

Reliability of different radioisotopic techniques in diagnosing solitary hot spots in the spine of patients with malignant neoplasm

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KEY WORDS

bone scintigraphy,
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ABSTRACT

INTRODUCTION Early diagnosis of spinal metastases is of key importance in further therapeutic management.

OBJECTIVES The aim of the study was to assess the reliability of single-photon emission computed tomography (SPECT) or SPECT and computed tomography (SPECT/CT) in the diagnosis of solitary hot nodules in the spine identified by scintigraphy.

PATIENTS AND METHODS In this retrospective study, 70 patients with neoplastic disease and a solitary nodule detected in the spine were analyzed. Using a SPECT/CT γ-camera, the type and site of the foci in the vertebra were analyzed. Bone scintigraphy, SPECT, and CT were performed. Reliability of the results was assessed depending on the applied technique.

RESULTS In malignant lesions, increased isotope uptake was observed in the vertebral body with the posterior arch (89%), the body and both arches (67%), and the body alone (14%). In benign lesions, increased uptake was observed in the body area or in the joint area. Using SPECT, 25 of 27 cases (93%) of foci were properly classified as malignant. Using SPECT/CT, malignant lesions were observed in 26 of 27 cases (96%). Using SPECT, 19 of 43 cases were identified as benign (44%), and using SPECT/CT, 31 of 43 were identified as benign (72%). The agreement between SPECT and SPECT/CT was higher for malignant lesions (89%) than for benign lesions (67%). The use of CT in SPECT/CT examinations allowed to change the SPECT diagnosis of malignant lesions to that of benign lesions in 50% of the cases.

CONCLUSIONS The criteria used in the diagnosis of solitary nodules in the spine direct the diagnosis largely towards noncancerous lesions. Reliability of positive assessment was significantly lower than that of negative one – 51% in SPECT and 68% in SPECT/CT. A hybrid SPECT/CT camera is more reliable than SPECT alone in the assessment of spinal lesions.

INTRODUCTION The skeletal system together with parenchymal organs, such as the liver and lungs, are the most common sites of metastases. In prostate and breast cancer, bone metastases can be observed in 47% to 85% of the patients, while in the lung, urinary bladder, and kidney cancer, they are present in 30% to 45% of

the cases. The most common site of bone metastases is the lumbosacral segment of the spine.^{1,2}

The early diagnosis of metastases to the skeletal system in patients with malignant tumors is particularly important for further therapeutic management. An accurate diagnosis of solitary hot spots in the spine is crucial in patients who are referred for bone scintigraphy.

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Scintigraphy is a routine examination when bone metastasis is suspected because it allows to evaluate the entire skeletal system. Thus, it enables to quickly identify foci in the spine, even those with minimal destruction, namely, of 5% to 10%. The method is superior to classical radiographic methods and tomography because it allows to identify abnormal changes even several months earlier. The sensitivity of this technique is estimated at 62% to 100% and specificity at 78% to 100%.^{3,4}

The presence of a solitary lesion shown only on whole-body scintigraphy is difficult to interpret and requires further diagnostic work-up. It could be a benign lesion but also malignant metastasis; thus, early diagnosis is important for further therapy and overall survival rates.⁵⁻⁹ By combining scintigraphy with single-photon emission computed tomography (SPECT) of the selected area, the site of a lesion within a vertebra may be visualized in 3 planes. This technique can help determine the character of a detected focus. In 20% to 50% of the patients, SPECT examination allows to identify additional foci, which would not be visible in a planar whole-body examination. Sensitivity and specificity of SPECT in the diagnosis of bone metastases are 91% and 93%, respectively.¹⁰

The use of an advanced technique of hybrid SPECT and computed tomography (SPECT/CT) offers yet additional diagnostic possibilities. The hot spot visible in SPECT can be precisely located within the bone tissue, and its morphology can be assessed owing to a simultaneous CT examination.

The aim of this study was to assess reliability of SPECT and SPECT/CT in the diagnosis of solitary hot spots in the spine identified by whole-body scintigraphy.

PATIENTS AND METHODS This retrospective study included 70 patients with neoplastic disease, with a solitary hot spot in the spine detected during further diagnostic work-up. The radioisotopic data of these patients sent between 2009 and 2011 to the Institute of Nuclear Medicine were analyzed. The type and malignancy of a neoplasm in those patients were assessed in specialized centers. Patients were referred for bone scintigraphy to identify neoplastic metastases. Of 70 patients with neoplastic disease (32 women, 38 men; mean age, 36 years; age range, 7–92 years), breast carcinoma was reported in 27 patients, prostate carcinoma in 26, lung carcinoma in 7, renal carcinoma in 5, neuroblastoma in 1 (a child patient), endometrial carcinoma in 2, and bowel carcinoma in 2. In all patients, scintigraphy revealed a solitary hot spot in the spine. The nature of foci was determined by modern diagnostic imaging methods (SPECT and SPECT/CT). Patients underwent further clinical examination in the centers that referred them for a radioisotope examination. They underwent radioisotope examinations (bone scintigraphy, SPECT, and CT) and, depending on the technological advancement of the equipment, we established whether the lesion was correctly

diagnosed as benign or malignant. Radioisotope examinations did not include any additional techniques to determine the character of a solitary hot spot (malignant or benign). Any additional examinations were at the discretion of the centers that referred patients for a radioisotope examination. Reliability of the diagnosis was determined during further diagnostic work-up (in the referring centers), including CT, nuclear magnetic resonance imaging, another scintigraphy, pathomorphological examination, and others.

All examinations were performed with a hybrid SPECT/CT camera 3 hours after the intravenous application of 1-hydroxyethane 1,1-diphosphonic acid with technetium-99m (^{99m}Tc-HEDP). Whole-body scintigraphy was followed by SPECT/CT of the specific vertebral segment where a hot spot was visible on scintigraphy. SPECT data were collected in a step-and-shoot mode with an angular range of 180° in 3° increments and duration of 30 s each. Directly after the SPECT examination, without changing the patient's body position, the same area of the spine was examined by CT. The images were assessed by specialists of nuclear medicine and radiology – SPECT images were assessed first followed by SPECT/CT images. Using SPECT, location of the lesion within the vertebrae was evaluated in 3 planes: axial, sagittal, and coronal. Using SPECT/CT, the regions of increased isotope uptake were precisely identified. Using CT, the specific areas were selected on the basis of fusion studies, and their anatomical structure was evaluated together with the tissues surrounding the foci.

Using the criteria of isotope uptake intensity, location of the lesion within the vertebral structures, and symmetry of isotope uptake, the detected lesions were classified either as malignant or benign.

Malignant lesions 1) SPECT studies: increased isotope uptake (much higher than in the adjacent vertebrae); symmetrical (homogeneous) or asymmetrical (areas where no isotope uptake is present), within the body of a vertebra or within the body and including one or both pedicles; 2) SPECT/CT studies: additionally, bone tissue destruction visible, osteolytic or osteosclerotic lesions, presence of pathological masses in the surrounding tissues.

Benign lesions 1) SPECT studies: increased isotope uptake (slightly higher than in the adjacent vertebrae); asymmetrical uptake in the vertebral body, beyond its margins, or symmetrical projected over the region of the facet joints; 2) SPECT/CT studies: additionally visible segmental sclerosis of the vertebral bodies, degenerative changes of the joints, intervertebral discs, and on the vertebral margins.

Diagnosis Using the above criteria, a preliminary diagnosis was established for all patients on the basis of SPECT. Next, SPECT/CT fusion

TABLE 1 Uptake patterns detected by single-photon emission computed tomography classified as benign or malignant (n = 70)

Location of increased isotope uptake	n	Malignant		Benign	
		n	%	n	%
entire vertebral body	21	3	14	18	86
vertebral body + 1 pedicle	18	16	88	2	12
vertebral body + 2 pedicles	12	8	67	4	33
changes beyond the margins of vertebral body	9	0	0	9	100
facet joints	10	0	0	10	100
total	70	27	–	43	–

TABLE 2 Characteristics of morphological changes on computed tomography in the areas of increased isotope uptake visible on single-photon emission computed tomography, together with their differentiation into malignant and benign lesions

Location of increased isotope uptake	Entire vertebral body		Vertebral body and 1 pedicle		Vertebral body and 2 pedicles		Beyond the margins of vertebral body		Facet joints	
	M	B	M	B	M	B	M	B	M	B
differentiation: M/B	3	18	16	2	8	4	0	9	0	10
CT findings	number of lesions									
osteosclerotic / osteolytic lesions	2		13		3					
destruction of vertebral body	1 + 2	11	2 + 3		2 + 2					
destruction of vertebral body and pedicles		4	1		3	3				
degenerative changes; osteophytes, osteochondrosis		6		2		1		9		
degenerative changes in facet joints				3		1 + 3				10
pathological mass in the surrounding tissues	+ 1		+ 2		+ 2					

“+” indicates other findings on CT

Abbreviations: B – benign, CT – computed tomography, M – malignant

images were examined and morphology of specific lesions was assessed by CT, and a definitive diagnosis was established using imaging techniques.

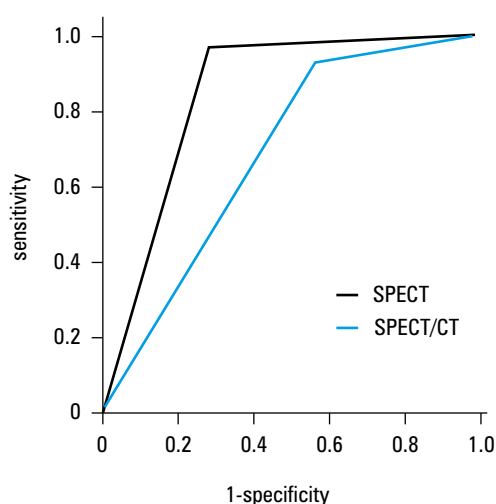
Statistical analysis The parameters were compared between the groups using the χ^2 test for categorical data and nonparametric tests of significance for interval data: the Mann–Whitney test for comparison of distributions in 2 independent groups. The McNemar’s test was used to assess sensitivity, specificity, accuracy, negative predictive value (NPV), and positive predictive value (PPV). A P-value of less than ≤ 0.05 was considered statistically significant. Calculations were performed using the Statistica 9.1 software.

RESULTS The sites of increased isotope uptake observed by SPECT in benign and malignant lesions in vertebral structures are presented in [TABLE 1](#). The morphological characteristics of the lesions (benign or malignant) observed on CT in the sites of increased isotope uptake in SPECT are presented in [TABLE 2](#).

In our material, assessing only SPECT performed in the range defined on the basis of the whole-body examination, the lesions were

properly classified as malignant in 25 of 27 foci (93%). Increased isotope uptake in the vertebral body with 1 or both sides transferring to the posterior arches, the pattern suspected of metastatic nature was observed in 24 patients: in 16 patients (88%), it involved the vertebral body and one of the posterior arches and, in 8 patients (67%), it involved the body and double-sided seizure of the posterior arches. However, in 1 patient, increased isotope uptake was observed in the vertebral body without a visible transfer into the arches. The morphological changes in these sites could be visualized owing to the use of a hybrid SPECT/CT camera. In 17 cases, focal lesions were shown in vertebral bodies as isolated sclerotic and lytic foci or focal lesions with accompanying vertebra destruction of varied extent. In 4 cases, only advanced destruction of the body could be observed and in another 4 cases, the destruction involved the body and posterior arches. In 5 patients, pathological tissue masses were visible in the perivertebral area. The morphological changes shown on CT were typical for metastatic lesions and confirmed the reliability of SPECT examination. Only 2 of 27 cases (7%) were incorrectly classified as having benign lesions; the isotope in

FIGURE 1 Comparison of receiver-operating characteristic curves for SPECT and SPECT/CT methods



much less intense level covered the whole, clearly narrowed body without the seizure of the arches. Using SPECT/CT, the lesions were classified as malignant in 26 of 27 cases (96%). Of note, in none of the malignant cases, did we observe increased isotope intake in the anterior and peripheral parts of the vertebral body or in the facet joint projection, which proved to be typical for benign degenerative lesions (100%).

We obtained much worse results by SPECT while assessing lesions verified as benign. Only 19 of 43 cases (44%) were correctly classified. In 9 patients, increased isotope uptake was observed in the periphery of the vertebral body or outside its outline; in 10 patients, it was visible in the posterior parts of the vertebra in facet joint projection. Moreover, 24 of 43 cases (56%) were wrongly classified as malignant. Isotope uptake was observed in the whole body in 18 cases, in

the whole body and one of the arches in 2 cases, and in the whole body and both posterior arches in 4 cases. These 24 cases were wrongly classified by SPECT as metastatic lesions and the pattern of isotope accumulation was considered malignant. An increased uptake involved the whole vertebral bodies in 18 patients or bodies with the posterior arches in 6 patients.

In 12 patients (50%), on analyzing SPECT/CT and CT, we changed the diagnosis of a malignant lesion into that of a benign lesion. In 6 patients with isotope uptake in the whole body on CT, massive generative lesions in the form of superstructures on the body edges were visible; in 3 patients, vertebral bodies were compressively broken; and in another 3 cases in which SPECT showed the uptake in the whole body and both arches, the destruction of the body was shown with accompanying degenerative changes in facet joints and nucleus pulposus. In the remaining 12 cases of increased isotope uptake in the body (8 patients) or in the body and posterior arches (4 patients), CT showed a massive destruction of the vertebral bodies and posterior arches without lesions suggesting the degenerative and proliferative nature. In these cases, we had no grounds for changing the diagnosis of a malignant metastasis to that of a benign lesion. Using SPECT/CT, 31 of 43 patients (72%) were properly classified as having benign lesions. Diagnostic accuracy of SPECT and SPECT/CT is presented in [TABLE 3](#).

The agreement between SPECT and SPECT/CT for all analyzed patients was 76%. In the assessment of malignant lesions, the agreement between SPECT and SPECT/CT was 89% and in the assessment of benign lesions it was 67%. The difference in proper classification of malignant versus benign lesions between the 2 methods was significant ($P = 0.049$). The number of correctly diagnosed benign lesions was significantly lower in SPECT alone than in SPECT/CT. The NPV of SPECT/CT was significantly higher than the PPV. The probability of the correct classification, described by the size of the area under the receiver operating characteristic curve was significantly higher for SPECT/CT than for SPECT alone ([FIGURE 1](#)). The selected results of our study are presented in [FIGURES 2–5](#).

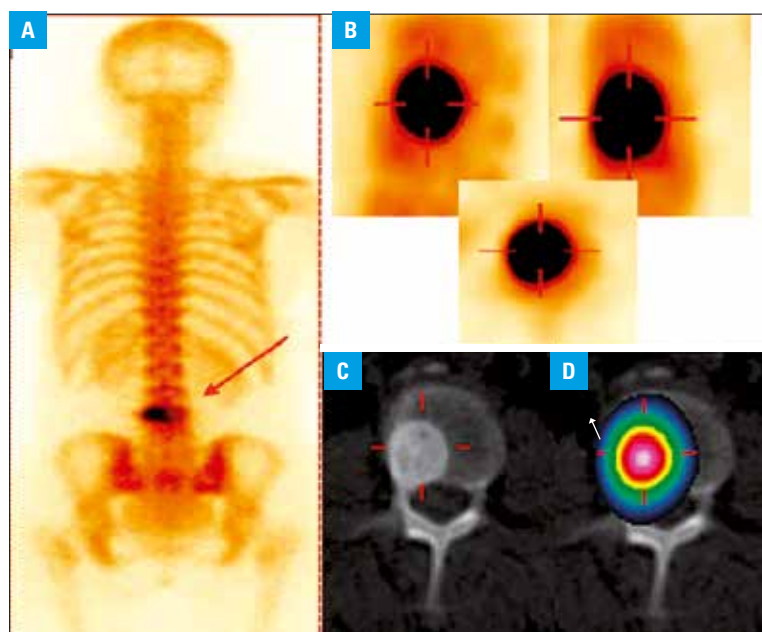


FIGURE 2 Planar bone spot in a patient with prostate cancer and a single hot focus in lumbar vertebra ([A](#)); SPECT images show the focus of increased tracer uptake in the vertebral body ([B](#)); transverse fused image shows hot focus in the posterior part of the vertebral body ([C](#)); transverse CT image shows highly dense sclerotic lesion corresponding to metastasis ([D](#))

DISCUSSION Early diagnosis of metastases to the skeletal system is crucial for further patient management. Numerous hot spots visible on whole-body bone scintigraphy in patients with recognized neoplastic disease do not constitute a greater diagnostic challenge.^{10,11} Whole-body bone scintigraphy is a highly sensitive method because it allows to detect all lesions that involve bone remodeling. However, the specificity of this method is decreased by the fact that remodeling may occur both in malignant and benign lesions. In the differential diagnosis, other bone diseases, such as osteoporosis, and risk of fractures should also be considered.^{12–15}

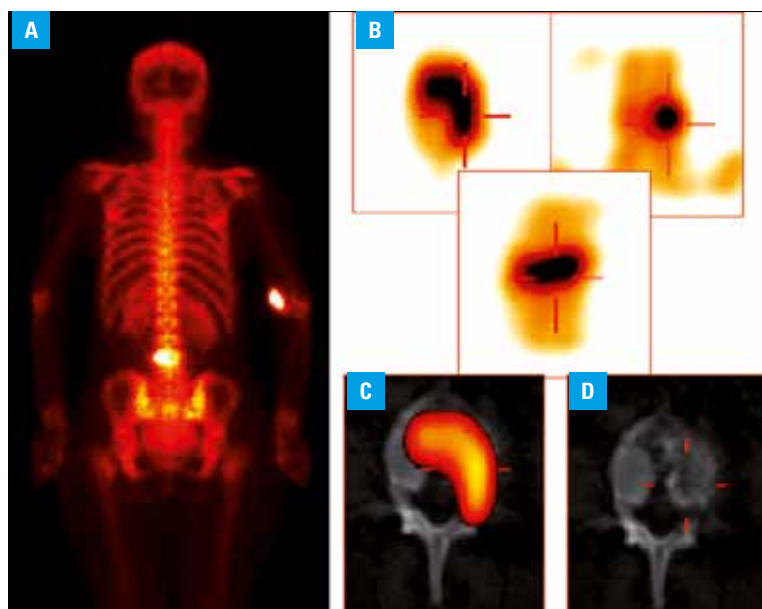


FIGURE 3 Planar bone spot in a patient with breast cancer and a single hot focus in lumbar vertebra (A); SPECT images show increased tracer uptake in the vertebral body and posterior left pedicle (B); transverse fused image shows increased tracer uptake in the posterior part of the vertebral body and left pedicle (C); transverse CT image shows the fracture of the vertebral body (D); finally, after verification, this proved to be bone metastasis

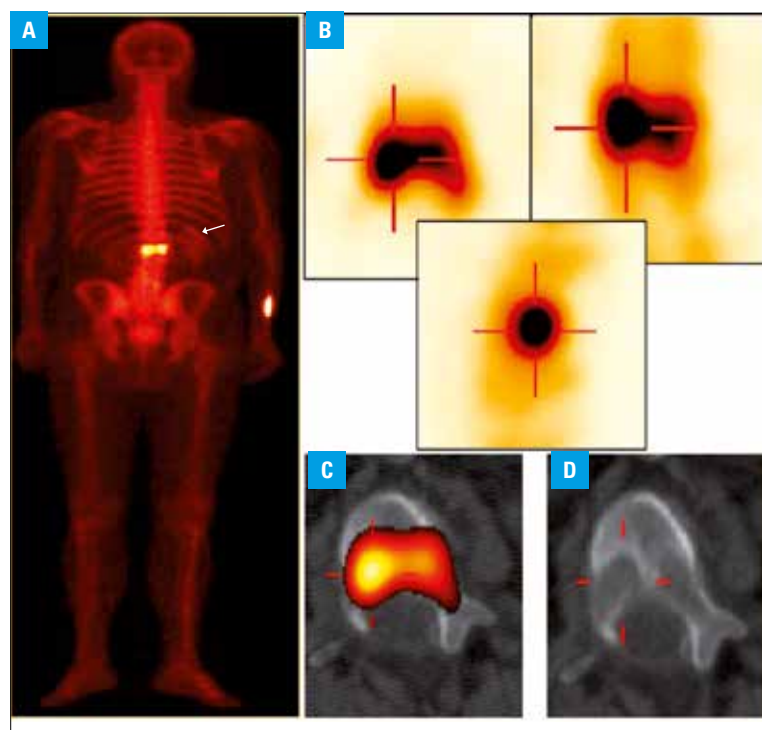


FIGURE 4 Planar bone spot in a patient with prostate cancer and a single hot focus in lumbar vertebra (A); SPECT images show increased tracer uptake in the vertebral body (B); transverse fused image shows increased tracer uptake in the posterior part of the vertebral body and pedicle (C); transverse CT image shows osteolytic destruction of the right vertebral pedicle (D); finally, after verification, this proved to be bone metastasis

In the spine, degenerative, metastatic, and inflammatory lesions can be observed. Metastatic foci can be lytic, sclerotic, or mixed. The early detection of metastases and early start of therapy are crucial to improve patient's

survival.¹⁶⁻¹⁸ Similarly, in other cases, scintigraphy can play an important role in disease monitoring.¹⁹ The differentiation of a solitary hot spot by using scintigraphy alone is still questionable. The presence of a large number of intervertebral and costovertebral joints, as well the structure of the intervertebral discs, predisposes the spine to degenerative changes. The anatomy of a vertebral body and, especially, the presence of a large amount of well-vascularized bone marrow together with well-developed venous circulation provide excellent conditions for the accumulation of cancerous cells and further development of metastases.^{8,20-22} Therefore, increased isotope uptake that can be observed in SPECT, encompassing the vertebral body and the posterior structures of the vertebra, suggests a metastatic lesion. The increased isotope uptake in the vertebral body, especially its anterior part or isolated covering of the posterior arch, spinous process, and facet joints, is usually benign. Lesions in the entire vertebral body or its posterior arch should be interpreted with caution because they can be either malignant or benign.^{1,23-25}

In most cases, the use of SPECT/CT to examine the bone structures and the surrounding tissues allows to determine whether the foci detected by scintigraphy are malignant or benign.^{11,26,27}

The morphological changes typical for metastatic lesions observed in CT confirmed the reliability of SPECT examination. Our results are in line with those of other authors who reported that the pattern of increased isotope intake in the vertebral body and posterior arches suggested the malignant character of the lesions in 87% to 100% of the cases (93% in our study).²⁵

In our study, the image of isotope accumulation in the vertebral body observed on one side or, less frequently, on both sides of the posterior arches proved to be more characteristic for metastatic lesions. Similar observations were described by other authors.^{22,24}

Of note, in none of the malignant cases did we observe an increased isotope uptake in the anterior part of the vertebral body or in the projection of facet joints, which turned out to be typical for benign degenerative lesions. The agreement between SPECT and SPECT/CT in the assessment of malignant lesions was high (89%), which shows that we chose appropriate criteria to identify malignant lesions.

We obtained worse results by SPECT while assessing lesions classified as benign. They were adequately classified only in 44% of the patients. Our results are in line with those reported by other authors.^{26,28} In 24 of 43 patients (56%), the observed lesions were classified as malignant. These 24 cases were wrongly classified after SPECT examination as metastatic lesions, and the pattern of isotope uptake was considered malignant. The foci of the metastatic scatter located in the marrow of the vertebral body may cause an increase of isotope uptake only in its area (40%–60%), the accumulation in the vertebral body with

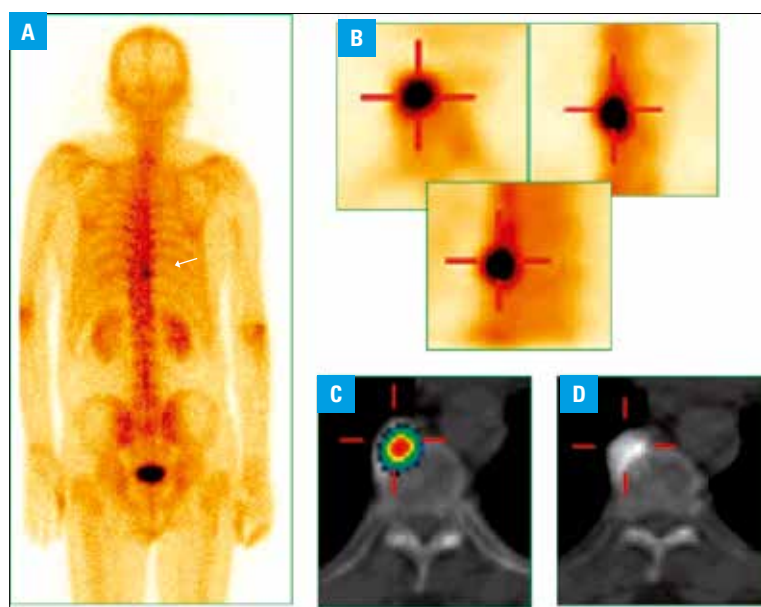


FIGURE 5 Planar bone spot in a patient with breast cancer and a single hot focus in thoracic vertebra (A); SPECT images show increased tracer uptake in the anterior part and outside of the vertebral body (B); transverse fused image shows increased tracer uptake outside the anterior part of the vertebral body (C); transverse CT image shows spondylosis responsible for localized hypermetabolism, excluding malignancy (D)

the involvement of the posterior arches may be characteristic for lesions that are more progressive (80%–100%). Therefore, based on the generally approved criteria, we considered these lesions as malignant. While analyzing the results of SPECT/CT and CT, of 24 cases classified as malignant, we changed the diagnosis into that of a benign lesion in 12 patients. In the remaining 12 cases of increased isotope uptake in the vertebral body (8 patients) or in the body and arches (4 patients), the results of SPECT/CT did not provide the grounds for changing the diagnosis into that of a benign lesion. The agreement between SPECT and SPECT/CT was 67%, which was much lower for the assessment of benign lesions compared with that of malignant lesions.

In our study, the greatest challenge was in evaluating the lesions in 21 patients with increased or more or less homogeneous uptake that included the entire vertebral body. In 18 patients (86%), these lesions were benign, and malignancy was confirmed only in 3 cases (14%). Other authors observed the presence of malignant lesions in the vertebral body, as shown in SPECT, only in 6% of the cases.^{22,25,28} These data show that, in cases with isolated seizure of the whole vertebral body (which in our study constituted 86% of the patients with benign lesions), the examiners are highly cautious and prefer to classify these changes as malignant. The morphological assessment of these findings on SPECT/CT allowed to change the diagnosis in 50% of these cases, which with the use of a nondiagnostic low-dose CT scanner may be considered as a good result. It is often impossible to determine the cause of vertebral destruction only on the basis of CT images and, in some cases, an additional examination

of the patient is necessary.^{29–32} Similarly, in our study, additional diagnostic work-up performed outside our institute had a crucial role in the establishment of the final diagnosis.

By fusing the images from 2 different studies in 1 session with a hybrid SPECT/CT camera, it is possible to evaluate metabolic and morphological changes, increase the specificity of SPECT, and determine the nature of lesions in a large percentage of cases. In our study, the use of a hybrid scanner with its numerous advanced features allowed us to accurately diagnose 44 cases (63%) and add additional 12 cases (18%) to this group after changing their diagnosis on the basis of CT; thus, we obtained the accuracy of 81%. Similar results were reported by other scientists who achieved a diagnostic accuracy of 85%.¹⁷

Our study confirms that the hybrid technique of SPECT/CT is currently one of the most optimal techniques in nuclear medicine available for clinical examination and diagnosis. The technique allows to evaluate lesions that show to be metabolically active in scintigraphy as well as assess the underlying morphological changes in a given area of isotope uptake; thus, it allows to correctly diagnose the majority of lesions that cannot be determined by SPECT. Our findings are in line with those of numerous authors who showed the diagnostic accuracy of the SPECT/CT technique to be near 100%.^{33–36}

Conclusions The applied credibility criteria for the assessment of a solitary hot spot in the spine allow for the direction of diagnosis mainly towards the lesions of noncancerous nature.

The studies showed high reliability in terms of the negative results. The NPV in SPECT was 90% and 97% in SPECT and SPECT/CT, respectively. Reliability in terms of the positive results was significantly lower. The PPV was 68% in SPECT/CT and 51% in SPECT alone. This is because SPECT/CT offers an additional possibility to perform a morphological assessment of the lesions. After scintigraphy shows a solitary hot spot in the spine of patients with malignant carcinoma, it is recommended to examine the patient with a SPECT/CT camera, which is more reliable than the assessment by SPECT alone and allows to differentiate between malignant and benign lesions with a higher probability of a correct diagnosis.

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Wiarygodność różnych technik radioizotopowych w diagnostyce pojedynczych gorących guzów w kręgosłupie u pacjentów z nowotworem złośliwym

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SŁOWA KLUCZOWE

pojedyncze ognisko
w kręgosłupie,
scyntygrafia kości,
SPECT, SPECT/CT,
urządzenie hybrydowe

STRESZCZENIE

WPROWADZENIE Wczesne rozpoznanie przerzutów do kręgosłupa jest kluczowe w dalszym postępowaniu terapeutycznym.

CELE Celem badania była ocena wiarygodności rozpoznania w zależności od aparatury tomografii emisyjnej pojedynczego fotonu (*single-photon emission computed tomography* – SPECT) lub tomografii emisyjnej pojedynczego fotonu i tomografii komputerowej (SPECT/*computed tomography* – SPECT/CT) w diagnozowaniu pojedynczych guzków gorących w kręgosłupie stwierdzonych w scyntygrafii.

PACJENCI I METODY W badaniu retrospektywnym analizowano 70 pacjentów z chorobą nowotworową, z wykrytym pojedynczym guzkiem w kręgosłupie. Za pomocą γ-kamery SPECT/CT analizowano rodzaj i lokalizację ogniska w kręgu. Wykonywano scyntyografię kośćca, SPECT i CT. Wiarygodność rozpoznania ustalano w zależności od zastosowanej aparatury.

WYNIKI W zmianach złośliwych wzmożony wychwyt znacznika obejmował: trzon z zajęciem tylnego łuku (88%), trzon i oba łuki (67%), trzon kręgu (14%). W zmianach łagodnych obserwowano wzmożony wychwyt na obwodzie trzonu lub w rzucie powierzchni stawowych. Przy użyciu SPECT 25 spośród 27 przypadków (93%) ognisk zakwalifikowano prawidłowo jako zmiany złośliwe. Przy użyciu SPECT/CT, spośród 27 przypadków, zmiany złośliwe obserwowano w 26 (96%). Przy użyciu SPECT, 19 spośród 43 przypadków (44%) uznano za zmiany łagodne, a przy użyciu SPECT/CT 31 spośród 43 przypadków (72%). Zgodność rozpoznania za pomocą SPECT i SPECT/CT była większa w przypadku zmian złośliwych (89%) niż zmian łagodnych (67%). Dzięki CT w badaniach SPECT/CT zmieniono rozpoznanie w 50% przypadków ze zmiany złośliwej na niezłośliwą.

WNIOSKI Zastosowane kryteria wiarygodności diagnostyki pojedynczych guzków w kręgosłupie ukierunkowują rozpoznanie głównie w stronę zmian o charakterze nienowotworowym. Wiarygodność oceny dodatkowo była znacznie mniejsza niż ujemnej wynosząc 51% w badaniu SPECT a 68% w SPECT/CT. Kamera hybrydowa SPECT/CT daje większą wiarygodność oceny zmian w kręgosłupie niż badanie SPECT.

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