

# Analysis of Midbrain Area Echogenicity in Diagnostic Transcranial Ultrasound Images

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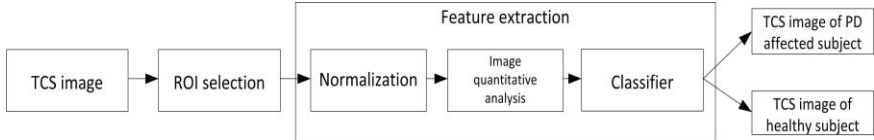
**Introduction.** Parkinson's disease (PD) is the most common neurodegenerative disease. The incidence of PD is about 0.3% of the whole population in industrialized countries [1]. At this moment not all Parkinsonism forms are diagnosed properly. Subjective inspection of clinical symptoms performed by physician is the most popular used method for PD detection [2]. In such way early diagnosis of PD becomes impossible, because clinical symptoms appear then substantial parts of substantia nigra (SN) neurons in the brain stem are irreparably damaged. It is very important to diagnose PD at a very early stage because the symptoms of PD can be alleviated by the administration of drugs. Transcranial B-mode sonography (TCS) proposed by Becker et al. [3] in 1995 could be used for this purpose. It was demonstrated that TCS can be applied as a diagnostic technique for supporting the clinical diagnosis of PD. SN appears hyperechogenic (increment of signal intensity and size of the area) in TCS images in about 90 % of patients with PD, despite its normal appearance on MRI or CT scans [4] and serves as main biomarker in ultrasound based PD diagnostics [5, 6]. Authors [7] recommended to diagnose neurological disorder, including PD, when the size of SN area exceeds 0.20 cm<sup>2</sup>.

Ultrasonography is quick to do, relatively cheap and harmless to patients, but one of the main drawbacks of TCS examination is a poor image quality [8]. The neurological evaluation of TCS images is quite subjective, because the physician does it by regarding anatomical knowledge and following own intuition. In recent years, researchers are trying to discover an effective TCS image analysis method which would help physicians to diagnose the PD.

The aim of this paper is to present the proposed method for quantitative analysis of TCS images based on statistical moments.

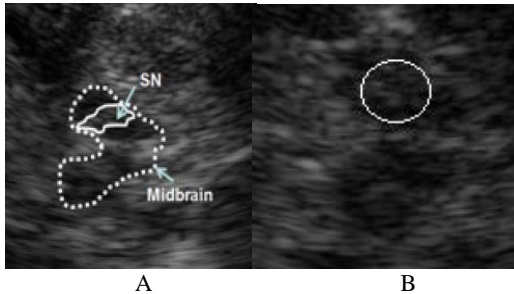
**Materials and Methods.** One hundred and eight subjects were examined during this study, 60 of them had clinical PD diagnosis and another 48 were healthy patients. The TCS images were carried out by the same experienced sonographer in Neurology clinic at Lithuanian University of Health Sciences. The scanning was performed using PA2-5 wide band phased array sector transducer ( $f_0=1.4$  MHz, band with: 1.3 – 4 MHz, footprint 20×14 mm (128 elements)) driven by the ultrasound scanner *Voluson 730* which was manufactured in *GE Healthcare* (Austria). The sonographer performed scanning at 18.5 cm depth and adapted scanning parameters (TGC curve, gain, zoom), in order to get the best possible image.

We proposed to use automated algorithm (see scheme Fig. 1) for the image based recognition of PD affected and healthy subjects. First of all, the TCS images were prepared for analysis by selecting the region of interested (ROI). The upper half of midbrain (closer to the scanning probe) served as ROI in our study. The upper half of midbrain was selected, because in the lower half of midbrain may result loss of contrast, resolution and SNR resulting from the increased scanning depth. Fig. 2 (A) presents an example of TCS image with manually delineated structures of interest.



**Fig. 1.** The scheme applied for TCS images analysis

In this study selection of ROI was performed by manually masking an image with constant geometric shape circle (see Fig. 2 B). The center of circle was interactively selected in TCS images.



**Fig. 2.** The midbrain segment with outlined SN area in diagnostic TCS image (A), and the ROI selection by using circle example (B).

The set of TCS images (600×800, BMP image data format) were acquired using two different zooming levels (sizes of pixel: 0.421, and 0.33 mm). The circles were set respectively to the scale of a pixel: in ex. if the size of pixel was 0.421 mm, the investigated diameters of circle were 12, 14 and 16 mm, and it was rescaled respectively to size of the pixel. In the second stage, amplitudes of all TCS images were normalized in respect of median of ROI pixels. Normalization was applied with aim to compensate scanning settings adjusted by scanning performing physician (such as gain, time gain compensation etc.) influence to amplitude.

Thirdly, the analysis of TCS images was performed computing nine statistical moments of intensity levels in the ROI: mean, range, skewness, kurtosis, variance, standard deviation, entropy, first and second Hu moments [9]. 511 combinations were obtained from chosen nine statistical moments by

combinatorial principles. Finally, the moments were used for classification task. The classifier was based on Mahalanobis [10] distance (see Formula (1)). Mahalanobis distance is defined as distance between two feature vectors (sample and training)  $\mathbf{x}=(x_1, \dots, x_p)^T$  and  $\mathbf{y}=(y_1, \dots, y_p)^T$  in the p-dimensional space  $R^p$ :

$$d_s(\mathbf{x}, \mathbf{y}) = \sqrt{(\mathbf{x} - \boldsymbol{\mu}_y)^T \mathbf{S}^{-1} (\mathbf{x} - \boldsymbol{\mu}_y)} \quad (1)$$

$\mathbf{S}$  – covariance matrix of training set,  $\boldsymbol{\mu}_y$  – mean training feature vector.

All TCS images were separated into two equal groups. The first one was used like sample set and the second – training set. The sample set consisted of 54 images (30 PD affected and 24 healthy patients) and the training set consist of remained 54 images. Efficiency of classification was evaluated by classification rate, sensitivity and specificity.

**Results.** The results of classification of TCS images using statistical moments and varying diameter of circles are presented in Table 1.

**Table 1.** The results of TCS images classification

Diameters of ROI circle, mm	Combination	CR, %	SENS, %	SPEC, %
12 and 15.4	Entropy, first Hu moment	74.07	70.00	79.17
	Entropy, first and second Hu moments		76.67	70.83
14 and 17.9	Skewness, kurtosis, first Hu moment	75.93	96.67	50.00
	First Hu moment		90.00	58.33
16 and 20.48	Entropy, first and second Hu moments	74.07	80.00	66.67
	First Hu moment		90.00	54.17

CR – classification rate; SENS – sensitivity; SPEC – specificity.

**Discussion and Conclusions.** In the present research analysis of TCS images was performed with the aim to separate images obtained examining PD affected and healthy subjects. The best classification rate (75.93%) was obtained when ROI was extracted using 14 mm diameter circle. After increment of diameters of circles till 16 and 20.48 mm, the result of classification rate didn't become better. The reason of this result could be the fact that more pixels (what are outside segment of SN) with higher intensity values fell inside to increased ROI. In all study and all tried ROI diameters, the most dominant characteristics were first and second Hu moments. Less dominant characteristics were entropy, skewness and kurtosis. In summary it could be noticed that the intensity of pixels representing hyperechogenic SN region in TCS images affect the statistical moments. The obtained classification results weren't good enough that would be used in practice, but viable and could serve as a decision support for physician. The proposed method could be improved by adding a set of indicators providing information about spectral properties of ROI.

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The aim of this paper is to evaluate statistical moments potentiality for separation of transcranial sonography images obtained evaluating healthy (48 subjects) and Parkinson's disease affected (60 subjects) patients. Closer to scanning probe upper half of midbrain with substantia nigra area was selected as region of interest for analysis outlining it manually by the circles with: 12, 14, 16 mm diameters. The transcranial sonography images were analysed with combinations of statistical image features obtained applying 9 statistical moments. All images were classified with Mahalanobis distance based classifier to groups: healthy and PD affected. Efficiency of classification was evaluated with classification rate, sensitivity and specificity.