The Distribution of Skeletal Metastases in Breast and Pulmonary Cancer: Concise Communication

Michael A. Wilson* and Ford W. Calhoun

The Mount Sinai School of Medicine of The City University of New York, New York, New York

In a review of all radionuclide bone scans performed in a 3-mo period, 318 patients with established tumor diagnosis were studied. In this tumor population the incidence of skeletal metastases was statistically similar ($p = 0.7$), and the regional distribution of lesion involvement was, in decreasing order, thorax, spine, pelvis, limbs, and skull. In the two largest tumor groups (breast and lung) the regional distribution of metastases was not different when examined for both the presence and the number of lesions ($p > 0.1$). In particular, the incidence of rib metastases was similar ($p > 0.99$) as was their frequency distribution (0.78). Indeed, the frequency distribution of rib metastases was similar for all major tumor categories ($p = 0.83$).

J Nucl Med 22: 594–597, 1981

Radionuclide bone scanning is a sensitive indicator of skeletal metastases (*1,2*), but while the procedure is sensitive it is also nonspecific. False-positive results occur and these are especially likely when the scan abnormality is solitary (*3–5*). The distribution of skeletal metastases as determined by radionuclide bone scanning has been reported, but the methods of data collection and analysis have differed (*6–8*). It has been reported that breast and lung cancer have different distributions of rib metastases (*7*), but the statistical significance of this conclusion was not established. The present study was undertaken to determine the distribution of skeletal metastases from soft-tissue neoplasms—particularly rib lesions in breast and lung cancer—and to determine whether statistically significant differences were present.

METHODS

In a 3-mo period, 486 patients were listed by our minicomputer data base as having been referred for bone scanning (*9*). Of these, 463 (96%) were available for review by one of us (MAW). Skeletal images were obtained 3 hr after the injection of 15 mCi of Tc-99m pyrophosphate. Focal scan abnormalities (regions of abnormally increased tracer uptake) were identified, then charted according to their anatomical site (and region). Fifteen sites (and five regions) were included: rib, clavicle, sternum, scapula (thoracic); thoracic, lumbar, and cervical spine (vertebral); ilium, ischium, pubis, sacrum, and sacroiliac regions (pelvic); upper and lower extremities (limb); and skull vault (skull). In the subset of patients with a final diagnosis of tumor as provided by the referring clinicians, the etiologies of the focal scan abnormalities were determined by the scan pattern, along with any temporal changes noted in these patterns when the current study was compared with previous or subsequent studies. Typical scan patterns included those of multiple metastases, Paget's disease, dental disease, and trauma (e.g., linear array in ribs). Radiographic correlation was carried out when suitable radiographs were available, and these were especially sought when the scan pattern suggested degenerative joint disease.

The distribution of lesions for the different tumor types was analyzed according to the presence or absence of lesions as well as the number and percentage of the patient's total lesions at each site and region. Contin-

* Current address: The University of Wisconsin Center for Health Sciences, Madison, WI 53792.

Received Nov. 21, 1980; revision accepted Feb. 11, 1981.

For reprints contact: Michael A. Wilson, MB, Ch.B, Section of Nuclear Medicine, Dept. of Radiology, Center for Health Sciences, 600 Highland Ave., Madison, WI 53792.

gency tables were constructed and chi-square analysis was used to determine significant differences in distributions; the level of significance chosen was 0.05, and the null hypothesis used was that the populations were identical.

RESULTS

Of the 463 patients imaged during this 3-mo period, 387 were referred for workup of possible neoplastic disease, and 318 (69%) were considered by their referring clinicians to have a soft-tissue tumor established. Indeed, the majority (65%) of these patients were being followed up with repeat bone scans. In the 318 established tumor patients there were 110 bone scans with focal abnormalities, and these were ascribed to causes primarily based on a classical scan pattern (54), multiple studies (49), or associated radiographs and gallium scans (5). In 53 instances the lesion's etiology was established by several criteria, e.g., multiple scans, a typical scan pattern, and associated tests. The typical scan pattern of multiple metastases (average 10.6 lesions per patient) was seen in all 39 patients that were imaged on only one occasion. The final etiology of the scan abnormalities was attributed to metastases in 76, osteoarthritis in 15, trauma or dental disease in 12, Paget's disease in 5, and unknown in 2. Because of the lack of evidence in these two patients (bladder and endometrial cancer with scan lesions confirmed to the limbs), they were excluded from the metastatic group. As they did not belong to the largest tumor groups, their omission does not affect the distribution data.

The incidence of metastatic lesions for the major tumor categories is listed in Table 1. There is no statistical difference in the incidence for this patient series. For all tumors, the distribution of skeletal metastases listed by the presence and percentage of total lesions in different regions is shown in Table 2. Sixty-one of the 76 patients with metastases (83%) were identified by imaging the thoracic region alone, and the optimized regional imaging order to detect disease in the remaining patients was: vertebral, pelvic, limb, and then skull. There were 11 patients with solitary focal lesions for which primary sources were established.

TABLE 1. INCIDENCE OF METASTASES IN MAJOR TUMOR CATEGORIES

Tumor	No. of patients	Metastases present (%)*
Breast	94	26 (28%)
Lung	59	13 (22%)
Gastrointestinal	36	7 (19%)
Lymphoma	27	5 (19%)
Prostate	17	6 (35%)
Miscellaneous	85	19 (22%)
Total	318	76 (24%)

* Chi-square = 2.99, df = 5, p = 0.70.

TABLE 2. REGIONAL DISTRIBUTION OF METASTASES

Anatomic region	Patients with lesions present (%)	No. of lesions (% of total)
Thoracic	61 (83%)	269 (37%)
Vertebral	46 (65%)	186 (26%)
Pelvic	37 (52%)	118 (16%)
Limb	37 (52%)	105 (15%)
Skull	24 (34%)	46 (6%)
Total	76	724

In the major tumor groups (breast, lung, prostate, and gastrointestinal tract) and the miscellaneous other tumors, the frequency distribution of rib metastases (Table 3) was found to be similar (p = 0.83). This was also found for the two largest tumor groups (breast and lung) when examined separately (p = 0.78). The regional distributions of skeletal metastases in the two largest tumor groups were compared (Table 4) and found not significantly different when analyzed for presence (p = 0.42), or number (p = 0.11) of lesions, or the average number of lesions, when present, for each region (p = 0.87). In patients with metastatic breast and lung cancer, rib involvement occurred in 92% (p = 0.99), and these lesions represented 37% (92 of 252) and 42% (53 of 125), respectively, of the total lesions (p = 0.27).

DISCUSSION

While several reports address the distribution of metastases for different tumor types using either the presence or absence of regional involvement (*6,8*) or the percentage of total lesions in these regions (*7*), the absence of statistical evaluation and differences of method

TABLE 3. FREQUENCY DISTRIBUTION OF RIB METASTASES IN THE MAJOR TUMOR CATEGORIES

Tumor*	No. of rib metastases 1	2–3	4–5	6–7	8–9
Breast†	9‡	4	6	3	2
Lung	2	4	4	1	1
Prostate	2	1	0	0	1
Gastrointestinal tract	3	0	1	0	1
Miscellaneous tumors	6	5	3	2	0

* All tumors: chi square = 10.69, df = 16, p = 0.83.
† Breast and lung tumors only: chi square = 3.21, df = 4, p = 0.78.
‡ Number of patients.

TABLE 4. REGIONAL DISTRIBUTION OF METASTASES IN BREAST AND LUNG TUMORS

Region	Patients with lesions*		No. of lesions†		Average no. lesions when present‡	
	Breast	Lung	Breast	Lung	Breast	Lung
Thoracic	24	12	92	53	3.8	4.4
Vertebral	19	11	74	37	3.9	3.3
Pelvic	17	3	46	10	2.7	3.3
Limbs	13	7	24	14	1.8	2.0
Skull	12	3	16	11	1.3	3.7

* Chi square = 3.9, df = 4, p = 0.42.
† Chi square = 7.6, df = 4, p = 0.11.
‡ Chi square = 1.24, df = 4, p = 0.87.

make interpretation and comparison of these studies difficult. This study was an attempt to overcome such limitations by using both common methods of evaluating lesion distributions (i.e., presence and number) and applying statistical tests to determine whether any observed differences were significant.

In a study where etiologies cannot always be ascribed to all scan abnormalities, there is the potential to misclassify a particular lesion. With several scan patterns it is particularly difficult for the interpreter to distinguish benign from malignant disease; these patterns include solitary lesions and lesions confined to the limbs or skull. The incidence of solitary metastases found in this study (14%) did correlate well with the 14% reported in the literature (*4*). Of the tumor patients in this study, only two did not have their scan lesions classified definitively, and both had lesions confined to the extremities. In one patient, previous scans established the lesion to be stable and therefore likely to represent degenerative disease. In both patients, the referring clinicians did not feel that further investigations were warranted. So while these patients are classified as undetermined, they could well be considered benign but lacked corroborating evidence.

In the entire tumor group, the thoracic skeleton was most frequently metastasized (83% of patients), and no significant difference in the frequency distribution of rib lesions was found among the different tumor types ($p = 0.83$). In particular, this distribution was nearly identical in breast and lung tumors, where 92% of each patient group had rib metastases, and these represented 37 and 42%, respectively, of their total lesion burden.

In the available literature that includes data about the regional presence or absence of skeletal metastases (*6,8*), the reported incidence of thoracic lesions in metastatic lung and breast cancer was statistically similar to our findings when chi-square contingency tables were constructed comparing these data ($p = 0.69$ and 0.85, respectively). The combined studies included 797 patients, of whom 430 had metastases. Comparing our data with the single report that provides information on the percentage of lesions at different sites (*7*), we find concordance with the lung cancer patients ($p = 0.90$) but not in the breast cancer group ($p = 0.0001$). Because our data (a) include more breast cancer patients, and demonstrate that (b) there is concordance with the breast cancer patients concerning regional presence of metastases, and (c) that the frequency distribution of rib metastases in breast tumors was similar to those of all the other major tumors; we believe that the incidence and distribution of rib metastases is similar in patients with breast and lung cancer. This is probably to be expected, since the mode of spread (hematogenous) and organ metastasized (skeleton) is common to both tumor groups.

The importance of considering the regional presence of lesions as well as their number in drawing conclusions about distribution patterns is illustrated by the fact that while only 37% of the patients' total lesions were found in the thoracic region, 83% of patients with skeletal metastases were identified by imaging that region alone. The data also demonstrate that while 15% of the total lesions were in the limbs and 52% of patients with skeletal metastases had limb lesions—figures similar to those reported in the literature (*10,11*)—only two new patients were identified by limb imaging. Both patients had malignant melanoma and were identified on the gallium-67 citrate scans routinely performed in the metastatic workup of their primary tumor. We believe, therefore, that the prevalence of appendicular metastases tends to exaggerate the clinical utility of whole-body imaging.

ACKNOWLEDGMENTS

The cooperation of Dr. S. Goldsmith, Director of Nuclear Medicine, Mount Sinai Hospital, and Dr. A. Safir, Director of the Institute of Computer Science, Mount Sinai School of Medicine, is greatly appreciated. The work was supported by the NLM Graduate Research Training Grant 1 T15 LM 07008-03/03 from the National Institutes of Health, and Public Health Service Grant No. EY 00336. Computer time for SAS was provided without charge by the University Computer Center of the City University of New York.

REFERENCES

1. GALASKO CSB: Skeletal metastases and mammary cancer. *Ann R Coll Surg Engl* 50:3-28, 1972
2. PISTENMA DA, MCDOUGALL IR, KRISS JP: Screening for bone metastases: Are only scans necessary? *JAMA* 231: 46-50, 1975
3. PABST HW, LANGHAMMER H: Detection and differential diagnosis of bone lesions by scintigraphy. *Eur J Nucl Med* 2:261-268, 1977
4. CORCORAN RJ, THRALL JH, KYLE RW, et al: Solitary abnormalities in bone scans of patients with extraosseous malignancies. *Radiology* 121:663-667, 1976
5. SHIRAZI PH, RAYUDU GVS, FORDHAM EW: Review of solitary ^{18}F bone scan lesions. *Radiology* 112:369-372, 1974
6. BELLIVEAU RE, SPENCER RP: Incidence and sites of bone lesions detected by ^{99m}Tc-polyphosphate scans in patients with tumors. *Cancer* 36:359-363, 1975
7. KRISHNAMURTHY GT, TUBIS M, HISS J, et al: Distribution pattern of metastatic bone disease. A need for total body skeletal imaging. *JAMA* 237:2504-2506, 1977
8. TOFE AJ, FRANCIS MD, HARVEY WJ: Correlation of neoplasms with incidence and localization of skeletal metastases: An analysis of 1,355 diphosphonate bone scans. *J Nucl Med* 16:986-989, 1975
9. WILSON MA, CALHOUN FW, GOLDSMITH SJ: The role of radionuclide imaging in metastatic disease: The Mount Sinai experience. *Mt Sinai J Med* 47:251-254, 1980
10. SHIRAZI PH, RAYUDU GVS, FORDHAM EW: ^{18}F bone scanning: Review of indications and results of 1,500 scans. *Radiology* 112:361-368, 1974
11. TOFE AJ, FRANCIS MD, HARVEY WJ: Incidence of solitary skull and extremity involvement in whole-body scintigrams. *J Nucl Med* 17:755-756, 1976 (Letter to the Editor)

ANNOUNCEMENT

The Education and Research Foundation of the Society of Nuclear Medicine welcomes applications for Student Fellowship and Pilot Research grants. These awards are made possible through donations from SNM members as well as from various commercial firms whose products are used in the practice of Nuclear Medicine. Applications received prior to December 15 of any year will be evaluted by the ERF Board on a competitive basis. Awards will be announced on or about February 15 of the following year.

STUDENT FELLOWSHIP GRANTS

These awards are designed to stimulate interest among students in the United States and Canada in the field of Nuclear Medicine. The awards are intended to provide an opportunity to spend elective quarters and/or summers in active departments working and associating with experts in the field. Maximum grant: $1,500. Letters of application should be submitted in duplicate and should contain the following: applicant's name, address, birth date, period for which support is requested, name and institution of sponsor, previous education, previous research, and brief summary of the proposed project, including an appropriate bibliography.

PILOT RESEARCH GRANTS

The goal of this research support is to provide money to young scientists working in Nuclear Medicine who desire support for a research project. Priority will be given to those proposals that are of a pilot nature in either clinical or basic research. The grants are not intended to support salaries, purchase major equipment, or for travel, but are designed to provide essential materials so that innovative ideas can be quickly tested. Maximum grant: $3,000.

SPECIAL ANNOUNCEMENT: FIRST TETALMAN MEMORIAL AWARD

A fund has been established in the ERF by friends of Marc Tetalman, M.D. who was a tragic homicide victim while attending the SNM meeting in Atlanta in June, 1979. This fund will permit an award of $3,000 to be made in June, 1981 to a young investigator (35 years of age or younger) who is pursuing a career in Nuclear Medicine. This award is to be repeated annually. It is possible that additional contributions to our fund will permit the stipend to be increased in future years. Applicants should submit prior to March 1, 1981 a curriculum vitae together with a summary of proposed research work.

All letters and applications should be addressed to:

Merle K. Loken, M.D.
President, E & R Foundation
c/o Society of Nuclear Medicine
475 Park Avenue South
New York, NY 10016