European Journal of Ophthalmology / Vol. 17 no. 3, 2007 / pp. 287-293

Eyeball muscles' diameters versus volume estimated by numerical image segmentation

A. MAJOS[1], P. GRZELAK[1], W. MŁYNARCZYK[2], L. STEFAŃCZYK[1]

[1]Radiology Department, Medical University of Lodz, Lodz
[2]Department of Microelectronic and Computer Science, Technical University of Lodz, Lodz - Poland

PURPOSE. *To determine the clinical usefulness of the numerical segmentation image technique (NSI) in estimating the volume of extraocular muscles and to compare this value to widely used measurements of single diameters of the muscles.*

METHODS. *Forty-five patients underwent magnetic resonance examinations in 1.5-T scanner. SE T1 sequences in transversal and coronal planes were provided and data were sent to a personal computer, where the degree of exophthalmos, horizontal diameter of medial rectus muscles, and vertical diameter of inferior rectus muscles were determined on the basis of two-dimensional images. The quantity estimation of all eye muscles volumes using NSI application in three-dimensional space was carried out with use of level set segmentation algorithm.*

RESULTS. *A strong correlation between the total eye muscle volume and degree of exophthalmos was determined. The usefulness of measuring single diameters for estimating the muscles' enlargement was confirmed. The difference between a single muscle's volume and its width also was confirmed. Estimates of muscle volume correlate with the degree of exophthalmos more accurately than measurements of single diameters.*

CONCLUSIONS. *The NSI technique is a clinically useful application, providing objective data calculated individually for each orbit. It allows an objective estimation of the pathologic processes leading to exophthalmos and may be especially helpful in monitoring discrete changes in the muscles volume during treatment. (Eur J Ophthalmol 2007; 17: 287-93)*

KEY WORDS. *Computer applications, Exophthalmos, Extraocular muscles, Graves' ophthalmopathy, Volume calculation*

Accepted: December 4, 2006

INTRODUCTION

Exophthalmos classification can be based on clinical criteria or different imaging modalities. Magnetic resonance imaging (MRI) is widely accepted as a method of the highest diagnostic value allowing precise and credible assessment of small orbital structures.

Various protocols of intraorbital structure quantity estimation are used; determination of muscle width is the simplest (1-4). More complex techniques are based on estimating muscle volume, which is considered a more accurate estimate of muscle size (5-11). These are precise and reliable but also time consuming and resource and labor intensive, therefore difficult to perform in everyday clinical practice.

In recent years, computer systems have allowed for the introduction of numerical analysis of medical images. Therefore, it seems possible to create a software application that could calculate the volume of anatomic structures imaged by MRI automatically.

The aim of our study was to determine the clinical usefulness of the numerical segmentation image technique (NSI) application in estimating extraocular muscle volume and to compare those values to widely used measurements of single diameters of the muscles.

Presented at the 22nd annual meeting of the European Society for Magnetic Resonance in Medicine and Biology; Basel, Switzerland; September 15–18, 2005

1120-6721/287-07$15.00/0

MATERIALS AND METHODS

The degree of exophthalmos was determined clinically by Hertel's exophthalmometer. Afterwards, it was defined on the basis of a single MR image obtained in a horizontal plane at the level of eyeball equator in relation to interzygomaticus line, which was carried out between the two most protruding points of the right and left zygomaticus bones (1, 4).

The MRI study

All patients underwent MR examinations in 1.5 T scanner Siemens, Vision+. Transversal sections were positioned parallel to medial rectus and lateral rectus muscles, coronal sections were perpendicular to the optic nerve.

Because of small sizes of intraorbital structures and complex topography of the orbit, 3 mm sections were used (2, 12-14). Parameters for SE T1 diagnostic sequences were as follows: repetition time 450 ms, echo time14 ms, FA 90°, field of view 250 mm, number of layers 15, thickness of layers 3, dis. factor 0.1, matrix 192x512, number of acquisitions 3, time 4 min 22 s.

NSI technique

Data from MR sequences were sent to a personal computer and saved on the workstation hard disc in DICOM format. Images used to estimate volume were characterized by 512x512x14 voxel resolution, at the size of single voxel of 1x1x3 mm.

For the purpose of image processing the open source ITK library (The Insight Software Consortium, The Insight Toolkit [ITK]; http://www.itk.org/) was used. The algorithms employed were cubic spline resampling and Level Set segmentation. For the description of abovementioned algorithms we referred to the ITK library reference manual (ITK Software Guide, Kitware, Inc., Ibanez, Schroeder, Ng, Cates; http://www.itk.org/Itk-SoftwareGuide.pdf).

In the first step of our procedure, the radiologist roughly marked the position of the muscle on an MR image. This operation created a mask image that was further used as an initial condition for the Level Set segmentation algorithm. In the second step both the MRI and the mask images were resampled into 1x1x1 mm isotropic voxel size by cubic spline resampling algorithm. All further processing was done on the resampled MRI and mask images. In the third step both resampled MRI and mask images were input into Level Set segmentation algorithm in order to obtain a segmented image that was refined and provided a more accurate position of the muscle. The radiologist had the opportunity to control the number of iterations of the algorithm and to introduce manual corrections into segmented image. This step essentially classified every voxel of an image into two classes: containing the muscle or not. Finally, the volume of the muscle was estimated by multiplying the number of voxels in the area of the muscle by the volume of one voxel.

The total muscle volume was obtained by adding the separately calculated volumes of all six muscles.

Statistical analysis

Parametric methods of statistical analysis were used because of the large trial size (n>50). The assessment of differences between the mean of analyzed parameters in separate points of the examination (after the confirmation of normal data distribution by Shapiro-Wilk test) with the use of Student *t*-test for independent trials was carried out.

Relations between characteristics were described using the Pearson linear correlation coefficient with the assessment of its significance and linear regression equations. The parameters of linear regression equations were calculated by the smallest squares method.

Participants

Forty-five patients (90 orbits) were qualified into the study: 6 men and 39 women, 19–72 years of age (mean 55 yr). The most frequent indication for MRI examinations was Graves' ophthalmopathy. Others included suspicion of myopia and paranasal sinuses diseases, all without disruption of the bone wall integrity.

The study was approved by the local ethical committee of the Medical University of Lodz (decision nb KBUM/23/04) in accordance with the Declaration of Helsinki.

RESULTS

The degree of the exophthalmos in a study group was determined by Hertel's method as follows: for the right eye: the mean value, 16.998 mm, SD 2.925; for the left

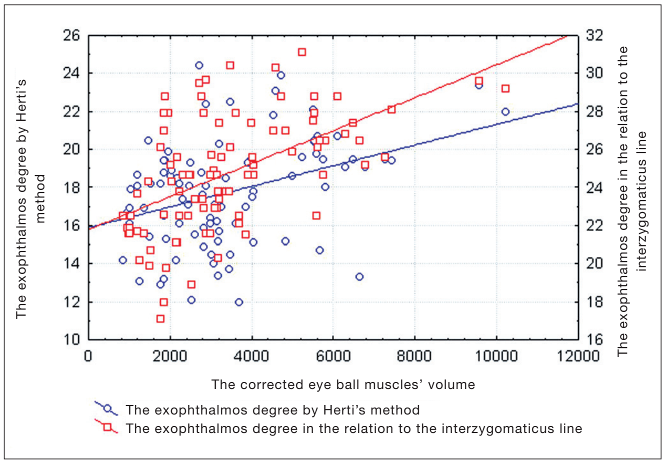


Fig. 1 - *The correlation between the degree of exophthalmos measured by Hertel's method and in relation to the interzygomaticus line and the total muscle volume calculated by the numerical segmentation image technique.*

eye: the mean value, 17.741 mm, SD 2.75.
The degree of the exophthalmos in relation to interzygomaticus line was as follows: for the right eye: the mean value, 22.173 mm, SD 2.908; for the left eye: the mean value, 24.744 mm, SD 3.041.

The eyeball muscles

Strong correlation was established between the total eye muscle volume determined by NSI technique and the exophthalmos degree both measured in Hertel's method and in relation to the interzygomaticus line (Fig. 1 and Tab. I).

The simple measurements

The usefulness of single diameters for estimating the muscle enlargement was confirmed; transverse diameters of MM and vertical of IM correlate significantly with the degree of exophthalmos defined both by Hertel's method as well as according to the zygomaticus line (Figs. 2 and 3 and Tab. II).
In addition, the difference between the muscle volume and single diameters was proved. The muscle volumes do not correlate exactly with single diameter measurements of the same muscles (Figs. 4–7).

DISCUSSION

Simple measurements

The list of parameters proposed in the literature for estimating eye muscle size in computed tomographic (CT) and MR imaging is quite long. One of the most common is an index of the largest width of the chosen muscle given in the absolute value or in relation to the optic nerve width to correct for individual variability (1-4, 15, 16).
Feldon et al measured the maximum width of MM on a single CT section at the level of the optic nerve that was to correlate with the muscle volume (17). Nugent et al presented another method that used a quotient of the largest transversal or longitudinal diameter of a muscle affected by Graves' disease to the normal value in healthy subjects (9). Another proposed parameter was the product of longitudinal and transverse diameter of each muscle (12, 18). The relation of muscle width to the orbits' transverse diameter in different planes was also proposed (17, 19).

TABLE I - THE STATISTICAL VALUES OF CORRELATIONS

	Statistical analysis	Exophthalmos measured by Hertel's method	Exophthalmos measured in relation to the interzygomaticus line
Corrected muscle volume	Linear correlation coefficient	r = 0.376 p = 0.000258	r = 0.543 p = 3.13396 E-08
	Spearman correlation coefficient	R = 0.320 p = 0.00209	R = 0.546 p = 2.61963 E-08
Muscle volume calculated automatically	Linear correlation coefficient	r = 0.357 p = 0.000552	r = 0.511 p = 2.59221 E-07
	Spearman correlation coefficient	R = 0.341 p = 0.00166	R = 0.546 p = 2.61963 E-08

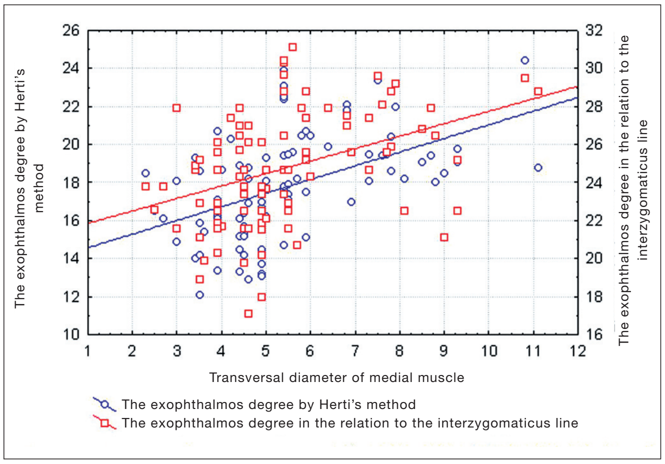


Fig. 2 - *The correlation between the degree of exophthalmos measured by Hertel's method and in relation to the interzygomaticus line and the transversal diameter of medial rectus muscles.*

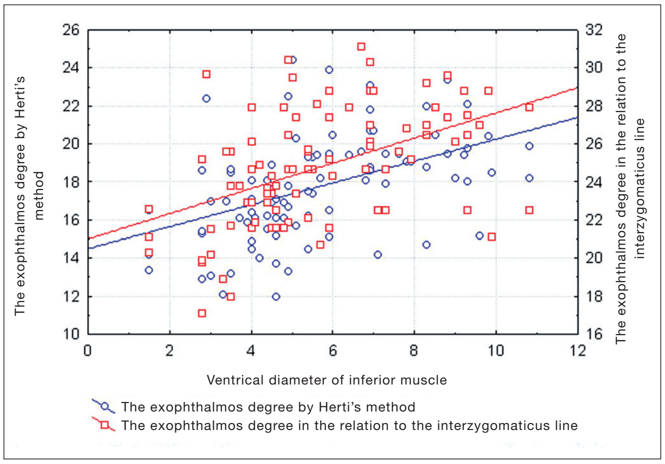


Fig. 3 - *The correlation between the degree of exophthalmos measured by Hertel's method and in relation to the interzygomaticus line and the ventricle diameter of inferior rectus muscles.*

TABLE II - THE STATISTICAL VALUES OF CORRELATIONS

	Statistical analysis	Exophthalmos measured by Hertel's method	Exophthalmos measured in relation to the interzygomaticus line
Transversal diameter of medial muscle	Linear correlation coefficient	r=0.473 p=2.49482 E-06	r=0.389 p=0.000145
	Spearman correlation coefficient	R=0.511 p = 2.63937 E-07	R=0.407 p = 6.71951 E-05
Vertical diameter of inferior muscle	Linear correlation coefficient	r=0.473 p=2.49482 E-06	r=0.479 p = 1.75149 E-06
	Spearman correlation coefficient	R=0.524 p=1.121859 E-07	R=0.509 p=3.02429 E-07

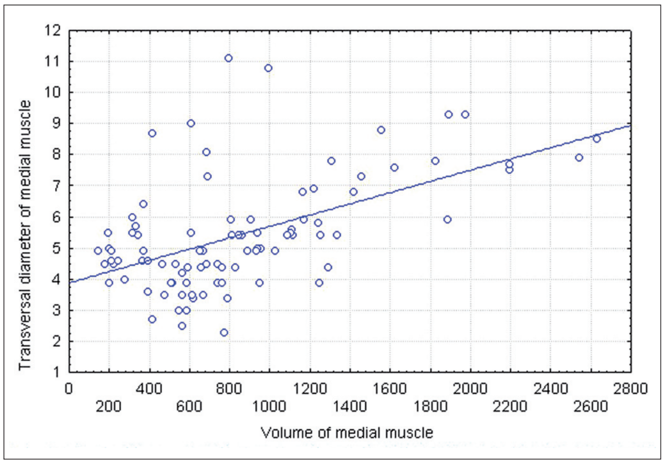


Fig. 4 - *The correlation between the transversal diameter of medial rectus muscles (MM) (y) and the volume of MM (x). Linear correlation coefficient r=0.546337, p=2.55 E-08, and Spearman correlation coefficient R=0.463152, p=4.29 E-06.*

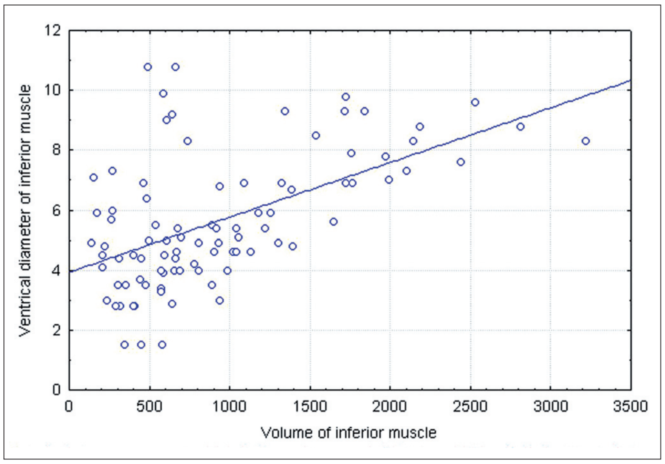
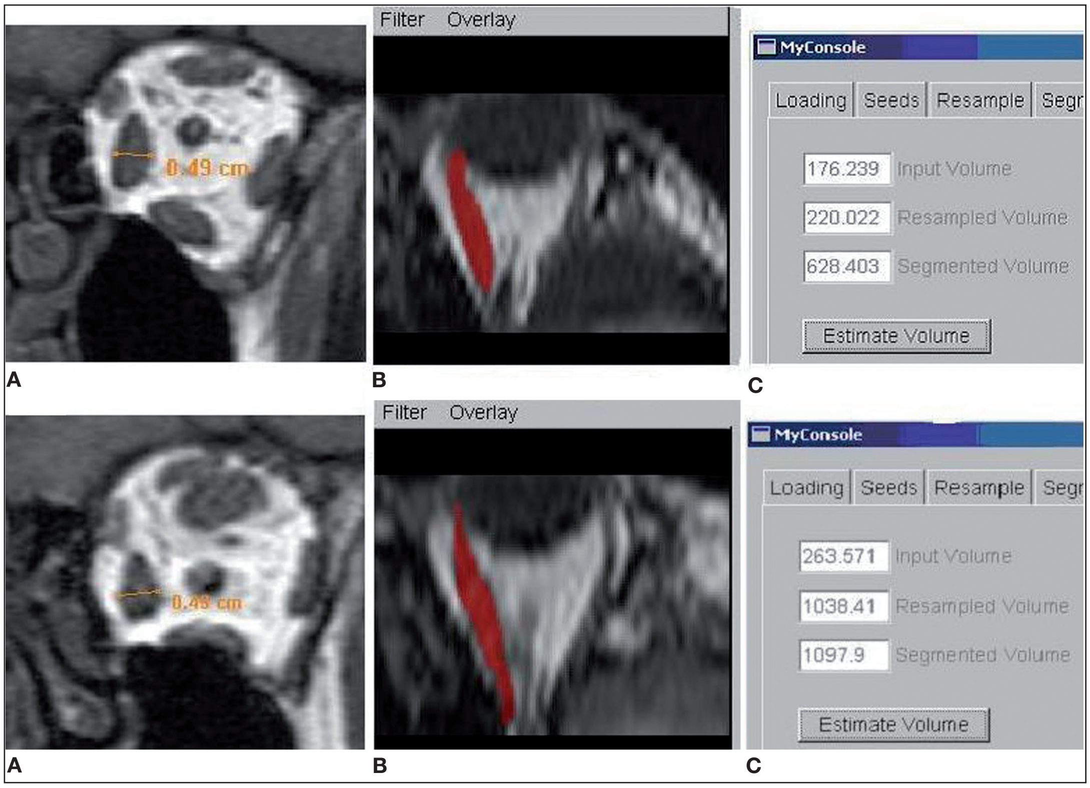


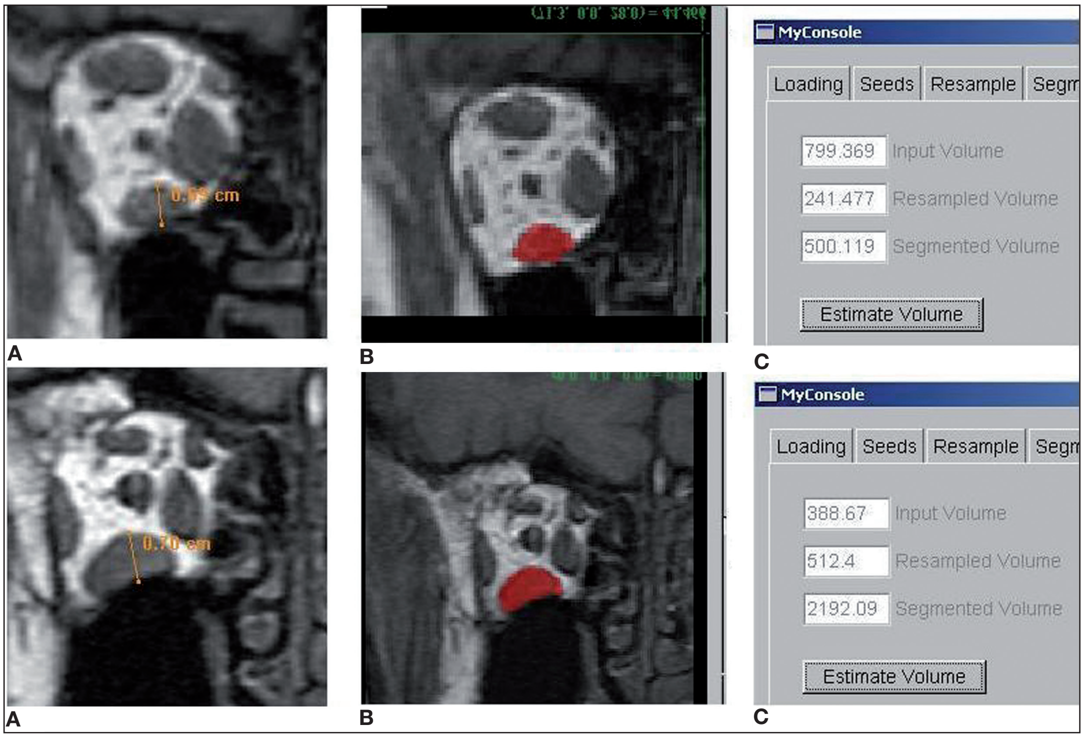
Fig. 5 - *The correlation between the vertical diameter of inferior rectus muscles (IM) (y) and the volume of IM (x). Linear correlation coefficient r=0.518943, p=1.61 E-07 and Spearman correlation coefficient R=0.528118, p=8.82 E-08.*



176.239 Input Volume
220.022 Resampled Volume
628.403 Segmented Volume

263.571 Input Volume
1038.41 Resampled Volume
1097.9 Segmented Volume

Fig. 6 - *An example of two patients with the identical transversal diameters of medial rectus muscles (MM) (4.9 mm) and significantly different volumes of these muscles (**A**) taking the transversal diameter of MM using a DicomWorks application, (**B**) covering an area of interest on the muscle section on MR images in X plane using the numerical segmentation image technique (NSI), and (**C**) the results: segmented volume is the final value calculated by the NSI application, for Patient 1 628.403 mm^3, for Patient 2 1097.9 mm^3.*



799.369 Input Volume
241.477 Resampled Volume
500.119 Segmented Volume

388.67 Input Volume
512.4 Resampled Volume
2192.09 Segmented Volume

Fig. 7 - *An example of two patients with identical vertical diameter of inferior rectus muscles (IM) (6.9–7.0 mm) and significantly different volumes of these muscles (**A**) taking the vertical diameter of IM using a DicomWorks application, (**B**) covering an area of interest on the muscle section on MR images in Z plane using the NSI technique, (**C**) the results: for Patient 1 500.1 19 mm^3, for Patient 2 2192.09 mm^3.*

In our study, the transverse diameter of MM and the horizontal diameter of IM in relation to the optic nerve width were determined as these enlarge the most frequently in the course of Graves' ophthalmopathy. Significant correlations were found between these parameters and the degree of exophthalmos. This observation was consistent with other articles, where similar relationships are reported (2, 9).

Figures 4–7 present correlations between single parameters of chosen muscles and their volume. Although they illustrate the lack of full agreement between these parameters, estimating the degree of muscle enlargement on this basis must be accepted as clinically useful. They correlate significantly with the degree of exophthalmos and can be a source of initial information about muscle enlargement and impact on the eyeball position (3). The most serious limitation of calculations based on single diameters, even if assuming their high exactness, is the lack of absolutely precise criteria for carrying them out. This could complicate the comparison of obtained data not only between different patients but also of the same subject in the course of the disease. The conclusions made about the effectiveness of treatment on such a basis can be controversial.

Volume calculation

MRI technique is widely used for muscle volume estimation. Gorman, Nugent et al, Prummel et al, and Szucs-Farkas et al proposed methods of manual outlining of chosen section areas of muscles as their volume index (8-11). Gupta et al, Tian et al, and Niniaris et al multiplied the sum of section areas covering the whole muscle by the thickness of MRI layers (13, 14, 18). Firbank et al drew out a semiautomated technique of volume estimation based on the muscle segmentation from the MR image, on the basis of the brightness level (6).

Methods of real volume calculation are more precise and objective than estimation of the muscle size on the basis of their single diameters. However, the individual choice of cross sections, subjective criteria for defining muscles borders (especially complex in the vicinity of an orbital apex and near the eyeball attachments), are the source of serious divergences in results among authors. This limits usefulness in everyday radiologic practice as all of them are labor intense and time consuming. In addition, they demand specialist computer software and specific equipment requirements for CT or MRI scanner (12).

The NSI application makes it possible to obtain credible computing results of real volumes for all analyzed intraorbital structures almost automatically and in a relatively short time. The time for calculation for all the six eye muscles was from 3 to 6 minutes, mean value 4 minutes 42 seconds for each orbit.

Our results determined by the NSI application confirmed the strong correlation between the whole extraocular muscle volume and the degree of exophthalmos as is the case in the published literature (3, 6, 11, 13).

These volumes are objective measurements correlating with the current pathophysiologic state of eye muscles. Diagnostic information precisely describing each muscle and therefore its influence on the relocation of other intraorbital structures is highly desirable in the course of therapeutic management, for both the proper choice of treatment as well as assessing its effectiveness. The total volume of all muscles is important for pharmacologic therapy and radiotherapy.

The possibility of changing the contour toleration created in the NSI application as well as including manual alterations greatly extends usefulness of this technique. When heterogeneity of examined anatomic elements exists, the program still works properly: for example, in cases of fat degeneration or fibrosis, as in advanced stages of Graves' ophthalmopathy. It is possible to change the evolution of the contour precisely, even several times, until achieving the exact overlapping of an area of interest on the chosen anatomic element in MR image. Therefore it is possible to use the NSI technique for monitoring intraorbital anatomic structures regardless of any underlying pathophysiologic processes.

CONCLUSIONS

The NSI technique is a clinically useful application, providing objective data calculated individually for each orbit. It is justified to use the measurements of single diameters of the muscles as a source of initial information about muscle enlargement. The NSI technique allows more objective estimation of the pathologic processes leading to exophthalmos; it may be helpful specifically in monitoring discrete changes of muscle volume during treatment.

The authors report no grants, funding support, or proprietary interest.

Reprint requests to:
Agata Majos, MD
Lagiewnicka 143a
91-863 Lodz, Poland
egnys@poczta.onet.pl

REFERENCES

1. Nishikawa M, Yoshimura M, Toyoda N, et al. Correlation orbital muscle changes evaluated by magnetic resonance imaging and thyroid-stimulating antibody in patients with Graves' ophthalmopathy. Acta Endocrinol 1993; 129: 213-9.
2. Ozgen A, Ariyurek M. Normative measurements of orbital structures using CT. AJR Am J Roentgenol 1998; 170: 1093-6.
3. Ozgen A, Alp MN, Ariyurek M, Tutuncu N, Can I, Gunalp I. Quantitative CT of the orbit in Graves' disease. BJR 1999; 72: 757-62.
4. Villadolid MC, Yokohama N, Izumi M, et al. Untreated Graves' disease patients without clinical ophthalmopathy demonstrate a high frequency of extraocular muscle (EOM) enlargement by magnetic resonance. J Clin Endocrinol Metab 1995; 80: 2830-3.
5. Carlow TJ, Deooer MH, Orrison WW. MR of extraocular muscles in chronic progressive external ophthalmoplegia. AJNR Am J Neuroradiol 1998; 19: 95-9.
6. Firbank MJ, Harrison RM, Williams ED, Coulthard A. Measuring extraocular muscle volume using dynamic contours. Magn Reson Imaging 2001; 19: 257-65.
7. Forbes G, Gerhing DG, Gorman CA, Brennan MD, Jackson IT. Volume measurements of normal orbital structures by computed tomographic analysis. AJR Am J Roentgenol 1985; 145: 149-54.
8. Gorman CA. The measurements of change in Graves' ophthalmopathy. Thyroid 1998; 8: 539-43.
9. Nugent RA, Belkin RI, Neigel JM, et al. Graves' orbitopathy: 6. Correlation of CT and clinical findings. Radiology 1990; 177: 675-82.
10. Prummel M, Gerding MN, Zonneveld FW, Wiersinga WM. The usefulness of quantitative orbital magnetic resonance imaging in Graves' ophthalmopathy. Clin Endocrinol 2001; 54: 205-9.
11. Szucs-Farkas Z, Toto J, Balazs E, et al. Using morphologic parameters of extraocular muscles for diagnosis and follow-up of Graves` ophthalmopathy: diameters, areas, or values? AJR Am J Roentgenol 2002; 179: 1005-10.
12. Aydin K, Guven K, Sencer S, Cikim A, Gul N, Minareci O. A new MRI method for the quantitative evaluation of extraocular muscle size in thyroid ophthalmopathy. Neuroradiology 2003; 5: 184-7.
13. Gupta MK, Perl J, Beham R, et al. Effect of 131 iodine therapy on the course of Graves' ophthalmopathy: a quantitative analysis of extraocular muscle volumes using orbital magnetic resonance imaging. Thyroid 2001; 11: 959-65.
14. Tian S, Nishida Y, Isberg B, Lennerstrand G. MRI measurements of normal extraocular muscles and other orbital structures. Graefes Arch Clin Exp Ophthalmol 2000; 238: 393-404.
15. Ozgen A, Aydingoz U. Normative measurements of orbital structures using MRI. J Comput Assist Tomogr 2000; 24: 493-6.
16. Trokel SL, Jakobiec FA. Correlation of CT scanning and pathologic features of ophthalmic Graves' disease. Ophthalmology 1981; 88: 553-64.
17. Feldon SE, Celina P, Saundra K, Muramatsu MS, Weiner JM. Quantitative computed tomography of Graves' ophthalmopathy. Extraocular muscle and orbital fat in development of optic neuropathy. Arch Ophthalmol 1985; 103: 213-5.
18. Niniaris N, Hutwitz J, Chen JC. Correlation between computed tomography and magnetic resonance imaging in Graves' ophthalmopathy. Can J Ophthalmol 1994; 29: 9-12.
19. So NMC, Lam WWM, Cheng G, Metreweli C, Lam D. Assessment of optic nerve compression in Graves' ophthalmopathy. Acta Radiol 2000; 41: 559-61.