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Radiation osteoporosis – an assessment using single energy quantitative computed tomography*

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Abstract. Radiation osteoporosis was assessed with single energy quantitative computed tomography (QCT) on 23 patients with cervical cancer. Eleven cases formed the radiation group, who received irradiation to the lumbar column. The other 12 cases formed the control group and were not irradiated. The absorbed dose to the lumbar column was 45 Gy over 5 weeks in nine cases and 22.5 Gy over 5 weeks in two cases. Bone mineral content (BMC) at the 3rd lumbar vertebra was scanned with QCT. BMC reduction was substantial in the radiation group and not evident in the control group. The mean reduction of the former was 52 mg/cm^3 at the end of irradiation. The difference in changes of BMC between the two groups was statistically significant ($p = 0.01$). The two cases who received 22.5 Gy revealed similar BMC reduction to those who received 45 Gy. QCT performed at the end of irradiation demonstrated that more than 22.5 Gy over 5 weeks induced substantial osteoporotic changes.

Key words: Radiotherapy – Bone injury – Osteoporosis – Quantitative computed tomography

Introduction

Bone atrophy is frequently seen following radiotherapy [1, 2], occasionally resulting in fracture or necrosis as late sequelae. Such damage may affect the quality of life of cancer patients, especially long survivors. However, owing to the difficulty of quantitative analysis, details of radiation osteoporosis have not been sufficiently investigated.

Recently, several none-invasive techniques have been developed to evaluate bone mineral content (BMC) quantitatively [3, 4]. In these non-invasive modalities, single energy quantitative computed tomography (QCT) provided a low-cost and easy assessment of BMC. In this study, radiation osteoporosis was analysed with QCT.

Materials and methods

From 1989 to 1990, 23 patients with uterine cervix carcinoma were treated in the Department of Radiology of Kansai Rosai Hospital. They were divided into two groups. Eleven cases in the radiation group received prophylactic irradiation to paraaortic lymph nodes. The field included lumbar vertebrae. The other 12 cases in the control group did not receive irradiation to lumbar vertebrae. Differences in age, cancer stage and post-menopausal duration were not significant between the two groups (Table 1).

In the radiation group, high energy photons of 4 MV were administrated via anterior and posterior opposite portals in nine cases and via box field in two cases. The level of the fields was from the 12th thoracic vertebra to the 4th lumbar vertebra. The anterior and posterior fields included spine. However, irradiation of the vertebrae through lateral portals was avoided in the two cases

Table 1. Subjects

	Radiation group	Control group	
Case number	11	12	NS[a]
Age (mean)	53	57	NS[a]
Stage			NS[b]
I	5	4	
II	4	6	
III	2	2	
Mean post-menopausal duration (year)	5.6	10.0	NS[a]

NS, not significant
[a] Non-paired *t*-test
[b] Chi-square test

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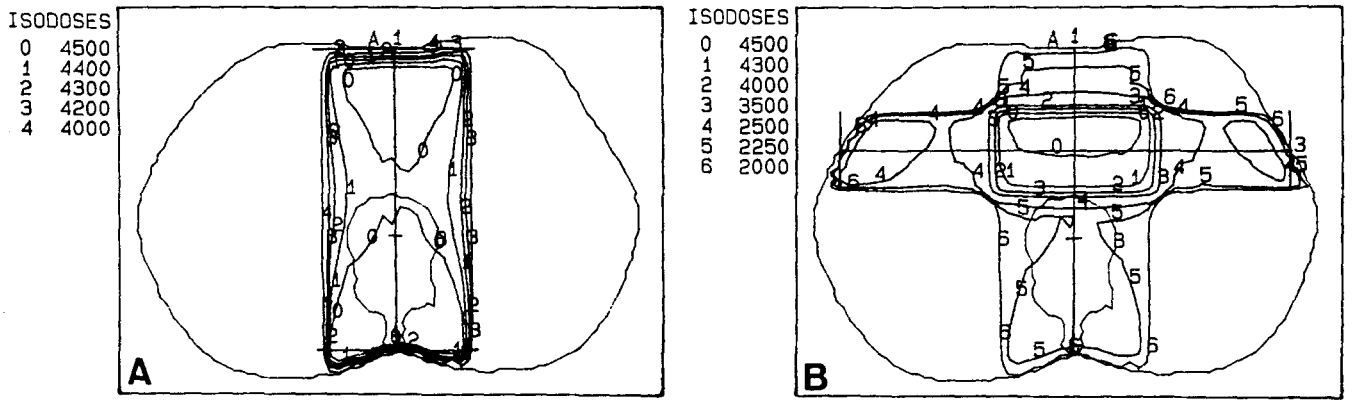

Fig. 1 A Radiation field of anterior and posterior portals: inner countour expresses the vertebra. The vertebra is covered b the curve of 4500 cGy. **B** Box field: the right and left portals do not include the spine. The vertebra is covered by the curve of 2250 cGy

treated via box field. Radiation was delivered at the rate of 1.8 Gy, 5 times a week. The total dose to the paraaortic lymph nodes was 45 Gy over 5 weeks in all cases of the radiation group. The absorbed dose of the spine was 45 Gy over 5 weeks in nine cases of anterior and posterior opposite portals and was 22.5 Gy over 5 weeks in the two cases treated via box field (Fig. 1).

Details of the QCT are shown in Table 2. Patients were scanned with a bone phantom containing five rods of bone substitutes (composed of $CaCO_3$) of known concentration placed under their backs. The scan level was at the nutrition foramen of the 3rd lumbar vertebra. The unit of BMC used was mg $CaCO_3$ eq/cm^3. The attenuation values of each bone substitute and trabecular bone of the 3rd lumbar vertebra were measured. A regression line formula was calculated between the attenuation values and $CaCO_3$ concentration of bone substitutes. With this formula, the attenuation value of trabecular bone was transformed into a value of BMC. This system is demonstrated in Fig. 2.

QCT was performed as shown in Fig. 3. Eight patients in the radiation group also received QCT at 5 weeks, just after the end of radiation. Chi-square and *t*-test were used for statistical analysis.

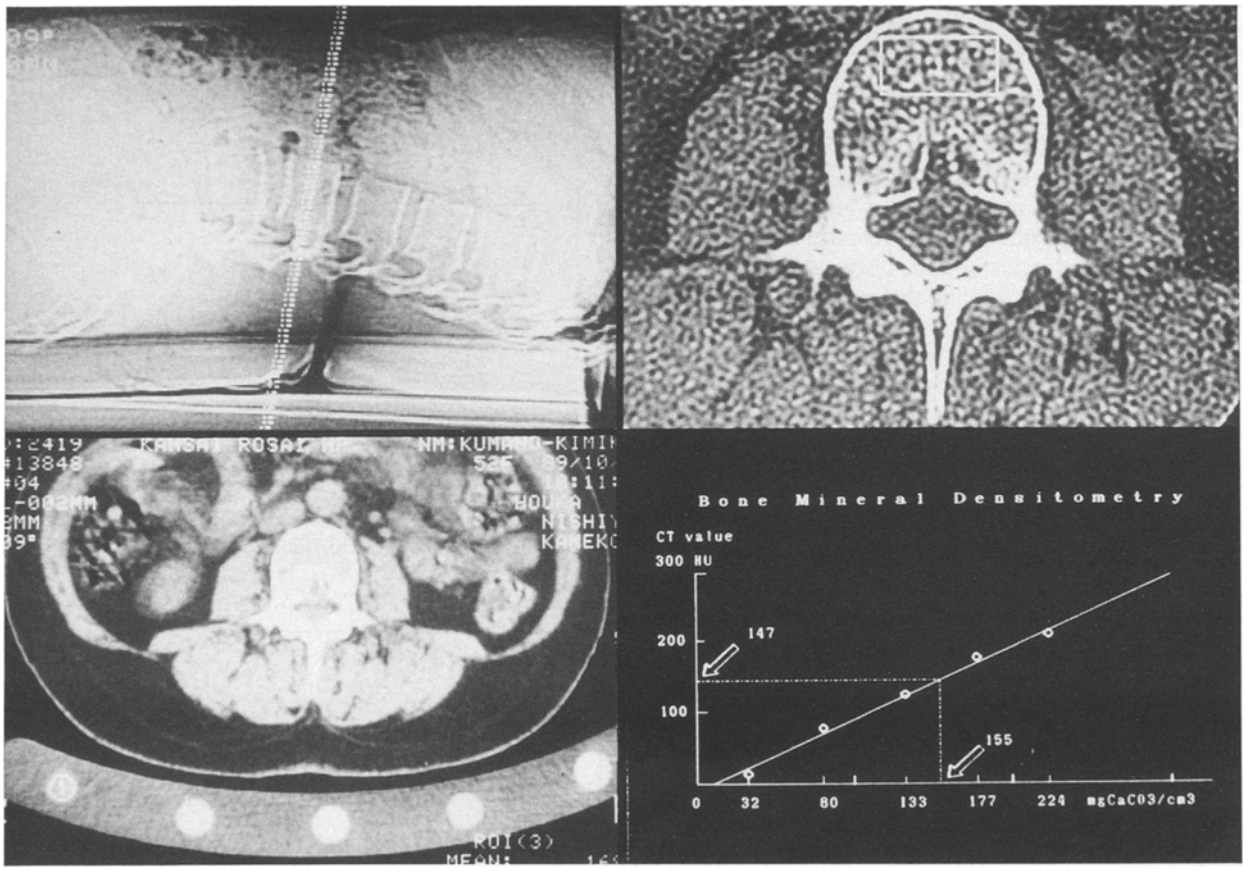

Fig. 2. Calculation system of QCT

Table 2. Details of QCT

CT scanner	GE 9200
Tube potential	120 kVp
Slice thickness	2 mm
Scan level	Nutrition foramen of the 3rd lumbar spine
Target	Trabecular bone of the 3rd lumbar spine
Bone phantom	B-MAS $CaCO_3$ phantom
CT calculation algorithm	
Phantom	Standard
Trabecular bone	Bone

Table 3. Mean BMC (mg $CaCO_3$ eg/cm^3) of both groups. Numbers in parentheses are SD

	Pretreatment	5 weeks	3 months	6 months	12 months
Radiation group	140 (57)	95 (59)	84 (56)	74 (45)	71 (48)
Control group	118 (53)		117 (54)	107 (54)	111 (51)

Results

The changes of BMC in the radiation group following irradiation and the control group are shown in Table 3. Pretreatment BMC of both groups was not statistically different. BMC of the control group was stable. There was no statistical difference between BMC of pretreatment and post-treatment in the control group, whereas BMC of the radiation group was substantially reduced after irradiation. In the radiation group, the mean amounts of BMC reduction were 52, 55, 66 and 69 mg/cm^3 at 5 weeks, 3, 6 and 12 months, respectively. In the radiation group, the results revealed significant differences in mean BMC between pretreatment and 5 weeks ($p = 0.01$, paired t-test) and between 3 and 6 months ($p = 0.05$, paired t-test). The difference in BMC between 6 and 12 months was not significant. Reduction of the radiation group was statistically different from that of the control group at 3, 6 and 12 months ($p = 0.01$, non-paired t-test).

Correlation between pretreatment BMC and BMC change at 3 months is shown in Fig. 4. BMC change in the control group ranged from +28 mg to −22 mg. BMC change in the radiation group ranged from −36 mg to −81 mg with an average of −55 mg. Reduction of BMC in the radiation group was not related to pretreatment BMC.

In Fig. 5, BMC change of low dose (22.5 Gy) cases is compared with that of moderate dose (45 Gy) cases. No difference in BMC reduction was seen between the two groups.

In one case from the radiation group, a compression fracture of the 2nd lumbar vertebra was seen 6 months after irradiation. For this case, BMC of the 3rd lumbar vertebra pretreatment and at 6 months were 75 and 18 mg/cm^3, respectively (Fig. 6.).

Discussion

It is well known that irradiation of mature bone sometimes causes several types of late damage [5]. Dahl [6] reported that radiation injured both osteoblast and osteoclast and that the former was more injured than the latter; this process led to bone mineral reduction. Therefore, bone change (a term that is preferred to bone atrophy) due to irradiation is a type of low turnover osteoporosis.

This type of bone change, radiation osteoporosis, has usually been examined radiographically. Recently, several modalities of higher sensitivity, such as QCT, dual photon absorptiometry and dual energy X-ray absorptiometry, have become available [3, 4]. QCT has the advantage that it can separately measure BMC of trabecular bone, which is more sensitive than compact bone. Reproducibility of the measurement in human subjects with QCT is no more than 2% [7].

Howland et al. [8] reported on post-irradiation bone change in detail. Their study demonstrated that bone change of an irradiated shoulder was seen by radiography

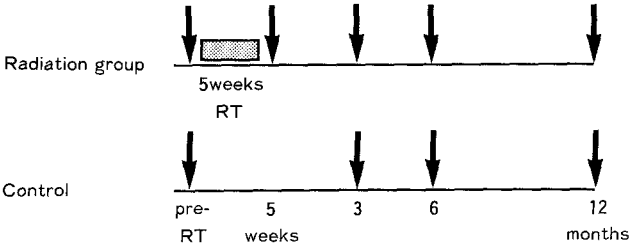

Fig. 3. Schedule of QCT. Eight cases in the radiation group were examined 5 weeks after irradiation

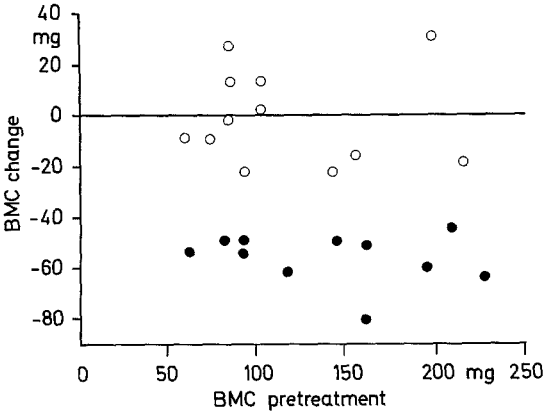

Fig. 4. Pretreatment BMC versus change of BMC at 3 months. Open circle, control group; closed circle, radiation group

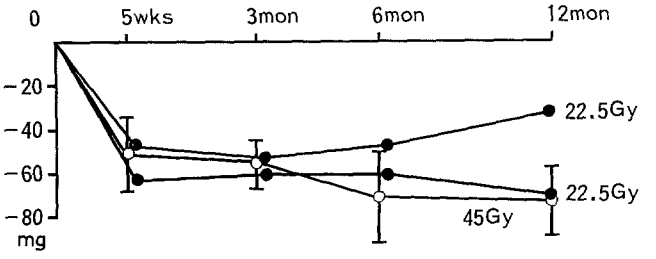

Fig. 5. BMC reduction versus absorbed dose. Open circle, 45 Gy; closed circle, 22.5 Gy

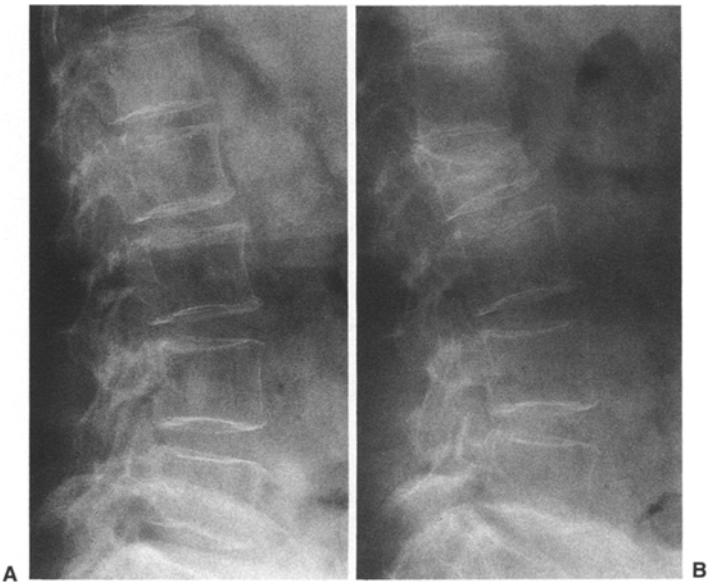

Fig. 6 A, B. Compression fracture of the 2nd lumbar vertebra 6 months after irradiation. **A** Pretreatment; **B** 6 months after irradiation

in 17 out of 70 cases who were treated with 25 MeV Betatron or telecobalt. QCT can detect subtle changes of BMC and all irradiated cases revealed BMC reduction in our study.

The study of Sengupta and Prathap [9] noted that bone changes did not become demonstrable until 2 or more years after irradiation. In our study, BMC of all eight cases that were examined at the end of irradiation was substantially reduced, thus it seems to occur during irradiation. However, radiograms of these cases revealed no objective changes.

To avoid BMC reduction due to irradiation, the radiation dose to vertebrae was decreased by use of the box field technique. Absorbed doses of the vertebrae decreased from 45 Gy to 22.5 Gy over 5 weeks with this technique. However, BMC reduction at 22.5 Gy was quite similar to that at 45 Gy. Radiation osteoporosis is one of the non-stochastic effects that have dose thresholds. The results in this study revealed that the dose threshold of BMC reduction seems to be below 22.5 Gy.

Studies on vertebral fracture due to senile osteoporosis using QCT demonstrated a high risk of fracture below 60 mg K_2HPO_4/cm^3, that is approximately 65 mg $CaCO_3/cm^3$ [10, 11]. Since BMC reduction due to irradiation is approximately 60 mg/cm^3, patients with BMC below 125 mg/cm^3 (= 65 + 60 mg/cm^3) might become high risk after irradiation. In such cases, careful follow-up of radiation osteoporosis and fracture is important.

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