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Assessment of the volume of intraorbital structures using the numerical segmentation image technique (NSI): the extraocular muscles

Ocena objętości struktur wewnątrzoczodołowych przy zastosowaniu techniki cyfrowej segmentacji obrazów (NSI): mięśnie zewnątrzgałkowe

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Abstract

Introduction: In recent years the use of computer systems has allowed numerical analysis of medical images to be introduced and has speeded up the conversion of numerical data into clinically valuable information. The creation of a software application that could almost automatically calculate the volume of anatomical structures imaged by MRI has seemed possible. The aim of our study was to determine the clinical usefulness of an numerical segmentation image technique (NSI) software application in estimating the volume of extraocular muscles.
Material and methods: The study group was formed of 45 patients (90 orbits). All the patients underwent MRI examinations of the orbits by a 1.5 T scanner using a head coil. The degree of exophthalmos was determined clinically and radiologically in relation to the interzygomaticus line. The quantitative assessment of all eye muscles was carried out using the NSI application, a new software program introduced by the authors.
Results: A close correlation between muscle volume and the degree of exophthalmos was revealed and confirmed by statistical analysis ($r = 0.543$, $p = 3.13396E-08$) in agreement with other papers.
Conclusions: The NSI software program is an application which offers a reliable and precise estimation of eye muscle volume. It is therefore useful in the diagnosis of the pathological processes leading to exophthalmos. It has special clinical value for monitoring discrete volume changes of muscles during treatment.

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Key words: *exophthalmos, volume calculation, extraocular muscles, computer applications*

Streszczenie

Wstęp: Stosowane współcześnie układy obliczeniowe i ich oprogramowanie pozwalają na analizę obrazów medycznych i znaczne przyspieszenie przetwarzania danych liczbowych w informacje użyteczne klinicznie. Realne jest stworzenie aplikacji automatycznie obliczających objętość struktur obrazowanych w badaniu MR. Celem pracy była ocena przydatności klinicznej metody cyfrowej segmentacji objętościowej (NSI, *numerical segmentation image*) w określaniu objętości mięśni wewnątrzgałkowych.
Materiał i metody: Do badania włączono 45 chorych (90 oczodołów). Wszyscy pacjenci zostali podani badaniu metodą rezonansu magnetycznego oczodołów w skanerze 1,5 T przy użyciu cewki głowowej. Stopień wytrzeszczu określono klinicznie, jak i radiologicznie w stosunku do linii międzyjarzmowej. Ocenę ilościową wszystkich mięśni zewnątrzgałkowych przeprowadzono przy użyciu aplikacji NSI, stanowiącej nowy program komputerowy opracowany przez autorów.
Wyniki: Stwierdzono silną korelację statystyczną pomiędzy objętością mięśni gałkoruchowych a stopniem wytrzeszczu ($r = 0,543$, $p = 3,13396E-08$), co jest zgodne z innymi doniesieniami.
Wnioski: Program NSI jest aplikacją umożliwiającą wiarygodną i precyzyjną ocenę objętości mięśni zewnątrzgałkowych. Jest tym samym użyteczny w diagnozowaniu procesów patologicznych prowadzących do wytrzeszczu. Technika NSI może być przydatna zwłaszcza w monitorowaniu dyskretnych zmian objętości mięśni w trakcie leczenia.

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Słowa kluczowe: *wytrzeszcz, obliczanie objętości, mięśnie zewnątrzgałkowe, programy komputerowe*

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Introduction

Classification of exophthalmos may be based on clinical criteria such as measurements taken by Hertel's exophthalmometer or the use of different kinds of imaging modalities. Magnetic resonance imaging (MRI) is widely accepted as a method of the highest diagnostic value, enabling assessment of small orbital structures to be made precisely and reliably in any chosen plane.

Various protocols are currently in use for the quantitative evaluation of intraorbital structures. Determination of muscle width is the simplest of these [1–4]. More complex techniques are based on estimating muscle volume, providing the most objective morphological information concerning the size of the muscles [5–11]. These techniques are precise and reliable but also time-consuming and labour-intensive and are therefore difficult to adopt in everyday clinical practice.

In recent years, the use of computer systems has allowed for the introduction of numerical analysis of medical images and has speeded up the conversion of numerical data into clinically valuable information. It therefore seemed possible to create a software application that could calculate the volume of anatomical structures imaged by MRI almost automatically.

The objective of our work was to provide such a program specifically for anatomical elements located in the orbital space and to determine the clinical usefulness of the numerical segmentation image technique (NSI) software application in estimating extraocular muscle volume.

Materials and methods

A total of 45 patients (90 orbits) were evaluated in the study, 6 men and 39 women aged between 19 and 72 years (mean age 55 years). Patients in whom pathological processes, post-traumatic effects or surgical intervention had disrupted the integrity of the orbit bone walls were excluded from the study. All underwent MRI examination of the orbits. Table I contains detailed information about the clinical diagnosis and degree of exophthalmos.

All subjects were fully informed as to the nature of the study and all gave their consent to participation in accordance with the Helsinki Declaration. The study was approved by the Local Ethical Committee of the Medical University of Łódź (decision no KBUM/23/04).

Exophthalmos evaluation

The degree of exophthalmos was determined in relation to the interzygomaticus line on the basis of a single MR image obtained in a horizontal section at the level of the eyeball equator. This lane extended between the two most protruding points of the right and left zygomatic bones. The distance between the interzygomaticus line and the cornea apex was measured perpendicularly to this line [6, 7]. The data obtained (in millimetres) were noted down in the report sheets (Table I).

The degree of exophthalmos in a study group was determined 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 MRI study

All patients underwent MR examinations by a Siemens Vision+ 1.5 T scanner using a head coil. Patients were asked to close their eyes during examination to avoid movement artefacts related to blinking or fatigue from looking at one point.

Table I
Clinical diagnosis and the location of the eyeball in the study group in relation to the interzygomaticus line

Tabela I
Zestawienie rozpoznań i stopnia wytrzeszczu w grupie badanej; przedziały wartości stopnia wytrzeszczu mierzonego względem linii dwujarzmowej

Diagnosis	Percentage	The measurement of the eyeball location in relation to interzygomatic line /mm/			
		17.1–20.6	20.7–24.1	24.2–27.6	27.7–31.1
Without pathology inside the orbit	8 (8.9%)	4	1	–	–
Myopia	4 (4.4%)	1	1	–	–
Graves' Ophthalmopathy	68 (75.5%)	2	27	31	17
Suspicion of intraorbital tumour	10 (11.1%)	–	2	3	1
All	90 (100%)	7	31	34	18

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The MRI examinations lasted not longer than 35 minutes and were carried out as follows:

— in axial planes, transverse sections parallel to the medial and lateral muscles TR/ms/–390, TE/ms/–14, FA/°/–90, FOV/mm/–230, number of layers — 11, thickness of layers — 3 mm, distance factor — 0.1, matrix — 192 × 512, number of acquisitions — 4, time of sequence — 5 min 2 s;
— in coronal planes, perpendicular to the course of the optic nerve and therefore tantamount to the long axis of the orbit TR/ms/–450, TE/ms/–14, FA/°/–90, FOV/mm/–250, number of layers — 15, thickness of layers — 3, distance factor — 0,1, matrix — 192 × × 512, number of acquisitions — 3, time of sequence — 4 min 22 s.

The numerical segmentation image technique (NSI)

The quantitative assessment of eye muscle volume was carried using the contour extension variant of the NSI technique. For the purpose of image processing the open source ITK library [The Insight Software Consortium Insight Toolkit (ITK) http://www.itk.org/] was used. The algorithms employed were cubic spline re-sampling and level set segmentation. For a description of the above-mentioned algorithms we referred to the ITK library reference manual [Ibanez, Schroeder, Ng, Cates Internet: http://www.itk.org/ItkSoftwareGuide.pdf].

Data from resonance sequences were sent to a computer and saved in DICOM format. The MRI images were in the form of two-dimensional section runs. The chosen run was loaded into the program in an appropriate catalogue, and then all the images were combined into one three-dimensional image. The images used for volume assessment were characterised by 512 × 512 × × 14 voxel resolution, with the size of a single voxel at 1 × 1 × 3 mm.

After the images had been loaded into the program they were designated as F1. In the first stage of our procedure the radiologist roughly marked the position of the muscle on an MRI image. This operation created a mask image that was further used as an initial condition for the level set segmentation algorithm. It was necessary to indicate the area of interest on each section, but usually only ten sections were included in the analysis. The M1 mask was obtained on the F1 image as a result, where M1(x) = 1 in indicated points × and M1(x) = 0 in others. The application gave the possibility of going through reviewing all the sections all the sections easily. At the second stage both the MRI and the mask images were re-sampled into 1 × 1 × 1 mm isotropic voxel size by means of a cubic spline re-sampling algorithm. The images obtained were designated as F2.

Three convolutions were made of the M1 mask with a Gaussian function along each of the axes. The $Sigma_i$ parameter of the Gaussian function was 0.95 w_i, where w_i was the size of the voxel along the corresponding axis. An M1a mask was obtained as a result. Next M1a was resampled with B-spline interpolation to the F2 image voxel size so that an M1b mask was obtained. The M2 mask was received from the M1b mask by use of a threshold, so that M2(**x**) = 1 for M1b(**x**)/0.5 and M2(**x**) = 0 for M1b(**x**) < 0.5. All further processing was done on the re-sampled MRI and mask images.

In the third step both the re-sampled MRI and the mask images were put into the level set segmentation algorithm in order to obtain a segmented image, in fact a refined and more accurate position of the muscle. The algorithm was based on the contour evolution. The contour was determined as the set of points of a higher dimensional function termed the level set function Ψ (x, t), the value of which is 0. The initialisation Ψ (x, t) function was determined by the radiologist in an earlier operation by characterising the area of interest. Next, the contour was processed until its shape fitted the anatomical structure. In the level set algorithms the contour was then evolved under the control of a differential equation:

$$\frac{d}{dt}\Psi = -\alpha \mathrm{A}(x) \times \nabla\Psi - \beta P(x)|\nabla\Psi| + \gamma Z(x)\kappa|\nabla\Psi|$$

where **A** is an advection term, P is a propagation (expansion) term and Z is a spatial modifier term for the mean curvature k. The scalar constants a, b, and g weight the relative influence of each of the terms on the movement of the interface.

In our implementation A was a gradient of the F2 image and P was the F2 absolute value of a gradient of the F2 image. Initialisation of the Ψ function was based on the M2 mask.

The radiologist had the opportunity to control the number of iterations of the algorithm and to introduce manual corrections into the segmented image. This step essentially allocates all voxels an image into two classes, those containing the muscle and those not. The operation could even be repeated a number of times until complete coverage is obtained of an area of interest on the MR sections of the muscle.

At the fourth step of our procedure 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 calculation time for all six eye muscles in the automatic segmentation method ranged from 3 to 6 minutes, with a mean value of 4 minutes 42 seconds for each orbit (Fig. 1).

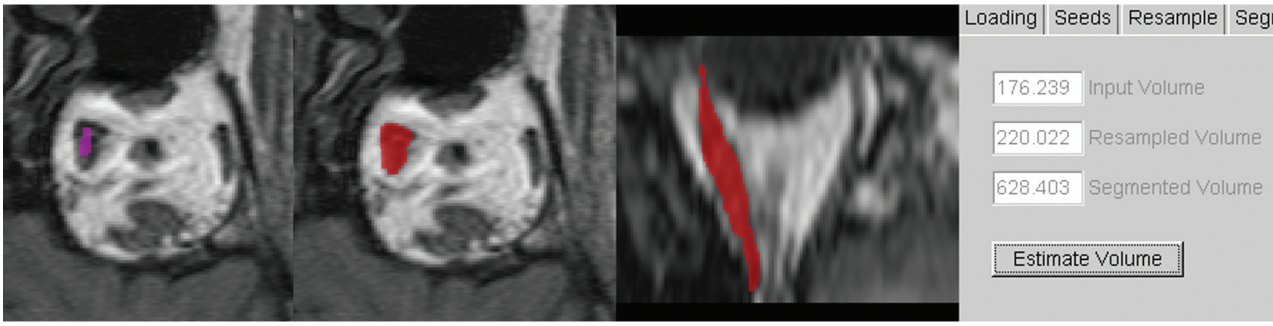

Figure 1. *The muscle volumes calculated by the NSI application; indication of area of interest in the muscle interior, fitting the area inside the contour to the chosen element of the MR image and determination of the last value*

Rycina 1. *Obliczanie objętości mięśni metodą CSO; zaznaczenie obszaru zainteresowania, dopasowanie obszaru zainteresowania do konturów wybranego elementu obrazu RM i określanie wartości końcowej*

Statistical analysis

The correlation between the degree of exophthalmos (in millimetres) measured in relation to the interzygomatic line and muscle volumes (in cubic millimetres) was evaluated.

The minimum and maximum for the continuous parameters expressed in the range scale were provided. The following values were also calculated: mean, median, standard deviation, standard error and variation coefficient. Because of the large trial size ($n > 50$) parametrical methods of statistical analysis were used.

Assessment of the differences between the mean of the analysed parameters at separate points in the examination (after the confirmation of normal data distribution by the Shapiro-Wilk test) was carried out with the use of Student's t test for independent trials. Relations between characteristics were described using Pearson's linear correlation coefficient, with assessment of its significance and linear regression equations. The parameters of linear regression equations were calculated by the least squares method.

Results

The degree of exophthalmos in the study group was determined in relation to the interzygomaticus line as following:

— for the right eye: mean value — 22.173 mm, stand. dev. 2.908;

— for the left eye: mean value — 24.744 mm, stand. dev. 3.041.

The influence of the muscle volume on the degree of exophthalmos in relation to the whole volume of the intraorbital structures was proved to be statistically very strong (linear correlation coefficient $r = 0.543$ $p = 3.13396E-08$, Spearman's correlation coefficient $R = 0.546$ $p = 2.61963$ E-08).

Discussion

Magnetic resonanse imaging is widely accepted as a technique of the highest diagnostic value in the assessment of intraorbital structures, although serious difficulties are encountered in determination of their volume [12, 13]. Many protocols are reported in the literature for indirect estimation of their size [8–12, 14, 15].

Extraocular muscles

The simplest parameter used in the assessment of eye muscle volumes is determination of the largest width of a chosen muscle given in absolute value or in relation to the optic nerve width to correct for individual variability [7, 16, 17]. The most important advantage of such methods is the speed and simplicity of obtaining the calculations. The 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. Even the choice of a section plane is a subjective decision. Measurement of the widest parameters of muscle bellies can therefore be used only for rough estimation of their size. What is more, the real importance is not the volume of a single muscle, but that of all six muscles as a whole. The error in defining the volume of each individual muscle is then multiplied. Because of small absolute muscle sizes this situation can result in serious mistakes in the determination of the real pathological state of muscles necessary for assessment of disease development and treatment decisions.

The assessment of the volume of muscles indicates size more precisely than measurements of any single diameter [8, 18].

Gorman, Nugent, Prummel and Szucs-Farkas suggest that chosen section areas of the muscle should be outlined manually [15, 18–20].

Tian and Gupta calculated the whole muscle volume by multiplying the sum of the section areas covering the whole muscle by the thickness of the slices [9, 21]. Carlow, in order to shorten evaluation time, limited the outlining of muscle contours to the five middle sections [8].

Szucs-Farkas analysed the relationships between maximum single muscle diameters, calculated areas of the surface of their sections and their volumes, using an author's original computer application for manual outlying the muscle borders [15].

Firbank drew up a semi-automated technique of volume estimation based on the coronal sections of the muscles [22]. The segmentation of muscles from the MRI image was carried out on the basis of brightness level. The method became unreliable when the muscles were in close proximity with structures of greatly different signal intensity. Manual outlining of an area of interest then became necessary. The semi-automated technique was used in 25% of the population of volunteers and patients studied.

Methods of calculating real volume are more precise and objective than estimation of muscle size on the basis of single diameters. However, judging by the repetitiveness of the results, they are not sufficient. Individual choice of imaging sections, subjective criteria for defining muscle borders, especially complex in the vicinity of an orbital apex and near attachments to the eyeball, are sources of serious divergence in the results of different authors. Their main limitation remains the lack of feasibility of use in every day clinical practice. All methods based on manual outlining of the muscles are extremely laborious and time consuming. What is more, they demand special computer software and specific requirements in an MRI scanner [23].

The NSI application creates the possibility of obtaining almost automatically reliable computed results of real volume for all intraorbital structures analysed; therefore objectively and in a relatively short time.

Our results, as determined by the NSI application, confirmed, in agreement with many other reports, the strong correlation between the total muscle volume and the degree of exophthalmos, measured both clinically and radiologically [9, 10, 13, 15, 17, 24] (Fig. 2). These volumes are objective measurements which correlate with the current pathophysiological state of the eye muscles. Diagnostic information describing precisely each muscle and the volume relations between all the intraorbital structures is highly desirable in the course of therapeutic management, both for the proper choice of treatment and assessment of its effectiveness. The total volume of muscles is important for pharmacological therapy and radiotherapy, while the volumes of single muscles are important for surgical treatment.

The possibility of changing the contour toleration created in the NSI technique as well as introducing manual alterations greatly extends its usefulness. When there is heterogeneity of the anatomical elements examined, which is a characteristic feature of the fatty degeneration or fibrosis that often occurs in the advanced stages of Graves' ophthalmopathy, the program still works properly and is not invalidated because of lack

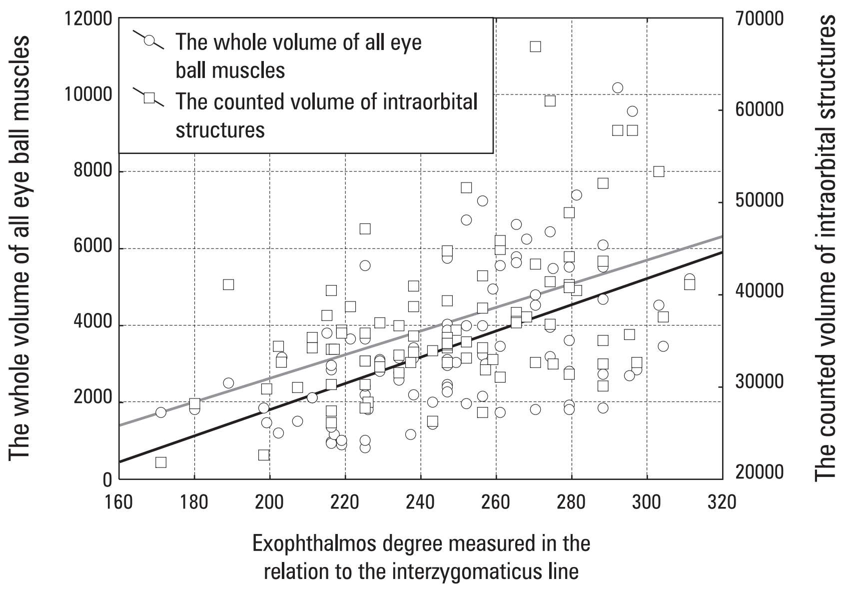

Figure 2. *The correlation between exophthalmos degree measured in the relation to the interzygomatic line, the whole volume of eye-ball muscles and the calculated volume of the intraorbital structures*

Rycina 2. *Zależność między wytrzeszczem określanym względem linii dwujarzmowej a objętością mięśni zewnątrzgałkowych oraz obliczoną objętością struktur wewnątrzoczodołowych* of accuracy. It is possible to change the evolution of the contour precisely, and even to do so several times, to achieve exact coverage of an area of interest on the chosen anatomical element in the MRI image. It is therefore possible to use the NSI technique for monitoring the intraorbital anatomical structures involved by pathophysiological processes going on inside them.

The NSI technique exceeds by its accuracy and the reliability of its results the methods reported earlier which assess muscle volume on the basis of single measurements. It also eliminates an excessive amount of work and time in comparison with methods which enable the volume of selected anatomical structures to be determined.

Conclusion

The NSI software program is an application which offers a reliable and precise estimation of eye muscle volume. It is therefore useful in assessing quantitatively the pathological processes leading to exophthalmos. It has special clinical value in monitoring discrete volume changes of muscles during treatment.

References

1. Barret L, Glatt HJ, Burde RM et al. Optic nerve dysfunction in thyroid eye disease: CT. Radiology 1988; 167: 503–507.
2. Inoue Y, Tsuboi T, Kouzaki A et al. Ophthalmic surgery in dysthyroid ophthalmopathy. Thyroid 2002; 12: 257–263.
3. Forbes G, Gerhing DG, Gorman CA et al. Volume measurements of normal orbital structures by computed tomographic analysis. AJR 1985; 145: 149–154.
4. Kung AWC, Michon J, Tai KS et al. The effect of somatostatin versus corticosteroid in the treatment of Graves' ophthalmopathy. Thyroid 1996; 6: 381–384.
5. Yeatts RP. Graves' ophthalmopathy. Med Clin North Am 1995; 79: 195–209.
6. Nishida Y, Tian S, Isberg B et al. Significance of orbital fatty tissue for exophthalmos in thyroid-associated ophthalmopathy. Graefes Arch Clin Exp Ophthalmol 2002; 240: 515–520.
7. 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: 2830–2833.
8. Carlow TJ, Depper MH, Orrison WW. MR of extraocular muscles in chronic progressive external ophthalmoplegia. AJNR 1998; 19: 95–99.
9. 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: 959–965.
10. Ozgen A, Alp MN, Ariyurek M et al. Quantitive CT of the orbit in Graves' disease. BJR 1999; 72: 757–762.
11. Ozgen A, Aydingoz U. Normative measurements of orbital structures using MRI. JCAT 2000; 24: 493–496.
12. Sosnowski P, Stajgis M. Possibilities of MR evaluation in thyroid orbitopathy. Przegl Lek 2004; 61: 829–832.
13. Karolczak-Kulesza M, Zalecki K, Sosnowski P, Starega M. Image and diagnostic value of ultrasonography and magnetic resonance in selected cases of orbital diseases. Klin Oczna 1995; 97: 328–333.
14. So NMC, Lam WWM, Cheng G et al. Assessment of optic nerve compression in Graves' ophthalmopathy. Acta Radiologica 2000; 41: 559–561
15. 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 2002; 179: 1005–1010.
16. 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: 213–219.
17. Sosnowski P. Roentgenometric evaluation of the orbital content in thyroid-related ophthalmopathy by computerized tomography. Pol Przegl Radiol 1987; 51: 229–233.
18. Gorman CA. The measurements of change in Graves' ophthalmopathy. Thyroid 1998; 8: 539–43.
19. Nugent RA, Belkin RI, Neigel JM et al. Graves' orbitopathy: 6. Correlation of CT and clinical findings. Radiology 1990; 177: 675–682.
20. Prummel M, Gerding MN, Zonneveld FW et al. The usefulness of quantitative orbital magnetic resonance imaging in Graves' ophthalmopathy. Clin Endocrinol 2001; 54: 205–209.
21. Tian S, Nishida Y, Isberg B et al. MRI measurements of normal extraocular muscles and other orbital structures. Graefes Arch Clin Exp Ophthalmol 2000; 238: 393–404.
22. Firbank MJ, Harrison RM, Williams ED et al. Measuring extraocular muscle volume using dynamic contours. Magn Reson Imaging 2001; 19: 257–265.
23. Aydin K, Guven K, Sencer S et al. A new MRI method for the quantitative evaluation of extraocular muscle size in thyroid ophthalmopathy. Neuroradiology 2003; 5: 184–187.
24. Firbank MJ, Coulthard A. Evaluation of a technique for estimation of extraocular muscle volume using 2D MRI. BJR 2000; 73: 1282–1289.