

## Evaluation by Microdensitometry and Dual Energy X-ray Absorptiometry of Changes in Bone Metabolism after Gastrectomy

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## Abstract

We used microdensitometry (MD) and dual energy X-ray absorptiometry (DXA) to evaluate impaired bone metabolism in 79 patients who had undergone gastrectomy. With MD, radiographs are simultaneously taken of the second metacarpal bone and an aluminum step-wedge, and the images were analyzed by computer. DXA was used to measure the bone mineral density of the second through fourth vertebrae and the estimated volumetoric bone mineral density (EstVBMD) was assessed. Significant positive correlations were obtained between EstVBMD as determined by DXA and metacarpal index (MCI) (r=0.413, P<0.01), peak of the cortex (GSmax) (r=0.362, P<0.05), peak of the middle portion of the bone marrow (GSmin) (r=0.412, P<0.01), and metacarpal bone mineral density (mBMD) (r=0.413, P<0.01) as determined by MD. When EstVBMD was compared with MCI, GSmax, GSmin, and mBMD according to sex, age, type of operation, and interval after operation, generally similar trends were obtained. We conclude that the determination by MD of various indices of bone metabolism is useful in the diagnosis of osteopathy after gastrectomy.

## Introduction

Osteopathy has recently received considerable attention as a postoperative complication of gastrectomy. Various mechanisms may cause osteopathy, including abnormal calcium metabolism<sup>1-3</sup>), impaired absorption of vitamin  $D^{4-6}$ , lactose intolerance<sup>3, 7</sup>), and secondary hyperparathyroidism<sup>7</sup>). However, the pathogenesis of this condition is complex and poorly understood. In the past, osteopathy was usually diagnosed solely on the basis of simple radiographs, and early detection and evaluation of treatment response were inadequate. Recent years have witnessed the development of new techniques for the quantification of bone mineral density, such as microden-

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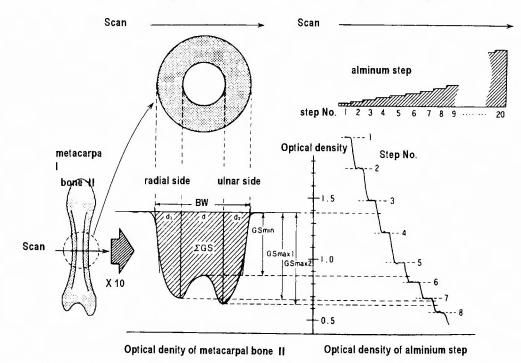
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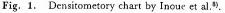
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sitometry (MD), single energy X-ray absorptiometry, dual energy X-ray absorptiometry (DXA), quantitative computed tomography (QCT), and ultrasound bone densitometry. These techniques have gradually demonstrated changes in bone mineral density after gastrectomy. Among these techniques, MD is the most convenient for the measurement of bone mineral density<sup>8</sup>). With MD, radiographs are simultaneously taken of the second metacarpal bone and an aluminum step-wedge, and the images are analyzed by computer. DXA, a technique that provides highly reproducible results<sup>9, 10</sup>), is used to measure the bone mineral density of the lumbar vertebrae, which contain abundant cancellous bone highly susceptible to osteopathy. In the present study, we evaluated osteopathy by means of MD and DXA in patients who had undergone gastrectomy to assess the usefulness and advantages of these techniques.

## Patients and methods

The study group consisted of 79 patients (54 men and 25 women) who had undergone gastrectomy. Bone mineral density was measured by MD and DXA on the same day at the Department of Surgery, Juntendo Izunagaoka Hospital, Juntendo University School of Medicine. No subject had concurrent diseases that affect bone metabolism or marked deformity of the lumbar spine; no subject regularly received drugs that affect bone metabolism, such as steroids, vitamin D, or calcium preparations. At the time of measuring bone mineral density, the mean age of the subjects was  $64.4\pm8.5$ 





BW, bone width; d, marrow width; d1, cortical width on the radial side; d2, cortical width on the ulnar side; GSmax1, peak of the cortex on the radial side; GSmax2, peak of the cortex on the ulnar side; GSmin, peak of the middle portion of the bone marrow. MD indices: 1) metacarpal index method (MCI)=d1+d2/BW; 2) d; 3) GSmax=(GSmax1+GSmax2)/2; 4) GSmin; 5) mBMD= $\Sigma$ GS/BW; 6) densimetric pattern.

(range, 45 to 77) years. Seventeen patients were younger than 60 years of age, 39 were from 60 to 69 years or younger, and 23 were 70 years or older. Fifteen patients had peptic ulcer, and 64 had gastric cancer. The surgical procedure was total gastrectomy in 22 patients (Roux-en-Y reconstruction, 21; jejunal interposition, 1) and distal gastrectomy in 57 (Billroth I reconstruction, 51; Billroth II reconstruction, 6). All patients with gastric cancer underwent radical operation, and none had recurrence. The interval from operation to the measurement of bone mineral density ranged from 1 to 49 years.

MD was developed by Inoue et al.<sup>8</sup>). Radiographs of an aluminum step-wedge and the patient's hands were taken on the same piece of X-ray film. Light transmission was continuously scanned with the use of a microdensitometer along the transverse longitudinal axis of the second metacarpal bone. The following variables were measured: bone width (BW), marrow width (d), cortical width on the radial side (d1), cortical width on the ulnar side (d2), peak of the cortex on the radial side (GSmax1), peak of the cortex on the ulnar side (GSmax2), peak of the middle portion of the bone marrow (GSmin), and a value obtained optico-densitometrically and converted into the number of steps on the aluminum step-wedge. Osteopathy was evaluated on the basis of 1) metacarpal index (MCI)=d1+d2/BW; 2) d; 3) GSmax=(GSmax1+GSmax2)/2; 4) GSmin; 5) mBMD= $\Sigma$ GS/BW; and 6) densimetric pattern. A value determined as computer integrating the pattern area is obtained optico-densitometrically and converted into the number of steps on the aluminum step-wedge (Fig. 1). Criteria for assessment of the severity were shown in Table 1<sup>8</sup>).

Indices Score	MCI, GSmax, GSmin, mBMD	d	Densitometoric pattern
0	Above the mormal regression line	Below the mormal regression line	Same as normal
1	Between the normal regression line and - $\sigma$ regression line	Between the normal regression line and + $\sigma$ regression line	1 rank aggravalion
2	Between - $\sigma$ regression line and -2 $\sigma$ regression line	Between + $\sigma$ regression line and +2 $\sigma$ regression line	2 rank aggravalion
3	Below -2 $\sigma$ regression line	Above +2 $\sigma$ regression line	3 rank aggravalion

Table 1. Criteria for asses	sment the severity	y by Inoue et al. method <sup>8)</sup> .
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Table 2. Criterion for synthetic assessment of the severity by Inoue et al. method<sup>8</sup>).

Severity as synthetically judged	Sum of given scores		
Normal	0 - 3		
Intial stage	4 - 6		
Degree I	7 - 9		
Degree II	10 - 12		
Degree III	13 - 18		

Based on the sum of the given scores, as shown in Table 1, the severity of bone atrophy was classified as normal, initial stage, degree I, degree II, or degree III (Table 2). The cases with osteopathy were defined as those presenting initial or more advanced stages.

Recently, bone width is abbreviated as BW rather than D, and  $\Sigma GS/D$  is expressed as metacarpal bone mineral density (mBMD)<sup>11</sup>. These new terms will be used in this report.

DXA was performed with a Hologic model QDR-2000 bone densitometer (Waltham, Maryland, USA). The bone mineral density of the second through fourth lumbar vertebrae was measured anteroposteriorly (AP) and laterally (Lat). For three-dimensional analysis, the estimated volumetric bone mineral density (EstVBMD) was assessed by dividing by the bone mineral content in a lateral plane by the vertebral volume. The vertebral volume was calculated by the following formula; vertebral volume=vertebral area on lateral images × width on anteroposterior images. Results are expressed as the mean  $\pm$  SD. The data were analyzed by Student's t-test and Pearson's correlation coefficients were calculated. P values less than 0.05 were considered to indicate statistical significance.

## Results

The relations between EstVBMD as determined by DXA and the 5 indices obtained by MD were studied. There were significant positive correlations of EstVBMD with MCI (r=0.413, P<0.01), GSmax (r=0.362, P<0.05), GSmin (r=0.421, P<0.01), and mBMD (r=0.413, P<0.01) (Fig. 2-A, B, C, D). However, there was no correlation between EstVBMD and d (Fig. 2-E). The indices obtained by MD and EstVBMD as determined by DXA were compared between men and women. mBMD, MCI, GSmax, GSmin, and EstVBMD were significantly lower in

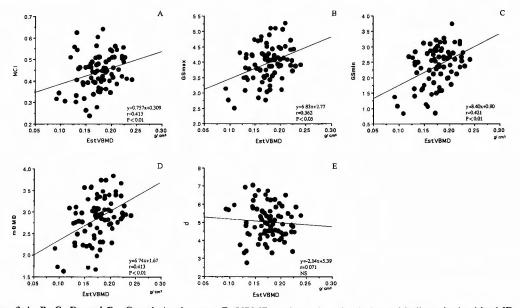


Fig. 2-A, B, C, D, and E Correlation between EstVBMD as determined by DXA and indices obtained by MD. There were significant positive correlations of EstVBMD with MCI (r=0.413, P<0.01), GSmax (r=0.362, P<0.05), GSmin (r=0.421, P<0.01), and mBMD (r=0.413, P<0.01) (Fig. 2-A, B, C, D). However, there was no correlation between EstVBMD and d (Fig. 2-E). N.S., not significant

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women than in men (P < 0.01, P < 0.05, P < 0.01, P < 0.01, P < 0.05) (Table 3). The indices obtained by MD and EstVBMD as determined by DXA were compared between normal and osteopathy cases in men and women. In men, mBMD, MCI, GSmax, and GSmin were significantly lower in osteopathy than in normal cases (P < 0.01, P < 0.01, I and I

MD					DXA	
	mBMD	ма	GSmax	GSmin	EstVBMD	
male (n=54)	3.03±0.40 -	0.445±0.077*	4.12±0.48 -	2.58±0.49	0.180±0.028	
female (n=25)	2.45±0.50 —	0.410±0.089-	3.62±0.64 —	1.91 ±0.65 —	0.163±0.034 —	

 Table 3.
 Comparison of indices obtained by MD and EstVBMD as determined by DXA between men and women.

\* P < 0.05, \*\*P < 0.01 Values are expressed as means  $\pm$  SD.

 Table 4-A and B.
 Comparison of indices obtained by MD and EstVBMD as determined by DXA between normal and osteopathy cases in men and women.

A						
	MD				EstVBMD	
	mBMD	ма	GSmax	G6min	EstVBMD	
normal (n=43)	3.11±0.33 -	0.478±0.06	44.21 ±0.43	2.70±0.37	0.182±0.029 ** 0.167±0.025NS	
osteopathy (n=11)	2.58±0.38 -	0.354±0.04	93.60±0.46	1.99 ±0.51	0.167±0.025	
в						
		·····	MD		EstVBMD	
	mBMD	ма	GSmax	GSmin	EstVBMD	
nor mal (n=17)	2.69±0.39 -	0.453±0.06	9 - 3.85±0.57	2.27±0.42	0.177±0.027 ** 0.134±0.031_NS	
osteopathy (n=8)	1.94±0.27 -	0.319±0.04	7 3.13±0.49	1.15±0.24	0.134±0.031 _	

\* P<0.05, \*\* P<0.01 Values are expressed as means  $\pm\,SD.$ 

N.S., not significant

mBMD, MCI, GSmax, and GSmin were also significantly lower in osteopathy than in normal cases (P<0.01, P<0.01, P<0.01, P<0.01) (Table 4-B). In men and women, EstVBMD was slightly but not significantly lower in osteopathy than in normal cases. The indices obtained by MD and EstVBMD as determined by DXA were compared between patients aged less than 60 years, those aged 60 to 69 years, and those aged 70 years or more in men and women at the time of examination. In men, MCI, GSmax, GSmin, and mBMD, and EstVBMD did not differ significantly among patients aged less than 60 years, those aged 60 to 69 years, and those aged 70 years or more (Table 5-A). In women, mBMD, MCI, Gsmax and Gsmin were significantly lower in patients aged 70 years or older than in those aged less than 60 years (P<0.01, P<0.01, P<0.05, P<0.01, respectively). mBMD and GSmin were significantly lower in women aged 60 to 69 years than in those aged less than 60 years (P<0.05, P<0.05, respectively). EstVBMD as determined by DXA was significantly lower in women aged 60 to 69 years and those aged 70 years or older than in women aged less than 60 years (P<0.01, P<0.01, respectively) (Table 5-B). The indices obtained by MD and EstVBMD as determined by DXA were compared according to the surgical procedure in men and women younger than 70 years. In men, mBMD, MCI, GSmax, and GSmin were slightly but not significantly higher and EstVBMD was slightly but not significantly lower after distal gastrectomy than after total

		DXA			
	mBMD	ма	GSmax	G&min	Est VBMD
<60 ( n=9)	3.23±0.39 NS	0.455±0.091 NS	4.43±0.47 *	2.71±0.64	0.183±0.019
60-69 (n=29)	3.01 ±0.32 =	0.465±0.077 =	4.04±0.41 =	2.59±0 39 =	0.183±0.031 =
70≦ (n≃16)	2.95±0.50	0.440±0.069	4.09±0.58	2.47 ±0.54	0.174±0.029 🔟

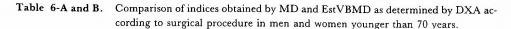
 Table 5-A and B.
 Comparison of indices obtained by MD and EstVBMD as determined by DXA according to age bracket in men and women.

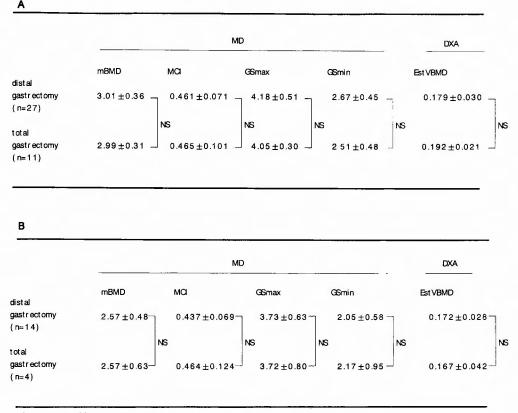
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	MD			DXA	
	mBMD	MCI	GSmax	GSmin	Est VBMD
<60 (n=8)	2.84±0.43	0.482±0.081	4.04±0.67	2.45±0.46	0.194±0.023
69 - 69 n=10)	2.36±0.46 = *	* 0.411±0.069	* * 3.48±0.54 NS	* 1.77±0.39 =	* * 0.153±0.024 = NS
′0≦ n=7)	2.15±0.39	0.327±0.040	3.34±0.54	1.47±0.54	0.143±0.036 🔟 📖

\* P<0.05, \*\* P<0.01 Values are expressed as means±SD. N.S., not significant

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\* P<0.05, \*\* P<0.01 Values are expressed as means±SD. N.S., not significant

Table 7.Interval after operation and change in indices obtained by MD and EstVBMD as determined<br/>by DXA (men younger than 70 years).

	MD				DXA
	mBMD	ма	GSmax	Gesmin	EstVBMD
<3 (n=14)	3.06±0.33	0.448±0.092	4.12±0.37 NS	2.60 ±0.51	0.193±0.022
3—9.9 (n=14)	2.90±0.27	0.492±0.082 = NS	3.90±0.37 -	2.53±0.44 =	0.172±0.029 - NS
10≦ (n=10)	3.25±0.37	0.444±0.045	4.45±0.46	2.77±0.44	0.183±0.031

\* P<0.05, \*\* P<0.01 Values are expressed as means  $\pm$  SD.

N.S., not significant

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gastrectomy (Table 6-A). In women, MCI, GSmax, GSmin, and mBMD and EstVBMD were similar after distal gastrectomy and total gastrectomy (Table 6-B). The relation between the indices obtained by MD and EstVBMD as determined by DXA and the interval after gastrectomy was studied in 38 men younger than 70 years. When the indices of bone mineral density were compared among patients less than 3 years after operation, those 3 to 9.9 years after operation, and those 10 years or more after operation, mBMD, MCI, GSmax, and Gsmin were slightly lower after 3 to 9.9 years than after less than 3 years, but the differences were not significant. mBMD and GSmax were significantly higher 10 years or more after operation than 3 to 9.9 years after operation (P<0.05, P<0.01). EstVBMD was significantly lower after 3 to 9.9 years than after less than 3 years (P<0.05). EstVBMD was slightly but not significantly higher after 10 years or more than after 3 to 9.9 years (Table 7).

## Discussion

MD is a technique developed by Inoue et al.<sup>8)</sup> to measure bone mineral density. Radiographs, taken simultaneously of an aluminum step-wedge and the hands, are analyzed with a microdensitometer. If simple X-ray equipment and an aluminum step-wedge are available, the analysis of the obtained X-ray films can be requested to an outside institution, which provides the examination results. MD is thus the most simple and convenient technique for estimating bone mineral density; it does not require expensive equipment. When MD was first developed, the coefficient of variation (CV) for reproducibility ranged from 2% to 4% for MCI and d, as compared with 3% to 7% for the other indices<sup>8)</sup>. Owing to the development of improved techniques, the CV for mBMD is now 0.2% to 1.2% and that for MCI is 0.4% to  $2.0\%^{12}$ .

MD has several disadvantages. Indices of the metacarpal bones are measured, whereas those of the lumbar vertebrae and neck of the femur, which have a high fracture risk, are not. Since metabolic abnormalities tend to occur in cancellous bone, whether or not it is meaningful to measure the second metacarpal bone is controversial. We therefore compared the results obtained by MD with those obtained by DXA of the lumbar spine in the same patients to study the correlation between the values.

DXA is superior in terms of image quality and reproducibility to other methods for the quantification of bone mineral density. The scanning time is extremely short, and the patient is exposed to a very low dose of radiation<sup>9</sup>. Since DXA uses X-rays derived from two different types of energy and measures the bone itself, it is very accurate and reliable. In this study we estimated the VBMD by measuring the lateral aspect of vertebrae to obtain very accurate values for bone mineral density of the lumbar spine. The use of AP measurements, widely employed in clinical practice, overestimates bone mineral density because of the age-related effects of osteoarthritis and aortic calcification. The use of Lat eliminates posterior components and provides measurements of the spine, composed mainly of cancellous bone. It is therefore useful in the detection of osteopenia. Conventionally, Lat is determined by shifting the patient from the standing to the lateral position. However, since the ribs overlie the second lumbar vertebra and the pelvis overlies the fourth lumbar vertebra, the measured region is small, and reproducibility is poor because the lateral body thickness is greater than the frontal thickness<sup>13</sup>. Recently, densitometers that permit measurement in a supine position (Hologic model QDR-2000 bone densitometer) have been developed, and accuracy of measurement has been improved. Suzuki<sup>13</sup> reported that when Lat is measured with the subject in a supine position, the mean CV for the second through fourth lumbar vertebrae was 0.84% in healthy subjects. In the present study, we performed more accurate measurements with the same model bone densitometer. Although Lat is a more accurate measurement than AP, it does not take into account body build and consequently results in high values in patients with a broad transverse dimension of the vertebral body. We therefore determined estimated VBMD, which provides volumetric indices of bone mineral density. Sabin et al.<sup>14</sup> studied the relation between EstVBMD of the lumbar spine in cadavers and the value obtained by measuring the actual mineral content of the bone ash. A very strong correlation (r=0.998) was reported. EstVBMD thus very closely approximates the actual value.

When severity determined as described by Inoue et al.<sup>8)</sup> is compared with EstVBMD as determined by DXA of the lumbar spine, higher severity is associated with a trend toward lower mean values of EstVBMD, but there is no correlation because of large intersubject variations. Terata et al.<sup>15)</sup> also measured the second metacarpal bone by MD in patients after gastrectomy and compared the results with the bone mineral density of the second through fourth lumbar vertebrae as determined by DXA of the anteroposterior aspect. They found no correlation between severity as assessed by MD and bone mineral density as measured by DXA. We therefore studied the relations of the five indices measured by MD (mBMD, MCI, d, GSmax, GSmin) to EstVBMD. When men were compared with women, mBMD, MCI, GSmax, and GSmin as well as EstVBMD were significantly higher in men. When bone mineral density was compared according to age group, in men there were no significant differences except for GSmax, whereas in women all indices differed significantly between patients younger than 60 years and those who were between 60 and 69 years of age or 70 years or older. Kin et al.<sup>16)</sup> reported that in healthy Japanese women bone mineral density starts to decrease before menopause and markedly decreases after reaching 50 years of age. Arlot et al.<sup>17</sup>) demonstrated that bone mineral density in women decreases rapidly within 10 years after menopause. Suzuki<sup>13)</sup> measured the bone mineral density of the lumbar spine by DXA of AP and Lat in females in their second to seventh decade and found no change up to and including the fourth decade. A distinct age-related decrease in bone mineral density was found in women in their fifth decade or older. The higher bone mineral density in men than women and the decrease in women aged 60 years or older suggest that menopausal changes in female hormones strongly affect bone mineral density in women. Men and women therefore must be studied separately to assess changes in bone mineral density after gastrectomy.

As for the relation between the surgical procedure and bone mineral density, there was no major difference in indices obtained by MD and EstVBMD between distal gastrectomy and total gastrectomy in either sex. In studies performed by MD, Sugiyama et al.<sup>18)</sup> showed that the incidence of postoperative osteopathy was significantly higher after total gastrectomy (42.2%) than after distal gastrectomy (38.8%). In similar studies, Tanaka et al.<sup>19)</sup> found that the incidence of osteopathy was 51.0% after total gastrectomy as compared with 37.2% after distal gastrectomy with Billroth I reconstruction. Hirano et al.<sup>20)</sup> reported that the incidence of osteopathy was 68.8% after subtotal gastrectomy and 48.3% after total gastrectomy. In studies of AP values by DXA, Inoue et al.<sup>21)</sup> reported no significant difference in postoperative bone mineral density among patients who underwent distal gastrectomy. Similarly, Nihei et al.<sup>22)</sup> found no significant difference in postoperative bone mineral density index as determined by QCT between distal gastrectomy and total gastrectomy.

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To eliminate the effects of female hormones and aging on bone metabolism, we studied changes in bone mineral density associated with the interval after gastrectomy in men only who were less than 70 years of age. We found that mBMD, GSmax, GSmin, and EstVBMD were lower in men less than 3 years after operation as compared with those 3 to 9.9 years after operation, and the difference in EstVBMD was significant. In men 10 years or more after operation, MD indices other than MCI and EstVBMD were higher than those in men 3 to 9.9 years after operation, and the differences were significant for mBMD and GSmax. As for studies performed with the use of MD by other investigators, Sugiyama et al.<sup>1)</sup> reported that the initial stage of osteopathy developed 5 years after partial gastrectomy and 1 year 6 months after total gastrectomy. Tanaka et al.<sup>19)</sup> studied the incidence of bone changes and the interval after operation and found an incidence of 33.3% up to 1 year after operation, 39.2% from 1.1 to 2 years, 43.4% from 2.1 to 5 years, 49.9% from 5.1 to 10 years, and 33.3% from 10.1 years onward. Bone changes thus gradually increased up to 10 years after operation. In addition, they noted that a time-related decrease in MCI, GSmin, and  $\Sigma$ GS/D (mBMD) 6 to 24 months after operation. Momose<sup>23)</sup> reported that the incidence of bone disturbances was 57.1% 5 years or less after operation as compared with 42.9% 6 years or more after operation, but this difference was not significant. In studies by DXA, Inoue et al.<sup>21)</sup> showed that as compared with healthy controls bone mineral density was significantly lower 2 to 5 years after gastrectomy in patients aged 50 to 69 years at the time of operation. In studies by QCT, Nihei et al.<sup>22)</sup> found that the mineral density index was significantly lower in patients 1 to 2 years after operation as compared with those less than 6 months after operation.

When the correlation between the indices derived by MD and EstVBMD was studied, the correlation coefficient was highest for GSmin (0.421), followed by those for MCI and mBMD (both 0.413) and that for GSmax (0.326). Inoue et al.<sup>8)</sup> investigated the correlation with bone mineral content as determined by photon absorptiometry and obtained correlation coefficients of 0.7390 for GSmin, 0.7932 for  $\Sigma$ GS/D (mBMD), 0.6354 for GSmax, and 0.4407 for MCI. Hayashi et al.<sup>24)</sup> reported that since bone mineral analyzers, which can most accurately determine bone atrophy, are all based on integrals of bone concentration, only  $\Sigma$ GS/D (mBMD) can be used as an index of the degree of bone atrophy. We feel that the global evaluation of MCI, GSmax, GSmin, and mBMD is useful in the detection of osteopathy.

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## 和文抄録

# Microdensitometory 法と dual energy X-ray absorptiometory 法を 用いた胃切除術後骨障害の検討

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胃切除術後患者79例の骨障害を最も手軽な測定法で ある microdensitometory (MD) 法と最も再現性の高い dual energy X-ray absorptiometory (DXA) 法の単位体 積当たりの計測値 (estimated volumetoric bone mineraldensity: EstVBMD) で評価した. MD 法では第 2 中手骨を DXA 法では第 2 - 4 腰椎を検査した.

DXA 法の EstVBMD と MD 法の指標の MCI (骨皮 質幅指数), GSmax (骨皮質部分のみの骨塩量の指標), GSmin (骨皮質+骨髄質の骨塩量の指標), mBMD (単 位骨幅当たりの平均の骨塩量を表わす指標)とはそれ ぞれ r=0.413 (P<0.01), r=0.362 (P<0.05), r=0.421 (P<0.01), r=0.413 (P<0.01) と有意な正の相関関係が 認められた. 性別,年代別,手術術式,術後経過期間 において EstVBMD と MCI, GSmax, GSmin, mBMD を比較するとほぼ同様の変動を示していた.

胃切除術後の骨障害を容易に診断する方法として, MD 法の個々の指標の変化を知ることが有効である と思われた.