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Kohonen's Algorithm Applied to the Scintigraphic Image for an Aid in the Diagnosis of Prostate Cancer Metastasis

Boucar Ndong[1], El Hadji Amadou Lamine Bathily[1], Mamoudou Salif Djigo[1], Mamadou Lamine Mboup[2], François Kaly[3], Kanta Ka[4], Ousseynou Diop[1], Ibrahima Thiam[4], Gora Mbaye[5], Omar Ndoye[1], Mamadou Mbodj[1]

[1]Biophysics and Nuclear Medicine Laboratory, Cheikh Anta Diop University, Dakar, Senegal
[2]Sustainable Development and Society Doctoral School, Thies University, Thies, Senegal
[3]Laboratoire du traitement de l'information/ESP/UCAD, Senegal
[4]Radiotherapy Department of the National Hospital University Center, Dalal Jamm, Guédiawaye, Dakar, Sénégal
[5]Physics Pharmaceutical Laboratory, Cheikh Anta Diop University, Dakar, Senegal
Email: ndongboucar73@yahoo.fr

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Abstract

To partition the scintigraphic image, several methods are used, among which is Kohonen's self-organizing map algorithm. The objective of this study was to perform an ascending hierarchical classification (HAC) on the results of the Kohonen self-organizing map. This makes it possible to carry out the second phase necessary for the elaboration of the classifier by grouping the neurons as well as possible into 3 classes then by reconstituting the scintigraphic image from the 3 classes. This partition proceeds by successive groups, thus merging at each iteration two subsets of neurons using a measure of similarity which is Ward's method. In this method, the algorithm aggregates the nearest neurons into classes. This allows us to obtain a dendrogram that looks like a tree. And this one needs to be cut. And to have an adequate cut-off level, we have established the variation of the Davies Bouldin index as a function of the number of classes. The minimum value of this index gave the optimal number of classes which corresponded to 3 in the study. These three groups A, B, C have a variable intensity. This intensity can be high, it can be medium or low. The high, medium and low intensities corresponded respectively to metastases for class A, to degenerative or inflammatory phenomena for class B and to normal radiopharmaceutical uptake for class C. To confirm this strong suspicion, we performed reconstructions using a filter. And after this reconstruction, we had images like at the entrance. And for the interpretation of these images, we used a visual metric. This enabled us to note that for the interval [0 - 50[, the image is not contrasted and no lesion could be detected. Over the interval [50 -

200[, we observed the distribution of the radiopharmaceutical over the entire skeletal whole body. On this reconstruction interval, the visual metric shows hypofixation in the bladder and areas suspected of metastases. Over the interval [200 - 250[, we detected hyperfixations linked to degenerative, inflammatory or metastatic lesions. And finally, in the last interval, [250 - 252], we found regions that showed strong uptake (bladder, sternum, etc.). This capture is physiological. Apart from physiological hyperfixation, the other types of hyperfixation were considered metastatic according to the two nuclear scientists who interpreted these images. In total, the HAC allowed us to sub-classify the data into 3 groups which were subsequently reconstructed. And this reconstruction technique highlighted the periarticular metastases belonging to the class [250 - 252]. This allowed us to highlight the oligo-metastases and to carry out in most of these patients a radical prostatectomy.

Keywords

Neural Networks, Hierarchical Ascending Classification, Scintigraph

1. Introduction

Prostate cancer is an osteophilic cancer. Bone metastases are most often found. When metastases are present and they are less than 4 prostatectomies is always recommended. Beyond these oligo-metastases, we observe an important turning point in the natural history of the cancerous disease because at this stage only a palliative treatment is possible [1]. Whole-body bone scans play an important role in the early detection of metastases from osteophilic cancers, especially prostate cancer. The high sensitivity of scintigraphy gives it a special place in the diagnosis and post-therapeutic follow-up of cancers. However, this test is characterized by its low specificity. It may not detect periarticular metastatic bone lesion. To minimize the risk of missing these metastatic lesions, we are implementing an artificial intelligence technique, particularly unsupervised learning. This technique uses artificial neural networks with topological Kohonen maps. These Kohonen maps allow, by learning from the data, to partition all available observations into similar groupings. These proposed groupings have the particularity of having a neighborhood structure materialized using a small-dimension lattice on which the neighborhood structures are taken into account by the model. The neurons are arranged on a regular grid and are connected to each other by a neighborhood relationship. This creates the map topology. In order to better group neurons, similarity methods are proposed, the best known of which is Ward's method for performing a good classification [2].

The objective of this work was to carry out neural learning via Kohonen's self-organizing maps to highlight peri-articular metastases.

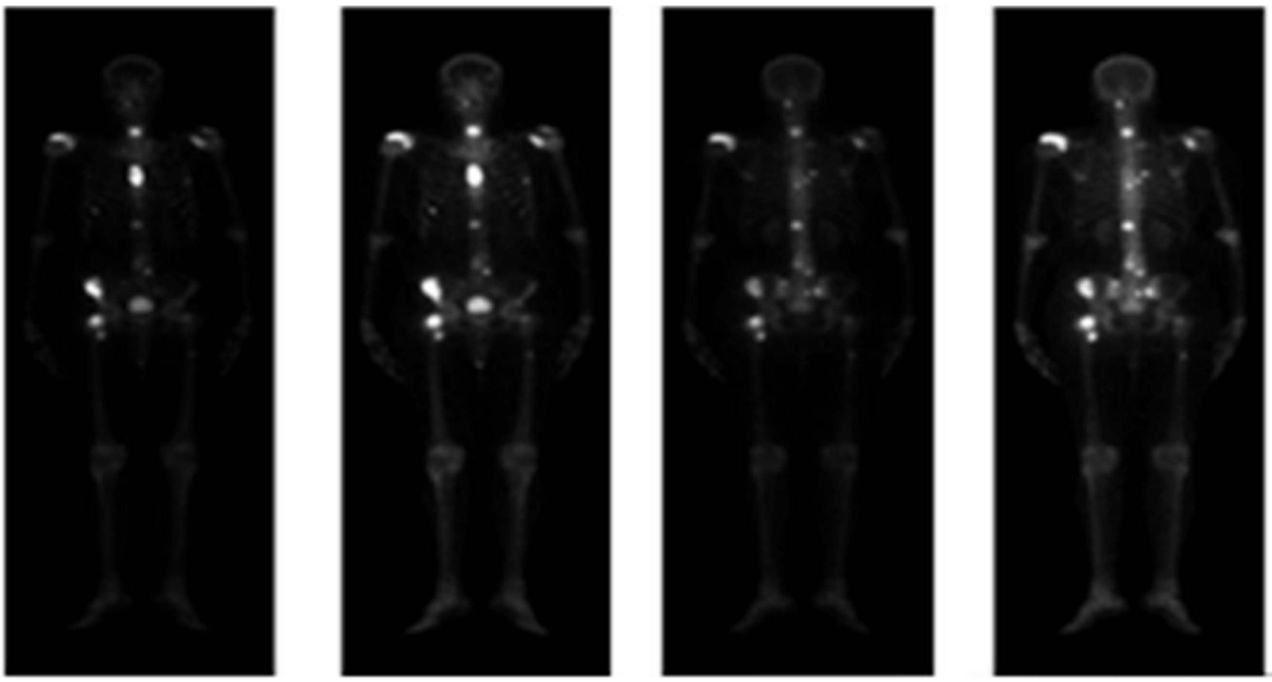
2. Materials and Methods

In this study, we used an artificial neural network algorithm. It is an unsupervised technique that takes place in two stages. The first step is to use Kohonen's self-organizing map to cluster the pixels of the scintigraphic image. Thus, the clustering gave a large number of classes (400) which corresponded to the number of neurons. In order to facilitate the interpretation of the results, the second step consists in carrying out a second classification. This is the hierarchical ascending classification. This technique made it possible to considerably reduce the number of classes which initially was equal to the number of neurons (400). Thus, we go from 400 classes to 3 classes. A reconstruction of these classes was carried out and allowed identification of the lesions using a semi-quantified scale.

2.1. Material

We used a preprocessing consisting in extracting four scintigraphic images **Figures 1(a)-(d)** which represent scintigraphic images of the whole body. Thus image (a) represents a front view. Image B shows a front view with enhanced contrast. Image (c) is a posterior view. And finally image (d) represents a posterior view with contrast enhancement

The pixels have a variable intensity gray level ranging from zero to 252 and will be presented as input after having produced a topological Kohonen map in two dimensions, via Somtoolbox. Then different architectures were tested and the best result was a topological map of 20 × 20 neurons. This allowed us to very finely separate the situations we had at the start and thus manage to keep the information on small scales. After preprocessing, we applied the Kohonen algorithm



(a) (b) (c) (d)

Figure 1. Scintigraphic images (Image (a): anterior face, Image (b): anterior face with contrast enhancement, Image (c): posterior face, Image (d): posterior face with contrast enhancement).

on these scintigraphic images. Thus we obtained a self-organized Kohonen map of 400 neurons (20 × 20).

2.1.1. Self-Organizing Map of Kohonen

The Kohonen algorithm allows a classification belonging to the family of unsupervised learning neural networks. It consists of two fully connected sofas [3]. The first layer (or input layer) is used to present the observations. The second layer is a regular grid of neurons representing the map. Each neuron is associated with a reference vector which has the dimension of the data and is statistically representative of all the data of the neuron. Kohonen's algorithm projects data into a low-dimensional space, usually 2 or 3 dimensions, called a map. The map is made up of a set of interconnected neurons. The map has a topological order. This means that the neighboring neurons on the map represent similar situations, while the furthest neurons on the map represent different situations. The referent vectors are determined by a learning process [3], minimizing a nonlinear cost function. Generally, Kohonen's algorithm is used for statistical research, but it can be used for all sorts of purposes, especially in health research. This self-organized map yielded 400 neurons where each neuron represents a class with several pixels of a certain intensity. And given the large number of neurons on the map, it was difficult to study each neuron. This is why we used the higher ascending classification in order to obtain a much smaller number of classes.

2.1.2. Hierarchical Ascending Classification (HAC)

HAC is an iterative classification method whose principle consists of a set of partitions K of n elements into less and less fine classes obtained by successive groupings. It is a method which, in this study, makes it possible from the topological map to create a hierarchy of partitions, each partition making it possible to group the neurons of the map in a different way. The different partitions of the hierarchy are determined iteratively, starting with the finest partition. Hierarchical clustering uses this initial partition and proceeds by successive clusters by merging two subsets of neurons at each iteration. The choice of the two subsets which will merge at a given step is made using a measure of similarity defined between two subsets. Among all the pairs of subsets that constitute the partition at this stage, the two most similar subsets of neurons, in the sense of the chosen distance measure. These successive groupings produce a binary classification tree called a dendrogram. This dendrogram represents a hierarchy of partitions. We can then choose a partition by cutting the tree at a given level. This level is chosen according to more objective criteria. Different measures of similarity are proposed in the literature [4]. The best-known similarity measure is Ward's method. This method consists in grouping the data in such a way that the sum of the inertias of the groupings obtained remains as low as possible

2.2. Methodology

In this work, we used the Kohonen self-organizing map with the pixels of the scintigraphic image as input data. These pixels represented the data and were initially estimated at 177,639 pixels. With these data, several maps were made and we selected the best map based on the topological error. After learning, the input data is captured by the neurons. These neurons were 400 in number. And each neuron had captured a set of data (pixels). This is why each neuron was considered as a group or a class. This number of classes which was equal to 400 was very large to be studied correctly. This is why we have reduced these classes thanks to the ascending classification. The criterion that allowed us to make this classification is Ward's criterion (**Figure 2**). This criterion is based on the calculation of a Euclidean distance. This allowed us to group the closest neurons into a class as we went along. **Figure 3** presents the process implemented in this study. In this specific case, the height was the distance between two classes. The distances between the classes are listed in a table of matrix values. The two closest classes are aggregated, that is, combined into a single class, and so on. When two classes have the lowest height and one of them results from an aggregation, then the minimum hop algorithm determines the height of the aggregation. This dendrogram is in the form of a tree whose cut-off level indicates the number of

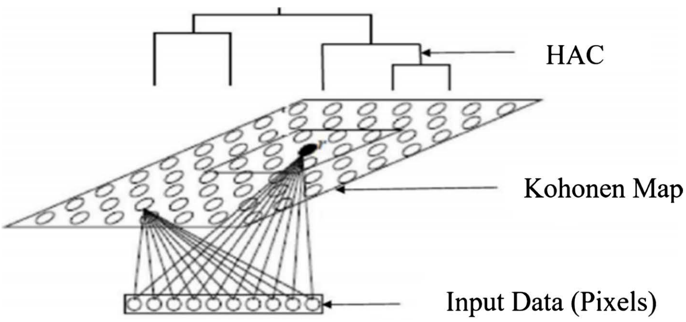


Figure 2. Kohonen map applied to the hierarchical ascending classification.

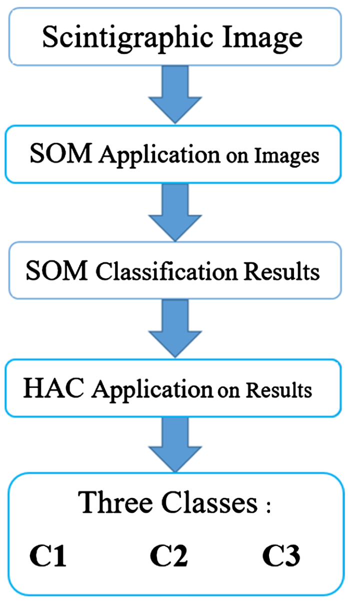


Figure 3. Presentation of the structure of our methodology.

classes to be retained. To obtain the best possible classification, several classifications were carried out. First we looked at the whole map, then we ranked up to 15 classes. For each classification, the Davies Bouldin index is calculated (Figure 4). This index measures the separability and compactness of classes. The lower the index, the better the classification.

Once the dendrogram has been established, the Davis Bouldin index allows us to retain the best classification which is that in 3 classes (Figure 4). This allowed us to choose a well-defined level as shown in Figure 5 allowing to have 3 classes.

3. Results

3.1. Dendrogram and Cutoff

The ascending hierarchical classification on the 400 neurons allowed us to have 3 classes. For Figure 6, we have a class C1 composed of 330 neurons (red color) of low intensity. This class is followed by the 2nd class C2 containing 58 neurons

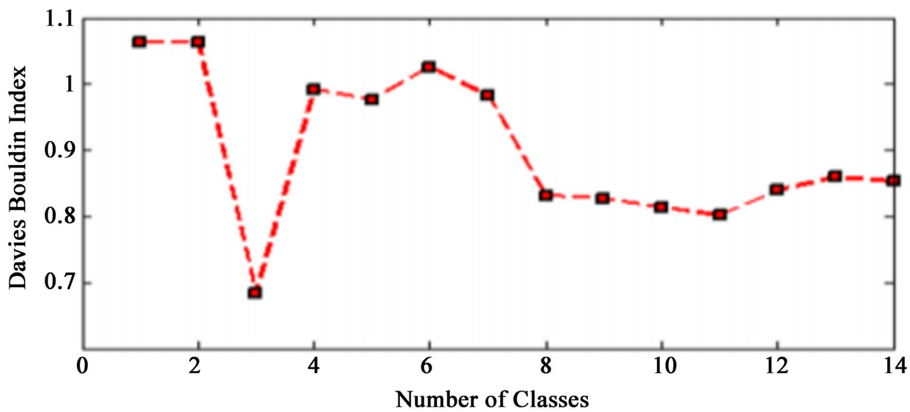


Figure 4. The davies and Bouldin index.

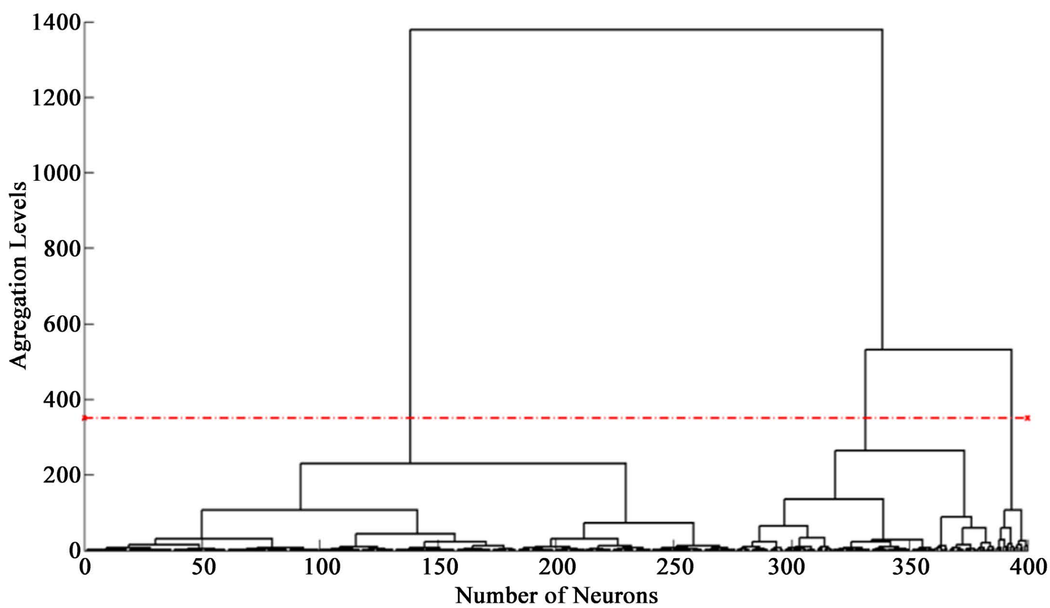


Figure 5. Dendrogram with a 3 class cut-off level.

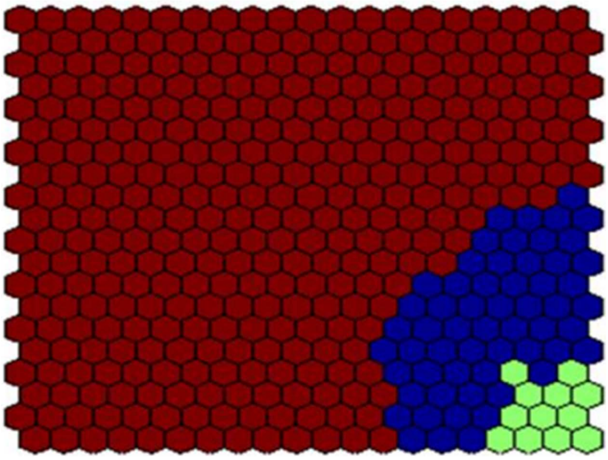


Figure 6. Highlighting of the different classes obtained after neural hierarchical ascending classification.

(blue color) of average intensity. And finally the last C3 class of high intensity and containing 12 neurons (in green)The hierarchical ascending classification algorithm (HAC) allowed us to find the intensity intervals of the three classes C1: [50 - 200[, in red, C2: [200 - 250[in blue, C3: [250 - 252] in green. These three reconstituted classes gave the scintigraphic image

3.2. Reconstruction of the Scintigraphic Image after HAC

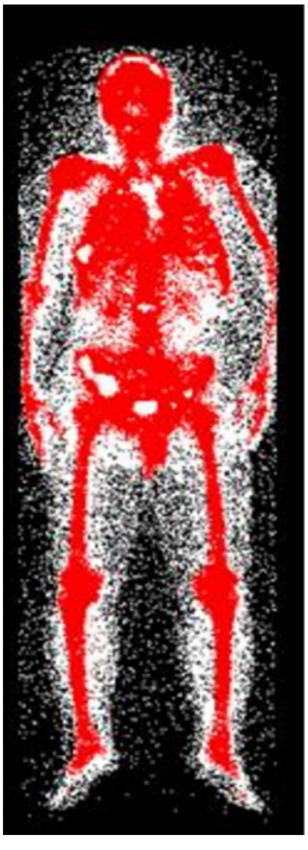


Figure 7. Reconstruction of C1 class.

Figure 8. Reconstruction of C2 class.

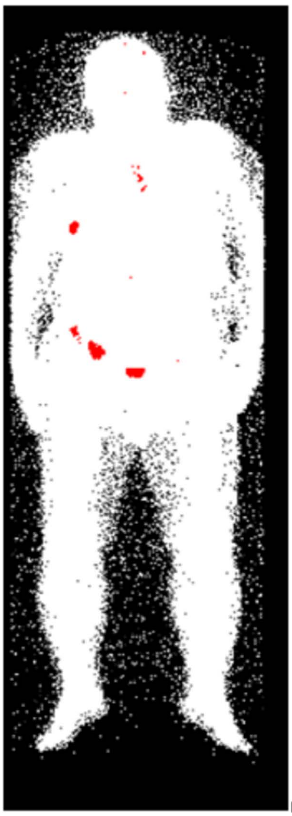


Figure 9. Reconstruction of C3 class.

4. Discussion

4.1. Dendrogram and Cutoff

In this classification, we considered 400 neurons which captured all the pixels of the scintigraphic image. In this specific case, there are 400 neurons or classes. And as it is difficult to study all these classes, the HAC allowed us to obtain a dendrogram by Ward's method whose threshold is determined by the Davies-Bouldin index. This Davies and Bouldin index is a metric for evaluating clustering algorithms. It is an internal evaluation system. The validation of the quality to which the classification has been subjected is carried out using parameters. These parameters quantify the intrinsic properties of the processed data. This index makes it possible to treat each class individually and seeks to measure its resemblance to the others. For each class i of the partition, we seek the class j which maximizes the similarity index. The best partition is the one that minimizes the average of the value established for each class. In other words, the best partition is the one that maximizes intra-class similarity and minimizes inter-class similarity [5]. Therefore, the intra-class variability is zero and the inter-class variability is equal to 1. Thus, two different classes have almost no similarity. In this case, the lowest Davis and Bouldin index makes it possible to indicate the best choice, *i.e.* the number of optimal classes [6] [7]. This allowed us to adjust the tree cut level to have 3 classes (C1, C2 and C3). This is clearly illustrated by **Figure 5** and **Figure 4**, **Figure 6**.

4.2. Reconstruction of the Different Classes in the Scintigraphic Images

For class C1, where the pixel intensities are between 50 and 200, we highlighted by white spots (**Figure 7**) the lesions corresponding to osteoarthritis, metastases of the costal grid and the iliac wing law. The white spots found on the sternum and the bladder correspond to physiological hyperfixation in conventional scintigraphy. For class C2, where the pixel intensities are between 200 and 250, we find a physiological hyperfixation (in red) at the level of the sternum, the bladder and the skull and the pathological hyperfixations which can be degenerative phenomena, arthritis or peri-articular metastases (**Figure 8**). We cannot distinguish these lesions at all. For class C3 whose pixel intensities are between 250 and 252, there is no more joint hyperfixation whose intensity is less than 250 (**Figure 9**). In Matlab there is a pointer which makes it possible to find these intensities as in the Hounsfield classification in X-ray scanner. Despite the peri-articular localization, we have thanks to this semi-quantitative function to find peri-articular metastases with pixels of intensity greater than 250 found a capture at this site with semi-quantization that found pixel values of intensity 250 This method is very interesting because it avoids under and over diagnosis of metastases. This allows urological surgeons to indicate or contraindicate radical prostatectomy. The Kohonen algorithm has a higher discriminating power to separate the different classes than the K-Means algorithm [8] [9] due to the topological constraint between the different neurons.

Our method has limitations because we did not biopsy the metastatics lesions. The biopsy is traumatic. The lesions are focal and difficult to reach. Hence the risk of false negatives. To obtain results comparable to those of the biopsy, we had two highly trained nuclear doctors, the PSA level and the Gleason score. This allowed us to validate our interesting results and to compare them with those of the literature. Indeed, authors like Nikolaos Papandrianos et al. have used a similar technique (convolution Neural Net work: CNN) to identify bone metastases from prostate cancer. Their technique is very close to ours. This technique enabled automatic feature extraction by applying filters to the input images and, through an advanced learning process, was able to highlight bone metastases. These studies can be compared to ours. Indeed, despite the limitation of our technique related to the absence of biopsy of the lesions, we found a good sensitivity (90%) and a specificity of 87%. These results are comparable to those of Nikolaos Papandrianos and al. They found an accuracy of the classification tests at 97.38%, for an average sensitivity of around 95.8%. These authors showed that the CNN method is superior to well-known popular CNN architectures for medical imaging, such as VGG16, ResNet50, GoogleNet, and Mobile Net. The classification results demonstrated that the proposed CNN-based approach outperforms popular CNN methods in nuclear medicine for the diagnosis of prostate cancer metastasis.

5. Conclusion

The most common bone locations are prostate cancer metastases. They expose to poorly tolerated bone pain, most often contraindicating a radical prostatectomy beyond the oligo-metastases. Whole body CT may be insufficient. SPECT-CT allows a more precise approach, especially when the location is periarticular. In the absence of this hybrid imagery in most developing countries like ours, artificial intelligence in the context of unsupervised learning using Kohonen topological maps followed by ascending hierarchical classification and d a reconstruction of the scintigraphic image using classification. And when the intensities of the pixels are between 250 and 252, a comparison with the opinion of the nuclear medicine specialist shows that it is about metastases. And the diagnosis of excess or lack of metastases can radically change the course of treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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