Signature: © Pol J Radiol, 2012; 77(4): 7-12

Polish Journal of Radiology
www.PolRadiol.com
ORIGINAL ARTICLE

Received: 2012.08.02
Accepted: 2012.09.04

Signal intensity and T2 time of extraocular muscles in assessment of their physiological status in MR imaging in healthy subjects

Michał Pająk, Piotr Loba, Julia Wieczorek-Pastusiak, Aneta Antosik-Biernacka, Ludomir Stefańczyk, Agata Majos

Department of Radiology – Diagnostic Imaging Medical University, Łódź, Poland

Author's address: Agata Majos, Department of Radiology – Diagnostic Imaging Medical University, Kopcińskiego 22 St., 90-153 Łódź, Poland, e-mail: agata.majos@umed.lodz.pl

Summary

Background: Lack of standardised orbital MR protocols leads to a situation, when each institution/centre may arbitrarily choose sequence parameters. Therefore, the results obtained and published by the authors may not be compared freely, and what is most important may not be considered fully reliable. Signal intensity (IS) and T2 time (T2) are important parameters in estimation of inflammatory processes of extraocular muscles in the clinical practice.

The aim of this study was to determine the reference values (i.e. cut-off values) for absolute signal intensity and T2 relaxation time in healthy subjects, their relativised values to white matter (WM) and temporal muscles (TM) and to evaluate the correlation between those parameters.

Material/Methods: The orbital examination was performed in healthy volunteers according to the protocol prepared in the Radiology-Imaging Diagnostic Department of the Medical University of Lodz for patients with suspected/diagnosed thyroid orbitopathy. Using two of the standard sequences IS and T2 time were calculated for the muscles and two relativisation tissues in realtion to WM and TM. Subsequently cut-off values for healthy volunteers were calculated.

Results: The differences between muscles for IS, IS MAX, IS/TM, IS/WM, IS MAX/TM, IS MAX/WM and T2 MAX/WM were not statistically significant. Therefore one cut-off value of these parameters for all the rectus muscles was calculated. T2-relaxation time and T2 relativised to white matter had to be calculated separately for each muscle.

Conclusions: No statistical correlation was found between IS and T2-time for extraocular muscles in healthy volunteers. We calculated the reference ranges (cut-off values) for absolute IS and T2-time values and relativised parameters. In the clinical practice the objectification of IS and T2-time values should be done to WM, than to IS or T2 of the temporal muscle. The T2 MAX/WM seems to have the highest clinical utility for the assessment of the pathophysiological status of extraocular muscles.

Key words: extraocular muscles • signal intensity • T2 time • reference values

PDF file: http://www.polradiol.com/fulltxt.php?ICID=883622

Background

The improvement in imagining techniques using magnetic resonance (MR) phenomenon observed in the last two decades allows for its utilisation in broader spectrum of indications. It includes the diagnostic of orbital diseases and monitoring of their therapy. In contrast to other imaging techniques, such as computed tomography or ultrasound examinations (US), MR possess valuable advantages over other modalities i.e. lack of ionizing radiation and very high tissue resolution, required especially in imaging of

difficult orbital cone space. It allows for multiple examination repetitions without the risk of adverse effects.

The issue of imaging of the extraocular muscles was raised by many authors [1–8]. It is generally agreed that MR is currently the best modality for imaging small intraorbital structures [9–11]. It allows for evaluating not only morphological parameters, but their pathophysiological status as well.

It is almost impossible to find in the literature reports establishing reference values evaluating the physiological status of imagined tissues, i.e. signal intensity in T2-weighted images (SI) and T2 relaxation time (T2).

Lack of standardised orbital MR protocols leads to a situation, when each institution/centre may arbitrarily choose sequence parameters. Therefore, the results obtained and published by the authors may not be compared freely, and what is most important may not be considered fully reliable. They cannot be directly transferred and utilised in every MR laboratory. Thus, it seems reasonable to introduce parameters relativising the absolute values of the measured parameters [4,12].

The aim of this study was to determine the reference values (i.e. cut-off values) for absolute signal intensity and T2 relaxation time in healthy subjects, their relativised values to white matter and temporal muscles and to evaluate the correlation between those parameters.

Material and Methods

This study constitutes a part of larger one being a doctoral dissertation of one of us (MP). The study was approved by the Bioethical Committee of the Medical University of Lodz (No RNN/28/12/KE).

The study group consisted of 7 healthy volunteers, 14 orbits (4 women and 3 men, age: mean 39.78, range 30–55 years).

The exclusion criteria included: lack of consent for participation, diseases of the intraorbital structures of any ethiology, the presence of any ferromagnetic or electronic materials in the subjects' body, claustrophobia and excessive overweight.

The orbital examination was performed according to the protocol prepared in the Radiology Department of the Medical University of Lodz for patients with suspected/diagnosed thyroid orbitopathy. The subjects were placed on the table, and their heades were immobilised using sponge pads. The head coil was placed and the subjects were asked to close his/her lids and to lie calmly and motionlessly.

The examination protocol included sequences providing morphological and physiological data:

a. T2 TSE FS-PARA COR performed in coronal plane, one for each orbit, with layers perpendicular to the orbit long axis: TR=4640, TE=108, FA-150, FOV-90×120, layer thickness-3mm, acquisition time 2: 43;
b. T2 SE COR 16-ECHO performed in coronal plane, one for both orbits TR=3000, TE=22,44,…, 330,352, FA-180, FOV-90×120, layer thickness – 5 mm, acquisition time 8: 23.

Data analysis

Signal intensity determination

The images with best visible muscle bellies were selected among those obtained using T2 _ TSE _FS _PARA _ COR sequence. Circular region of interest (ROI) was selected and placed threefold over different parts of each muscle and the mean and maximal brightness (greyscale) of pixels and respective standard deviation were calculated. Depending on the quality of the obtained images, data from one or two slices were calculated and transferred to Excel spreadsheet application and a mean and maximal value from these three to six measurements were calculated.

The signal intensity for the white matter (WM) of frontal lobes of both hemispheres and temporal muscles (TM) were similarly obtained.

Calculation of T2-relaxation time

The images with best visible muscle bellies were selected among those obtained using T2 _ T2_SE_COR_16-ECHO sequence and slice position was determined. Subsequently, having 16 images for different TE time and utilising scanners own software (Dynamic Evaluation –> T2) the following images were created: 1) image of T2-relaxation times and 2) image of proton density. The latter provided better outlined and well-defined muscle representation. As with the signal intensity measurements, the circular region of interest was selected. It was placed over muscle outline on proton density image, and then image was switched to T2-relaxation time and without moving the ROI the mean and maximal value of T2-time were obtained. Such a procedure was repeated threefold for each muscle with a given slice position. Three to six such measurements were utilised for eventual calculation of mean and maximal T2-time value for each muscle. The T2-time for the WM of frontal lobes of both hemispheres was obtained similarly. The example of T2-time calculation is presented on Figure 1.

Calculations

All measurements concerning data obtained during magnetic resonance tomography were performed using ImageJ software, available on a freeware basis (*rsbweb.nih.gov/ij/).*

For each muscle the following parameters were calculated:

A. T2/T2 WM
B. T2 MAX/T2 WM
C. IS/IS WM
D. IS/IS TM
E. IS MAX/IS WM
F. IS MAX/IS TM

Statistical analysis was performed using STATISTICA software (licence No. AXAP202E504303AR-A).

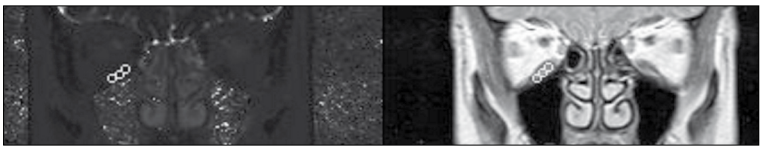

Figure 1. The proton density and T2-relaxation time images obtained using the scanners software. The method of calculating T2-time is presented.

Table 1. H values of Kruskal-Wallis test and p-values for parameters differences among individual rectus muscles; the statistically significant differences for individual muscles are underlined.

	H (3, N 56)	p
IS	2.42	0.4904
IS MAX	2.91	0.4050
T2	14.48281	0.0023
T2 MAX	10.09958	0.0177
IS/TM	3.394695	0.3347
IS/WM	3.303464	0.3472
IS MAX/MS	4.290977	0.2317
IS MAX/TM	4.730820	0.1926
T2/TM	12.98317	0.0047
T2 MAX/TM	6.914194	0.0747

The mean, median and standard deviation were calculated for each of the above-mentioned parameters and absolute IS and T2 values.

The statistical significance between obtained values for individual muscles and correlation between these parameters were determined, as well. A non-parametric Kruskal-Wallis test was performed, and the results are presented in Table 1 (Spearman R).

Due to the non-parametric nature of the tests (small sample size) the reference values were selected as these not exceeding a cut-off value, defined as 95th percentile.

Results

Tables 2 and 3 present the results obtained for rectus muscles.

Slight differences of the calculated parameters for individual muscles inspired the authors to determine the statistical significance of differences of the parameters values among the muscles – Table 3.

The correlation between IS and T2 and respective parameters are presented in Table 4, statistically significant are underlined.

Discussion

The assessment of inflammation activity taking place within the orbit requires not only the morphological analysis of particular intraorbital structures, most commonly associated with the evaluation of their size. Signal intensity and T2-relaxation time are both parameters, which value is determined by the disease activity, and are well correlated with tissue hydratation. Thus, they may be treated as an indicator for inflammation intensity.

Among these two parameters the T2-time value seems to be more objective, as contrary to IS, it should be independent of sequence parameters, and constitutes a specific feature of a given tissue/structure. However, the calculation of T2-time requires a specially equipped scanner, which enables to perform multiple-echo sequences, with software able to compile the obtained data, determine the transverse magnetisation decay curve and basing on the latter to calculate the required value. As not every scanner is able to perform such a procedure we calculated the reference values both for IS (for a given sequence protocol) and T2-time. Whenever possible, the diagnosis should me made basing rather on T2-time. Although the sequence utilising many TE values is

Table 2. Results (absolute values and defined parameters) for the medial rectus and lateral rectus muscles.

	Medial rectus muscle					Lateral rectus muscle				
	Mean	Median	Minimum	Maximum	SD	Mean	Median	Minimum	Maximum	SD
IS	135.13	134.30	97.22	164.25	19.02	139.00	142.21	102.35	185.08	25.68
T2	82.32	83.24	68.70	93.33	7.36	100.91	98.48	82.81	139.09	14.96
IS/TM	2.43	2.35	2.07	3.07	0.31	2.48	2.44	1.89	2.96	0.33
IS/WM	0.90	0.88	0.79	1.16	0.11	0.92	0.91	0.75	1.11	0.11
IS MAX/TM	3.57	3.51	3.03	4.31	0.37	3.56	3.58	2.80	4.30	0.42
IS MAX/WM	1.33	1.32	1.10	1.67	0.16	1.32	1.30	1.14	1.52	0.12
T2/WM	0.98	1.02	0.82	1.18	0.12	1.21	1.14	1.02	1.71	0.19
T2 MAX/WM	1.25	1.21	1.02	1.53	0.16	1.45	1.38	1.15	2.09	0.24

Table 3. Results (absolute values and defined parameters) for the inferior rectus and superior rectus.

	Inferior rectus muscle					Superior rectus muscle				
	Mean	Median	Minimum	Maximum	SD	Mean	Median	Minimum	Maximum	SD
IS	136.27	134.42	84.88	185.63	28.02	127.65	121.54	89.40	171.94	22.13
T2	89.46	88.17	73.17	110.67	10.36	90.68	91.23	74.22	108.31	9.18
IS/TM	2.43	2.46	1.77	3.05	0.38	2.28	2.23	1.89	2.85	0.29
IS/WM	0.90	0.91	0.72	1.16	0.13	0.85	0.82	0.73	1.01	0.09
IS MAX/TM	3.82	3.65	2.99	5.06	0.60	3.46	3.36	2.73	4.49	0.44
IS MAX/WM	1.41	1.46	1.15	1.64	0.15	1.28	1.29	1.04	1.63	0.17
T2/WM	1.07	1.06	0.89	1.38	0.13	1.08	1.07	0.91	1.23	0.10
T2 MAX/WM	1.33	1.35	1.08	1.57	0.14	1.30	1.23	1.11	1.67	0.18

Table 4. Correlation between IS and T2 and respective parameters.

	IRM	SRM	MRM	LRM	Altogether
IS to T2	–0.05	0.45	–0.21	–0.09	0.00
IS to T2 MAX	–0.11	0.39	–0.22	–0.25	0.02
IS MAX to T2	0.08	0.64	–0.31	0.09	0.13
IS MAX to T2 MAX	0.00	0.56	–0.21	–0.09	0.13

usually longer than standard ones, the T2-time calculation is a very simple and not a time-consuming (few minutes) task.

Apart from SRM no correlation between the T2-time and IS values was observed in our reference group. Yet, in contrary to other rectus muscles, SRM does not constitute a separate structure. It forms, indeed, a part of a complex with levator palpabrae, and bands of connective and fat tissue, which may significantly influence the obtained results.

It is interesting, however, that in some studies, a statistically significant correlation between T2-time, signal intensity and muscle volume was observed in patients with Graves orbithopathy [4,12]. The preliminary results of the above-mentioned doctoral dissertation reveal that this is not the case in healthy volunteers.

It seems justified though to establish reference values for healthy subjects. Such values may not, however, concern only the absolute values, measured directly, as it may be associated with bias secondary to scanner type and parameters of the sequences utilised for intraorbital structure evaluation. It finds it confirmation in reports from many studies. Almost all authors analysing the intraorbital structures in patients with Graves disease calculated their own reference ranges for IS and T2-time.

Tachibana et al. determined absolute values of T2-time for all muscles to be at the level of 60 ms [11]. The difference between their and our results is as high as 70–80%, as our calculations range from 90 to 110 ms. Such a difference may be attributed to various subjects populations – Asian *vs.* Caucasian. It may be confirmed by a study of Prummel, who studied the Dutch population and obtained results similar to ours – the differences do not exceed 10% [13]. On the other hand, Pauleita et al. assumed T2-time of 60 ms to constitute their reference value, which is similar to the results of Tachibana et al. [3]. Such discrepancy directly questions the usefulness of absolute T2-time value.

One of the possibilities to cope with such discrepancy is to objectivise the obtained data through their relativisation to the same parameters but calculated for structures localised outside the orbit and not affected by any orbital disease. Two ways of relativisation of absolute values, most commonly described in the literature, i.e. the frontal lobe white matter and temporal muscle belly are utilised for that reason. Both structures are visible in typical orbital MR examination. Data obtained from these regions are collected simultaneously and may be considered reliable and specific for a given patient, sequence parameters, current status of the magnetic field etc. In our study we calculated the relativised values both to temporal muscle and cerebral white mater.

Similarly to our project, Kirsh et al. determined IS/TM index, yet they chose only one rectus muscle with the highest signal in T2-weighted images [14]. Such calculated index for IRM was 1.18–2.4 (mean 1.63), whereas in our study it was 1.77–3.05 (mean 2.43). The clear difference in both range and mean value may suggest that IS/TM parameter may not be freely utilised for extraocular muscle evaluation.

Our own experience suggests that objectification of the results to white matter seems more useful in comparison to relativisation to temporal muscle. The area of frontal lobe white matter visible in the orbital MR images is larger and

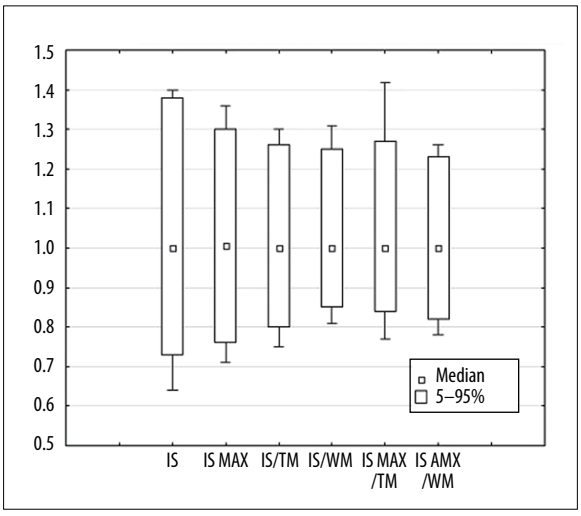

Figure 2. Reference range for IS and its relativised parameters. The absolute values and parameters were calculated so, that the median was equal 1 in each case. IS – signal intensity, T2 – T2-relaxation time, WM – white matter, TM – temporal muscle, IS MAX – maximal signal intensity of three to six measurments.

more homogenous. On the other hand, the temporal muscle on frontal sections is narrow, which results in possible bias consisting in including other-than-muscle tissues in the analysis. The range of index in percentage of relativised parameters is thus smaller for WM than for TM. The analysis of the kurtosis for IS/TM and IS/WM allows for an observation, that it is higher for IRM and MRM, than for LRM. It means, that by relativising the absolute values to WM the obtained collection of data is more homogenous with higher results grouping about the mean value (Figure 2).

It should be emphasised that median values of IS/WM for all muscles lie near 0.9 and do not exceed 1.46, and T2/WM are near 1.1 and do not exceed 1.35, which confirms the above-mentioned observations.

In clinical practice, the determination of normal (reference) values is more influenced by extremes not mean values, as the radiological evaluation requires individual approach to every examined person. Thus, IS MAX/WM value is 1.1 and do not exceed 1.67, whereas T2 MAX/WM is 1.5 and do not exceed 2.1. If the calculated values be higher in subjects with intraorbital pathology, the separable ranges for these values could be determined for healthy subjects and diseased patients, which is of great clinical significance. The studies concerned this issue are in progress.

The similar spread of mean and maximal values with higher T2 MAX/WM value allows for a similar statement as was done for T2/WM that relativised T2-time is more suitable for the assessment of inflammation activity than IS.

The analysis of our results and slight differences between absolute values and calculated secondary parameters induced us to determine the statistical significance of differences between individual muscles. The differences for IS, IS MAX, IS/TM, IS/WM, IS MAX/TM, IS MAX/WM and T2 MAX/WM were not statistically significant. Thus these parameters may be treated as on group for all muscles, and only one reference range has to be calculated for all rectus muscles. The statistical significance was showed only for T2, T2 MAX and T2/TM.

The clinical value of IS was assessed in other studies concerning inflammation activity in patients with Graves disease, and its good correlation with muscle size and good predictive value for treatment response were observed [15,16].

Taking into account the above considerations we recommend using T2 MAX/WM index in the assessment of pathophysiological status of rectus muscles, and would it be impossible to calculate this parameter, a IS/WM index should be provided.

We suggest that reference values for particular parameters should be as follows – Table 5.

In the available literature no studies were found concerning the utilisation of most of the parameters calculated in our study. It may constitute a baseline for further research.

Conclusions

1. No statistical correlation was found between IS and T2-time for extraocular muscles in healthy volunteers.
2. We calculated the reference ranges for absolute and relativised IS and T2-time values.

Table 5. Reference values for IS and T2 and respective parameters.

	IRM	SRM	MRM	LRM
IS		<183.5		
T2	<100	<103	<93	<113
IS/WM		**<1.11**		
IS MAX/WM		<1.63		
T2/ WM	1.38	1.23	1.18	1.71
T2 MAX/ WM		**<1.67**		

SRM – superior rectus muscle; IRM – inferior rectus muscle; MRM – medial rectus muscle; LRM – lateral rectus muscle; IS – signal intensity; T2 – T2-relaxation time; WM – white matter; TM – temporal muscle; IS MAX – maximal signal intensity of three to six measurments; T2 MAX – maximal T2-relaxation time of three to six measurments.

3. In clinical practice relation to IS and T2 time for MW than IS and T2 time for MS is more reliable and usable for objectification of these parameters.
4. The T2 MAX/WM seems to have the highest clinical utility for the assessment of the pathophysiological status of extraocular muscles.

References:

1. Jiang H, Wang Z, Xian J et al: Evaluation of rectus extraocular muscles using dynamic contrast-enhanced MR imaging in patients with Graves' ophthalmopathy for assessment of disease activity. Acta Radiol, 2012; 53(1): 87–94
2. Ohnishi T, Noguchi S, Murakami N et al: Extraocular muscles in Graves ophthalmopathy: usefulness of T2 relaxation time measurements. Radiology, 1994; 190(3): 857–62
3. Pauleit D, Schüller H, Textor J et al: MR relaxation time measurements with and without selective fat suppression (SPIR) in endocrine orbitopathy. Rofo, 1997; 167(6): 557–64
4. Majos A, Pajak M, Grzelak P et al: Magnetic Resonance evaluation of disease activity in Graves' ophthalmopathy: T2-time and signal intensity of extraocular muscles. Med Sci Monit, 2007; 13(Suppl.1): 44–48
5. Cakirer S, Cakirer D, Basak M et al: Evaluation of extraocular muscles in the edematous phase of Graves ophthalmopathy on contrast-enhanced fat-suppressed magnetic resonance imaging. J Comput Assist Tomogr, 2004; 28(1): 80–86
6. Demer JL,Clark RA, Lim KH et al: Magnetic Resonance Imaging of Innervational And Extraocular Muscle Abnormalities In Duane-Radial Ray Syndrome. Invest Ophthalmol Vis Sci, 2007; 48(12): 5505–11
7. Jiao YH, Zhao KX, Wang ZC et al: Magnetic resonance imaging of the extraocular muscles and corresponding cranial nerves in patients with special forms of strabismus. Chin Med J, 2009; 122(24): 2998–3002
8. Demer JL, Dushyanth A: T2-weighted fast spin-echo magnetic resonance imaging of extraocular muscles. J AAPOS, 2011; 15(1): 17–23
9. Khitri MR, Demer JL: Magnetic Resonance Imaging of Tissues Compatible with Supernumerary Extraocular Muscles. Am J Ophthalmol, 2010; 150(6): 925–31
10. Karakas HM, Tasali N, Cakir B: Normal magnetic resonance contrast enhancement of extraocular muscles: a quantitative analysis. Ophthalmologica, 2002; 216(2): 85–89
11. Tachibana S, Murakami T, Noguchi H: Orbital magnetic resonance imaging combined with clinical activity score can improve the sensitivity of detection of disease activity and prediction of response to immunosuppressive therapy for Graves' ophthalmopathy. Endoc J, 2010; 57(10): 853–61
12. Majos A, Pajak M, Elgalal M et al: Lateral rectus muscle as a new reference point in estimation of Grave's ophthalmopathy activity. Med Sci Monit, 2010; 16(Suppl.1): 80–85
13. Prummel MF, Gerding MN, Zonneveld FW et al: The usefulness of quantitative orbital magnetic resonance imaging in Graves' ophthalmopathy. Clin Endocrinol, 2001: 54(2): 205–9
14. Kirsch EC, Kaim AH, Oliveira MG et al: Correlation of signal intensity ratio on orbital MRI-TIRM and clinical activity score as a possible predictor of therapy response in Graves' orbitopathy – a pilot study at 1.5 T. Neuroradiology, 2010; 52(2): 91–97
15. Yokoyama N, Nagataki S, Uetani M et al: Role of magnetic resonance imaging in the assessment of disease activity in thyroid-associated ophthalmopathy. Thyroid, 2002; 12(3): 223–27
16. Lennerstrand G, Tian S, Isberg B et al: Magnetic resonance imaging and ultrasound measurements of extraocular muscles in thyroid-associated ophthalmopathy at different stages of the disease. Acta Ophthalmol Scand, 2007; 85(2): 192–201