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Application of artificial neural network algorithm to detection of parathyroid adenoma

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Abstract

Background: The most common radionuclide procedures for parathyroid imaging are ^{99m}Tc-MIBI/^{99m}Tc pertechnetate subtraction scintigraphy and ^{99m}Tc-MIBI double-phase imaging, with estimation of MIBI wash-out rate. Those two methods are by some authors regarded as complementary techniques, yielding the best evaluation of parathyroid gland if performed conjointly. By such an approach it seems reasonable to substitute the visual assessment of neck scintigrams and semiquantitative evaluation of MIBI wash-out rate with a single, common procedure. The aim of this study was application of the Artificial Neural Network (ANN) simulated by the computer program to detection and localisation of pathological parathyroid tissue in the planar neck scintigrams.

Material and methods: The applied algorithm was based on simultaneous data processing in sets of 3 single pixels, each of them belonging to one of the three consecutive neck scintigrams generated 20 min. after $^{99m}TcO_4^-$ administration, 10 min. after ^{99m}Tc-MIBI injection and 120 min. after ^{99m}Tc-MIBI injection, respectively. Those scintigrams were aligned which each other according to the same vertical and horizontal co-ordinates. The training patterns were obtained from 25 patients by searching for maximum count numbers within small ROIs drawn in selected scintigraphic areas, arbitrarily classified and coded in a numerical scale. In 10 pts the results of ANN simulation were compared with those obtained by common conventional assessment of two radionuclide parathyroid examinations: subtraction method and ^{99m}Tc-MIBI double-phase imaging.

Results: The training patterns processed by the neural network showed a close relationship with the results of visual assessment of original neck scintigrams, with R square coefficient $R^2 = 0.717$, and standard error equal to 0.243. Similar comparison between original data and results of multidimensional regression analysis yielded weaker relationship, with $R^2 = 0.543$ and standard error 0.567. Parametric images obtained by the neural network presented regions with homogeneously distributed, relatively high activity, greater than or equal to 750 cts/ /pixel, visualized in areas of confirmed abnormal parathyroid location.

In all 10 patients with suspected parathyroid adenoma results obtained by ANN simulation agreed with those by conventional methods. In five of these cases no parathyroid abnormalities were found. In the remaining 5 subjects results of both approaches were positive but the abnormalities were depicted more distinctly and visualised more clearly in parametric images received by ANN than in original scans.

Conclusions: Application of trained ANN enables objective and quantitative detection and localisation of parathyroid adenoma and is a good alternative for conventional radionuclide imaging procedures used in diagnosing parathyroid abnormality.

Including in neural network simulation not only scintigraphic data, but also clinical symptoms and/or some other indicators of parathyroid abnormality, parathormone level first of all, should be a next step in developing a procedure for assessing parathyroid abnormality, of high diagnostic accuracy.

Key words: parathyroid adenoma, artificial neural networks, parametric image

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Introduction

A variety of radionuclide methods of abnormal parathyroid glands imaging have been described [1–3] and their value has been confirmed intraoperatively [4] Among those methods two procedures are the most common: ^{99m}Tc-MIBI/^{99m}Tc pertechnetate subtraction scintigraphy and ^{99m}Tc-MIBI double-phase imaging, with estimation of MIBI wash-out rate. A wide variation in the sensitivity and specificity of each of the above procedures exists between various reports but a consistent finding is that the sensitivity of detecting primary parathyroid adenoma is much higher than that of hyperplastic gland. The reason for the differences in observed sensitivities is unclear, but the scan interpretation may be considered an important factor [4]. Because of those differences and not always overlapping results of both examinations, subtraction scintigraphy and MIBI double-phase imaging are by some authors regarded not as alternatives but as complementary techniques, yielding the best evaluation of parathyroid gland if performed conjointly [2].

By such an approach it seems reasonable to substitute the visual assessment of neck scintigrams and semiquantitative measurement of MIBI wash-out rate with single common procedure. Hence, it seems justified to look for a new method which might improve the parathyroid diagnosis with radionuclides.

Application of Artificial Neural Network (ANN) to this purpose may be considered a good solution. It may be presumed that evaluation of $^{99m}TcO_4^-$ neck images combined with that of early and delayed ^{99m}Tc-MIBI images by means of Artificial Neural Network may become a valuable tool in diagnosing parathyroid pathology. To our knowledge such procedure was not described as yet.

The interest in neural network simulation started in 1943 when the mathematical model of neuron activity was described for the first time by McCulloch and Pitss [5], but most of the advanced neural network algorithms were developed in early eighties of the twenty century starting from publication by Hopfield [6]. A neural network is a set of simple processing units with structure similar to brain, which can learn to generalise, cluster, classify and organise the input data [7, 8]. The most important common features of ANN used as an analytical technique are abilities to find hidden relations between various phenomena and to recognise shape and texture patterns of graphical forms, as well as the non-linearity of signal processing, similar to that occurring in biological processes. Additionally, neural networks are able to model specific characteristic of a given phenomenon that cannot be obtained with any explicit mathematical formula [7, 8]. All the above advantages make those methods suitable for digital image evaluation, particularly in nuclear medicine. The aim of this study was the application of the Artificial Neural Network (ANN) simulated by the computer to detection and localisation of pathologic parathyroid tissue, based on the data obtained from the planar scintigraphic images.

Material and methods

The study was based on an assumption that some latent specific relations exist between activities within regions of thyroid gland, parathyroid adenoma, and background, arbitrarily selected in the three corresponding neck images: $^{99m}TcO_4^-$ peretechnate image, ^{99m}Tc-MIBI early image and ^{99m}Tc-MIBI delayed (wash out) image. The examinations were performed using two-day protocol. On the first day the scintigraphic image was obtained 20 min. after *iv* injection of $^{99m}TcO_4^-$. On the second day ^{99m}Tc-MIBI was administered intravenously and 2 scintigrams were registered — first

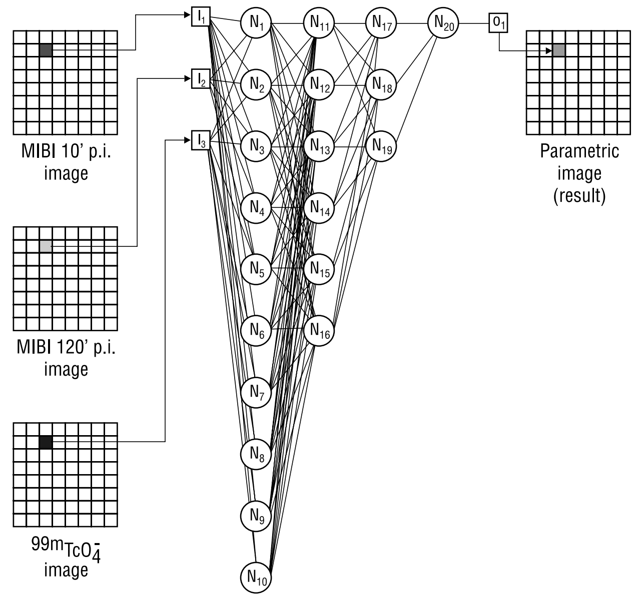

Figure 1. Construction of a parametric image from the three original neck scintigrams.

of them 20 min. after injection; the second one — 120 min. after injection. All examinations were performed using small field of view gamma camera Picker CX-250s, equipped with high resolution, low energy collimator. For the $^{99m}TcO_4^-$ scintigraphy 200 kcts/image were collected. Both MIBI scans were obtained with preset time mode, using 10 min/image. In all examinations the acquired data were collected in 128 $\times$ 128 computer matrix (pixel size 1.78 mm). After termination of acquisition, the scintigrams were converted into 64 $\times$ 64 matrix to perform the neural network processing.

For the above processing, a network structure was created automatically by an evolutionary optimizer procedure, using standard feed-forward, back-propagation and non-linear sigmoid transfer function (Fig. 1). The obtained network structure included 3 input nodes, sets of 10, 6 and 3 neurons, each of them in a corresponding hidden layer and 1 output node. Connections between neurons have been fixed with initially randomised weights. Each neuronal output (O_n) was calculated according to the following formula:

$$O_n = F(\sum_k J_k \times W_{kn})$$

where:

J_κ — neuronal inputs,

k — number of inputs,

W_{kn} — the neurons weights initially set to random values from 0 to 1,

F — the sigmoid activation function: $1/\{1 + Exp[-4.5*(x-0.5)]\}$.

The neural network data processing was performed in a single pixel of each of the 3 above scintigraphic images simultaneously, each of those pixels of the same location (x_i , y_i) in the computer matrix. For that purpose the scintigrams were aligned with each other — translated and rotated if necessary — according to the same vertical and horizontal co-ordinates. This procedure was supported by topographic information, yielded by location of suprasternal notch and salivary glands. By that alignment an excellent agreement was obtained between all images, as regards shape, size and location of regions selected for thyroid, parathyroid gland and background, respectively.

The training patterns were obtained from 25 patients by searching maximum count numbers within small 5 × 5 pixels ROIs drawn in arbitrarily selected and classified scintigraphic areas coded in the following numerical scale: 1 — visually detectable parathyroid adenoma, 0.5 — probable parathyroid adenoma, 0 — background and/or outside body area and –1 — thyroid gland. In those training patterns count numbers in all areas were expressed as a fraction of maximum activity within thyroid region.

The trained network applied to process 3 acquired neck scintigrams resulted in values ranging from –1 to +1 on the network output of each pixel (x_i, y_i). Those numerical data were used to constitute a parametric image. In this procedure the negative values were replaced with 0. Then the data were multiplied by 1000 and converted into an integer which made them possible to be presented in form of a widely accepted interfile format. The obtained parametric images were smoothed and presented with the cut-off window threshold set on 50%. A parathyroid adenoma was diagnosed when a circular region with homogeneously distributed activity equal to or higher than 750 cts/pixel was visualised in the typical location. Additionally, the obtained training patterns were analysed by multidimensional regression analysis and the results were compared with those received by the neural network. The ANN simulation was employed in 10 subjects with suspected parathyroid adenoma, including 2 men and 8 women, aged 20––68 years, on average 42.3 years. The obtained results were compared with those of conventional evaluation of both radionuclide procedures applied in the study, *i.e.* the subtraction technique and the ^{99m}Tc MIBI double-phase imaging. For that comparison only those neck scintigrams were used which were assessed in consensus by two independent observers.

Results

It was found that the training patterns processed by the neural network showed a close relationship with the results of visual assessment of original neck scintigrams, with R square coefficient $R^2 = 0.717$, and standard error equal to 0.243 (Fig. 2). Similar comparison performed between original data and results of multidimensional regression analysis yielded weaker relationship, with $R^2 = 0.543$ and standard error 0.567 (Fig. 3).

The above data indicate that ANN processing gave better results than parametric images generated as a linear combination of the 3 original neck scintigrams.

Parametric images obtained by the neural network presented regions with homogeneously distributed, relatively high activity, greater than or equal to 750 cts/pixel, visualized in areas of confirmed abnormal parathyroid location. Homogenous regions with 500–750 cts/pixel were classified as probable parathyroid. However, a high activity noise greater than 500 cts/pixel but with different distribution pattern from that of the parathyroid activity was also observed in those images.

In all 10 patients with suspected parathyroid adenoma results obtained by ANN simulation agreed with those by conventional methods. In five of these cases no parathyroid abnormalities were found (Fig. 4). In the remaining 5 subjects results of both approaches were positive but the abnormalities were depicted more distinctly and visualised more clearly in parametric images received by ANN than in original scans. (Fig. 5 and 6).

Discussion

Radionuclide evaluation based on only visual assessment of scintigraphic images is strongly dependent on individual experience of the investigator and for that reason is commonly regarded as non-sufficiently reliable. Hence, various methods are pro-

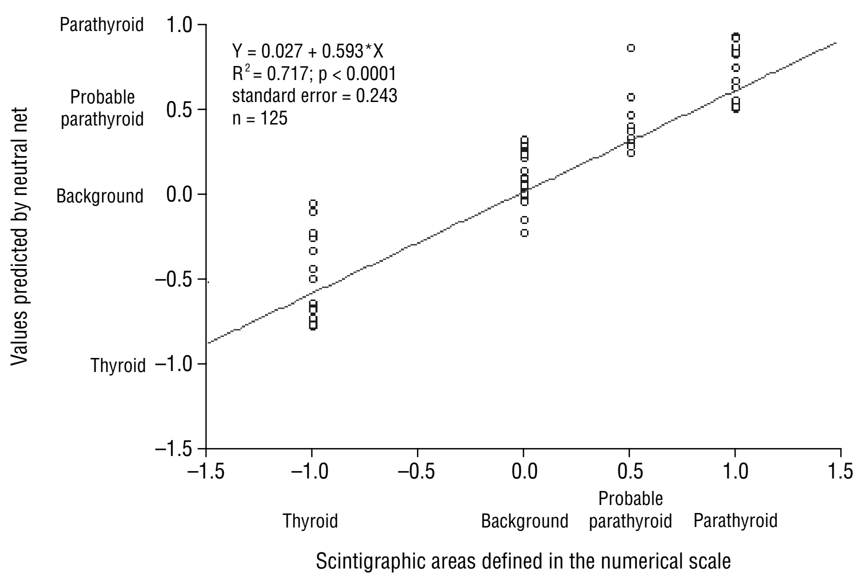

Figure 2. Relationship between values used to classify scintigraphic regions and data obtained from learning patterns processed by the neural net.

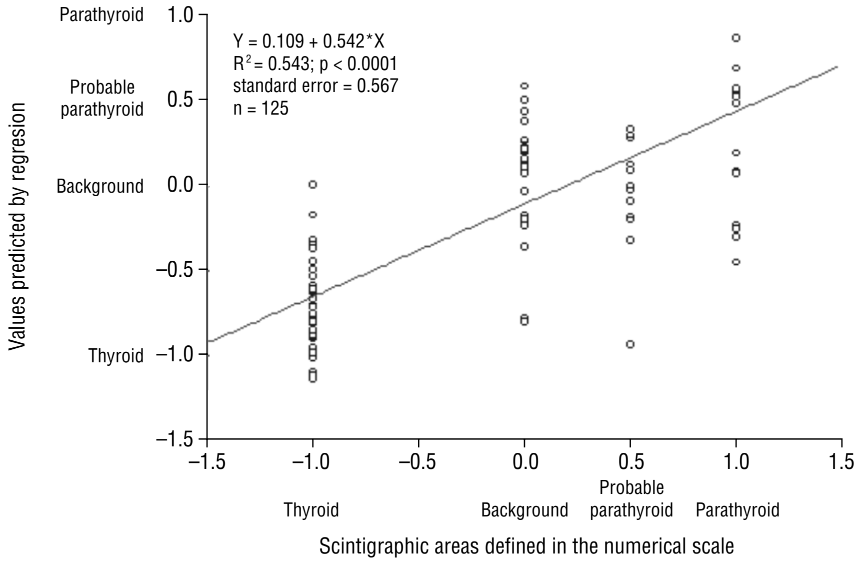

Figure 3. Relationship between values used to classify scintigraphic regions and data obtained from multidimensional linear regression of learning pattern.

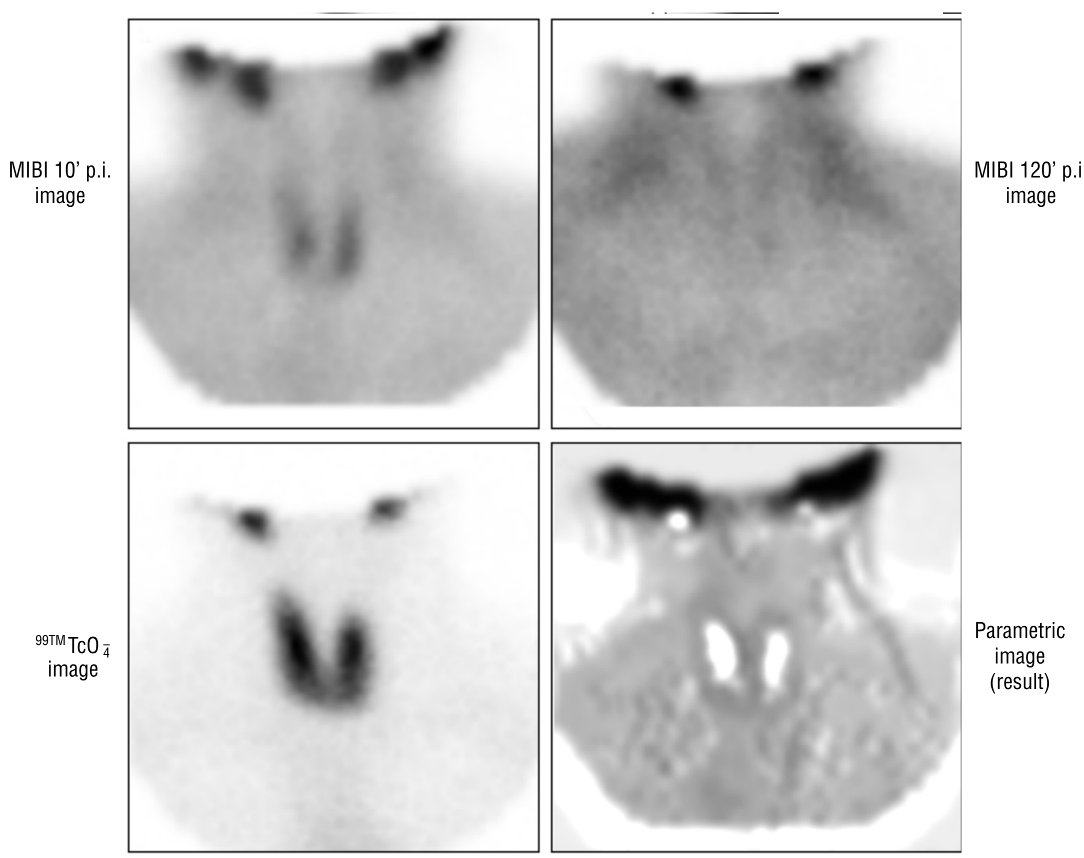

Figure 4. Planar neck scintigrams and the parametric image generated by ANN in a patient without parathyroid adenoma.

posed to quantify the results and make them objective. Among those methods the neural network simulation is of special importance. A trained neural networks are known as a efficient classification tools [9] and are proposed in a wide range of tasks, including assessment of digital images [7, 10]. In nuclear medicine artificial intelligence simulated by the computer has been so far not very commonly applied and usually limited only to the scientific applications. Its main domain has been the image processing in cardiac examinations, myocardial perfusion studies first of all [7, 11–13]. Besides, ANN has been used in evaluation of brain perfu-

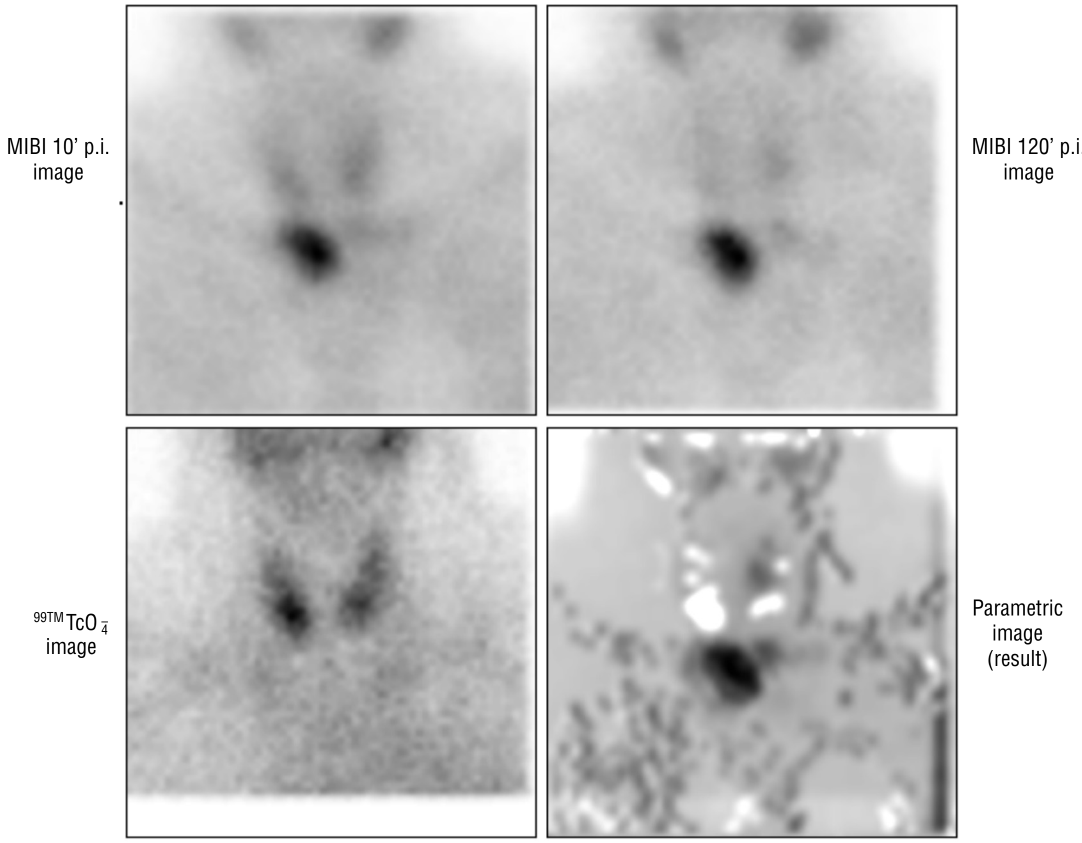

Figure 5. Planar neck scintigrams and the parametric image generated by ANN in a patient with parathyroid adenoma.

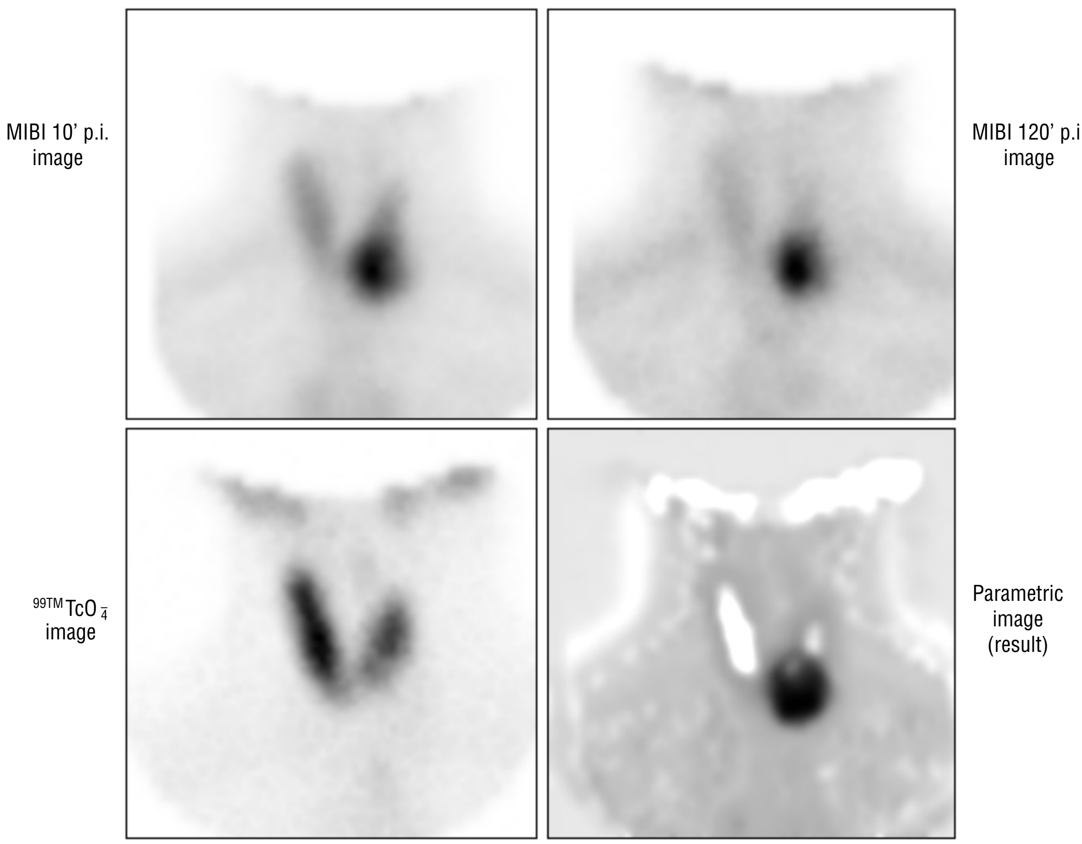

Figure 6. Planar neck scintigrams and the parametric image generated by ANN in a patient with parathyroid adenoma.

sion [9, 14], kidney function [15], diffuse parenchymal liver diseases [16], and lung ventilation and perfusion, especially in patients with suspected pulmonary embolism [10]. Neural networks may be also helpful in computer-assisted diagnosis of various pathologic conditions [17], by SPECT data reconstruction [18] or as a cross talk scatter correction method [19].

It may be presumed that ANN may be useful in a variety of other nuclear medicine procedures, among them in evaluation of parathyroid imaging. To our knowledge, application of ANN to parathyroid gland scintigraphy was not described in the literature as yet. The most common procedures for parathyroid radionuclide imaging, i.e. ^{99m}Tc-MIBI/^{99m}Tc pertechnetate subtraction scintigraphy and ^{99m}Tc-MIBI double-phase imaging, with estimation of MIBI wash-out rate are by some authors regarded not as alternatives, but as complementary techniques, yielding the best evaluation of parathyroid gland if performed conjointly. By such an approach it seems reasonable to substitute the visual assessment of neck scintigrams and semiquantitative evaluation of MIBI wash-out rate with a single, common procedure. Application to that purpose ANN, which yields quantification of the results, makes them more objective and enables them to be presented in form of parametric images, was considered a reasonable solution, leading to a better detection and localisation of a pathologic parathyroid tissue.

Multidimensional linear regression might be regarded as an alternative to ANN. However, it was found that this method revealed only relatively weak interrelationships between training patterns based on cts numbers in selected pixels of the 3 corresponding neck scintigrams and output values coded in the described scale. This finding suggests that ANN processing gives results superior to the parametric images generated as a linear combination of the 3 original scintigrams.

The feed-forward, trained with back-propagation and non-linear neural network type which was chosen in the described method for parathyroid evaluation, is characterised by stability and repeatability of output results. The network of that type was also most frequently used for evaluation of scintigrams in the above mentioned applications in the nuclear medicine [9, 10, 13, 19]. Such networks usually operate on a set of input data of limited quantity which is processed in one step of network simulation, what means that the network may be equipped, for example, with 18, 24 or 30 inputs [7, 10, 13]. That limitation in quantity to few dozens [9, 19] of neural net inputs usually results in data reduction obtained by dividing image into several regions [7], averaging pixel count numbers, processing only a part of the scintigram, as well as two-dimensional Fourier [11, 13] or velvet components analysis.

In this study one step of data processing was used to classify relations between count values in sets of only 3 pixels in 3 corresponding images. In this way the proposed algorithm operates on minimum input data which are not dependent on local activity texture, shapes of thyroid and parathyroid glands nor locations of both glands areas which cannot be clearly defined. For the same reason it is not necessary to use any of the standard thyroid templates in computer matrix as it was previously proposed for lungs [10].

Application of arbitrarily assigned logical values to the input data in training patters is a typical procedure commonly used to differentiate between various organs and/or degrees of pathology, similar to the proposed earlier four-grade scale of abnormalities in myocardial bull's-eye images [12] or two-grade scale ("0" or "1") in detection of pulmonary embolism [10]. The proposed method contains a simplified procedure for area coding with various values for different region types, and with rejection of salivary glands activities usually registered at the edge of the image and visualised in delayed MIBI images. Salivary glands, if preserved in the training, would provide radioactivity patterns not connected with parathyroid abnormalities thus leading to erroneous results.

In the described method parametric images consisted of pixel count values ranged from 0 to 1000. For that reason they were smoothed, because it was necessary to decrease noise effects and to eliminate singular pixels outside patathyroid regions which showed relatively high activity. Besides, smoothing made the detected parathyroid adenoma regions more regular-shaped, and with more homogenous activity distribution.

Arbitrarily introduced grading scale in training patterns resulted in appearing areas of abnormal parathyroid tissue as regions with the highest cts/pixel values. Application of 50% cut-off level revealed regions with activities ranging 750–1000 cts/pixel, which were identified as parathyroid adenomas if located outside salivary glands.

Based on the obtained results it may be stated that the application of trained ANN enables objective and quantitative detection and localisation of parathyroid adenoma. Hence, that method seems to be a good alternative for conventional radionuclide imaging procedures used in diagnosing parathyroid abnormality. However, the value of that method should be confirmed in further studies, on larger study population. It may be also presumed that including in neural network simulation not only scintigraphic data, but also clinical symptoms and/or some other indicators of parathyroid abnormality, parathormone level first of all, may be a next step of significant importance in developing a procedure of high diagnostic accuracy.

Conclusions

Application of trained ANN enables objective and quantitative detection and localisation of parathyroid adenoma and is a good alternative for conventional radionuclide imaging evaluation procedures used in diagnosing parathyroid abnormality.

Including in neural network stimulation not only scintigraphic data, but also clinical symptoms and/or some other indicators of parathyroid abnormality, parathormone level first of all, should be a next step in developing a procedure for assessing parathyroid abnormality with high diagnostic accuracy.

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