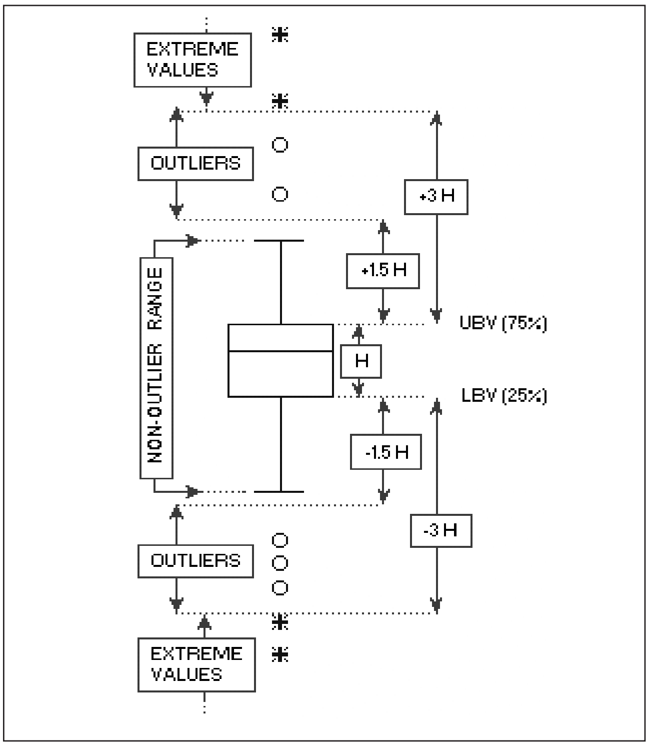

Figure 3: Box plot, definition of the non-outlier range, the outliers and the extreme values. Rectangular box: Median within the upper quartile (UBV) and the lower quartile (LBV), interquartile range H, non-outlier range, outliers (○) and extreme values (✱).

Results

Morphological characteristics of the subjects

At this time a cohort of 96 subjects were evaluated in this transversal analysis, i.e. 20 subjects for group 1 (control), 45 subjects for group 2 (moderate training) and 31 subjects for group 3 (extensive training). The morphological characteristics (weight, height, BMI) are summarised in *table 1* and *figure 4*.

Ages are homogeneously distributed between 25 and 45 years for all three groups (for group 3 up to 42 years only, for group 1 one subject 19 years old).

Morphology: The non-marathon runners (group 1) are obviously heavier than marathon runners, and marathon runners practising moderate training (group 2) heavier than marathon runners practising intensive training (group 3). The same observation is made for the height and for the BMI *(fig. 4)*. These differences seem to increase with the age, but are small or negligible at an age bellow 30 *(fig. 4)*.

	Nb.	**Weight** (kg)	**Height** (cm)	**BMI** (kg/m^2)
Group 1	20	78.7 ± 7.0	183 ± 6.7	23.36 ± 1.2
Group 2	45	71.4 ± 7.0	177 ± 5.7	22.6 ± 1.8
Group 3	31	65.8 ± 7.0	173 ± 6.2	22.2 ± 2.5
Total	**96**	**71.1 ± 8.3**	**177 ± 6.8**	**22.6 ± 1.8**

Table 1: Morphological characteristics of the measured subjects. Mean value ± standard deviation.

Morphological characteristics in relationship to the age. Figure 4 shows that, on young subjects, marathon runners are lighter and slimmer, but also smaller than non-marathon runners. The difference between the groups increases with age, the marathon runners with intense training showing a difference to marathon runners with moderate training in the opposite way to the difference between marathon runners and non-marathon runners.

Densitometry of the ultradistal tibia

The bone mineral density of the distal part of the tibia is shown in table II and *figures 6* and *7*.

The boxplots of *figure 6* show that the bone density is larger in marathon runners, this effect being increased by the intensity of training. Particularly high values of trabecular bone density D50 (outliers) are shown in group 2 (moderate training). One of the subjects of group 2 presented the highest values, whereas subjects of group 1 and group 2 showned particularly low density values.

Bone density of the distal part of the tibia in relationship to the age. Figure 7 shows that the ultradistal total density D100 is rather constant with age, whereas the ultra distal trabecular density D50 shows a slight decrease. The density at the junction between the diaphysis and the metaphysis P100 seems to increase.

	D100 (mg/cm^3)	**D50** (mg/cm^3)	**P100** (mg/cm^3)
Group 1	548 ± 74	303 ± 53	1006 ± 122
Group 2	589 ± 81	340 ± 59	947 ± 124
Group 3	620 ± 81	363 ± 48	1201 ± 126
Total	**591 ± 83**	**340 ± 58**	**1054 ± 95**

Table II: Densitometrical characteristics of the measured subjects. Mean value ± standard deviation.

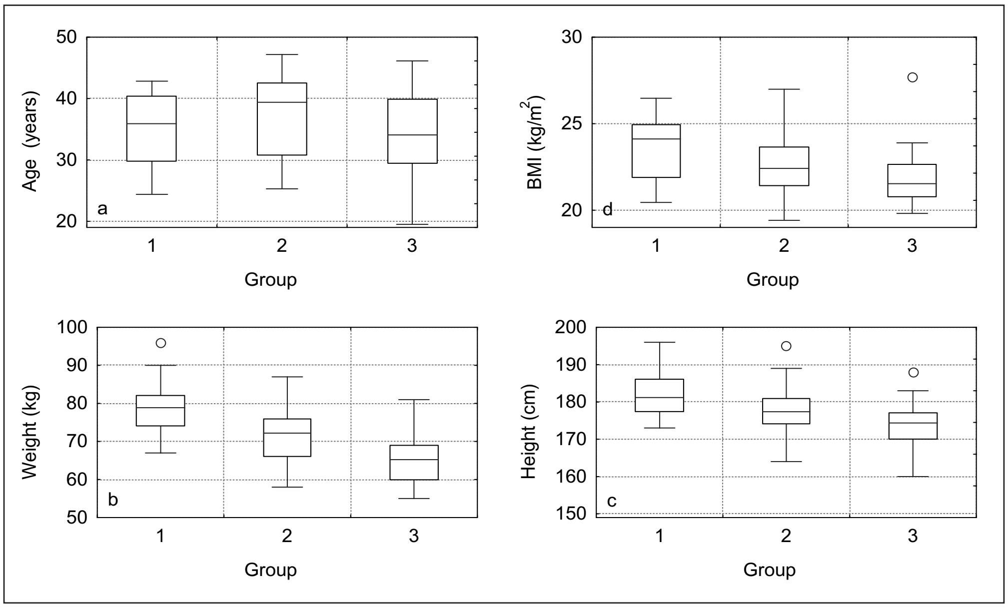

Figure 4: Boxplots of ages and morphological characteristics. The three groups were homogeneously distributed between 25 and 45 years. The morphological characteristics decrease when the training increases.

a. Boxplot of age
b. Boxplot of weight
c. Boxplot of height
d. Boxplot of BMI

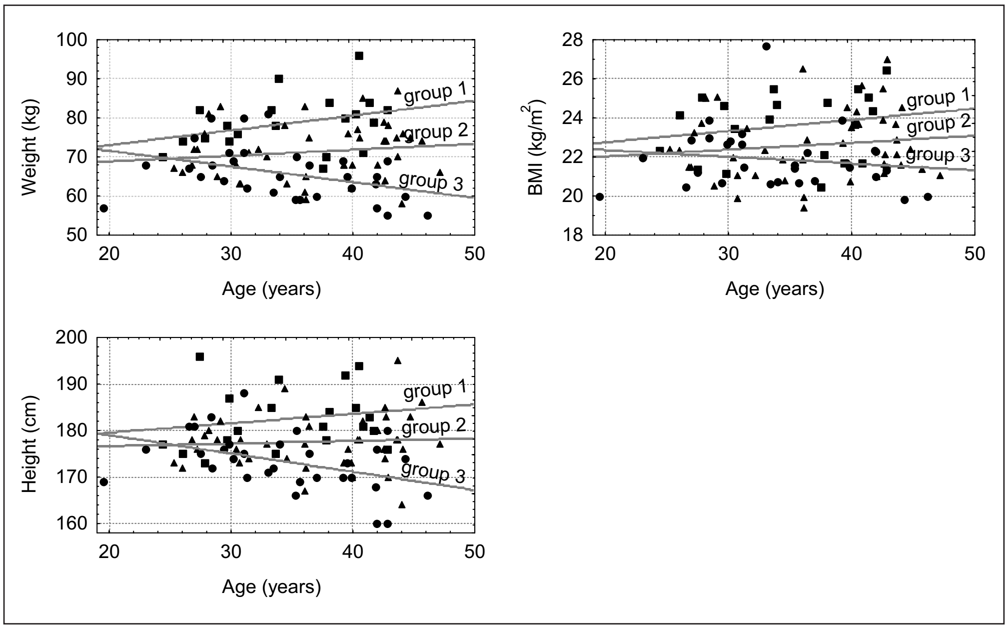

Figure 5: Morphological characteristics in relationship to the age of the subjects. The lines are the linear regressions for the three groups. The differences are rather small for young subjects and tend to increase with age.

■ Group 1 (non-marathon runners)
▲ Group 2 (moderate training)
● Group 3 (intensive training)

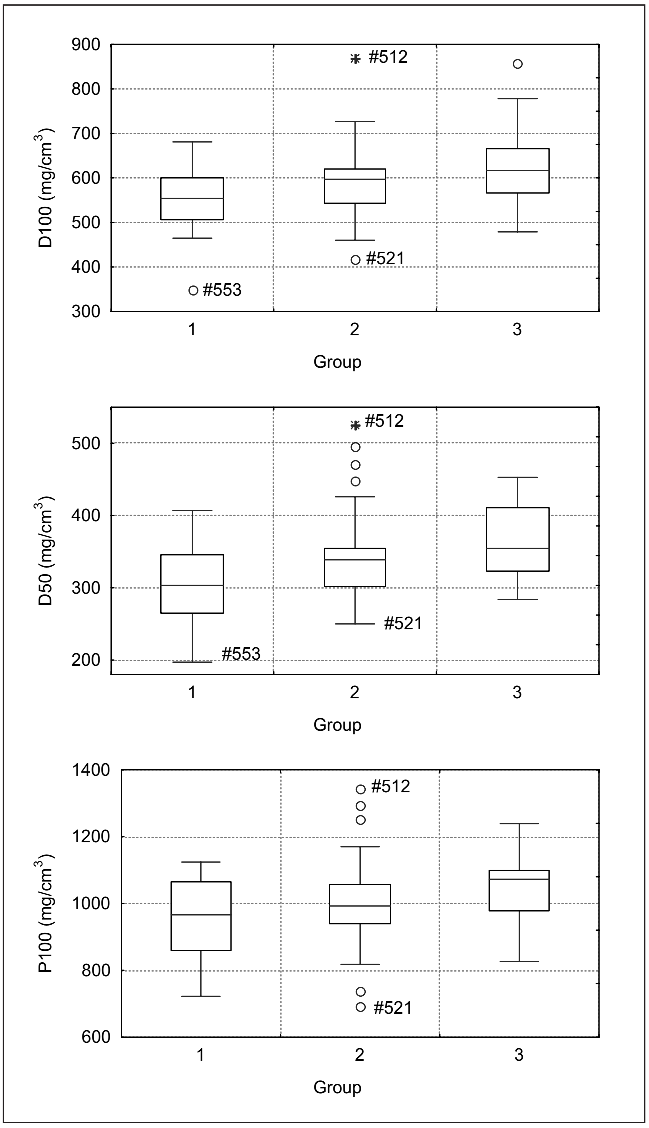

Figure 6: Boxplots of bone density of the distal tibia. Marathon runners with moderate training show in average higher values than non-marathon runners, and marathon runners with intensive training higher values than marathon runners with moderate training. ■ Group 1 (non-marathon runners), ▲ Group 2 (moderate training), ● Group 3 (intensive training)

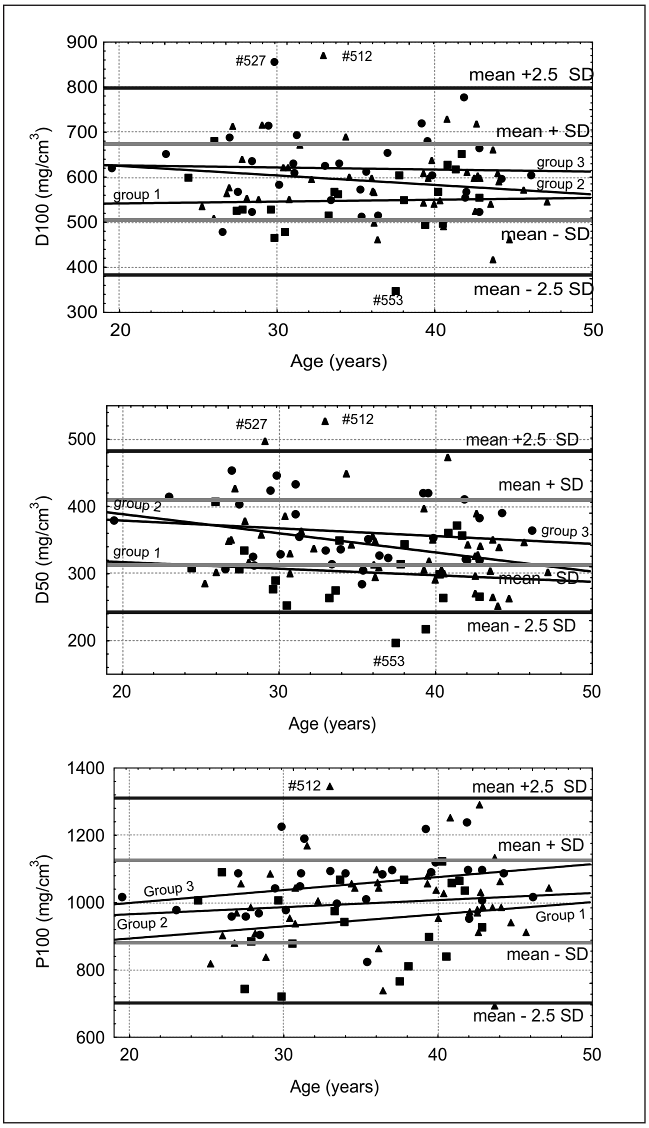

Figure 7: Bone density of the distal tibia in relationship to the age. Confidence intervals are displayed by the mean value of all the measurements ± 2.5 standard deviation. ■ Group 1 (non-marathon runners), ▲ Group 2 (moderate training), ● Group 3 (intensive training)

Discussion

What do the results mean?

Our results mean that either 1) the morphology (height, weight, body mass index) or 2) the bone density (D100, D50, P100, i.e. trabecular and bone density) differ between the groups of varying training. In average, the density of group 1 < density of group 2 < density of group 3 for either D100 or D50 or P50.

Why does the density not decrease after 40? Indeed, it is widely accepted that bone density reaches a maximum value at about 25–30 years, and afterward decreases in average. *Figure 7* does not show such an age-related behaviour: It is rather constant for the ultra-distal total density (D100 is the addition of the contribution of cortical bone, which is a fine shell at this level, and of trabecular bone). At this level, the trabecular bone density D50 seems to slightly decrease for all three groups. In contrast, the cortical bone P100 at dia-metaphyseal junction clearly tends to increase for the three groups. This rather unexpected behaviour might suggest that individual decrease is masked by a bias in the subject morphology. Our further investigation (i.e. the longitudinal study) will answer this question, whereby even a minute individual variation (in + or in –) will be revealed by our highly precise instrument.

The question remains, if the difference in bone density between the groups is only another way to display the difference in subject morphology, or if the difference in bone density expresses the effect of the difference of training. We used a rather complex statistical tool to answer this question: The principal component analysis (PCA), whereby the contribution of *all*[2] the measured values (which are correlated, i.e. not independent) allows to build new variables, the *principal components*, which are independent each other. For a better understanding of PCA, see for instance Falissard [25].

It is out of the scope of the present paper to present this analysis in details. This analysis established that the amount of exercise leads to increased bone density. Weight and height are only confounding factors. The most important contribution was due to the bone mineral density (38% of the total variance), the second contribution to the size of the subjects (height and weight – with a contribution of 22% to the total variance), and the third contribution to the body mass index BMI (with a contribution of 9% to the total variance). That means that the effect of the amount of training does indeed affect the bone density. It seems amazing that the body mass index, which is directly calculated from the weight and the height of the subjects, leads to an independent principal component. That means that height and weight describes mainly if the subjects are large or small, then BMI describes the corpulence of the subjects: more slender or more obese.

What is the benefit for the measured subjects?

For the subjects, that is a global and individual benefit, but also an individual risk. The individual risk results from the X-ray irradiation due to the computed tomograph. The Densiscan has been specially conceived to apply a negligible amount of irradiation, smaller than that of a transatlantic flight; furthermore this irradiation is applied to a non-sensible region (appendicular member). The global benefit relates to a better understanding of the bone adaptation to running activity, and improvement of this training. The individual benefit is of course more important for the subjects. A particularly low or high density may suggest inadequate training or other medical problems. This related to the medical follow-up of the subjects.

Further reports – further measurements

This report is restricted to our ultradistal measurements. Other measurements have been made on the proximal part of the tibia during the same measuring session and will be reported separately. The same volunteers supported also DEXA (Dual Energy X-ray Absorptiometry) at the whole body, the proximal femur and the spine. This investigation will also be reported separately. Furthermore, a longitudinal investigation is currently in progress, whereby the subjects were measured in a second session after about one year (currently ~50 subjects) and a third session after two years (6 subjects). It is too early to report these measurements, but they display a very high reproducibility, which proves (together with control phantom measurements made in routine at each session) the expected precision of the instrument.

Conclusions

- Either the ultradistal trabecular bone density or the dia-metaphyseal cortical bone density is in average higher for the groups with more intense training.
- This means that Wolff's law is corroborated by our measurements.
- As expected, more intense training leads to higher bone density.
- However, a particular attention has to be focused on individual subjects with osteopenia or with too high density (pathological or training problem?).
- A maximum in density at the age of about 25–35, followed by a decrease with increasing age, has been shown in none of our training groups.

Acknowledgements

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Notes

1 This is a true *physical* density (ratio mass/volume), and not a *projection* density (ratio mass/projection area) as measured using the conventional bone absorptiometry.
2 With *all* the variables means that PCA includes also the values of the proximal part of the tibia. These measurements are not reported here, and will be Part II of our transversal investigation.

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