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In a continuing study of bone biodynamics, established values for the 6th rib are used to predict the parameters of the 11th rib. Autopsy samples of the 6th and 11th rib are compared and the correlation is used to validate studies of the 11th rib in osteoporosis showing normal cross sectional area with enlarged marrow cavity. The values presented are considered provisional until larger numbers of patients are studied.—Ed.

Correlation of the Transverse Sizes of 6th and 11th Ribs in Normal and Osteoporotic Individuals*

F. Santoro, B.S.** **H. M. Frost, M.D.*****

Introduction

It is known that most patients who have postmenopausal (PMO) and senile osteoporosis (SO) have less bone than normal. It is a justifiable assumption that this is caused by a supernormal enlargement of the marrow cavity in adult life, which implies a supernormal excess of cortical-endosteal resorption relative to formation. Recently completed studies of Haversian and cortical-endosteal bone formation and resorption rates in SO and PMO, done by quantitative histological methods based on tetracycline bone labeling, appeared to confirm this assumption. For, while they varied largely from patient to patient, they revealed subnormal mean osteon formation and resorption rates yet a supernormal cortical-endosteal resorption rate. [18,19] The latter rate had to be estimated by making certain reasonable assumptions about the rate of enlargement (due to cortical-endosteal bone loss) of the marrow cavity in the aging normal 11th rib.[19]

Here we devise a test of these assumptions, and classify provisionally SO and PMO in terms of "envelope" sizes.

This study was addressed to two specific questions:

(1) Is the external, transverse size of a standard bone sample subnormal or normal in PMO and SO?† (See Footnote next page.)

(2) Is the amount of compacta normal in this sample?

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The procedure followed was to measure the cross section sizes of standard 6th and 11th rib samples of the same person. This was repeated in a group of persons and intersite correlations demonstrated. Then, scaling factors were computed which expressed certain parameters of size for one sampling site as a decimal fraction of the other. These factors plus established values for normal 6th rib were then used to predict parameters for the normal 11th rib, which were then compared to those observed in the 11th rib biopsies in a group of osteoporotic women.

Materials

The middle third of the 6th and anterior third of the 11th ribs were taken from each of 26 subjects at autopsy. This is the *study group*. It contained 18 males and eight females whose ages ranged from 7 to 72 years. They died from a variety of causes. None had known skeletal metastases, Paget's disease or other form of known localized bone disease. Their mean age was 55 years, and they are listed in Table I. Chronically ill patients were intentionally included in the study, because the effects of systemic illness on bone remodeling should be generally distributed throughout the skeleton and should produce the same quantitative *kinds* of changes in different regions. Furthermore an ideal parameter of such changes should remain valid in the presence of chronic disease. Correlations between different sampling sites in this parameter should also remain valid. Systemic illness would include the patterns of bone loss which lead to osteoporosis. The total cross section areas for the 6th rib sampling site in the study group averaged 20% larger than normal and displayed a threefold increase in variance over normal. This means that from the standpoint of the size of the ribs, we did include abnormal as well as normal material.

The anterior third of the 11th rib taken at biopsy was available in 18 women with clinically symptomatic PMO or SO. These have been the subjects of previous reports.[19,10] Their mean age was 56 years; and they are the *osteoporosis group*, listed in Table II. The code letters in this table identify a given patient and are identical with these patients' data in all publications from this laboratory.

Methods

Undecalcified cross sections of the ribs were made by hand grinding under running water to a thickness of 70 microns; stained with the Villanueva Osteochrome Stain,†† and mounted in H.S.R. synthetic resin for permanent reference.[17] Three sections per rib were studied for a total of 210 sections.

The total (A_t) and cortical (A_c) cross-section areas were measured by the grid method (Chalkley[1]; Hennig[9]; Frost[5]) to an accuracy of $0.6 mm^2$ and a precision of

†If bones in these diseases were systematically smaller than normal, they could then contain less actual compacta than normal and so be osteoporotic in that (absolute) sense, yet contain a relatively normal amount of compacta for the total size of the bone and so be nonosteoporotic in that (relative) sense.

‡"Osteochrome", Harleco, Pa.

Transverse Sizes of the 6th and 11th Ribs

Table I

Study Group: middle third of 6th rib, anterior third of 11th rib

No.	CODE	Age Years	Sex	Rib #	A_t,mm^2	A_c,mm^2	C/T	$C/T^6/C/T^{11}$
1	18-66	7	M	6	13.47	6.76	0.50	0.97
				11	9.35	4.85	0.52	
2	27-66	10	F	6	34.50	16.72	0.48	0.88
				11	23.90	13.11	0.55	
3	4-66	21	M	6	27.37	12.37	0.45	0.77
				11	10.58	6.21	0.59	
4	21-66	27	M	6	77.24	36.72	0.48	0.80
				11	29.10	17.21	0.59	
5	16-66	41	M	6	87.14	21.16	0.24	0.67
				11	41.45	14.98	0.36	
6	13-66	44	F	6	54.03	18.05	0.33	1.06
				11	30.87	9.76	0.32	
7	29-66	43	F	6	71.74	33.21	0.46*	1.15
				11	37.07	14.90	0.40	
8	14-66	48	M	6	68.45	27.97	0.41*	1.53
				11	36.02	9.61	0.27	
9	9-66	50	M	6	96.70	28.68	0.30*	0.70
				11	50.62	21.49	0.42	
10	24-66	50	M	6	103.42	19.40	0.19	0.72
				11	61.33	16.04	0.26	
11	20-66	51	M	6	96.96	23.82	0.25	0.67
				11	52.93	19.33	0.37	
12	7-66	52	F	6	49.32	22.00	0.43*	1.03
				11	25.99	10.78	0.41	
13	11-66	54	F	6	65.83	19.75	0.30	1.12
				11	52.82	14.15	0.28	
14	26-66	55	M	6	87.62	32.45	0.37*	1.44
				11	44.23	11.40	0.26	
15	5-66	56	F	6	41.99	14.12	0.33	0.77
				11	40.37	17.51	0.43	
16	8-66	58	M	6	82.00	17.24	0.21	1.04
				11	59.85	12.13	0.20	
17	25-66	59	F	6	43.62	10.34	0.24	0.63
				11	18.16	6.84	0.38	
18	22-66	60	M	6	77.63	19.43	0.25	0.72
				11	37.16	12.96	0.35	
19	23-66	60	F	6	45.32	20.56	0.45*	0.96
				11	22.96	10.81	0.47	
20	15-66	61	M	6	103.09	21.80	0.21	0.48
				11	30.85	13.69	0.44	
21	19-66	61	M	6	89.90	20.53	0.23	1.50
				11	57.83	8.80	0.15	
22	6-66	62	M	6	79.45	32.61	0.41*	0.92
				11	29.74	13.28	0.45	
23	12-66	65	M	6	89.22	18.65	0.21	0.66
				11	50.66	16.04	0.32	
24	2-66	66	M	6	113.59	20.07	0.18	0.84
				11	66.50	13.81	0.21	
25	3-66	71	M	6	92.42	24.08	0.26*	0.87
				11	39.90	11.91	0.30	
26	10-66	72	M	6	70.52	18.46	0.26*	0.61
				11	37.98	16.27	0.43	

The data are listed for the study group. Each measurement is the mean of three cross sections. A_t: total cross section area, an index of the transverse size of the periosteal envelope. A_c: cortical cross section area, an index of the amount of compacta, and the remainder when the endosteal envelope (i.e., marrow cavity) is subtracted from the periosteal envelope. The asterisk in the C/T column indicates that the ratio given was within one S.D. of normal for the age and sex of the patient, based on the study of Takahashi and Frost.[16]

$0.4 mm^2$ per section. The marrow cavity areas were computed by taking the difference between the two areas.

Among the numerous intersite relationships explored was the C/T ratio of Sedlin.[14] This is the cortical cross-section area (A_c) divided by the total cross-section area (A_t) of the rib, or in symbols:

$$C/T = A_c (A_t)^{-1}$$

This parameter expresses the decimal proportion of the periosteal envelope that is filled by compacta. Tables I and II list the data for each case. Table III summarizes some of these data and lists data for four other groups relevant to the subject.

Results

This study showed certain points of note:

1) The C/T ratio of the 6th averaged 0.90 (±.26) that of the 11th, with a correlation coefficient between the two of r = .71. The estimating equation is y = 0.13 + 0.76x, where y is the C/T ratio of the 6th rib, and x that for the 11th. This relationship or scaling factor did not correlate with age, sex, or with the kind, severity or duration of disease. This means that when the C/T ratio was abnormal in one bone it

Table II
18 Women with Osteoporosis, 11th Rib

Number	HFH ORL Code	Age Years	A_c,mm²	A_t,mm²	C/T
1	A_v	24	5.2	28.8	0.18
2	A_c	36	8.0	22.2	0.26
3	A_w	43	12.7	27.2	0.46
4	A_x	48	12.8	24.5	0.52
5	C_f	48	10.2	32.1	0.32
6	B_b	52	7.5	25.8	0.29
7	A_z	53	14.9	27.8	0.53
8	A_q	57	9.5	28.8	0.33
9	A_y	60	9.9	24.6	0.40
10	B_f	60	6.0	34.2	0.18
11	C_a	60	13.2	26.7	0.49
12	B_e	61	5.2	20.9	0.25
13	A_e	61	11.3	39.6	0.29
14	A_k	63	7.9	32.2	0.24
15	B_j	63	7.9	15.8	0.50
16	B_L	65	10.5	24.3	0.43
17	A_o	73	7.3	24.2	0.30
18	B_k	73	8.7	24.9	0.36

The data are listed for the osteoporosis group.

tended to be equally abnormal in the other. Figure 1 shows this relationship for each member of the study group.

2) C/T Ratio: By means of this scaling factor, normal mean female 11th rib C/T ratios were predicted from published 6th ratios for each age decade in 117 normal women.[16] Figure 2 shows that the curve of this predicted norm is significantly higher than the ratios found in the osteoporosis group, implying a relative decrease in the amount of compacta in the latter group. Three of the 26 osteoporotic patients had

Table III

Disease and number of subject in group	Study Group 11th rib (26)	—P.M.O.— —S.O.— Females 11th rib (18)	—S.O.— Male 11th rib (7)	Osteomalacia 11th rib (12)	Osteogenesis Imperfecta 11th rib (3)	Acromegaly 11th rib (2)
Mean Age Years	55	56	58	54	51	35
A_c	13.00	9.36	12.32	13.17	10.87	17.72
±1 S.D.	4.00	2.82	5.51	5.23	8.96	
A_t	38.39	26.89	36.43	32.78	15.90	65.51
±1 S.D.	15.28	5.36	17.00	14.92	6.48	
C/T	0.37	0.35	0.34	0.44	0.66	0.27
±1 S.D.	0.12	0.11	0.09	0.16	—	—

11th rib means for several different groups of patients are listed.

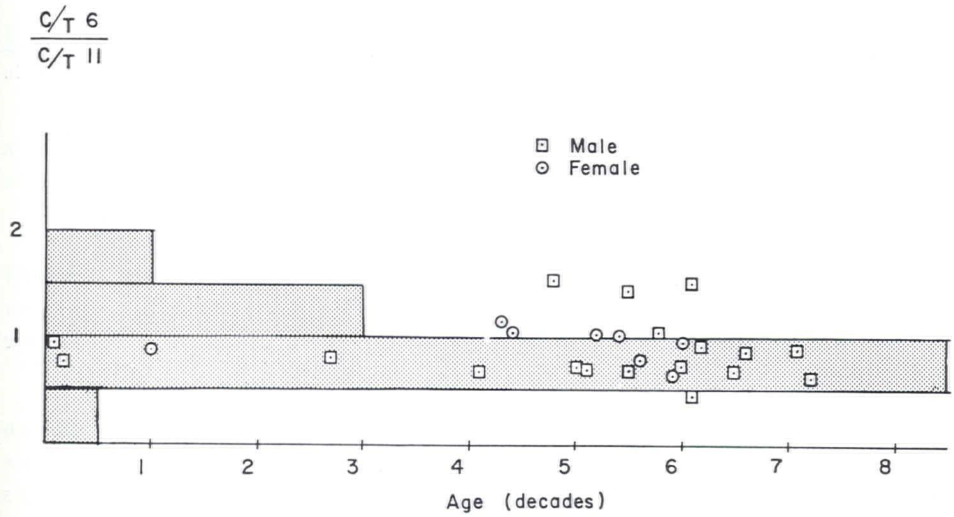

Figure 1

The ratios are plotted for each case in the study group of the C/T ratio of the middle 3rd of the 6th rib divided by that of the anterior 3rd of the 11th. The histogram constructed on the vertical axis suggests an approximately normal distribution.

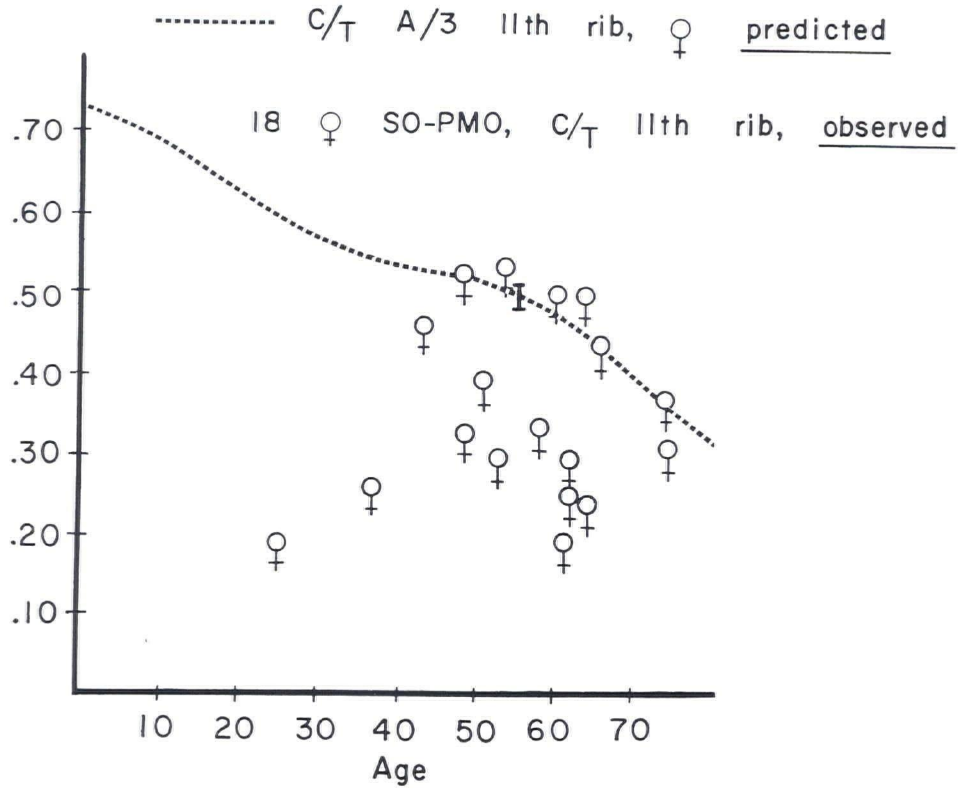

Figure 2

The curve shows the predicted C/T ratio for normal 11th rib. The observed value of the rib biopsy of each osteoporotic woman is plotted. They average significantly smaller values than normal. The small vertical bar is one standard error of the predicted norm and was computed as described in the legend of the next figure.

supernormal C/T ratios (implying more compacta than normal). This emphasizes a previous theory that more than a loss of bone is involved in clinically symptomatic osteoporosis.[7]

3) A_t: In the study group the 11th rib total cross section areas (mean: 38.4mm^2) averaged 55% ± 14% (S.E. 3.6%) those of the 6th (mean: 71.6mm^2). This factor was used to predict the normal 11th rib A_t from previously published norms for the female 6th rib.[16]

Figure 3 shows the observed normal 6th rib curve, the predicted normal 11th rib curve, and the actual A_t for the 11th rib biopsy of each woman in the osteoporosis group. The absolute mean external size of the osteoporotic ribs is greater than the predicted norm but this is not statistically significant ($p>.05$).

4) A_c: In the study group, the cortical cross section areas of the 11th ribs (13.0mm^2) averaged 64% ± 20% of (S.E. 5%) of the 6th (21.7mm^2).

Transverse Sizes of the 6th and 11th Ribs

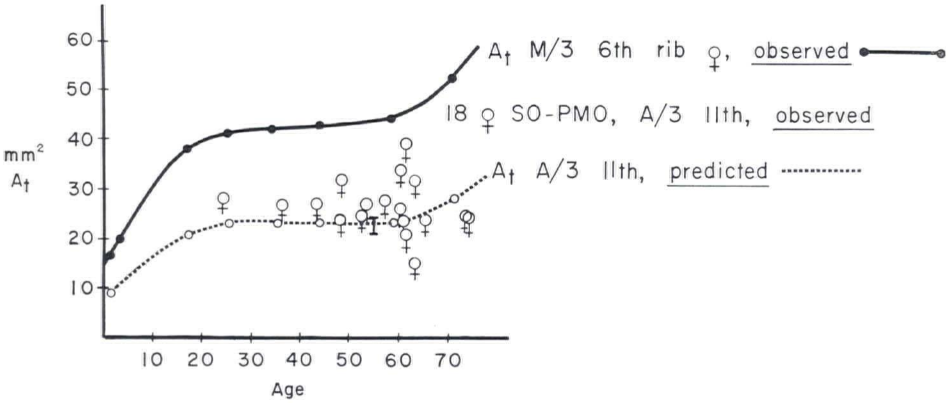

Figure 3

The dotted curve shows the predicted A_t for the normal 11th rib, plotted for each age decade. The A_t for each case in the ostoporosis group is plotted also, showing that these ribs are not smaller than normal. Therefore, the average osteoporotic did not have too little bone simply because she had bones that were too small in external, transverse dimensions. The small vertical bar on the predicted curve is one standard error and was computed on the basis that $N = 117$, after normalizing each age decade and its standard deviation to the curve. It was computed on the arbitrary assumption that there was no uncertainty in the numerical value of the conversion factor. This is not literally true because the coefficient of variation for this factor is .33, but it is justified on the basis that this factor showed no appreciable correlation with age, sex, severity or duration of disease.

Discussion

I: *Calibration of skeletal standards:* Sedlin's C/T ratio[14] provides a simple way to scale size parameters of the 6th to those of comparable 11th ribs. It showed the least scatter of the conversions we tested, and no systematic variation with age, sex or illness. Generalized, this lends support to (but does not prove) the idea that any skeletal sampling site has certain predictable cross-sectional size relationships to any other, and therefore to the whole skeleton. If true, suitable "calibration" factors might be used to infer certain properties of the whole skeleton from measurements of standard bone samples, assuming that localized bone disease is not present. The nature of this procedure, and the large interperson variance, mean that when evaluating the characteristic findings of a given disease entity, the evaluation must be based on the averaged values of a *group* of 20 or more patients who have the disease.

A logical extrapolation of this reasoning is that the mean size of a standard bone biopsy in a group of osteoporotic females could be compared to a norm for that biopsy site which is obtained by applying a scaling factor to a norm established by observation for another biopsy site. Such a comparison could be done with increasing statistical confidence as the number of subjects increases.

II: *Envelope classification of SO and PMO:* On cell-behavioral grounds, Frost introduced the concept that there are three kinds of bone surfaces or "envelopes" on which remodeling can occur: The periosteal, Haversian and endosteal.[6,7] These envelopes reveal considerable functional independence during aging and in disease.[2,3,13-19]

Table IV

Some Morphological Types of Osteoporosis Based on Cross Section Area Measurements of Standard Bone Samples

Envelope Sizes	Examples
1) Increased periosteal envelope Increased Haversian envelope Increased endosteal envelope	(acromegaly)[7] (111)
2) Normal periosteal envelope Increased Haversian envelope Increased endosteal envelope	(post-traumatic osteodystrophy)[7] (011)
3) Decreased periosteal envelope Increased Haversian envelope Decreased endosteal envelope	(osteogenesis imperfecta tarda)[1,17] (-11-1)
4) Decreased periosteal envelope Normal Haversian envelope Normal endosteal envelope	(Muscular dystrophy) (-100)
5) Normal periosteal envelope Normal Haversian envelope Increased endosteal envelope	SO, PMO[7] (001)

The parentheses on the right of each combination in this table show the vector notation Frost proposes to designate these states.[7] Here, plus one means *increased* in size, minus one *decreased*, and zero *normal*. The first term describes the periosteal, the second the Haversian and the third the endosteal envelope. The data in Table III suggest that the previous provisional classifications of acromegaly and osteogenesis imperfecta are correct, and that senile osteoporosis in men is probably the same disease morphologically and dynamically as it is in women.[7]

Mechanistically and in terms of envelope dynamics, this means that there is more than one way for a skeleton to become osteoporotic. For example, each combination of envelope sizes listed in Table IV is a morphologically and dynamically distinct* kind of osteoporosis.

Lacking specific information, any of these combinations could theoretically describe the anatomy of the bone loss in SO and PMO. However, our data indicate that the classification of (001), previously assigned provisionally to SO and PMO,[7] is probably correct. That is, the observed 11th rib total cross section areas in the SO and PMO patients were not less than a predicted norm, so these patients did not have bones that were too small. Therefore their decreased cortical cross section areas imply absolutely as well as relatively enlarged marrow cavities.

III: *Cortical-Endosteal bone loss in SO and PMO:* The scaling factors derived here can be used to evaluate the marrow cavity cross section areas in the osteoporotic 11th

*Dynamically distinct because each envelope size is the integral over time of all past resorption and formation of bone on the surface of that envelope.

rib biopsies. The areas are: 16.1mm^2 predicted normal at age 56*, and 17.5mm^2 observed in SO-PMO**, suggesting that by age 56 the average osteoporotic woman lost 1.4mm^2 more cortical-endosteal bone than normal. At age 25 the predicted normal female 11th rib marrow cavity is 12.9mm^2***, so the computed cortical-endosteal excess of resorption over formation between ages 25 and 56 is normally 3.2mm^2 but is 4.6mm^2 in osteoporosis (assuming both groups had normal sized marrow cavities at skeletal maturity). However reasonable it may appear, this latter assumption cannot be evaluated decisively with the evidence available in the literature up to now.

Wu *et al*,[19] who measured different sections of the 11th rib biopsies of these 18 women and obtained a mean A_c of 10.6mm^2, estimated their absolute cortical endosteal loss between ages 25 and 56 to 4.3mm^2. This is reasonably close to the 4.6mm^2 obtained here, so that the absolute excess of cortical-endosteal resorption inferred by Wu *et al*[19] in these 18 SO and PMO subjects is realistic. This study suggests it averaged 44% above normal.

IV: *Resorption generally in SO and PMO:* We must disagree with many authors who have assumed that a generalized increase exists in bone resorption in PMO and SO.[11,12] The "envelope" concept which we introduced,[6,7,13] and systematic studies we initiated of the behavior of these envelopes in health and disease[14,16-19] have indicated that the supernormal resorption *rate* which we have shown to exist on the cortical endosteal envelope in rib, does not exist on the Haversian or periosteal envelopes. This statement is based on direct measurements in biopsies of more than 50 patients with these diseases. The crucial point in our studies which is relevant to this argument (i.e., functional envelope independence) has recently been confirmed, by Garn and Hull,[8] and Smith and Walker[15] as well as by others.

Summary

In standard cross sections of the 6th and 11th ribs of 26 autopsied subjects: *(i)* Sedlin's C/T ratio of the 6th averaged 90% of the 11th (±26, r = .71); *(ii)* the total area of the 11th was 55%±14% of that of the 6th. These interrib ratios did not vary significantly with age, sex or disease. This implies that different skeletal sampling sites may have useful intersite correlations and predictable size relationships.

Using the above factors, and established values for normal 6th ribs, norms for the 11th rib were predicted and compared to values actually observed in 11th rib biopsies of a group of 18 osteoporotic females, revealing that in osteoporosis the ribs were not too small externally, yet too little compact bone was present. Consequently, both relatively and absolutely, the ostoeporotics had too large a marrow cavity.

In view of the large interperson variance encountered (expectedly) in this study, the numerical values of the above scaling factors are considered provisional.

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*N = 117; S.E. = .36
**N = 18; S.E. = .9
***N = 117; S.E. = .3

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