Can the effects of exercise on bone quality be detected using the CUBA clinical ultrasound system?

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Abstract

Objectives—To determine whether the CUBA clinical quantitative ultrasound bone analyser was able to distinguish variations in bone quality between groups categorised according to activity level.

Method—Eighty one white women aged 32 to 89 completed a confidential questionnaire on general health, diet, and exercise participation and underwent ultrasound testing at the right calcaneus utilising a CUBA clinical ultrasound system.

Results—The results confirmed the inverse relationship between age and the ultrasound indicators of bone quality: broadband ultrasound attenuation (BUA) ($r = -0.52$) and velocity of sound (VOS) ($r = -0.68$). Subject height weakly but significantly correlated with BUA ($r = 0.39$) and VOS ($r = 0.35$), and subject weight only correlated significantly with BUA ($r = 0.37$). Activity level was significantly associated ($p < 0.05$) with the changes in ultrasound attenuation (BUA). The use of hormone replacement therapy or the contraceptive pill, a family history of osteoporosis, and gross indicators of calcium consumption did not yield significant results.

Conclusion—Data obtained from the CUBA clinical system were sensitive enough to allow women to be classified into groups according to activity level. These data were within the range of "normal" ultrasound data and hence it is suggested that the machine has research as well as clinical value.

(Br J Sports Med 1998;32:162-166)

Keywords: CUBA; ultrasound; bone; exercise; osteoporosis

Osteoporosis is characterised by low bone mass and deterioration of bone tissue leading to fragility and increased risk of fracture.¹ A fractured bone can be a costly and painful outcome of the influence of a combination of risk factors that predispose an individual to a reduction in bone density. Osteoporosis continues to be a major health concern in our society, affecting one in four women in the United Kingdom.² The resulting cost to the NHS is estimated to be around £640 million a year, with £411 million of this being attributed to direct medical costs.³

Bone is ultimately affected by age,⁴ with age related or involutional loss beginning after the attainment of peak bone mass, which occurs

between the ages of 17 and 30.⁵⁻⁸ Subsequently bone loss may occur at 0.8% per year, accelerating to 1.0-3.0% per year after menopause because of the reduction in oestrogen production.⁹ However, it is suggested that women who have higher peak mass, although they experience similar age related losses to those with lower values, will tend to remain above the fracture threshold because of the higher initial values.¹⁰

Although aging is inevitable, mechanical loading, such as might occur in physical exercise at intensities above those experienced in normal activity, has been shown to alter or delay the reduction in bone mass associated with the aging process.¹¹⁻¹⁴ The strain resulting from this loading, if greater than the optimum strain for the bone being loaded, produces an osteogenic stimulus. This stimulus results in an increase in bone mass to reduce future strain.^{5, 15} In contrast, periods of prolonged inactivity are shown to result in bone atrophy.^{16, 17}

Evidence to support the importance of weight bearing activity relative to bone density comes, in the main, from cross sectional studies of resistance training,^{18, 19} aerobic training,²⁰ or a combination of the two,²¹⁻²³ and from longitudinal studies suggesting the importance of long term adherence to an exercise regimen.^{13, 24-26} Although the general relation between exercise and bone density is accepted, the effects of specific recreational and sporting activities, other than those mentioned above, have received little attention. It is suggested that this is, in part, due to limitations imposed by the experimental techniques currently available.

Bone mineral content and bone mineral density can only be directly measured using a bone biopsy sample from which the number of active bone cells can be determined. However, the surgical nature of this procedure precludes its use as a routine research or screening tool. Osteoporosis is commonly diagnosed after a fracture using standard x ray techniques.³ Unfortunately, up to 30% of bone density must be lost before it becomes detectable using this technique.²⁷ A more sensitive and frequently used technique is that of dual energy x ray absorptiometry. In this technique, photon attenuation per unit area is used as an indicator of bone density, and data may be obtained for a number of anatomical sites, including spine, femoral neck, and forearm, as well as estimates of total body skeletal density.²⁸ Although this technique is generally considered the most accurate method of indirect bone density measurement,¹⁰ it is very costly,

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Accepted for publication
9 October 1997

requires exposure to ionising radiation and the apparatus is non-portable.

More recently, a number of techniques based on the measurement of ultrasound velocity and attenuation have been developed. One such technique is the contact bone ultrasound analyser (CUBA) system developed by Langton.²⁹ The heel of the foot is placed between two directly contacting ultrasound transducers in a foot rest mechanism, and the velocity of sound (VOS) and broadband ultrasound attenuation (BUA) through the calcaneus are measured. The magnitude of the resulting VOS measurement is dependent on the elasticity and density of the calcaneus; the BUA value obtained is the gradient of the linear portion of the attenuation-frequency curve over the range 0.2–0.6 MHz and is related to density and structure. Although the technique is limited to this site in the body, it is of value because the calcaneus is composed primarily of trabecular bone as are the principal osteoporotic fracture sites, the proximal femur and the vertebra. Remodelling activity is greatest in trabecular bone, and, as a result, bone loss occurs here much earlier than in cortical bone.¹⁰ The calcaneus is therefore sensitive to osteoporotic change.

The low cost, portability, and relative safety of the CUBA system suggest that it may have value both in routine screening and for research use. However, although ultrasound bone analysers are said to be accurate, relatively poor precision has also been noted.²⁹ The aim of this study was to determine whether the limited precision of the CUBA system would prevent it from differentiating between subgroups of differently active women within the normal population and hence limit its value as a research tool.

Methods

Eighty one white female volunteers aged 30–89 were tested. The subjects were drawn from university staff, a local leisure centre running a general practitioner referral scheme, warden run retirement homes, and sport and leisure clubs in East Sussex. On receipt of a description of the purpose of the ultrasound testing, all subjects gave written consent.

Each subject was asked to complete a questionnaire. The questionnaire elicited general information about age, height, weight, and occupation. A general health section determined the current state of the subject's health and any family history of osteoporosis. Nutritional information was obtained, including allergies and use of dietary supplements. Data on current weekly consumption of milk and other high calcium foods was also obtained. Answers were then ranked as low, average, or above average calcium intake, depending on the regularity of consumption (0, rarely consumed if ever; 1, once to three times a week; 2, more than three times a week). An average was calculated using all foods selected for analysis, and a final score allocated, classifying the subject's intake as below average, average, or above average.

The questionnaire also sought to determine exercise participation and general activity

levels. Subjects were ranked as below average, average, or above average according to the hours of weight bearing leisure activity per week (0, zero to two hours; 1, two to five hours; 2, more than five hours). Activity levels in the home were scored according to the subject's self perception of exertion (0, inactive/relatively inactive; 1, moderately active/active; 2, very active). Activity levels at work were assessed by allocating a score for type of work (0, sedentary; 1, moderate or semimanual sometimes resulting in breathlessness or perspiration; 2, manual often causing breathlessness or perspiration) and hours spent working (0, >15; 1, 16–25; 2, 26+), and an average score was calculated. A combined exercise score was calculated using a mean score from results of activity in the home, at work, and during leisure time, and each subject classified as below average, average, or above average.

The subjects were tested at the university, leisure centre, home, or club as appropriate. The manufacturer of the CUBA system (McCue Ultrasonics, Winchester, Hants, UK) recommended that calibration checks were performed before each testing session. During a test, water based ultrasound gel was applied to the target site of the right calcaneus, and measurements were taken according to the manufacturer's instructions. For each subject this process was repeated three times and a mean score calculated.

Two readings were given as indications of bone quality: BUA and VOS through the calcaneus. In addition, age related BUA (%BUA_{age}) and VOS (%VOS_{age}) values were obtained. These were expressed as a percentage of the expected value for an individual of similar age based on normative data supplied by the manufacturer of the CUBA system.

A normal distribution in our cross sectional sample was confirmed by observation of the sample's descriptive statistics. Pearson correlation coefficients were calculated to identify relations between different proposed influential factors and the ultrasound measures of bone quality. Analyses of variance were performed between the proposed influential factors and each reading of bone quality. Homogeneity of variance tests was used to verify that the data were suitable for analysis via analysis of variance. For all tests a significance level of $p < 0.05$ was accepted.

Results

Table 1 gives a summary of statistics for the sample population and the mean ultrasound measures obtained. Sixty eight of the women had children. All of the women had menstruated or were menstruating with an average duration of 32.7 years. Thirty eight women had taken or were taking a contraceptive pill with a mean duration of 7.83 years, and 12 subjects had been taking the pill for more than 10 years. Seventeen women were on hormone replacement therapy (HRT) (average duration 1.9 years).

Table 2 summarises the significant correlations between the basic anthropometric descriptors of the sample and the four ultrasound

Table 1 Descriptive statistics for the sample population (n=81)

Factor	Mean	SD	Minimum	Maximum
BUA (dB/MHz)	74.60	19.21	23.7	125.0
VOS (m/s)	1587.6	47.80	1472.0	1682.0
%BUA _{age}	109.98	27.44	57.0	204.5
%VOS _{age}	101.6	2.60	96.0	107.0
Age (years)	59.2	15.10	32.0	89.0
Height (m)	1.62	0.80	1.37	1.78
Mass (kg)	66.29	12.23	45.45	98.64
Ponderal index	0.404	0.023	0.344	0.047

BUA, broadband ultrasound attenuation; VOS, velocity of sound.

Table 2 Significant ($p < 0.05$) correlations between affecting variables and the four ultrasound indicators of bone quality

	Pearson correlation coefficient (r)			
	BUA (dB/MHz)	%BUA _{age}	VOS (m/s)	%VOS _{age}
%BUA	0.638	—	0.322	0.474
VOS (m/s)	0.732	0.322	—	0.236
%VOS	NS	0.474	0.236	—
Age (years)	-0.516	NS	-0.683	0.490
Height (m)	0.385	NS	0.346	-0.279
Weight (kg)	0.365	NS	NS	-0.253
Ponderal index	NS	NS	0.246	NS

BUA, broadband ultrasound attenuation; VOS, velocity of sound; NS, not significant.

Table 3 Comparison of BUA and VOS for pre and post-menopausal women. Results are mean (SD)

	BUA (dB/MHz)	VOS (m/s)
Premenopausal (n=32)	82.75 (16.33)	1618.3 (43.5)
Postmenopausal (n=42)	66.00 (18.11)	1588.8 (33.3)

BUA, broadband ultrasound attenuation; VOS, velocity of sound.

Table 4 Variation in the ultrasound measures of BUA and VOS between activity level groups. Results are mean (SD)

	Combined activity level		
	Below average (n=24)	Average (n=39)	Above average
BUA (dB/MHz)	67.98 (22.63)	73.21 (16.81)	86.42 (14.09)*†
VOS (m/s)	1581 (50.1)	1582 (50.0)	1608 (35.1)

BUA, broadband ultrasound attenuation; VOS, velocity of sound.

* $p < 0.05$ v below average; † $p < 0.05$ v average.

Table 5 Mean BUA and VOS data for subjects grouped according to selected risk factors. Results are mean (SD)

	BUA (dB/MHz)	VOS (m/s)	Number
HRT use			
No	73.25 (18.92)	1587 (46.2)	64
Yes	79.67 (20.05)	1589 (55.1)	17
Contraceptive pill use			
No	67.58 (19.72)	1567 (41.9)	43
Yes	82.53 (15.32)*	1616 (44.2)*	38
Children			
No	76.92 (26.29)	1597.1 (64.2)	13
Yes	74.15 (17.77)	1585.8 (44.4)	68
Family history of osteoporosis			
No	73.21 (19.13)	1585.9 (48.6)	73
Yes	87.25 (15.87)*	1603.5 (39.9)	8

BUA, broadband ultrasound attenuation; VOS, velocity of sound; HRT, hormone replacement therapy.

* $p < 0.05$ v "No".

Table 6 Variation in the ultrasound measures between groups classified according to gross measure of calcium intake. Results are mean (SD)

	Calcium intake		
	Below average (n=25)	Average (n=42)	Above average (n=14)
BUA (dB/MHz)	68.50 (18.26)	77.19 (18.26)	77.70 (20.47)
VOS (m/s)	1575 (39.0)	1594 (49.8)	1588 (54.9)

BUA, broadband ultrasound attenuation; VOS, velocity of speed.

bone quality indicators. Age was shown to have a significant effect on BUA and VOS ($p < 0.05$). Indeed, when comparing pre- and post-menopausal subjects, there is a decline in mean BUA and VOS values of 16.75 dB/MHz and 59.5 m/s respectively (table 3). Subject height correlated significantly with both BUA and VOS. Subject weight correlated with BUA but not with VOS. Interestingly, ponderal index exhibited a reverse trend.

The correlation between VOS and BUA (table 2) was to be expected as both should reduce as bone quality deteriorates. The correlations between these measures and their age adjusted percentage values (%BUA_{age} and %VOS_{age}), although low, indicate a discrepancy between our sample and the normative data supplied by the manufacturer.

When subjected to one way analysis of variance, the individual measures of exercise at work, in leisure, and in the home produced non-significant variation in both of the ultrasound measures of bone quality. However, when the combined exercise scores were investigated, significant results were obtained ($p < 0.05$). Table 4 shows the mean BUA to be greater in those individuals exhibiting above average exercise levels, the difference being significant between the below average and above average groups and between the average and above average groups. Although the mean age of the above average activity level group was lower than the average and below average groups, this was not found to be statistically significant ($p > 0.05$). Although VOS showed an increasing trend, it was not significantly different between the groups.

Although the principal objective of this study was to investigate the relationship between the ultrasound measures BUA and VOS and activity level, additional data on known osteoporosis risk factors were obtained to account for contamination effects in the data. Table 5 summarises the effects of contraceptive pill use, HRT use, and family history of osteoporosis. A family history of osteoporosis produced a significant value for BUA, but not for VOS. Those using the contraceptive pill had significantly different results for both BUA and VOS ($p < 0.05$). However, only four women aged over 60 had taken the pill, and, when this age group was removed from the study, no significant differences were obtained. The mean age of the women in the HRT group was 55.5 years. Two of the 17 women on HRT had a family history of osteoporosis. One was aged 44, and the other, aged 77, had been treated for one year. HRT produced no detectable effect in this study. Similarly, there were no significant differences in BUA or VOS between low, medium, and high calcium intake groups ($p > 0.05$) (table 6). None of these factors was associated with significant differences in the means of %BUA_{age} or %VOS_{age}.

Discussion

A wealth of evidence exists to show that age related bone loss is an inherent part of an increased risk of fracture.²⁷⁻³⁰⁻³² The results of this study confirm that the ultrasound measures

Figure 1 Relation between broadband ultrasound attenuation (BUA) and age.

Figure 2 Relation between velocity of sound (VOS) and age.

BUA and VOS are sensitive to changes in bone quality with age (figs 1 and 2). The osseous tissues of the body are ultimately influenced by the aging process, and the factors relating bone loss to age appear to be irreversible.³³ Previous research has suggested that, if women are to maintain bone quality above clinical thresholds throughout adulthood, efforts must be made in the premenopausal years to maximise potential for peak bone mass and prevent or reduce bone loss thereafter.^{34 35} It has been observed that individuals who habitually take part in a high level of physical activity have greater bone density than less active individuals.^{34 36} However, conventional methods of determining bone density impose practical difficulties on studies investigating this relationship further. This study suggests that the CUBA technique is able to distinguish between groups classified according to activity level in terms of their mean BUA, a variable that is associated with bone density and structure.

The age range of this sample was large, and it might be expected that increasing age may have exerted an influence by decreasing exercise participation.³⁷ However, analysis of variance indicated that there were no significant differences between the ages of the exercise level classifications.

Exercise can positively affect bone mass, aiding the attainment of an individual's peak bone mass. However, measuring activity levels accurately is difficult, which reduces the likelihood of showing a relationship between exercise and bone quality.²³ Furthermore, Walker and Holm³⁸ suggest that it may be more valid to correlate bone quality with previous activity levels as opposed to short term or current activity; however, the former is much more difficult. An attempt at an historical analysis was made in this study. However, communication

with the subjects during completion of the questionnaire and the large number of nil responses indicated that these data were unreliable and it was therefore rejected.

It has been proposed that genetic factors may contribute 70–80% of the biological potential for peak bone mass attainment.^{39 40} Only eight subjects reported a family history of fractures and osteoporosis, which prevented a satisfactory statistical analysis in this study. Accurate reports of family history rely on the parents and grandparents living long enough to develop the condition and the diagnosis of the condition in a time when relatively little knowledge had been accumulated. In the present study we were unable to add to this debate except to conclude that this factor was unlikely to have affected the differences in BUA associated with exercise.

The contraceptive pill has been recognised as a protective factor which acts by adding to the oestrogen supply.⁴¹ This in turn acts as a store when natural hormone depletion occurs at menopause. Bone density may therefore be maintained at a higher level than in women who have not taken the pill before bone loss at menopause. This, however, was unsubstantiated by the findings of this study. Although highly significant *p* values for BUA and VOS were shown, a Pearson correlation coefficient of -0.486 between contraception and age suggests that, in part, these differences were age related. Indeed, most subjects over the age of 60 had never used the pill, and, when this age group was removed from the study, no significant differences were observed in either BUA or VOS between contraceptive pill users and the others.

HRT has been shown to be an effective method of preventing bone loss as a result of the menopause.⁴² Women who use HRT for at least five years, starting soon after menopause, reduce their risk of fracture by 50–60%.⁴³ HRT has been shown to be effective in reducing bone loss 10 years or more after the menopause, and it is safe for women to start and continue with treatment more than 15 years after menopause.⁴⁴ Seventeen subjects in this study were using HRT. Given their high mean age (55.5 years), it was possible that these individuals were utilising HRT as a preventive measure after menopause or to alleviate the symptoms of menopause. Of the two HRT users with a family history of osteoporosis, the younger subject (aged 44) had been using HRT for seven years, suggesting the aim was preventive. The older subject (aged 77) had been treated for just one year, indicating that use was not aimed at prevention of bone loss. No significant differences in BUA or VOS were observed between this group and the rest of the sample. Again it may be possible that this effect was swamped by the large age range, but comparison of an age matched subgroup also produced non-significant results.

Height and weight were highly significant variables affecting bone quality. An investigation into the ponderal index indicated that no subject was underweight for her height, a risk identified in a study by Falch *et al.*⁴⁵ Height and weight not only increases the loading on the

bones, but, according to Sowers *et al.*,⁴⁶ more fat tissue results in an increased production of oestrogen which slows bone loss. None of these factors correlated significantly with age.

Lack of weight is often associated with dietary inadequacies.⁴⁷ Data were obtained from which the subjects were classified according to calcium intake, and no effects were observed on the ultrasound measures of bone quality, leading us to conclude that dietary factors did not contaminate our exercise related results. No subject appeared to have an unusually low calcium intake and there were no significant differences in calcium intake between the exercise groups.

The lack of an ability to differentiate between the affecting factors, HRT and contraceptive pill use, may be associated with the relatively small sample size. Assuming a mean population BUA of 74 dB/MHz with a standard deviation of 20, power analysis would suggest that for deviations from the mean of 5% to be statistically significant at the 95% confidence level, a sample size in excess of 110 subjects per group would be required.

CONCLUSION

The results of this study are in accordance with previous research documenting the influence of certain variables on bone density. In particular, it has been shown that the ultrasound measures of BUA and VOS are related to age, height, and weight, and that it is possible to differentiate between subject groups within the female population classified according to activity level. This would suggest that the CUBA clinical machine has potential for low cost non-ionising investigation of similar subgroups, such as young athletes, the disabled, and in male populations. However, the limited precision of the data apparent in the relatively large standard deviations, particularly in the BUA measure, indicates that larger sample sizes are required for more detailed investigations and that these should preferably be matched for age, height, and weight. This latter observation may prove to be an important limiting factor of the technique. The limited precision also suggests that the technique may not be suitable for monitoring the effects of exercise over time on any given individual, which are are expected to be relatively small.

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