

# Absent or Faint Renal Uptake in Bone Scan: Etiology and Significance in Metastatic Bone Disease

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국문 초록 =

## 골 스캔에서 신장 영상 비출현의 원인 질환 및 전이성 골질환에서의 의의

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김상은 · 김덕윤 · 이동수 · 정준기 · 이명철 · 고창순

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국 성 수

골 스캔에서 신장이 희미하게 보이거나 전혀 안보이게 되는(이하 신장 영상 비출현이라 함) 원인 질환을 파악하고, 또 골 스캔에서 골전이 발견된 여러 악성종양에서 신장 영상 비출현의 빈도 및 신장 영상 비출현의 소견을 보이는 여러 악성종양의 골전이 범위를 관찰하기 위하여, 서울대학교 병원에서 최근 6년간 시행한 골 스캔 중 신장 영상 비출현의 소견을 보이는 889개를 재검토하였다.

신장영상 비출현의 원인 질환으로는 신부전이 대부분을 차지하였으나(816/889 : 91.8%), 신장 질환이 없는 경우에는 광범위한 골전이가 가장 많았으며(53/889 : 6.0%), 그 원발부위는 전립선암(19/53 : 35.8%), 위암(14/53 : 26.4%), 유방암(5/53 : 9.4%), 폐암(4/53 : 7.5%) 신세포암(2/53 : 3.8%), 방광암(1/53 : 1.9%), 원발부위 미상(8/53 : 15.1%)으로 전립선암과 위암이 가장 많았다. 특히 강직성 척추염 4예, 류마티오이드 관절염 3예, 성인형의 골화석증 1예에서 신장 영상 비출현의 소견을 보여 이채로왔으며, 이 밖에 원발성 부갑상선 기능항진증 및 그레이브스병이 각 1예씩 있었으며 원인을 알 수 없는 경우가 10예 있었다. 전립선암 140예중 골 스캔에서 골전이가 발견된 예는 108예(77.1%), 이중 신장 영상 비출현의 소견을 보이는 예는 19예(19/108, 17.6%)이었으며, 위암에서는 각각 328예, 162예(49.4%), 14예 (8.6%), 유방암에서는 각각 1754예, 730예(41.6%), 5예(0.7%), 폐암에서는 각각 1105예, 596예(53.9%), 4예(0.7%), 방광암에서는 각각 247예, 110예(44.5%), 1예(0.9%)로 전립선암에서 신장 영상 비출현의 빈도가 가장 높았으며, 특히 위암에서 골전이 및 신장 영상 비출현의 빈도가 높아 주목되었다. 골전이 및 신장 영상 비출현의 소견

을 보이는 악성종양 환자의 골 스캔그림 53개중 44개(83.0%)에서 척추 및 늑골에 미만성, 또는 다발성 침습이 관찰되었다. 또 골전이 부위를 두개골, 척추, 견대부, 늑골, 골반, 사지의 근위부 장골의 6개 부위로 나누어 분석할 경우 49개(92.5%)에서 3부위 이상에 전이가 발견되었고, 35개(66.0%)에서 4부위 이상에 전이가 발견되었으며, 5부위 이상, 6개 부위에 모두 전이가 발견된 것은 각각 20개(37.7%), 11개(20.8%)이었다.

이상의 성적으로 보아 악성종양 환자의 골 스캔그라피에서 신장 영상의 비출현은 종양의 광범위한 골전이를 간접적으로 시사하는 소견으로 생각된다. 여러 악성종양중 전립선암에서 신장 영상 비출현의 빈도가 가장 높았으며, 특히 위암에서 골전이 및 신장 영상 비출현의 빈도가 높음은 주목할 만한 것이라 하겠다.

## INTRODUCTION

Renal images obtained incidentally to bone scanning are frequently of value in detecting renal abnormalities<sup>1-3</sup>. However, absent or faint renal uptake during bone scanning is an unreliable sign of renal disease<sup>3</sup>. Sy et al<sup>4</sup> reported poor kidney visualization secondary to rapid and enhanced uptake of radiopharmaceutical by abnormal bone, usually representing widespread metastatic involvement. It was also reported that poor renal uptake occurs in a variety of metabolic<sup>5-15</sup> and hematologic diseases<sup>16-18</sup> as well as diffuse metastases<sup>4,18-23</sup>. Poor visualization of kidneys in bone scan, therefore, suggests the possibility of widespread bone disease<sup>4,20</sup>.

We retrospectively surveyed unselected bone scans and corresponding clinical records to identify the etiologies of absent or faint renal uptake in bone scan and its frequency in a variety of malignancies with skeletal metastasis. The extent of bone involvement in patients with metastatic bone disease showing absent or faint renal images in bone scan was then determined.

## MATERIALS AND METHODS

A total of 14,296 consecutive bone scans performed on the adult patients between February 1984 and February 1990 at Seoul National University

Hospital, Seoul, Korea and corresponding clinical records were reviewed by a nuclear medicine physician (KSE). Follow-up scan(s) of the same patient was included as an individual study. 7,102 scans were taken for the detection of bone metastases, and 7,194 for the evaluation of benign osseous diseases (Table 1). All studies were performed 2-4 hr following i.v. injection of 555-925 MBq (15~25mCi) of Tc-99m methylene diphosphonate (MDP) using large field-of-view gamma cameras equipped with low-energy, high resolution collimators. In virtually all cases, the entire skeletal system was imaged.

"Faint renal uptake" was defined as an undoubtedly diminished renal activity compared with rib activity on visual inspection<sup>18</sup>. Cases in which the reviewer could not make a clear decision were submitted to a second nuclear medicine physician (KCS) for examination, and a final interpretation was achieved by consensus.

Table 1. Clinical Indications for Bone Scanning

Indication	Number of patients
Detection of bone metastasis	
Breast cancer	1754
Lung cancer	1105
Stomach cancer	328
Bladder cancer	247
Prostate cancer	140
Others	3528
Evaluation of benign bone disease	7194
Total	14296

For establishing an individual scan lesion as a bone metastasis in patients with malignant disease, we reviewed all available correlative radiological studies for each scan lesion, but limited availability of concurrent radiographs of the lesion made the results mainly dependent on scan findings. Careful clinical review of trauma history or benign osseous disease including degenerative change was also made to reduce false positive cases or lesions. The following bone scan findings were excluded<sup>24)</sup>:

- 1) Two or more adjacent, aligned rib lesions in a pattern indicative of trauma.
- 2) Polyarticular increased uptake in the joints of the extremities.
- 3) Diffuse or focal increased uptake in the appendicular skeleton at sites of documented trauma.
- 4) Increased uptake in the maxilla or mandible indicative of dental pathology.

The extent of bone metastasis was determined as a function of number of involved regions. Six ana-

tomotic regions were defined: skull, spine, shoulder girdle (scapula and clavicle), ribs, pelvis, and proximal long bones of extremities.

## RESULTS

Of the 14,296 scans surveyed, 889 scans revealed absent or faint visualization of kidneys. The etiologies of absent or faint renal uptake and their frequencies are shown in Table 2. The majority of cases were associated with renal insufficiency (816/889; 91.8%), while prostate cancer with diffuse bone metastases was the most common cause in a group of patients without renal disease (19/889; 2.1%) followed by stomach cancer with widespread bone metastases (14/889; 1.6%)(Fig. 1, 2). Interestingly,

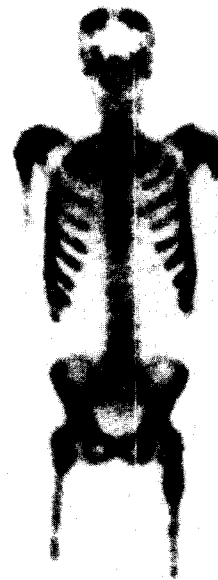


Fig. 1. Anterior bone scan of an 77-year-old man with prostate carcinoma shows diffuse, patchy areas of abnormally increased uptake in the axial skeleton and proximal long bones of the upper and lower extremities. Renal activity is markedly diminished, and a decreased uptake is noted in the greater part of the extremities.

Table 2. Etiologies of Absent or Faint Renal Uptake in Bone Scan

Etiology	Number of patients with absent or faint renal uptake in bone scan*
Renal insufficiency	816 (91.8%)
Widespread bone metastases	
Prostate cancer	19 ( 2.1%)
Stomach cancer	14 ( 1.6%)
Breast cancer	5 ( 0.6%)
Lung cancer	4 ( 0.4%)
Renal cell carcinoma	2 ( 0.2%)
Bladder cancer	1 ( 0.1%)
Unknown primary site	8 ( 0.9%)
Ankylosing spondylitis	4 ( 0.4%)
Rheumatoid arthritis	3 ( 0.3%)
Primary hyperparathyroidism	1 ( 0.1%)
Diffuse toxic goiter	1 ( 0.1%)
Osteopetrosis	1 ( 0.1%)
Unknown etiology	10 ( 1.1%)
<b>Total</b>	<b>889</b>

\* Percentage of patients in parentheses



**Fig. 2.** Anterior bone scan of an 45-year-old woman with stomach cancer shows diffuse high uptake mainly in the spine and pelvis with a faint uptake in both kidneys and in the greater part of the extremities.



**Fig. 3.** Anterior bone scan of an 32-year-old man with adult-form osteopetrosis shows strikingly increased uptake mainly in the long bones with markedly diminished renal uptake.

ankylosing spondylitis and rheumatoid arthritis, involving multiple joints, were occasional causes of poor renal uptake in bone scan (4 and 3 cases, respectively). A case of adult-form osteopetrosis, showing strikingly increased uptake mainly in the long bones with markedly diminished renal uptake, was also included in this study (Fig. 3).

The prevalence of skeletal metastasis in a variety of malignancies of unselected stages and the frequen-

cy of poor renal uptake on bone scan in a variety of malignant diseases with bone involvement are given in Table 3. Of the 140 patients with prostate cancer, 108(77.1%) had evidence of bone metastasis, 19 of whom(17.6%) revealed absent or faint renal uptake, showing that poor renal uptake is more frequently associated with prostate cancer than any other

**Table 3.** Prevalence of Bone Metastasis and Frequency of Absent or Faint Renal Uptake on Bone Scan in a Variety of Malignancies

	Total number of patients	Number of patients with bone metastasis* <sup>+</sup>	Number of patients with absent or faint renal uptake in bone scan**
Prostate cancer	140	108 (77.1%)	19 (17.6%)
Stomach cancer	328	162 (49.4%)	14 ( 8.6%)
Breast cancer	1754	730 (41.6%)	5 ( 0.7%)
Lung cancer	1105	596 (53.9%)	4 ( 0.7%)
Bladder cancer	247	110 (44.5%)	1 ( 0.9%)

\* Diagnosis of bone metastasis was made based mainly upon scan findings ; for details, see text.

+ Percentage of patients in parentheses

\*\* Percentage of patients to those with bone metastasis in parentheses

malignancies. Of note was that 162 out of the 328 patients with stomach cancer of varying stages(49.4%) had evidence of skeletal metastasis, as many as 14 of whom (8.6%) showed poor renal images in their bone scans. In contrast, only 5 of the 730 patients with breast cancer having evidence of bone metastasis (0.7%) showed absent or faint renal uptake. Similar results were observed in patients with lung cancer (4/596; 0.7%) and with bladder cancer(1/110; 0.9%).

Of the 53 bone scans with metastatic disease showing absent or faint renal uptake, 48 (90.6%) revealed malignant involvement in the ribs (multiple, except one case), and 46(86.8%) in the spine (diffuse or multiple, except two cases), mainly in thoracic and lumbar spine. As many as 44 out of the 53 scans (83.0%) showed evidence of metastases in both spine and ribs. The number of involved sites judged based upon predefined six anatomic regions in 53 bone scans with metastatic disease showing poor renal visualization were: 6;11 cases (20.8%), 5;9(17.0%), 4;15(28.3%), 3;14(26.4%), 2;4(7.5%); 49 of 53 scans(92.5%) revealed malignant involvement in 3 or more regions, and 35 of 53(66.0%) in 4 or more regions(Fig. 4).

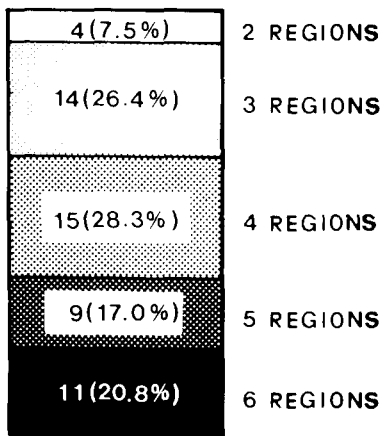


Fig. 4. Number of involved regions in 53 bone scans with metastatic disease showing absent or faint renal uptake.

## DISCUSSION

As a bone scan is invariably obtained to assess skeletal abnormalities, the detection of soft tissue abnormalities is usually an unexpected bonus. Most relevant information thus obtained relates to the kidney and urinary tract because of the high photon density achieved within this organ system during radiopharmaceutical excretion. The most specific signs of renal disease in bone scans can be classified as renal asymmetry, mass lesions, urinary or renal tract dilatation or abnormalities of uptake, size or displacement. Less valuable signs are bilateral decreased renal uptake and focal areas of increased uptake<sup>3,25</sup>. Sy et al<sup>4</sup> observed faint or absent renal activity at the time of bone imaging when there was diffuse metastatic involvement of the axial skeleton. They suggested that the rapid and enhanced uptake of tracer by the abnormal bone resulted in reduced radionuclide excretion by kidney, thereby making the renal images fainter in the bone scans. They therefore concluded that absent or faint kidney shadows on the bone scan suggest the possibility of widespread bone disease.

In the present study, 44 out of the 53 scans with metastatic disease showing absent or faint renal uptake (83.0%) revealed evidence of diffuse or multiple metastases in both spine and ribs. Furthermore, 49 of 53 scans(92.5%) showed malignant involvement in three or more regions amongst predefined six anatomic regions, and 35 of 53(66.0%) in four or more regions, suggesting widespread bone metastases in most cases. It was reported that patients with superscan, that is bone scan with uniformly increased bone to soft tissue ratio generally associated with faint or absent renal visualization<sup>4,19,20</sup>, excrete about 10% of the injected dose of Tc-99m MDP in 3hr compared with 60% for normal subjects and they achieve total bone to soft tissue uptake ratios of about 5 times higher than normal subjects<sup>26</sup>.

Adams et al<sup>27)</sup> reported that while intense epiphyseal concentration, cellulitis, and neuroblastoma were the usual causes of poor renal visualization in children without renal disease, extensive bone involvement by tumor was the most common cause in adults with no renal disease, which is in good agreement with our findings.

The superscan condition appears to be more frequently associated with prostate cancer than with other etiologies. Osmond et al<sup>28)</sup> used Tc-99m diphosphonate in 259 patients including 91 with prostate cancer and reported the superscan appearance in prostatic patients only. Of the seven superscan patients reported by Sy et al<sup>4)</sup>, six had prostate cancer and one had cancer of the bladder. Three probable superscan cases were reported by Thrupkaew et al<sup>19)</sup> using F-18 and Tc-99m diphosphonate. Two of these patients had breast carcinoma and the other had prostate carcinoma. In our series, 108 out of the 140 patients with prostate cancer (77.1%) had evidence of bone metastasis, 19 of whom (17.6%) revealed absent or faint renal uptake, showing that poor renal uptake is more frequently associated with prostate cancer than any other malignancies. Our findings are similar to the symmetrical skeletal uptake with absent or faint renal activity in 4 out of 31 patients with metastatic prostate carcinoma reported by Kane et al using Tc-99m pyrophosphate<sup>22)</sup>. Our results are also comparable to those of Constable et al<sup>26)</sup> who have reported that about 17% of patients with prostatic metastases could be expected to have superscans either at presentation or during follow-up, though we have examined bone scans focusing on "poor renal images", not on the superscan appearance (hence, only part of the scans showing poor renal uptake were in the category of so-called "superscan").

It is noteworthy that as many as 8.6% of the patients with stomach cancer having metastatic bone disease but no evidence of renal failure showed absent or faint renal visualization in their bone

scans, and a considerable number of them were diagnosed as having superscans. These findings may be partly related to the high prevalence of bone metastasis in stomach cancer shown in this study as discussed below. We are not aware of any other studies examining bone scan findings of stomach cancer with widespread skeletal metastases.

In our study, furthermore, surprisingly high prevalence of bone metastasis was noted in stomach cancer (49.4%) compared to the previous reports (0.3~9.0%)<sup>28-31)</sup>, whereas results from other malignancies were similar to prior studies<sup>32-33)</sup>. Although we established the diagnosis of bone metastasis mainly based upon scan findings and follow-up scan(s) of the same patient was included as an individual study, it is still unlikely that such a wide discrepancy in stomach cancer is totally related to the methods employed. We believe that it may, at least in part, be related to the prolonged survival in patients with stomach cancer secondary to the progress in therapy, thus allowing more chance to metastasize to bones, as well as high prevalence of stomach cancer in our country.

Absent or faint visualization of kidneys in bone scan, other than in diffuse metastatic disease, has been described in diffuse metabolic disease; renal osteodystrophy, secondary hyperparathyroidism<sup>5-6)</sup>, occasional primary hyperparathyroidism<sup>6-9)</sup>, hyperthyroidism<sup>10)</sup>, osteomalacia/rickets<sup>11-12)</sup>, Paget's disease<sup>13-14)</sup>, and hypervitaminosis D<sup>15)</sup>, hematologic disease; myelofibrosis<sup>16)</sup>, systemic mastocytosis<sup>17)</sup>, aplastic anemia, leukemia, and Waldenström's macroglobulinemia<sup>18)</sup> and fibrous dysplasia<sup>18)</sup>. In our series, interestingly, ankylosing spondylitis and rheumatoid arthritis, involving multiple joints, were occasional causes of poor renal uptake (4 and 3 cases, respectively). A case of adult form osteopetrosis, showing strikingly increased uptake mainly in the long bones with markedly diminished renal uptake, was also included in this study.

In summary, absent or faint renal uptake in bone scan provides a clue to the widespread bone disease when there is no evidence of renal disease. While absent or faint renal uptake appears to be more frequently associated with prostate cancer than with other etiologies but renal insufficiency, stomach cancer is one of the major causes of poor renal uptake. Although further studies are needed to confirm our data, we believe that the current prevalence of bone metastasis in stomach cancer may, at least in our country, be higher than previous reports.

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