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CORRELATION BETWEEN ATROPHY-TRACTION-NEOVASCULARIZATION GRADE FOR MYOPIC MACULOPATHY AND CLINICAL SEVERITY

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Purpose: To assess the reliability of the atrophy-traction-neovascularization (ATN) classification in patients with pathologic myopia (PM) and its correlation with best-corrected visual acuity (BCVA).

Methods: Cross-sectional study. Hundred highly myopic eyes with a spherical equivalent of >-6.0 diopters or axial length of >26 mm and a total ATN score of ≥ 3 underwent a complete ophthalmological examination, including fundus photography and swept-source optical coherence tomography. Five observers graded each eye using the ATN system. Mean A, T, and N scores were calculated and correlated with age, BCVA (in logarithm of the minimum angle of resolution), and axial length. Patients were considered to present severe PM if either A or T components were ≥ 3 and/or N was ≥ 2.

Results: Hundred eyes (53 left) from 91 patients (78 women) were classified. Mean age, BCVA, and axial length values were, respectively, 65.1 ± 11.7 years (range, 36–97 years), −0.63 ± 0.62 (−3.00 to 0.00), and 29.26 ± 2.7 mm (26.01–37.66 mm). Mean ATN grades for each component were as follows: A = 2.51 ± 0.78 (0.6–4.0), T = 0.88 ± 1.14 (0.0–5.0), and N = 1.31 ± 1.40 (0.0–3.0). Weighted interobserver agreement was 98.1%, 98.7%, and 94.6%, for A, T and N, respectively. In eyes with severe PM, BCVA was significantly lower and axial length was significantly longer.

Conclusion: The excellent interobserver rate in this study demonstrates that the updated ATN grading system is an accurate and reliable tool to classify patients with PM. These findings show that BCVA is more compromised in eyes with severe PM, particularly those graded ≥A3 and/or T3.

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High myopia affects approximately 500 million people worldwide and prevalence rates continue to increase, particularly in East Asia, where rates are greater than 20%.[1–3] Patients with high myopia are at risk of developing macular alterations secondary to changes in the posterior pole of the eye, leading to pathologic myopia (PM) and, potentially, loss of visual acuity.[4] Pathologic myopia is one of the leading causes of legal blindness in the world[4] and the prevalence of myopia-related complications is expected to continue rising in the future, presenting a major challenge for ophthalmologists.[5]

Given the potential negative impact of PM on the quality of life of patients, there is a clear need for a reliable, homogeneous grading system to simply and quickly classify PM. This would allow clinicians to properly classify the complex maculopathy in highly myopic eyes, which would in turn facilitate follow-up and treatment. Moreover, the availability of an accurate and reliable classification system would unify criteria, thus enabling more accurate comparisons of data obtained in clinical trials and other studies. Although several classification systems have been proposed, their value is somewhat limited because they generally grade either chorioretinal atrophy or traction-related changes, without accounting for neovascularization.[5,6] By contrast, the recently developed atrophy-traction-neovascularization (ATN) classification system was designed to

mirror the well-established and highly reliable TNM classification used in oncology.[7] The ATN considers the three main components of PM: chorioretinal atrophy (A), myopic traction maculopathy (T), and myopic choroidal neovascularization (N).[8] International validation studies have shown good intra- and interobserver correlation for all three components, demonstrating that the ATN is a reliable and highly reproducible classification method.[9] More recently, a large study has successfully applied the ATN system to grade myopic maculopathy.[10]

High myopia is commonly defined as a spherical equivalent of >-6.0 diopters (D) or an axial length (AL) of ≥ 26.0,[11,12] although some authors set the threshold at >-8.0 D.[5] Actually, PM was first defined by Curtin in 1977,[13] but—like high myopia—the definition proposed by Curtin is not without controversy. The first definition of PM was based on changes leading to vision loss in long, highly myopic eyes.[14,15] Although AL does seem to play a role in myopic maculopathy,[16] there are reports of emmetropic eyes showing posterior staphyloma- and myopia-related alterations.[17] Ohno-Matsui et al proposed that PM be defined as the presence of myopic maculopathy,[18] but no studies have been conducted till date to objectively correlate the presence of myopic morphological changes with visual acuity. According to the META-PM classification system, PM is defined as "the eyes having equal to or more serious than diffuse choroidal atrophy" or "the eyes having staphylomas."[19] This was justified as categories A0, A1, and A2, which do not imply significant vision loss. However, the precise point at which the T and N components are likely to compromise visual acuity remains undefined.

In this context, the aim of the present study was to evaluate the reliability of the ATN classification system in patients with severe PM by correlating the ATN grade with best-corrected visual acuity (BCVA). In addition, we aimed to establish a specific cutoff score for each component (atrophy, traction, and neovascularization) at which BCVA could be considered to be especially compromised.

Methods

This was a retrospective review of 100 eyes of patients diagnosed with PM at Puerta de Hierro-Majadahonda University Hospital (Madrid, Spain). This study adhered to the tenets of the Declaration of Helsinki and was approved by the hospital ethics committee.

Inclusion criteria were as follows: spherical equivalent (SE) >-6.0 D or >26 mm of AL and a score ≥ 3 on the ATN grading system. This latter criterion was included to ensure the inclusion of patients across the entire spectrum,[8] in part because the validation study for the ATN system was based on samples that skewed toward lower levels of PM on the ATN classification.[9] Exclusion criteria were the presence of any other ophthalmological or systemic disease or previous macular surgery.

All patients underwent a complete ophthalmological examination consisting of the following: BCVA (in logarithm of the minimum angle of resolution), optical biometry AL determination (IOL Master 500; Carl Zeiss, Germany), slit-lamp examination, Goldmann applanation tonometry, and multimodal imaging—fundus photography and swept-source optical coherence tomography (SS-OCT; Triton, Topcon, Co. Japan).

Five of the six retina specialists (J.R.M., I.F.-M., J.M.R.-M., K.O.-M., G.C., R.S.) involved in the original validation study of the ATN grading system graded the 100 patients in the present study (without any additional clinical data) using the updated version of the ATN classification (Table 1). Grading was based on fundus photography and two 12-mm, fovea-centered SS-OCT b-scans (vertical and horizontal), following the approach described in the validation study (Figure 1).[9] The grades were compared to determine interobserver agreement. The mean score for each component (A, T, and N) was calculated, and these values were then correlated with age, BCVA, and AL.

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Table 1. Updated ATN Classification System

Atrophic Component (A)	Tractional Component (T)	Neovascular Component (N)
A0: No myopic retinal lesions	T0: no macular schisis	N0: no myopic CNV
A1: Tessellated fundus only	T1: inner or outer foveoschisis OR *lamellar macular hole*	N1: lacquer cracks
A2: Diffuse chorioretinal atrophy	T2: inner + outer foveoschisis	***N2a: active CNV***
A3: Patchy chorioretinal atrophy	***T3: foveal detachment***	***N2s: scar/Fuch spot***
A4: Complete macular atrophy	***T4: full-thickness macular hole***	
	T5: macular hole + retinal detachment	

New update based on the original ATN grading system from Ruiz-Medrano J. *Prog Retin Eye Res* 2019;69:80–115.
Bold-italic: stages that define severe pathologic myopia.

Statistical Analysis

The statistical analyses were performed with SPSS for Windows, v.24.0 (IBM-SPSS, Chicago, IL) and Stata, v15.1 (StataCorp LLC, College Station, TX). Descriptive statistics were performed for all variables. Interobserver agreement was analyzed using Fleiss kappa statistics. The kappa statistic (k) was considered "moderate" if $k > 0.4$, "good" if $k > 0.6$, and "excellent" if $k > 0.8$. Bivariate correlations were evaluated using Spearman correlation coefficient. Student *t* test was used to compare groups when the data were normally distributed or the Mann–Whitney test for nonparametric tests. A *P* value of <0.05 was considered statistically significant.

Results

One-hundred eyes (53 left) from 91 patients (78 women) were classified. All eyes scored ≥3 on the ATN. Mean patient age was 65.1 ± 11.7 years (range, 36–97 years). Mean BCVA was −0.63 ± 0.62 (−3.00–0.00), and mean AL 29.26 ± 2.7 mm (range, 26.01–37.66 mm).

The mean ATN grade (Table 2) for each component was as follows: A = 2.51 ± 0.78 (range, 0.6–4.0), T = 0.88 ± 1.14 (range, 0.0–5.0), and N = 1.31 ± 1.40 (range, 0.0–3.0). The mean interobserver agreement for all graders was 77.0% (Table 3); by component, agreement was 74.2% (A), 77.6% (T), and 79.2% (N), respectively. The weighted Fleiss kappa (k) statistic (adjusted by the quadratic weight for disagreement) was excellent for all three categories, with correlations (k value) of 0.802 (A), 0.891 (T), and 0.850 (N), with interobserver agreement rates of 98.1%, 98.7% and 94.6%, respectively.

Intergrader agreement for each variable is shown in Table 4. The weakest agreement for all three components was observed in stages A1, T0, and N1, with correlation values of 0.366, 0.704, and 0.394, respectively. Correlation was good or excellent for all of the other stages, ranging from 0.615 to 0.926.

The bivariate analysis to determine correlation between the mean grade on each individual component (A/T/N) and age, BCVA, and AL showed a significant negative correlation (Spearman correlation test) between BCVA and A ($r = -0.259$, $P < 0.01$) and N ($r = -0.23$, $P = 0.02$) scores (Table 5). Axial length and T values were also significantly and positively correlated ($r = 0.67$, $P = 0.01$).

Patients with A score of ≥3 and/or T of ≥3 and/or N of ≥ 2 presented significantly worse BCVA. No between-group differences in age were observed. Axial length was significantly different in eyes with T score of <3 versus those of ≥3. There was no difference in AL between groups according to A and N (Table 6).

Discussion

In this study, patients presenting signs of advanced PM were classified using the criteria in the updated version of the ATN grading system, which now incorporates additional features, such as lamellar macular hole to improve the accuracy of the classification. A total of five specialists classified 100 eyes according to ATN criteria. Overall, the mean weighted interobserver agreement was

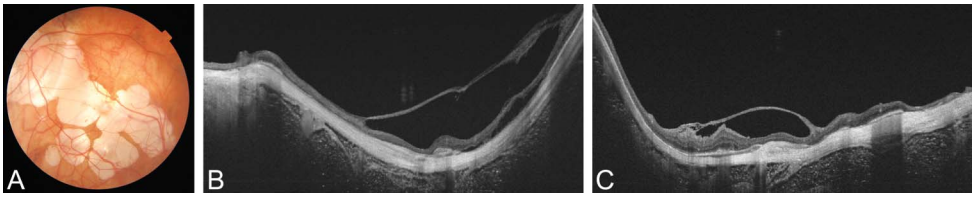

Fig. 1. Highly myopic patient showing a complete macular atrophy, inner and outer foveoschisis and a choroidal neovascularization scar (A4T2N2s).

Table 2. Demographics. Mean ATN Values

Variable	n	Mean	Standard Deviation	Minimum	Maximum
Age, years	100	65.12	11.72	36	97
BCVA (logMAR)	100	−0.63	0.62	−3.00	0.00
AL	74	29.26	2.7	26.01	37.66
Mean A	100	2.51	0.78	0.60	4.0
Mean T	100	0.88	1.14	0.00	5.0
Mean N	100	1.31	1.4	0.00	3.0

LogMAR, logarithm of the minimum angle of resolution.

97.1%, with Fleiss correlations (k) of 0.802 (A), 0.891 (T), and 0.850 (N). Interobserver agreement rates were 98.1%, 98.7%, and 94.6%, respectively. In eyes with severe PM, BCVA was significantly worse with longer AL, in eyes graded as ≥A3 and/or T3. The good interobserver correlation demonstrated in the present study confirms the reliability of the ATN grading system.

The establishment of an accepted and reliable grading system for PM is paramount to guarantee an accurate and homogenous classification and follow-up of patients in daily retina consultations, scientific publications, and most importantly, clinical trials. For this reason, our group developed the original ATN grading system for PM in 2018.[8] This system is modeled on the widely used TNM classification system commonly used to grade cancer.[7] The ATN grading system uses three letters and three numbers to grade each component, thus providing a straightforward classification of patients with PM. The reliability of the ATN system was evaluated in a previous study involving retina specialists from various countries. The excellent results of that study in terms of both intra- and interobserver correlation support the use of the ATN system.[9] Other groups have also used this scale to reliably classify patients with PM, with one study classifying more than 1,000 eyes.[10]

Although the concept of PM has not yet been clearly defined, there does seem to be general agreement regarding the changes in highly myopic eyes that lead to vision loss. In fact, in the study by Ohno-Matsui et al,[19] the presence of diffuse choroidal atrophy (Stage A2 in the ATN system) was defined as the point beyond which visual acuity is considered severely compromised.[3] Although posterior staphyloma is not the primary defect in PM, it can lead to important posterior pole alterations and an increased prevalence of atrophic[20] and tractional aggression,[21] together with a lower BCVA when compared with eyes without posterior staphyloma.[22]

Axial length and age should not be overlooked in these patients because both variables (i.e., longer AL and older age) seem to increase the odds of progression in eyes with posterior staphyloma[23] and PM-related alterations in the posterior pole.[24] In fact, the prevalence of posterior staphyloma—which is low in young, highly myopic patients—is greater than 53% in patients older than 60 years.[13] Lamellar macular hole was not included in the original version of the ATN classification, but because of the potential for lamellar macular hole to negatively impact BCVA and given its association with AL, its presence must be considered. Consequently, the updated version of the ATN classification now includes lamellar macular hole (T1 on the ATN

Table 3. Intergrader Agreement

Variable	% Agreement	k	95% CI
Atrophic*	74.2	0.619	0.542–0.696
Traction*	77.6	0.660	0.584–0.736
Neovascular*	79.2	0.693	0.631–0.756
Atrophic†	98.1	0.802	0.745–0.858
Traction†	98.7	0.891	0.831–0.950
Neovascular†	94.6	0.850	0.782–0.917

CI, confidence interval.

*Fleiss kappa statistic, without weights.

†Fleiss kappa statistic, with weights. Quadratic weight for disagreement: weights are defined as $1 - (k - 1)^2/(q_{max} - q_{min})^2$, where k and l refer to the actual ratings and q_{max} and q_{min} are the maximum and minimum of all observed ratings.

Table 4. Intergrader Agreement

Variable Atrophic	n	K
1	8	0.366
2	43	0.615
3	41	0.719
4	8	0.654
Variable Traction	**n**	**k**
0	45	0.704
1	31	0.714
2	15	0.843
3	3	0.926
4	4	0.913
5	2	0.907
Variable Neovascular	**N**	**K**
0	41	0.816
1	5	0.394
2a	24	0.665
2s	30	0.646

Fleiss kappa statistic.

Table 5. Bivariate Analysis

Grading	Variable	Correlation	P*
Atrophy	Age	0.102	0.312
	BCVA	−0.259	0.009
	AL	0.226	0.100
Traction	Age	0.018	0.860
	BCVA	−0.046	0.653
	AL	0.670	0.010
Neovascular	Age	0.029	0.776
	BCVA	−0.230	0.021
	AL	−0.113	0.418

*Spearman's correlation test.

scale).[25] Some published reports refer to the concept of "extreme myopia," defined as a clear surgical scope with an AL of >30 mm in patients whose surgical outcomes are worse than eyes with a shorter axial length (≤30 mm).[22] Nonetheless, the degree of traction associated with a possible loss of BCVA remains unclear.

Given this background, we performed the current study to assess the possible association between ATN grade and three variables (age, AL, and BCVA). Surprisingly, we did not find, despite our expectations, a statistically significant correlation between age and ATN grade, in contrast to previous reports.[20,26,27] This unexpected finding is probably the result of the study inclusion criteria, which required a combined ATN score of ≥3 and to the relatively high mean age of our cohort (the youngest patient was 36 years old). There was a negative correlation between BCVA and the ATN score for A and N, and AL positively correlated with T.

Considering our results in the context of previous research, we reached a consensus agreement to define severe PM as a score of ≥3 points on the A or T component and/or ≥2 on the N component, which we denominated a "significant myopic macular complication." Patients with severe PM presented significantly worse BCVA than those with common PM, defined by any of the three components of the ATN grading system (Table 6). Similarly, AL was significantly longer in patients with severe PM versus those with common PM (defined by the tractional component), although there were no differences in AL in patients with significant myopic macular complications, defined by either A or N. These findings are consistent with previous reports describing a positive correlation between myopic traction maculopathy and AL[21,26,27] and between the absence of a significant correlation between AL and myopic choroidal neovascularization (CNV), where a preserved choriocapillary is theoretically needed for the CNV complex to develop.[28] This finding raises questions about the true etiology of "myopic CNV," given that CNV resulting from other causes (such as punctate inner choroidopathy or idiopathic CNV) may be included in this category. More data are needed to reach more definitive conclusions regarding the origin of CNV in myopic eyes (our sample included four cases with a grade of N2 and A <2). For this reason, we suggest that only the A and T components of the ATN be considered when defining severe PM, at least until the definition of myopic CNV has been firmly established, which we expect will exclude cases of CNV with a low A component.

Table 6. Pathologic Myopia vs. Severe Pathologic Myopia Comparison

Grading	Variable	PM	Severe PM	P*
Atrophy	Age, years	n: 54 63.8 ± 11.6	n: 46 66.5 ± 11.8	0.19
	BCVA (logMAR)	n: 54 −0.52 ± 0.55	n: 46 −0.76 ± 0.68	0.02
	AL	n: 41 29.2 ± 2.7	n: 33 29.1 ± 2.3	0.49
Traction	Age, years	n: 92 65.0 ± 12.0	n: 8 65.8 ± 2.3	0.78
	BCVA (logMAR)	n: 92 −0.61 ± 0.63	n: 8 −0.91 ± 0.52	0.02
	AL	n: 66 28.8 ± 2.4	n: 8 32.3 ± 1.0	0.01
Neovascular	Age, years	n: 55 64.1 ±11.3	n: 45 66.2 ± 12.1	0.21
	BCVA (logMAR)	n: 55 −0.54 ± 0.60	n: 45 −0.75 ± 0.64	0.02
	AL	n: 37 30.2 ± 2.6	n: 37 28.1 ± 1.9	0.051

logMAR, logarithm of the minimum angle of resolution.
*Mann–Whitney test.

The association between chorioretinal atrophy and AL remains controversial. Although some authors argue that chorioretinal atrophy is present in large posterior staphyloma,[13,29,30] the association between atrophy and AL remains unclear, as evidenced by our findings, which were not statistically significant.

Study Strengths and Limitations

This study has several limitations. First, our sample did not include any patients younger than 36 years, which impeded our ability to assess the potential association between ATN grade and age. Moreover, the concept of myopic CNV remains undefined. In this regard, studies that include a wider range of age spans are needed. Although the present study had a larger sample size than the original validation study (100 vs. 60 eyes), larger studies would help to confirm the results obtained.

In conclusion, the findings of this study show that the updated ATN grading system is a simple, accurate, and reliable tool to classify patients with PM, with a strong interobserver correlation. Our results seem to support the definition of significant myopic macular complications in severe PM for patients with a grade of ≥A3 and/or T3 on the ATN classification system because these patients present significantly worse BCVA than those with lower (better) ATN grades.

Key words: myopic maculopathy, myopic traction maculopathy, myopic choroidal neovascularization, myopic atrophy, ATN classification.

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References

1. Koh V, Yang A, Saw SM, et al. Differences in prevalence of refractive errors in young asian males in Singapore between 1996–1997 and 2009–2010. Ophthalmic Epidemiol 2014;21: 247–255.
2. Lee JH, Jee D, Kwon JW, Lee WK. Prevalence and risk factors for myopia in a rural Korean population. Investig Ophthalmol Vis Sci 2013;54:5466–5470.
3. Morgan IG, Ohno-Matsui K, Saw SM. Myopia. The Lancet 2012;379:1739–1748.
4. Iwase A, Araie M, Tomidokoro A, et al. Prevalence and causes of low vision and blindness in a Japanese adult population. The Tajimi Study. Ophthalmology 2006;113:1354–1362.e1.
5. Shimada N, Tanaka Y, Tokoro T, Ohno-Matsui K. Natural course of myopic traction maculopathy and factors associated with progression or resolution. Am J Ophthalmol 2013;156: 948–957.e1.
6. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. Am J Ophthalmol 2015;159:877–883.e7.
7. Gospodarowicz MK, Miller D, Groome PA, et al. The process for continuous improvement of the TNM classification. Cancer 2004;100:1–5.
8. Ruiz-Medrano J, Montero JA, Flores-Moreno I, et al. Myopic maculopathy: current status and proposal for a new classification and grading system (ATN). Prog Retin Eye Res 2019;69: 80–115.
9. Ruiz-Medrano J, Flores-Moreno I, Ohno-Matsui K, et al. Validation of the recently developed atn classification and grading system for myopic maculopathy. Retina 2020;40:2113–2118.
10. Chen Q, He J, Hu G, et al. Morphological characteristics and risk factors of myopic maculopathy in an older high myopia population—based on the new classification system (ATN). Am J Ophthalmol 2019;208:356–366.
11. Wolf S, Balciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. Ophthalmology 2014;121:682–692.
12. Ohno-Matsui K. What is the fundamental nature of pathologic myopia? Retina 2017;37:1043–1048.
13. Curtin BJ. The posterior staphyloma of pathologic myopia. Trans Am Ophthalmol Soc 1977;75:67–86.
14. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology 2016;123:1036–1042.
15. Tokoro T. On the definition of pathologic myopia in group studies. Acta Ophthalmol 1988;66:107–108.
16. Moriyama M, Ohno-Matsui K, Hayashi K, et al. Topographic analyses of shape of eyes with pathologic myopia by high-resolution three-dimensional magnetic resonance imaging. Ophthalmology 2011;118:1626–1637.
17. Wang NK, Wu YM, Wang JP, et al. Clinical characteristics of posterior staphylomas in myopic eyes with axial length shorter than 26.5 millimeters. Am J Ophthalmol 2016;162:180–190.
18. Du R, Fang Y, Jonas J, et al. Clinical features of patchy chorioretinal atrophy in pathologic myopia. Retina 2020;40:951–959.
19. Ohno-Matsui K, Lai TY, Lai CC, Cheung CM. Updates of pathologic myopia. Prog Retin Eye Res 2016;52:156–187.
20. Ohno-Matsui K. Proposed classification of posterior staphylomas based on analyses of eye shape by three-dimensional magnetic resonance imaging and wide-field fundus imaging. Ophthalmology 2014;121:1798–1809.
21. Baba T, Ohno-Matsui K, Futagami S, et al. Prevalence and characteristics of foveal retinal detachment without macular hole in high myopia. Am J Ophthalmol 2003;135:338–342.
22. Ma J, Li H, Ding X, et al. Effectiveness of combined macular buckle under direct vision and vitrectomy with ILM peeling in refractory macular hole retinal detachment with extreme high axial myopia: a 24-month comparative study. Br J Ophthalmol 2017;101:1386–1394.
23. Gözüm N, Çakir M, Gücukoglu A, Sezen F. Relationship between retinal lesions and axial length, age and sex in high myopia. Eur J Ophthalmol 1997;7:277–282.
24. Chen SJ, Cheng CY, Li AF, et al. Prevalence and associated risk factors of myopic maculopathy in elderly Chinese: the Shihpai eye study. Investig Ophthalmol Vis Sci 2012;53: 4868–4873.
25. dell'Omo R, Virgili G, Bottoni F, et al. Lamellar macular holes in the eyes with pathological myopia. Graefes Arch Clin Exp Ophthalmol 2018;256:1281–1290.
26. Benhamou N, Massin P, Haouchine B, et al. Macular retinoschisis in highly myopic eyes. Am J Ophthalmol 2002;133: 794–800.

27. Hirakata A, Hida T. Vitrectomy for myopic posterior retinoschisis or foveal detachment. Jpn J Ophthalmol 2006;50:53–61.
28. Cheung CM, Arnold JJ, Holz FG, et al. Myopic choroidal neovascularization: review, guidance, and consensus statement on management. Ophthalmology 2017;124:1690–1711.
29. Steidl SM, Pruett RC. Macular complications associated with posterior staphyloma. Am J Ophthalmol 1997;123: 181–187.
30. Blach R, Jay B, Macfaul P. The concept of degenerative myopia. Proc R Soc Med 1965;58:109–112.