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**Author:**

Angel González-Sistal, MD, PhD

Department of Physiological Sciences II

Faculty of Medicine, University of Barcelona.

**Address correspondence to:**

Prof. Dr. Angel González-Sistal

Department of Physiological Sciences II

Faculty of Medicine, University of Barcelona.

Campus Bellvitge. C/ Feixa Llarga s/n Pavelló de Govern, 4<sup>a</sup> planta, lab. 41.57

08907 Hospitalet de Llobregat (Barcelona)

Spain.

Tel. +34 934029088

Fax. +34 934024268

e-mail: [angelgonzalez@ub.edu](mailto:angelgonzalez@ub.edu)

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## **Diagnostic imaging modalities of osteoblastic metastases**

Osteoblastic metastases are characterized by the neoformation of bone around tumor cell deposits. These cells secrete morphogens and growth factors (BMPs, IGF, TGF $\beta$ ,...) that stimulate osteoblasts to produce collagen, osteocalcin and alkaline phosphatases<sup>1</sup>. The newly formed bone is deposited on trabecular bone, making it more dense. These tumoral cells metastasize to the most vascularized parts of the skeleton, particularly the red bone marrow of the axial skeleton and the proximal ends of the long bones.

In 80% of the cases, the primary tumor originates in the breast or prostate<sup>2</sup>. Bone pain is the most common clinical consequence and could be the initial presenting symptom.

Imaging plays a major role given that early identification of skeletal metastases could lead to changes in patient management. Clinical evaluation demands multimodal diagnostic imaging owing to the limitations of the diagnostic techniques. Four main modalities are currently utilized: radiograph, computed tomography, scintigraphy and magnetic resonance imaging<sup>3-4</sup>. At present, positron emission tomography and single-photon emission computed tomography have a potential for evaluation<sup>5</sup>. These techniques differ in performance in terms of sensitivity and specificity, but none of the modalities alone seem to be able to yield a reliable diagnostic outcome. There is currently no agreement on which is the best modality for diagnosing the lesion and for assessing its response to treatment. In clinical practice, most oncologists do not even use the same criteria, which results in disparate assessments of bone metastases<sup>5</sup>.

Radiograph and scintigraphy are the most common imaging modalities used for detection.

Computerized tomography (using the bone window setting) offers better skeletal detail than radiographs because of its ability to visualize in sufficient anatomic detail.

Scintigraphy remains the technique of choice in asymptomatic patients in whom skeletal metastases are suspected. This technique visualizes increases in osteoblastic activity as hot spots. However, the technique, albeit very sensitive, is poorly specific, and thus a negative bone scan finding is double-checked with an additional examination.

Magnetic resonance imaging is the only technique that enables us to differentiate between bone marrow components. The major limitation of magnetic resonance imaging is the poor specificity of its findings, which could result in erroneous findings. The capability of magnetic resonance imaging to obtain sagittal views allows large sections of the skeleton to be assessed in one imaging session.

Computerized tomography and magnetic resonance imaging are used less frequently than radiographs because of the cost, the restricted availability and the scant data available on the sensitivity and specificity of these methods<sup>4-5</sup>.

### **New methods on digitized radiographs**

On radiographs these metastases appear as spots that are whiter than the surrounding healthy bone and are sometimes difficult to differentiate from it. This technique is commonly used to evaluate symptomatic sites and is a useful complement to scintigraphy for clarifying nonspecific or atypical findings or for following up cases in which clinical findings indicate bone pain but where scintigraphy findings are negative. This is not generally recommended as a screening method because of its poor sensitivity. Sensitivity depends partly on location. For instance, metastases to dense cortical bone are easier to detect than those involving trabecular bone. The advantages of this technique include its wide diffusion, low cost and improved patient comfort.

The digitized radiograph image is obtained by scanning the image of a radiograph film, which converts an analogue image into a digital one. This modality offers the possibility of studying anatomical locations from qualitative and quantitative points of view.

Radiological diagnosis produces false-negative findings may be due to a misperception of osteoblastic metastases. The major cause is a bone marrow sclerosis below the threshold for detection on radiograph. False- positive, on the other hand, are an incorrect analysis of radiological findings such as trauma, inflammation or healing<sup>5</sup>.

The accurate detection of osteoblastic metastases should improve by quantifying these lesions, thereby paving the way for computerized methods that would enable us to: standardize studies to draw general conclusions, calculate the ideal parameters, define patterns of normality and determine the pathology by evaluating deviations of these indexes.

Earlier works, using digitized radiographs, have reported a method designed to improve the differential diagnosis between healthy bone and osteoblastic metastases, the primary tumors of which was prostate and breast<sup>6-7</sup>. The material used was 144 radiographs of healthy bone and 35 of osteoblastic metastases of 179 subjects. The method is summarized on the algorithm as follows: (1) image acquisition, (2) selection of a region of interest, (3) filtering, (4) histogram, (5) characterization by parameters, (6) results analysis and, (7) discriminatory capacity of the parameters.

The results showed a good discriminatory ability of the parameters to distinguish between healthy trabecular / flat bones and osteoblastic metastases (area under the receiver operating characteristic (ROC) of 0.97 and 0.85, respectively)<sup>7</sup>.

This method can be helpful as a complementary method for a differential diagnosis and has the following advantages: 1) it accurately quantifies the selected regions of healthy and osteoblastic metastases, 2) it reduces subjectivity in the interpretation of the image,

3) it improves the information contained in the radiograph, 4) it implements in a personal computer, 5) it is automatic, 6) it obtains the results on the screen in a shorter time and 7) it diminishes the radiation of the patient since a second diagnosis is unnecessary in many cases.

## **Conclusion**

The aim of developing methods that quantify radiograph images is to improve the identification of these metastases given that the parameters accurately identify the tumoral areas. Consequently, new methods open up new horizons in early diagnosis and follow up. Moreover, they can be useful to study the evolution of these metastases under treatment.

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