The Value of Bone Scan in the Initial Staging of Lung Cancer

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^{99m}Tc-MDP 골스캔을 이용한 폐암의 병기결정에 대한 후향적 분석

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이 명 철 · 조 보 연 · 고 창 순

폐암은 비록 그 예후가 나쁜 것으로 되어 있으나, 각 환자에서의 정확한 병기결정은 치료방침과 예후결정에 중요하다. ^{99m}Tc-MDP를 이용한 골스캔은 단순 방사선학적 검사보다 골전이의 조기진단에 예민하므로, 병기결정에 유용하다고 인정되어 왔다. 저자들은 최근 2년간 조직학적으로 확진된 폐암 환자중 치료전의 골스캔을 구할 수 있었던 202예를 대상으로 후향적 분석을 하였다.

1) 전체적인 골스캔의 골전이 양성율은 43% (87/202)였으며, 비소세포폐암에서 44% (60/135), 소세포폐암에서 40% (27/67)로 나타났다.
2) 비소세포폐암 중에는 선암이 61% (19/31)의 가장높은 골전이 양성율을 보였고, 비소세포폐암의 임상적 stage II에서 29%, stage II에서 50%의 골전이 양성율을 보였다.
3) 87예의 골전이 양성중에서 고립성인 경우가 18예였으며, 다발성 69예의 골분포양상는 늑골이 가장 빈번했으며 요추, 대퇴골, 흉추 그리고 골반 순서로 나타났다.
4) 골통증이 있었던 환자 67예중 골스캔상 골전이가 양성인 경우가 57예, 골통증이 없었던 107예중 골전이 양성인 경우가 17예였고, 혈청 alkaline phosphatase가 증가되었던 65예중 47예에서 골스캔 양성이었고, 그 수치가 정상이었던 137예중 40예서 골스캔상 전이 소견을 보였다.
5) 전체적으로 증가추세에 있는 폐암 환자에 있어서 치료전의 골 스캔은 병기결정에 많은 도움을 줄 수 있는 유용한 검사라 하겠다.

INTRODUCTION

Despite the poor prognosis of lung cancer, it is very important that each patient with this disease be carefully investigated, as much can be done to relieve suffering and some can be cured of disease. Skeletal metastases in lung cancer are present in a significant number of patients at the time of initial staging. Therefore, demonstration of metastases often determines the particular mode of therapy to be employed. Bone scan has played an increasingly

principal role in the evaluation of patients with malignancies because of its superiority against radiographs in detecting early osseous metastatic lesions[1~3]. There are also some controversies about the efficacy of routine application of bone scan in lung cancer[4~6].

We analyzed the results of initial bone scan in histologically proven cases of 202 lung cancer during recent two years to know the initial impact of bone scan in staging work-up, overall positive rates, distribution and patterns of positive findings, and its correlation with serum alkaline phosphatase and bone pain.

SUBJECTS AND METHODS

Included in this study are 202 patients of lung cancer between Febuary, 1986 and January, 1988. The series included 170 male and 32 female patients, 28-79 years of age (mean:57 years). All had a 99m-Technetium-Methylenediphonate (MDP) bone scan using scintillation gamma camera (Picker Dyna 4/15, ON 410, and Siemens Rota). The dosage rate of the IV administered radiopharmaceuticals ranged from 10 mCi to 20 mCi. All had initial level of alkaline phosphatase and 157 patients had written records of presence or absence of bone pain. Without the chart description of bone pain, it seemed likely to have no bone pain but such an uncertain assumption was excluded.

Interpretations of original films of initial bone scan in conjunction with available radiographic films were correlated to minimize false positive rate of bone scan, but limited availability of concurrent radiographs of the lesion made the results mainly dependent on the finding of bone scan. In case of single regional hot spot, careful review of traumatic history or senile changes was made to reduce false postive fraction as far as possible.

Alkaline phosphatase values obtained before initiation of therapy were included in the study. Alkaline phosphatase levels greater than 115 IU/liter without concurrent elevation of SGOT/GPT levels were considerd elevated as an indicator of bone involvement. The pathology reports were reviewed for histologic classification and the results of clinical staging from charts were utilized.

RESULTS

Histologic classification is shown in Table 1. Nonsmall cell lung cancer (NSCLC) was twice as many as small cell lung cancer (SCLC). Squamous cell carcinoma was the most common cell type.

There were 87 (43%) patients with bone scans considered positive for bone metastases and 115 (57 %) with negative scans. No significant difference in positive rates between NSCLC and SCLC was found, and adenocarcinoma of lung had the highest positive rates of bone scan (19/31;61%) among NSCLC. Extensive stage of SCLC showed 64% of positive rate. Diagramatic illustrations of bone scan results according to cell type and stage are shown as Fig. 1 and 2. In 6 patients (6/21;29%) with clinical stage 2 NSCLC showed positive bone scan resulting in upgrading of stage. The regional distribution of lesions according to the number and percentage was rib, spine, femur, pelvis, and skull in the order of decreasing frequency (Table 2).

Of those with 87 positive scans, 47 (54%) had elevated alkaline phosphatase level. There were 18 patients with negative bone scans for metastases

Table 1. Cell Type (n=202)

1. NSCLC	
Squamous cell	94
Adenocarcinoma	31
Mixed	7
Large cell	2
Bronchioloalv.	1
	135 (66.8%)
2. SCLC	67 (33.2%)

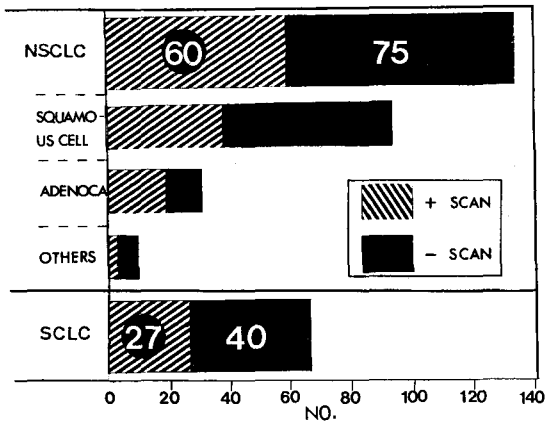

Fig. 1. Results of bone scans according to cell type. Positive fraction of dashed bar means positive bone scan results (43%).

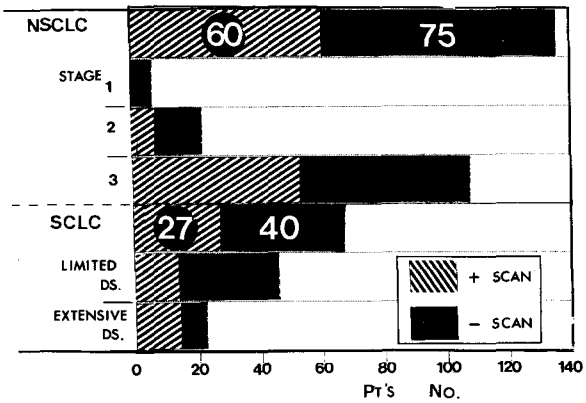

Fig. 2. Results of bone scans according to clinical stages.

who had elevated alkaline phophatase levels (Table 3). Of the 67 patients for whom records of bone pain were positive, 57 (85%) had positive bone scans for metastases. There were 17 patients with positive bone scans who had no evidence of subjective symptom of bone pain (Table 4). The sensitivity and specificity of the alkaline phosphatase and bone pain in comparison to the results of bone scan is shown in Table 5. Of 30 patients with elevated alkaline phosphatase and presence of bone pain, 28 (93%) patients had positive results of bone scan.

Associated findings of bone scans were hypertrophic pulmonary osteoarthropathy in 13 (6.3%) patients, unilateral increased thoracic accumulation in 10 (4.9%) patients, and suspected primary tumor uptake of radiotracer in 9 (4.5%) patients (Fig. 3).

Table 2. Pattern and Distribution of Bone Scan Result

	Single*	Multiple
NSCLC	9	51
SCLC	9	18
	18 (20.7%)	69 (79.3%)
Rib	8 (44.4%)	45 (65.2%)
L-spine	3	22 (31.9%)
Femur	–	20 (28.9%)
T-spine	2	19 (27.5%)
Pelvis	–	18 (26.1%)
Skull	–	16 (23.1%)
Scapula	1	7
Humerus	1	6
C-spine	3	5
Sterum	–	5

* Single hot uptake with history of trauma or senile change was excluded if possible.

Table 3. Correlation with Alk. P'tase (N = 202)

	Alk. P'tase	
	Elevated	Normal
+ Scan (87)		
NSCLC	33	27
SCLC	14	13
	47	40
– Scan (115)		
NSCLC	13	64
SCLC	5	33
	18	97
Total	65 (32%)	137

DISCUSSION

Radionuclide bone scan is very sensitive for detecting the altered local metabolism in areas of skeletal remodeling associated with metastases.

Table 4. Correlation with Bone Pain (N=157)

	Bone pain	
	+	−
+ Scan (74)		
NSCLC	45	12
SCLC	12	5
	57	17
− Scan (83)		
NSCLC	6	57
SCLC	4	16
	10	73
Total	67 (43%)	90

Bone scan requires as little as a 5 to 10% change in the lesion-to-normal bone ratio for an abnormal focus to be appreciated[7]. On the other hand, a 30 to 50% change in bone density is required before the same lesion can typically be detected radiographically. The scintigraphic patterns encountered in

Table 5. Single Test Sensitivity and Specificity According to Bone Scan

Test	Sensitivity	Specificity
Alk. P'tase	54.0%	84.3%
Bone pain	77.0%	87.9%

·Comparison to the result of bone scan was made.

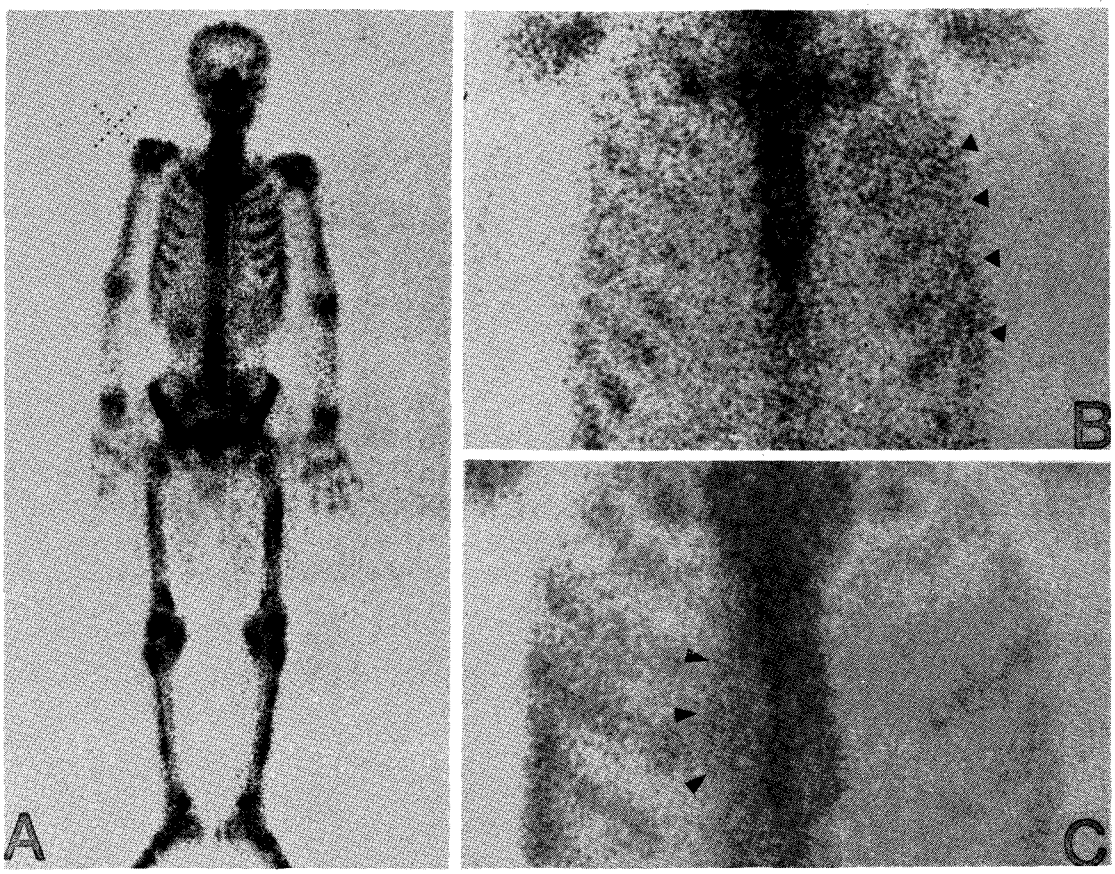

Fig. 3. Associated features of bone scans in lung cancer.
(A). Relatively symmetric increased activity along the cortex of lower extremities without focal abnormality.
(B). Unilateral thoracic accumulation of radioactivity (arrowheads) suggests possible pleural effusion.
(C). Abnormal radioactivity along the right infrahilar region which coincides with chest mass seen radiographically (arrowheads).

osseous metastases are variable, but typical patterns that provides the most diagnostic certainty is the presence of multiple randomly distributed focal lesions throughout the axial skeleton[8]. But there are other causes of multiple focal lesions including osteoporosis, osteomalacia, arthritis, trauma, surgical intervention, osteomyelitis, and Paget's disease[9]. It is mandatory to assess the pattern of scintigraphic abnormality with caution, but practical limitations of tissue diagnosis of the involved bone in malignancies would increase false positive fraction of bone scan results even though careful comparison with available radiographic images were attempted.

In general, incidence of bone metastases in lung cancer has been known 30-50 percent[10~13]. The usefulness of performing diagnostic staging tests including computed tomography and bone scan on patients thought to have operable lung cancer was acceptable[10,14]. This report showed relatively high positive rate of bone scan (43%) without histologic confirmation, so it may assumed that false positive fractions were included especially of single bone lesion[15]. Tumeh et al surveyed how much portion of solitary rib lesion had true metastatic cell with extraskeletal malignancies, and they found only 9.8 % of solitary rib lesions were true metastases[16]. So one should be meticulous to say that single abnormality by bone scan is due to metastasis from other malignancy especially in rib lesion. The distribution of bone metastases in lung cancer was mainly the axial skeleton of spines and appendicular skeleton of ribs, femur, sternum and average number of involved lesions was 2.6 anatomic sites which were not dissimilar to ours[17~19].

Various combination of laboratory tests and clinical evaluations for metastases can make exact diagnosis, but single test sensitivity of bone pain and alkaline phophatase were not satisfactory in this study. Front et al reported that 32% (21/66) having bone metastases in breast cancer didn't have bone pain[20]. There were some reports about significant value of bone scan and other radionuclide study in the initial staging of lung cancer as well as follow-up procedures[21,22].

Recently the "flare" response of bone scan has been the rule rather than the exeption after successful systemic therapy for bone metastases[23]. Additional findings of bone scan in lung cancer include hypertrophic pulmonary osteoarthropathy with parallel tract sign, direct tumor uptake, and unilateral thoracic soft-tissue accumulation of bone agent[24]. Our series showed 4.9% of unilateral thoracic activity of significantly lower percentage than Levy's series because our subjects were those of pretreatment state without radiation therapy.

In summary, bone scanning is of value during the initial evaluation to determine operability in patients with lung cancer and its impact on management will rise according to increasing prevalence of lung cancer in this country. Although bone scan is more sensitive than clinical symptomatology or alkaline phosphatase level, it is probably not sufficiently reliable to be used as the sole parameter in therapeutic decision-making, especially purely osteolytic lesions showing cold defect on bone scan. To eliminate many of these potential source of false negative results, scrutinizing follow-up of bone scan and radiographs of suspected area with established interval should be performed by oncologists.

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