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## Clinical Characteristics of Dome-shaped Macula in Highly Myopic Eyes among Chinese Han: Correlation with Maculopathy and Macular Complications

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4 1 **Clinical Characteristics of Dome-shaped Macula in Highly Myopic Eyes among Chinese Han:**  
5 2 **Correlation with Maculopathy and Macular Complications**

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17 10 Abbreviated Title: DSM in Chinese Han

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3 1 **Keywords:** dome-shaped macula, high myopia, maculopathy

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5 2 **Synopsis:** DSM is found in 10.77% of highly myopic eyes among Chinese Han. DSM is associated  
6 3 with decreased BCVA and an increased ratio of subfoveal to parafoveal CT, positively associated  
7 4 with the severity of myopic maculopathy.  
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## 1 Abstract

2 **Purpose:** To evaluate the prevalence of dome-shaped macula (DSM) in highly myopic eyes among  
3 Chinese Han and to detect the correlation with myopic maculopathy and macular complications.

4 **Methods:** A total of 736 Chinese Han patients (1384 eyes) with high myopia (refractive error  $<-6.0$   
5 diopters or axial length  $\geq 26.5$ mm) are reviewed based on information entered into a high myopia  
6 database at Zhongshan Ophthalmic Center. Subfoveal choroidal thickness (SFCT) and parafoveal CT  
7 (PFCT) are measured. The prevalence of DSM in patients with myopic maculopathy categorized  
8 from C0 to C4. Clinical features, including macular complications, SFCT and PFCT, are compared  
9 between myopic eyes with and without DSM.

10 **Results:** Among the 1384 eyes, 149 (10.77%) show DSM. The best corrected visual acuity is worse  
11 in eyes with DSM compared to those without in highly myopic eyes without other macular  
12 complications ( $P=0.002$ ). The ratio between subfoveal and parafoveal CT (S/PCT) ( $P=0.021$ ) is  
13 significantly elevated in the DSM group. The proportion of foveal schisis (17.24% vs. 62.86%) is  
14 much lower in eyes with DSM compared to those without DSM. However, the proportions of  
15 extrafoveal schisis (39.66% vs. 5.37%), foveal SRD (5.17% vs. 0) and ERM (24.14% vs. 10.74%)  
16 are much higher in eyes with DSM. The proportion of DSM was lower in C0 and C1, but higher  
17 proportion of DSM was found in C3 and C4.

18 **Conclusions:** DSM is found in 10.77% of highly myopic eyes among Chinese Han. DSM might be a  
19 protective mechanism for foveal schisis and a risk factor for extrafoveal schisis, SRD and ERM.

## 20 Strengths and limitations of this study

21 The study discusses DSM in the Chinese Han population, reports the prevalence of eight macular  
22 complications, and the relation to the choroidal changes.

23 The study compared the demographic characteristics between highly myopic eyes with and without  
24 DSM.

25 The sclera thickness, whose role in the formation of DSM has been hypothesized, was not  
26 investigated because the outer scleral border would be difficult to visualize in some cases, even if we  
27 used an SD-OCT in enhanced depth imaging modality.

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45 2 **Introduction**

6 3 Gaucher et al. first described the dome-shaped macula (DSM) as a morphologic feature in 2008 by  
7 4 characterizing it as an inward convexity or anterior deviation of the macula using optical coherence  
8 5 tomography (OCT)<sup>1</sup>. Although recent advances in OCT technology have helped to evaluate DSM, its  
9 6 physiopathology remains uncertain. Scleral infolding through the collapse of the posterior portion of  
10 7 the eye wall or vitreomacular traction were initially proposed as causes of DSM<sup>2</sup>. Subsequently,  
11 8 DSM was thought to be secondary to an ingrowth of the choroid, but recent research indicates that  
12 9 the main problem is focal scleral thickening in the foveal area<sup>3</sup>. However, the prevalence, clinical  
13 10 features, and mechanisms of this disease are still controversial.

14 11 Although DSM has been described in western countries and Japan, the clinical features of DSM are  
15 12 poorly documented in China. This study aims to analyze the frequency and morphologic features of  
16 13 DSM in a large series of highly myopic Chinese Han patients. The prevalence of DSM, the rate of  
17 14 myopic maculopathy and macular complications, such as foveal schisis, extrafoveal schisis, serous  
18 15 retinal detachment (SRD), epiretinal membrane (ERM), full thickness macular holes (FTMH),  
19 16 lamellar MH, choroidal neovascularization (CNV) and macular hemorrhage, are compared between  
20 17 eyes with and without DSM.

21 18 **Methods**

22 19 The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics  
23 20 Committee of the Zhongshan Ophthalmic Center. The medical records of 736 consecutive highly  
24 21 myopic patients totaling 1472 eyes were reviewed at the High Myopia Clinic at Zhongshan  
25 22 Ophthalmic Center from Jan 2014 to Jul 2016. High myopia was defined as a refractive error of  
26 23  $\leq -6.0$  diopters and axial length (AL) of  $\geq 26.5$  mm. Eighty-eight eyes (5.98%) were excluded due to  
27 24 AL less than 26.5 mm (12 eyes), rhegmatogenous retinal detachment (53 eyes), and poor-quality  
28 25 OCT images (23 eyes). Thus, 1384 eyes were enrolled in this study.

29 26 Comprehensive ocular examinations were performed in all participants. Spherical equivalent  
30 27 refraction (SER) was measured using an autorefractometer (KR-8900 version 1.07, Topcon  
31 28 Corporation, Tokyo, Japan) after complete cycloplegia for both eyes. Best-corrected visual acuity  
32 29 (BCVA) was determined with Snellen VA charts and was converted to the logarithm of the minimal  
33 30 angle of resolution (logMAR) for statistical analysis. AL was recorded using the IOL Master (Carl  
34 31 Zeiss, Tübingen, Germany) and fundus photographs (FP) were obtained using a TRC50LX (Topcon  
35 32 Corp.). OCT images were obtained with a spectral-domain OCT (SD-OCT, Heidelberg Engineering,  
36 33 Heidelberg, Germany) by a single experienced examiner who was masked to the clinical diagnosis.  
37 34 Vertical and horizontal scans that passed through the center of the fovea and raster scans which cover  
38 35 all the macular complications were obtained in each eye.

39 36 Two experienced retinal specialists (X.Z and X.D) read all of the FP and OCT. The presence of  
40 37 myopic maculopathy was defined and classified based on the International Photographic

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2  
3 1 Classification and Grading System for Myopic Maculopathy<sup>4</sup>. Eight macular complications were  
4 2 identified, including foveal schisis, extrafoveal schisis, SRD, ERM, FTMH, lamellar MH, CNV and  
5 3 macular hemorrhage. All cases of CNV were diagnosed through a combination of OCT and FFA.  
6 4 DSM was defined as the presence of an inward bulge of the macular retinal pigment epithelium  
7 5 (RPE) of >50 µm in the vertical, horizontal direction, or both, and was diagnosed with an OCT  
8 6 image according to the method designed by Ellabban and Ohsugi et al.<sup>5,6</sup> ERM was defined as an  
9 7 avascular, fibrocellular membrane on the inner retinal surface<sup>7</sup>. FTMH was characterized by a  
10 8 vertical split in the neurosensory layers of foveal region. Lamellar MH was defined as a partial  
11 9 thickness defect of the macular area, with an irregular foveal contour and a schisis between inner and  
12 10 outer retinal layers, with intact photoreceptors<sup>8</sup>. The CT was measured from the outer portion of the  
13 11 hyper-reflective line that corresponded to the RPE to the inner surface of the sclera using a single  
14 12 masked author<sup>9</sup>. Measurements were taken of the parafoveal choroid at 2 mm superiorly, inferiorly,  
15 13 temporally, and nasally to the fovea using a built-in caliber tool (Fig 1). The average value from  
16 14 these four locations is defined as the parafoveal choroidal thickness (PFCT). The ratio of the  
17 15 subfoveal to the parafoveal CT (S/PCT) was also calculated.

## 16 **Statistical analysis**

17 Age, SER, AL, BCVA, and ratios of subfoveal and parafoveal CT were compared between the two  
18 groups using independent sample *t*-tests. The subfoveal and parafoveal CT between the groups were  
19 compared using multiple linear regressions that paired the eyes based on both AL and age. The  
20 incidences of various macular complications and the distribution of myopic maculopathy between  
21 the groups were compared using chi-square tests or Fisher exact probability tests. A *P* value of <0.05  
22 was considered statistically significant.

## 23 **Results**

24 Out of the 1384 eyes, DSM was identified in 10.77% (149/1384), while 1235 highly myopic eyes  
25 without DSM served as the control. OCT imaging of the posterior pole showed that there were 88  
26 horizontal oval-shaped DSM, 9 vertical oval-shaped DSM, and 33 DSM with the shape of a round  
27 dome. No significant differences were observed based on gender, age, SRE, or AL between eyes with  
28 DSM and without DSM (Table 1). Furthermore, there was no significant difference in BCVA  
29 (0.67±0.57 vs. 0.55±0.56, *P*=0.464). The subfoveal CT tended to be thinner in the DSM group  
30 (60.10±46.61 vs. 73.81±53.54), but the difference was not significant (*P*=0.064). Moreover, the  
31 ratio between the subfoveal and parafoveal CT showed no difference between the two groups  
32 (1.17±0.72 vs. 0.97±0.76, *P*=0.073).

33 Since macular complications, such as CNV, macular holes, and foveal schisis, are highly associated  
34 with impairment of visual function and the choroidal structure, the potential effect of DSM might be  
35 sheltered by these complications. In order to clarify the correlation between DSM and BCVA and  
36 choroidal thickness, eyes with macular complications, such as foveal schisis, extrafoveal schisis,  
37 SRD, ERM, FTMH, lamellar MH, CNV, macular hemorrhage and macular atrophy, were excluded in  
38 the subgroup analysis. Thus, sixty-seven DSM eyes and 692 control eyes with the absence of  
39 macular complications were enrolled (Table 2). Notably, the BCVA was much worse in DSM eyes

1 compared to the control eyes ( $0.35\pm 0.36$  vs.  $0.55\pm 0.51$ ,  $P=0.002$ ). Again, the subfoveal CT showed  
2 no statistical difference between the two subgroups ( $69.04\pm 52.05$  vs.  $84.53\pm 57.94$ ,  $P=0.217$ ) (Fig 2).  
3 The mean parafoveal CT was  $66.09\pm 52.42$   $\mu\text{m}$  in the DSM group and  $94.80\pm 52.78$   $\mu\text{m}$  in the control  
4 group ( $P=0.586$ ). However, the ratio of subfoveal and parafoveal CT was significantly elevated in  
5 the DSM group ( $1.16\pm 0.62$  vs.  $0.93\pm 0.48$ ,  $P=0.021$ ). Moreover, the ratio of inferior and temporal CT  
6 were significantly elevated in the DSM group ( $1.47\pm 1.25$  vs.  $0.96\pm 0.57$ ,  $P<0.001$ ;  $1.24\pm 0.93$  vs.  
7  $0.95\pm 0.82$ ,  $P<0.001$ ), and there was no difference in superior CT ( $1.03\pm 0.69$  vs.  $0.85\pm 0.58$ ,  $P=0.189$ )  
8 or nasal CT ( $2.08\pm 1.19$  vs.  $1.59\pm 1.05$ ,  $P=0.203$ ).

9 No significant differences were observed based on age, AL, SRE and BCVA between eyes with DSM  
10 and without DSM with macular complications. The rate of macular complications was also compared  
11 between patients with and without DSM. Overall, the prevalence of complications was not  
12 significant different in eyes with DSM compared to eyes without ( $38.93\%$  vs.  $36.19\%$ ,  $P=0.513$ ).  
13 The proportion of foveal schisis ( $17.24\%$  vs.  $62.86\%$ ,  $P<0.001$ ) was significantly lower in eyes with  
14 DSM compared to eyes without, while foveal SRD ( $5.17\%$  vs.  $0\%$ ,  $P=0.001$ ), extrafoveal schisis  
15 ( $39.66\%$  vs.  $5.37\%$ ,  $P<0.001$ ) and ERM ( $24.14\%$  vs.  $10.74\%$ ,  $P=0.007$ ) were significantly more  
16 frequent in eyes with DSM compared to those without. However, there was no significant difference  
17 in the proportion of FTMH ( $3.45\%$  vs.  $10.74\%$ ,  $P=0.130$ ), lamellar MH ( $3.45\%$  vs.  $0.89\%$ ,  $P=0.144$ ),  
18 CNV ( $5.17\%$  vs.  $7.16\%$ ,  $P=0.785$ ), and macular hemorrhage ( $1.72\%$  vs.  $2.24\%$ ,  $P=0.801$ ) (Table 3).

19 The severity of myopic maculopathy was also determined in all 1384 eyes. The fundus was  
20 unremarkable in 91 eyes (C0), as was the tessellated fundus in 411 eyes (C1), diffuse chorioretinal  
21 atrophy in 668 eyes (C2), patchy chorioretinal atrophy in 94 eyes (C3), and macular atrophy in 120  
22 eyes (C4). DSM was observed in each stage of myopic maculopathy from C0 to C4. The proportion  
23 of DSM was lower in C0 and C1, but higher proportion of DSM was found in C2-C4. (Table 4).

## 24 Discussion

25 To our knowledge, this study includes one of the largest sample size of DSM. Our results show that  
26 DSM is found in 149 out of 1384 (10.77%) highly myopic eyes in hospital-based Chinese Han. This  
27 ratio is similar to other hospital-based researches, for example, rate of 10.7% reported by Gaucher et  
28 al.<sup>1</sup>, as well as Chebil et al<sup>10</sup>, who found DSM in 24 out of 200 highly myopic eyes (12.0%) and  
29 Garcia-Ben<sup>11</sup> who found DSM in 28 out of the 260 (10.7%) pathologically myopic eyes. However,  
30 DSM was observed in as much as 20.1% (225/1118) of Japanese subjects examined by Liang et al<sup>12</sup>.  
31 The differences in the inclusion criteria used in these studies may explain the variations in their  
32 findings. In Liang's study, the SRE was  $<-8.0$  diopters or axial length of  $\geq 26.5$  mm, which results in  
33 a narrower spectrum with a higher and more extensive myopia population. However, excluding the  
34 effect of the patient administration bias, the prevalence of DSM in Liang's study was still higher  
35 when compared with other studies. To reveal the effect of the refractive error on the prevalence of  
36 DSM, we performed a subgroup analysis according to the SRE. Only three out of 149 eyes with  $-8.0<$   
37  $\text{RE} \leq -6.0$  diopters showed DSM and 146 out of 1064 eyes with  $\leq -8.0\text{D}$  showed DSM, which  
38 demonstrates that most DSM occurs in eyes with  $\text{RE} \leq -8.0$  diopters. However, the adjusted  
39 prevalence was 13.72%, which was still lower than in Liang's study. Furthermore, other studies  
40 performed with small Japanese sample sizes reveal a relative low rate of DSM, at approximately



1 10%. For example, Ohsugi et al. reported a DSM rate of 9.3%<sup>6</sup>. Therefore, considering the patient  
2 administration bias, we suggest that the prevalence of DSM in high myopia populations is nearly  
3 consistent across ethnic groups worldwide. Notably, all of the documented data, including the  
4 present study, came from hospital-based patients and were clinically based studies. It is difficult to  
5 assess precisely the prevalence of DSM in the general population. Therefore, further  
6 population-based epidemiological studies are desirable to explore the real incidence of DSM.

7 Variations in CT are considered related to the evolution of DSM and its associated complications.  
8 The results thus far have been quite controversial. For instance, it is not clear if the choroid is  
9 thickened, normal, or atrophic in eyes with DSM. Some studies show a thickened choroid in DSM<sup>3,  
10 10</sup>, especially in eyes with SRD<sup>13</sup>, while others show that choroidal thickness decreases in DSM<sup>5</sup>.  
11 Some authors have recently suggested that thinning of the choroid is secondary to the elongation of  
12 the posterior staphyloma, or secondary to the sclera thickening. Furthermore, Caillaux et al.<sup>14</sup> show  
13 that the subfoveal choroid is thicker than the parafoveal choroid. The current study does not find any  
14 significant differences in either SFCT or PFCT between myopic eyes with and without DSM in both  
15 the overall population and the subgroup without other macular complications, while the ratio of  
16 subfoveal to parafoveal choroid appears to be significantly larger in patients with DSM without other  
17 complications. This was in accordance with the results reported by Ellabban et al.<sup>15</sup> who performed a  
18 longitudinal study that demonstrated a progressive thinning of the choroid and sclera in eyes with  
19 DSM in the paramacular area. Our results suggest that the thinning of the choroid occurs mainly  
20 outside the macular region in eyes with DSM, thus resulting in what appears to be a localized  
21 relative thickening of the sclera. The central macular choroidal area is preserved in eyes with DSM,  
22 while the paramacular choroid appears to be pathological.

23 In the current study, DSM is highly associated with the severity of myopic maculopathy, which is  
24 remarkable. According to META-PM study, myopic maculopathy is defined as C0-C4 from no  
25 macular lesions to macular atrophy, respectively. Categories 2 and above are classified as pathologic  
26 lesions, while Categories 1 and below are considered unremarkable<sup>4</sup>. Our data shows that DSM can  
27 be seen at any stage of myopic maculopathy, and the proportion of DSM increases with the  
28 progression of maculopathy. Only 1.10% and 4.87% of eyes with DSM fall into Categories 0 and 1,  
29 respectively, while 12.87% fall into Category 2, and 19.15% and 20.00% fall into Categories 3 and 4,  
30 respectively. To our knowledge, this is the first study to focus on the correlation between DSM and  
31 myopic maculopathy. These data show that DSM is not rare in eyes with advanced maculopathy;  
32 however, more careful OCT examinations are warranted to identify the particular entity. Furthermore,  
33 this study shows a dramatic increase in the prevalence of DSM between nonpathological category 1  
34 and pathological category 2. Our data provides novel clinical evidence for the definition and  
35 classification of pathological maculopathy.

36 Besides myopic maculopathy, potential vision-threatening macular complications, such as SRD, MH,  
37 LMH, foveal schisis, and extrafoveal schisis, are well-established complications in DSM,  
38 dependently or independently. Interestingly, foveal schisis (17.24% vs. 62.86%,  $P < 0.001$ ) is less  
39 frequent in groups with DSM compared to those without, while extrafoveal schisis (39.66% vs.  
40 5.37%,  $P < 0.001$ ), SRD (5.17% vs. 0,  $P = 0.001$ ) and ERM (24.14% vs. 10.74%,  $P = 0.007$ ) are  
41 more frequent in those with DSM compared to those without. On the other hand, the rate of FTMH,

1 lamellar MH, CNV and macular hemorrhage showed no significant differences between the two  
2 groups. Our data suggests that DSM might be a protective factor of foveal schisis, but a risk factor  
3 for extrafoveal schisis, SRD and ERM. It is well-documented that foveal schisis is mostly due to  
4 tangential and perpendicular vitreomacular traction. We speculate that the dome might play a role in  
5 reducing mechanical damage in the foveal area, but it may exaggerate the perpendicular  
6 vitreomacular traction in the parafoveal area as a result. Our data supports the hypothesis that passive  
7 resistance of the macular sclera occurs during the elongation of the peripheral staphyloma, thus  
8 providing new understanding of the mechanisms of DSM.

9  
10 SRD is extremely rare (3 eyes out of 149, 2.01%) in our study. Interestingly, the prevalence of SRD  
11 (sometimes called subretinal fluid, foveal detachment, or neuroretinal detachment in previous studies)  
12 ranges from 9.7% to 69%<sup>1, 10</sup> and is considered one of the major complications of DSM in western  
13 countries. SRD is present in 10 out of 15 eyes in the first study with DSM<sup>1</sup> and 52.1% (25 of 48 eyes)  
14 in the later study with the same group<sup>14</sup> even after ruling out SRD due to CNV. On the other hand,  
15 the prevalence of SRD is dramatically low in Asia (5.9% or 3 out of 51 patients)<sup>5</sup> and even lower in  
16 studies with large sample sizes<sup>12</sup>. The dramatic discrepancy in the frequency of SRD in DSM  
17 patients among ethnic populations is still elusive. Interestingly, in Imamura's study, patients are seen  
18 either in New York or Fukushima and the ethnic background of the patients with DSM is not  
19 mentioned<sup>3</sup>. The study shows a moderate rate of SRD with 8.70% (2 out of 23 patients), which  
20 seems to provide more evidence that there is a discrepancy in prevalence of SRD between different  
21 ethnic groups.

22  
23 Although SRD complicates a large proportion of DSM cases, its causes are poorly understood.  
24 Imamura et al.<sup>3</sup> hypothesize that SRD could result from the obstruction of outflow of choroidal fluid  
25 due to a thick sclera. However, others have noted that the submacular choroid is abnormally thick in  
26 eyes with SRD for this degree of myopia, thus suggesting a mechanism similar to central serous  
27 chorioretinopathy (CSC). Furthermore, the mean dome height is much higher in the study by  
28 Caillaux et al., and the difference in the dome height could be one of the causes of serious RD.  
29 Fortunately, the SRD has a relatively benign natural history in western studies<sup>16</sup>. In Suadier's study  
30 of 29 cases, SRD is present initially in 15 of 29 eyes, increases in four cases, and is resolved  
31 spontaneously in seven cases<sup>16</sup>.

32 This study has several limitations. First, this is a retrospective case study, and the potential inherent  
33 limitations are associated with the study's design. Second, the sclera thickness, whose role in the  
34 formation of DSM has been hypothesized, was not investigated because the outer scleral border  
35 would be difficult to visualize in some cases, even if we used an SD-OCT in enhanced depth  
36 imaging modality. Third, CT measurements were carried out manually using a built-in caliper.  
37 Further investigations using swept-source OCT, which allows for deeper tissue penetration into the  
38 choroid and the sclera with automatic measurement, would be beneficial. Despite these limitations,  
39 this is the first study to examine DSM among the Chinese Han population, and it is one of the largest  
40 case study of highly myopic patients with DSM.

41 In conclusion, DSM is a frequent subtype found in 10.77% of patients with high myopia. Visual

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1 acuity is compromised in eyes with DSM compared to those without. A comparison of highly  
2 myopic patients with and without DSM shows differences with western populations, while SRD  
3 remains a rare complication of DSM, at least in Asian populations. DSM may be a protective  
4 mechanism for foveal schisis, but it is positively associated with extrafoveal schisis, SRD and ERM.

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### Figure legend

Figure 1: Measurement protocol from horizontal and vertical scans obtained with spectral-domain optical coherence tomography (SD-OCT) in eyes with dome-shaped macula (DSM) configuration. The retinal and choroidal thickness were measured at subfoveal and at point 2000  $\mu\text{m}$  superior, nasal, temporal and inferior to the fovea. The dome base was measured tangent to the outer surface of the RPE at the bottom of the posterior staphyloma (a). Macular bulge height was measured from the dome base to the most convex vertical or horizontal OCT sections (b).

Figure 2: Comparison of dome-shaped macula (DSM) and non-DSM choroidal thickness in highly myopic eyes without macular complications.

Table 1. Demographic Characteristics of the 1384 Highly Myopic Eyes

	DSM		<i>P</i>
	Present (n=149)	Absent (n=1235)	
AL (mm±SD)	30.76±1.92	29.33±1.99	0.991
Sex (M/F)	55/93	221/426	0.489
Age (years±SD)	50.33±14.81	47.73±13.93	0.310
SER (SER±SD)	-17.42±5.30	-15.93±6.49	0.854
BCVA (logMAR±SD)	0.67±0.57	0.55±0.56	0.464
SFCT (µm±SD)	60.10±46.61	73.81±53.54	0.064
PFCT (µm±SD)	58.71±46.40	83.19±50.10	0.074
SF/PF	1.17±0.72	0.97±0.76	0.073

DSM: dome-shaped macula, AL: axial length, M: male, F: female, SER: spherical equivalent refraction, BCVA: best corrected visual acuity, SFCT: subfoveal choroidal thickness, PFCT: parafoveal choroidal thickness

Table 2 Comparison of eyes with and without DSM in 759 myopic eyes with normal macular architecture

	DSM		<i>P</i>
	Present (n=67)	Absent (n=692)	
Age	45.60±15.27	43.09±13.61	0.53
AL	30.66±2.04	29.38±2.07	0.869
SE	-17.48±5.23	-14.28±5.88	0.958
BCVA	0.55±0.51	0.35±0.36	0.002
SFCT	69.04±52.05	84.53±57.94	0.217
PFCT	66.09±52.42	94.80±52.78	0.586
SF/PF	1.16±0.62	0.93±0.48	0.021
SF/S	1.03±0.69	0.85±0.58	0.189
SF/I	1.47±1.25	0.96±0.57	0.000
SF/N	2.08±1.19	1.59±1.05	0.203
SF/T	1.24±0.93	0.95±0.82	0.016

DSM: dome-shaped macula, AL: axial length, SE: spherical equivalent, BCVA: best corrected visual acuity, SFCT: subfoveal choroidal thickness, PFCT: parafoveal choroidal thickness, S: superior, I: inferior, N: nasal, T: temporal

Table 3. Comparison of Eyes with and without DSM in 505 Myopic Eyes with Macular Complications

	DSM		<i>P</i>
	Present (n=58)	Absent (n=447)	
Age	57.95±12.47	54.64±11.02	0.084
AL	30.92±1.74	29.22±1.83	0.974
SRE	-17.31±5.46	-13.78±6.38	0.953
BCVA	0.82±0.62	0.88±0.67	0.420
Foveal schisis	10/58 (17.24%)	281/447 (62.86%)	0.000
Extrafoveal schisis	23/58 (39.66%)	24/447 (5.37%)	0.000
Foveal SRD	3/58 (5.17%)	0/447 (0%)	0.001
ERM	14/58 (24.14%)	48/447 (10.74%)	0.007
FTMH	2/58 (3.45%)	48/447 (10.74%)	0.130
Lamellar MH	2/58 (3.45%)	4/447 (0.89%)	0.144
CNV	3/58 (5.17%)	32/447 (7.16%)	0.785
Macular hemorrhage	1/58 (1.72%)	10/447 (2.24%)	0.801

DSM: dome-shaped macula, SRD: serous retinal detachment, ERM: epiretinal membrane, FTMH: full thickness macular hole, MH: macular hole, CNV: choroidal neovascularization

Table 4. Correlation of DSM and Myopic Maculopathy

Myopic Maculopathy	DSM		<i>P</i>
	Present (n=149)	Absent (n=1235)	
Category 0 (no macular lesions)	1/149 (0.67%)	90/1235 (7.29%)	0.001
Category 1 (tessellated fundus only)	20/149 (13.42%)	391/1235 (31.66%)	0.000
Category 2 (diffuse chorioretinal atrophy)	86/149 (57.72%)	582/1235 (47.13%)	0.015
Category 3 (patchy chorioretinal atrophy)	18/149 (12.08%)	76/1235 (6.15%)	0.007
Category 4 (macular atrophy)	24/149 (16.11%)	96/1235 (7.77%)	0.001

DSM: dome-shaped macula



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6 **Contributors** LL conceived the aims and overall design of the study. XZ and XD acquired the data  
7 and did the writing of the different sections, tables and figures. CL, SL, CJ and XL did the literature  
8 search and statistical analyses, XC, YL, ST, AZ and JL collected the data used in the study. All  
9 authors were involved in the study design, data analyses, data interpretation and revision of the paper.  
10  
11 The following authors had access to the full raw dataset: LL and ZXJ. The corresponding author had  
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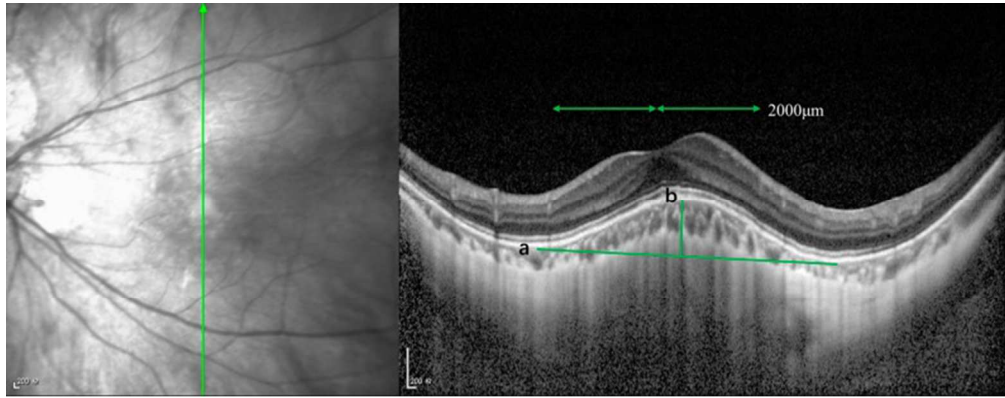
31 **Provenance and peer review** Not commissioned; externally peer reviewed.  
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33 **Data sharing statement** Original data are available on request. Please contact the corresponding  
34 author for further information.  
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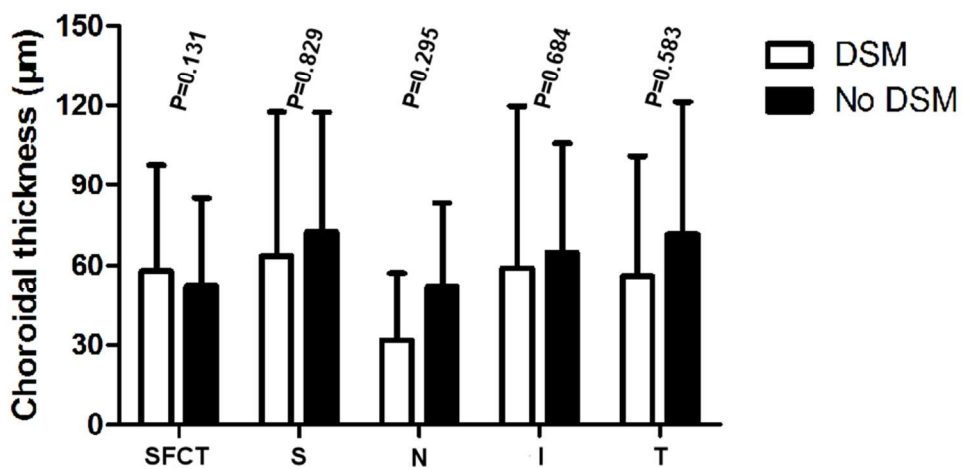
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Measurement protocol from horizontal and vertical scans obtained with spectral-domain optical coherence tomography (SD-OCT) in eyes with dome-shaped macula (DSM) configuration. The retinal and choroidal thickness were measured at subfoveal and at point 2000 µm superior, nasal, temporal and inferior to the fovea. The dome base was measured tangent to the outer surface of the RPE at the bottom of the posterior staphyloma (a). Macular bulge height was measured from the dome base to the most convex vertical or horizontal OCT sections (b).

279x110mm (300 x 300 DPI)

review only



Comparison of dome-shaped macula (DSM) and non-DSM choroidal thickness in highly myopic eyes without macular complications.

126x67mm (300 x 300 DPI)

Review only

# BMJ Open

## Observational Study of Clinical Characteristics of Dome-shaped Macula in Chinese Han with High Myopia at Zhongshan Ophthalmic Center

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<b>Primary Subject Heading</b>:	Ophthalmology
Secondary Subject Heading:	Ophthalmology
Keywords:	dome-shaped macula, high myopia, maculopathy

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4 1 **Observational Study of Clinical Characteristics of Dome-shaped Macula in Chinese Han with**  
5 2 **High Myopia at Zhongshan Ophthalmic Center**  
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9 4 Xiujuan Zhao\*, MD, PhD, Xiaoyan Ding\*, MD, PhD, Cancan Lyu, MD, PhD, Shiyi Li, MD, Yu Lian,  
10 5 Xiaohong Chen, MD, PhD, Silvia Tanumiharjo, MD, Aiyuan Zhang, B.S, Jinge Lu, B.S, Xiaoling  
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18 10 Abbreviated Title: DSM in Chinese Han  
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3 1 **Keywords:** dome-shaped macula, high myopia, maculopathy  
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5 2 **Synopsis:** DSM is found in 10.77% of highly myopic eyes among Chinese Han. DSM is associated  
6 with decreased BCVA and an increased ratio of subfoveal to parafoveal CT, positively associated with  
7 3 the severity of myopic maculopathy.  
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## 1 Abstract

2 **Purpose:** To evaluate the prevalence of dome-shaped macula (DSM) in highly myopic eyes among  
3 Chinese Han and to detect the correlation with myopic maculopathy and macular complications.

4 **Methods:** A total of 736 Chinese Han patients (1384 eyes) with high myopia (refractive error  $< -6.0$   
5 diopters or axial length  $\geq 26.5$ mm) are reviewed based on information entered into a high myopia  
6 database at Zhongshan Ophthalmic Center. Subfoveal choroidal thickness (SFCT) and parafoveal  
7 choroidal thickness (PFCT) are measured. The prevalence of DSM in patients with myopic  
8 maculopathy categorized from C0 to C4. Clinical features, including macular complications, SFCT  
9 and PFCT, are compared between myopic eyes with and without DSM.

10 **Results:** Among the 1384 eyes, 149 (10.77%) show DSM. In highly myopic eyes without macular  
11 complications, the best corrected visual acuity is significantly worse in patients with DSM ( $P=0.002$ ),  
12 and the ratio between subfoveal and parafoveal choroidal thickness (S/PCT) is significantly elevated  
13 in patients with DSM ( $P=0.021$ ). The proportion of foveal schisis (17.24% vs. 62.86%) is much lower  
14 in eyes with DSM compared to those without DSM. However, the proportions of extrafoveal schisis  
15 (39.66% vs. 5.37%), foveal serous retinal detachment (SRD) (5.17% vs. 0) and epiretinal membrane  
16 (ERM) (24.14% vs. 10.74%) are much higher in eyes with DSM. The proportion of DSM was lower  
17 in C0 and C1, but higher proportion of DSM was found in C3 and C4.

18 **Conclusions:** DSM is found in 10.77% of highly myopic eyes among Chinese Han. DSM might be a  
19 protective mechanism for foveal schisis and a risk factor for extrafoveal schisis, SRD and ERM.

## 20 Strengths and limitations of this study

21 The study discusses DSM in the Chinese Han population, reports the prevalence of eight macular  
22 complications, and the relation to the choroidal changes.

23 The study compared the demographic characteristics between highly myopic eyes with and without  
24 DSM.

25 The sclera thickness, whose role in the formation of DSM has been hypothesized, was not investigated  
26 because the outer scleral border would be difficult to visualize in some cases, even if we used an SD-  
27 OCT in enhanced depth imaging modality.



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## 1 Introduction

Gaucher et al. first described the dome-shaped macula (DSM) as a morphologic feature in 2008 by characterizing it as an inward convexity or anterior deviation of the macula using optical coherence tomography (OCT)<sup>1</sup>. Although recent advances in OCT technology have helped to evaluate DSM, its physiopathology remains uncertain. Scleral infolding through the collapse of the posterior portion of the eye wall or vitreomacular traction were initially proposed as causes of DSM<sup>2</sup>. Subsequently, DSM was thought to be secondary to an ingrowth of the choroid, but recent research indicates that the main problem is focal scleral thickening in the foveal area<sup>3</sup>. However, the prevalence, clinical features, and mechanisms of this disease are still controversial.

Although DSM has been described in western countries and Japan, the clinical features of DSM are poorly documented in China. This study aims to analyze the frequency and morphologic features of DSM in a large series of highly myopic Chinese Han patients. The prevalence of DSM, the rate of myopic maculopathy and macular complications, such as foveal schisis, extrafoveal schisis, serous retinal detachment (SRD), epiretinal membrane (ERM), full thickness macular holes (FTMH), lamellar macular hole (MH), choroidal neovascularization (CNV) and macular hemorrhage, are compared between eyes with and without DSM.

## 18 Methods

The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Zhongshan Ophthalmic Center. The medical records of 736 consecutive highly myopic patients totaling 1472 eyes were reviewed at the High Myopia Clinic at Zhongshan Ophthalmic Center from Jan 2014 to Jul 2016. High myopia was defined as a refractive error of  $\leq -6.0$  diopters and axial length (AL) of  $\geq 26.5$  mm. Eighty-eight eyes (5.98%) were excluded due to AL less than 26.5 mm (12 eyes), rhegmatogenous retinal detachment (53 eyes), and poor-quality OCT images (23 eyes). Thus, 1384 eyes were enrolled in this study.

Comprehensive ocular examinations were performed in all participants. Spherical equivalent refraction (SER) was measured using an autorefractometer (KR-8900 version 1.07, Topcon Corporation, Tokyo, Japan) after complete cycloplegia for both eyes. Best-corrected visual acuity (BCVA) was determined with Snellen VA charts and was converted to the logarithm of the minimal angle of resolution (logMAR) for statistical analysis. AL was recorded using the IOL Master (Carl Zeiss, Tubingen, Germany) and fundus photographs (FP) were obtained using a TRC50LX (Topcon Corp.). OCT images were obtained with a spectral-domain OCT (SD-OCT, Heidelberg Engineering, Heidelberg, Germany) by a single experienced examiner who was masked to the clinical diagnosis. Vertical and horizontal scans that passed through the center of the fovea and raster scans which cover all the macular complications were obtained in each eye.

Two experienced retinal specialists (X.Z and X.D) read all of the FP and OCT. The presence of myopic maculopathy was defined and classified based on the International Photographic Classification and

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3 1 Grading System for Myopic Maculopathy<sup>4</sup>. Eight macular complications were identified, including  
4 2 foveal schisis, extrafoveal schisis, SRD, ERM, FTMH, lamellar MH, CNV and macular hemorrhage.  
5 3 All cases of CNV were diagnosed through a combination of OCT and FFA. DSM was defined as the  
6 4 presence of an inward bulge of the macular retinal pigment epithelium (RPE) of  $>50\ \mu\text{m}$  in the vertical,  
7 5 horizontal direction, or both, and was diagnosed with an OCT image according to the method designed  
8 6 by Ellabban and Ohsugi et al.<sup>5, 6</sup> ERM was defined as an avascular, fibrocellular membrane on the  
9 7 inner retinal surface<sup>7</sup>. FTMH was characterized by a vertical split in the neurosensory layers of foveal  
10 8 region. Lamellar MH was defined as a partial thickness defect of the macular area, with an irregular  
11 9 foveal contour and a schisis between inner and outer retinal layers, with intact photoreceptors<sup>8</sup>. The  
12 10 choroidal thickness (CT) was measured from the outer portion of the hyper-reflective line that  
13 11 corresponded to the RPE to the inner surface of the sclera using a single masked author<sup>9</sup>. Measurements  
14 12 were taken of the parafoveal choroid at 2 mm superiorly, inferiorly, temporally, and nasally to the  
15 13 fovea using a built-in caliber tool (Fig 1). The average value from these four locations is defined as  
16 14 the parafoveal choroidal thickness (PFCT). The ratio of the subfoveal to the parafoveal CT (S/PCT)  
17 15 was also calculated.

## 16 **Statistical analysis**

17 17 Age, SER, AL, BCVA, and ratios of subfoveal and parafoveal CT were compared between the two  
18 18 groups using independent sample *t*-tests. The subfoveal and parafoveal CT between the groups were  
19 19 compared using multiple linear regressions that paired the eyes based on AL, age and SER. The  
20 20 incidences of various macular complications and the distribution of myopic maculopathy between the  
21 21 groups were compared using chi-square tests or Fisher exact probability tests. A *P* value of  $<0.05$  was  
22 22 considered statistically significant.

## 23 **Patient and public involvement**

24 24 No patients or the public were involved in the study protocol design, the specific aims or the research  
25 25 questions, and the plans for the design or implementation of the current study. No patients or the public  
26 26 were involved in the interpretation of the results of the study or preparation of the manuscript. There  
27 27 are no plans to disseminate the results of the research to study participants.

## 28 **Results**

29 29 Out of the 1384 eyes, DSM was identified in 10.77% (149/1384), while 1235 highly myopic eyes  
30 30 without DSM served as the control. OCT imaging of the posterior pole showed that there were 88  
31 31 horizontal oval-shaped DSM, 9 vertical oval-shaped DSM, and 33 DSM with the shape of a round  
32 32 dome. No significant differences were observed based on gender, age, SER, or AL between eyes with  
33 33 DSM and without DSM (Table 1). Furthermore, there was no significant difference in BCVA  
34 34 ( $0.67\pm 0.57$  vs.  $0.55\pm 0.56$ ,  $P=0.464$ ). The subfoveal CT tended to be thinner in the DSM group  
35 35 ( $60.10\pm 46.61$  vs.  $73.81\pm 53.54$ ), but the difference was not significant ( $P=0.064$ ). Moreover, the ratio  
36 36 between the subfoveal and parafoveal CT showed no difference between the two groups ( $1.17\pm 0.72$   
37 37 vs.  $0.97\pm 0.76$ ,  $P=0.073$ ).

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3 1 Since macular complications, such as CNV, macular holes, and foveal schisis, are highly associated  
4 2 with impairment of visual function and the choroidal structure, the potential effect of DSM might be  
5 3 sheltered by these complications. In order to clarify the correlation between DSM and BCVA and  
6 4 choroidal thickness, eyes with macular complications, such as foveal schisis, extrafoveal schisis, SRD,  
7 5 ERM, FTMH, lamellar MH, CNV, macular hemorrhage and macular atrophy, were excluded in the  
8 6 subgroup analysis. Thus, sixty-seven DSM eyes and 692 control eyes with the absence of macular  
9 7 complications were enrolled (Table 2). Notably, the BCVA was much worse in DSM eyes compared  
10 8 to the control eyes ( $0.35\pm 0.36$  vs.  $0.55\pm 0.51$ ,  $P=0.002$ ). Again, the subfoveal CT showed no statistical  
11 9 difference between the two subgroups ( $69.04\pm 52.05$  vs.  $84.53\pm 57.94$ ,  $P=0.217$ ) (Fig 2). The mean  
12 10 parafoveal CT was  $66.09\pm 52.42$   $\mu\text{m}$  in the DSM group and  $94.80\pm 52.78$   $\mu\text{m}$  in the control group ( $P=$   
13 11  $0.586$ ). However, the ratio of subfoveal and parafoveal CT was significantly elevated in the DSM  
14 12 group ( $1.16\pm 0.62$  vs.  $0.93\pm 0.48$ ,  $P=0.021$ ). Moreover, the ratio of inferior and temporal CT were  
15 13 significantly elevated in the DSM group ( $1.47\pm 1.25$  vs.  $0.96\pm 0.57$ ,  $P<0.001$ ;  $1.24\pm 0.93$  vs.  $0.95\pm 0.82$ ,  
16 14  $P<0.001$ ), and there was no difference in superior CT ( $1.03\pm 0.69$  vs.  $0.85\pm 0.58$ ,  $P=0.189$ ) or nasal CT  
17 15 ( $2.08\pm 1.19$  vs.  $1.59\pm 1.05$ ,  $P=0.203$ ).

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20 16 No significant differences were observed based on age, AL, SER and BCVA between eyes with DSM  
21 17 and without DSM with macular complications. The rate of macular complications was also compared  
22 18 between patients with and without DSM. Overall, the prevalence of complications was not significant  
23 19 different in eyes with DSM compared to eyes without ( $38.93\%$  vs.  $36.19\%$ ,  $P=0.513$ ). The proportion  
24 20 of foveal schisis ( $17.24\%$  vs.  $62.86\%$ ,  $P<0.001$ ) was significantly lower in eyes with DSM compared  
25 21 to eyes without, while foveal SRD ( $5.17\%$  vs.  $0\%$ ,  $P=0.001$ ), extrafoveal schisis ( $39.66\%$  vs.  $5.37\%$ ,  
26 22  $P<0.001$ ) and ERM ( $24.14\%$  vs.  $10.74\%$ ,  $P=0.007$ ) were significantly more frequent in eyes with DSM  
27 23 compared to those without. However, there was no significant difference in the proportion of FTMH  
28 24 ( $3.45\%$  vs.  $10.74\%$ ,  $P=0.130$ ), lamellar MH ( $3.45\%$  vs.  $0.89\%$ ,  $P=0.144$ ), CNV ( $5.17\%$  vs.  $7.16\%$ ,  
29 25  $P=0.785$ ), and macular hemorrhage ( $1.72\%$  vs.  $2.24\%$ ,  $P=0.801$ ) (Table 3).

30 26 The severity of myopic maculopathy was also determined in all 1384 eyes. The fundus was  
31 27 unremarkable in 91 eyes (C0), as was the tessellated fundus in 411 eyes (C1), diffuse chorioretinal  
32 28 atrophy in 668 eyes (C2), patchy chorioretinal atrophy in 94 eyes (C3), and macular atrophy in 120  
33 29 eyes (C4). DSM was observed in each stage of myopic maculopathy from C0 to C4. The proportion  
34 30 of DSM was lower in C0 and C1, but higher proportion of DSM was found in C2-C4. (Table 4).

## 35 31 Discussion

36 32 To our knowledge, this study includes one of the largest sample size of DSM. Our results show that  
37 33 DSM is found in 149 out of 1384 (10.77%) highly myopic eyes in hospital-based Chinese Han. This  
38 34 ratio is similar to other hospital-based researches, for example, rate of 10.7% reported by Gaucher et  
39 35 al.<sup>1</sup>, as well as Chebil et al<sup>10</sup>, who found DSM in 24 out of 200 highly myopic eyes (12.0%) and Garcia-  
40 36 Ben<sup>11</sup> who found DSM in 28 out of the 260 (10.7%) pathologically myopic eyes. However, DSM was  
41 37 observed in as much as 20.1% (225/1118) of Japanese subjects examined by Liang et al<sup>12</sup>. The  
42 38 differences in the inclusion criteria used in these studies may explain the variations in their findings.  
43 39 In Liang's study, the SER was  $<-8.0$  diopters or axial length of  $\geq 26.5$  mm, which results in a narrower  
44 40 spectrum with a higher and more extensive myopia population. However, excluding the effect of the

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3 1 patient selection bias, the prevalence of DSM in Liang's study was still higher when compared with  
4 2 other studies. Furthermore, other studies performed with small Japanese sample sizes reveal a relative  
5 3 low rate of DSM, at approximately 10%. For example, Ohsugi et al. reported a DSM rate of 9.3%<sup>6</sup>.  
6 4 Therefore, considering the patient selection bias, we suggest that the prevalence of DSM in high  
7 5 myopia populations is nearly consistent across ethnic groups worldwide. Notably, all of the  
8 6 documented data, including the present study, came from hospital-based patients and were clinically  
9 7 based studies. It is difficult to assess precisely the prevalence of DSM in the general population.  
10 8 Therefore, further population-based epidemiological studies are desirable to explore the real incidence  
11 9 of DSM.

12 10 Variations in CT are considered related to the evolution of DSM and its associated complications. The  
13 11 results thus far have been quite controversial. For instance, it is not clear if the choroid is thickened,  
14 12 normal, or atrophic in eyes with DSM. Some studies show a thickened choroid in DSM<sup>3, 10</sup>, especially  
15 13 in eyes with SRD<sup>13</sup>, while others show that choroidal thickness decreases in DSM<sup>5</sup>. Some authors have  
16 14 recently suggested that thinning of the choroid is secondary to the elongation of the posterior  
17 15 staphyloma, or secondary to the sclera thickening. Furthermore, Caillaux et al.<sup>14</sup> show that the  
18 16 subfoveal choroid is thicker than the parafoveal choroid. The current study does not find any  
19 17 significant differences in either SFCT or PFCT between myopic eyes with and without DSM in both  
20 18 the overall population and the subgroup without other macular complications, while the ratio of  
21 19 subfoveal to parafoveal choroid appears to be significantly larger in patients with DSM without other  
22 20 complications. This was in accordance with the results reported by Ellabban et al.<sup>15</sup> who performed a  
23 21 longitudinal study that demonstrated a progressive thinning of the choroid and sclera in eyes with DSM  
24 22 in the paramacular area. Our results suggest that the thinning of the choroid occurs mainly outside the  
25 23 macular region in eyes with DSM, thus resulting in what appears to be a localized relative thickening  
26 24 of the sclera. The central macular choroidal area is preserved in eyes with DSM, while the paramacular  
27 25 choroid appears to be pathological.

28 26 In the current study, DSM is highly associated with the severity of myopic maculopathy, which is  
29 27 remarkable. According to META-PM study, myopic maculopathy is defined as C0-C4 from no  
30 28 macular lesions to macular atrophy, respectively. Categories 2 and above are classified as pathologic  
31 29 lesions, while Categories 1 and below are considered unremarkable<sup>4</sup>. Our data shows that DSM can  
32 30 be seen at any stage of myopic maculopathy, and the proportion of DSM increases with the progression  
33 31 of maculopathy. Only 1.10% and 4.87% of eyes with DSM fall into Categories 0 and 1, respectively,  
34 32 while 12.87% fall into Category 2, and 19.15% and 20.00% fall into Categories 3 and 4, respectively.  
35 33 To our knowledge, this is the first study to focus on the correlation between DSM and myopic  
36 34 maculopathy. These data show that DSM is not rare in eyes with advanced maculopathy; however,  
37 35 more careful OCT examinations are warranted to identify the particular entity. Furthermore, this study  
38 36 shows a dramatic increase in the prevalence of DSM between nonpathological category 1 and  
39 37 pathological category 2. Our data provides novel clinical evidence for the definition and classification  
40 38 of pathological maculopathy.

41 39 Besides myopic maculopathy, potential vision-threatening macular complications, such as SRD,  
42 40 FTMH, LMH, foveal schisis, and extrafoveal schisis, are well-established complications in DSM,  
43 41 dependently or independently. Interestingly, foveal schisis (17.24% vs. 62.86%,  $P < 0.001$ ) is less

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4 1 frequent in groups with DSM compared to those without, while extrafoveal schisis (39.66% vs. 5.37%,  
5 2  $P < 0.001$ ), SRD (5.17% vs. 0,  $P = 0.001$ ) and ERM (24.14% vs. 10.74%,  $P = 0.007$ ) are more frequent  
6 3 in those with DSM compared to those without. On the other hand, the rate of FTMH, lamellar MH,  
7 4 CNV and macular hemorrhage showed no significant differences between the two groups.  
8 5 Interestingly, FTMH with DSM was reported to be stable for 3-5 years without progression to retinal  
9 6 detachment even with extremely high myopia. The indentation effect induced by the DSM may prevent  
10 7 FTMH from progressing<sup>16</sup>. Our data suggests that DSM might be a protective factor of foveal schisis,  
11 8 but a risk factor for extrafoveal schisis, SRD and ERM, which was consistent with García-Ben at el<sup>17</sup>.  
12 9 García-Ben at el reported that the protective effect in patients with DSM by reducing the AL. However,  
13 10 in our study, the AL was longer in patients with DSM than those without DSM. It is well-documented  
14 11 that foveal schisis is mostly due to tangential and perpendicular vitreomacular traction. We speculate  
15 12 that the dome might play a role in reducing mechanical damage in the foveal area, but it may  
16 13 exaggerate the perpendicular vitreomacular traction in the parafoveal area as a result. Our data supports  
17 14 the hypothesis that passive resistance of the macular sclera occurs during the elongation of the  
18 15 peripheral staphyloma, thus providing new understanding of the mechanisms of DSM.  
19 16 SRD is extremely rare (3 eyes out of 149, 2.01%) in our study. Interestingly, the prevalence of SRD  
20 17 (sometimes called subretinal fluid, foveal detachment, or neuroretinal detachment in previous studies)  
21 18 ranges from 9.7% to 69%<sup>1, 10</sup> and is considered one of the major complications of DSM in western  
22 19 countries. SRD is present in 10 out of 15 eyes in the first study with DSM<sup>1</sup> and 52.1% (25 of 48 eyes)  
23 20 in the later study with the same group<sup>14</sup> even after ruling out SRD due to CNV. On the other hand, the  
24 21 prevalence of SRD is dramatically low in Asia (5.9% or 3 out of 51 patients)<sup>5</sup> and even lower in studies  
25 22 with large sample sizes<sup>12</sup>. The dramatic discrepancy in the frequency of SRD in DSM patients among  
26 23 ethnic populations is still elusive. Interestingly, in Imamura's study, patients are seen either in New  
27 24 York or Fukushima and the ethnic background of the patients with DSM is not mentioned<sup>3</sup>. The study  
28 25 shows a moderate rate of SRD with 8.70% (2 out of 23 patients), which seems to provide more  
29 26 evidence that there is a discrepancy in prevalence of SRD between different ethnic groups.

30 27  
31 28 Although SRD complicates a large proportion of DSM cases, its causes are poorly understood.  
32 29 Imamura et al.<sup>3</sup> hypothesize that SRD could result from the obstruction of outflow of choroidal fluid  
33 30 due to a thick sclera. However, others have noted that the submacular choroid is abnormally thick in  
34 31 eyes with SRD for this degree of myopia, thus suggesting a mechanism similar to central serous  
35 32 chorioretinopathy (CSC)<sup>13</sup>. Furthermore, the mean dome height is much higher in the study by Caillaux  
36 33 et al., and the difference in the dome height could be one of the causes of serious RD. Fortunately, the  
37 34 SRD has a relatively benign natural history in western studies<sup>18</sup>. In Suadier's study of 29 cases, SRD  
38 35 is present initially in 15 of 29 eyes, increases in four cases, and is resolved spontaneously in seven  
39 36 cases<sup>18</sup>.

40 37 This study has several limitations. First, this is a retrospective case study, and the potential inherent  
41 38 limitations are associated with the study's design. Second, the sclera thickness, whose role in the  
42 39 formation of DSM has been hypothesized, was not investigated because the outer scleral border would  
43 40 be difficult to visualize in some cases, even if we used an SD-OCT in enhanced depth imaging  
44 41 modality. Third, CT measurements were carried out manually using a built-in caliper. Further  
45 42 investigations using swept-source OCT, which allows for deeper tissue penetration into the choroid

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1 and the sclera with automatic measurement, would be beneficial. Despite these limitations, this is the  
2 first study to examine DSM among the Chinese Han population, and it is one of the largest case study  
3 of highly myopic patients with DSM.

4 In conclusion, DSM is a frequent subtype found in 10.77% of patients with high myopia. Visual acuity  
5 is compromised in eyes with DSM compared to those without. A comparison of highly myopic patients  
6 with and without DSM shows differences with western populations, while SRD remains a rare  
7 complication of DSM, at least in Asian populations. DSM may be a protective mechanism for foveal  
8 schisis, but it is positively associated with extrafoveal schisis, SRD and ERM.

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4 **Figure legend**

5 Figure 1: Measurement protocol from horizontal and vertical scans obtained with spectral-domain  
6 optical coherence tomography (SD-OCT) in eyes with dome-shaped macula (DSM) configuration. The  
7 retinal and choroidal thickness were measured at subfoveal and at point 2000  $\mu\text{m}$  superior, nasal,  
8 temporal and inferior to the fovea.  
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16 Figure 2: Comparison of dome-shaped macula (DSM) and non-DSM choroidal thickness in highly  
17 myopic eyes without macular complications.  
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Table 1. Demographic Characteristics of the 1384 Highly Myopic Eyes

	DSM		<i>P</i>
	Present (n=149)	Absent (n=1235)	
AL (mm±SD)	30.76±1.92	29.33±1.99	0.991
Sex (M/F)	55/93	221/426	0.489
Age (years±SD)	50.33±14.81	47.73±13.93	0.310
SER (SER±SD)	-17.42±5.30	-15.93±6.49	0.854
BCVA (logMAR±SD)	0.67±0.57	0.55±0.56	0.464
SFCT (µm±SD)	60.10±46.61	73.81±53.54	0.064
PFCT (µm±SD)	58.71±46.40	83.19±50.10	0.074
SF/PF	1.17±0.72	0.97±0.76	0.073

DSM: dome-shaped macula, AL: axial length, M: male, F: female, SER: spherical equivalent refraction, BCVA: best corrected visual acuity, SFCT: subfoveal choroidal thickness, PFCT: parafoveal choroidal thickness



Table 2 Comparison of eyes with and without DSM in 759 myopic eyes with normal macular architecture

	DSM		<i>P</i>
	Present (n=67)	Absent (n=692)	
Age	45.60±15.27	43.09±13.61	0.53
AL	30.66±2.04	29.38±2.07	0.869
SER	-17.48±5.23	-14.28±5.88	0.958
BCVA	0.55±0.51	0.35±0.36	0.002
SFCT	69.04±52.05	84.53±57.94	0.217
PFCT	66.09±52.42	94.80±52.78	0.586
SF/PF	1.16±0.62	0.93±0.48	0.021
SF/S	1.03±0.69	0.85±0.58	0.189
SF/I	1.47±1.25	0.96±0.57	0.000
SF/N	2.08±1.19	1.59±1.05	0.203
SF/T	1.24±0.93	0.95±0.82	0.016

DSM: dome-shaped macula, AL: axial length, SER: spherical equivalent refraction, BCVA: best corrected visual acuity, SFCT: subfoveal choroidal thickness, PFCT: parafoveal choroidal thickness, S: superior, I: inferior, N: nasal, T: temporal

Table 3. Comparison of Eyes with and without DSM in 505 Myopic Eyes with Macular Complications

	DSM		<i>P</i>
	Present (n=58)	Absent (n=447)	
Age	57.95±12.47	54.64±11.02	0.084
AL	30.92±1.74	29.22±1.83	0.974
SER	-17.31±5.46	-13.78±6.38	0.953
BCVA	0.82±0.62	0.88±0.67	0.420
Foveal schisis	10/58 (17.24%)	281/447 (62.86%)	0.000
Extrafoveal schisis	23/58 (39.66%)	24/447 (5.37%)	0.000
Foveal SRD	3/58 (5.17%)	0/447 (0%)	0.001
ERM	14/58 (24.14%)	48/447 (10.74%)	0.007
FTMH	2/58 (3.45%)	48/447 (10.74%)	0.130
Lamellar MH	2/58 (3.45%)	4/447 (0.89%)	0.144
CNV	3/58 (5.17%)	32/447 (7.16%)	0.785
Macular hemorrhage	1/58 (1.72%)	10/447 (2.24%)	0.801

DSM: dome-shaped macula, SER: spherical equivalent refraction, SRD: serous retinal detachment, ERM: epiretinal membrane, FTMH: full thickness macular hole, MH: macular hole, CNV: choroidal neovascularization

Table 4. Correlation of DSM and Myopic Maculopathy

Myopic Maculopathy	DSM		<i>P</i>
	Present (n=149)	Absent (n=1235)	
Category 0 (no macular lesions)	1/149 (0.67%)	90/1235 (7.29%)	0.001
Category 1 (tessellated fundus only)	20/149 (13.42%)	391/1235 (31.66%)	0.000
Category 2 (diffuse chorioretinal atrophy)	86/149 (57.72%)	582/1235 (47.13%)	0.015
Category 3 (patchy chorioretinal atrophy)	18/149 (12.08%)	76/1235 (6.15%)	0.007
Category 4 (macular atrophy)	24/149 (16.11%)	96/1235 (7.77%)	0.001

DSM: dome-shaped macula

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5

6 **Contributors** LL conceived the aims and overall design of the study. XZ and XD acquired the data  
7 and did the writing of the different sections, tables and figures. CL, SL, CJ and XL did the literature  
8 search and statistical analyses, XC, YL, ST, AZ and JL collected the data used in the study. All authors  
9 were involved in the study design, data analyses, data interpretation and revision of the paper. The  
10 following authors had access to the full raw dataset: LL and ZXJ. The corresponding author had the  
11 final responsibility to submit for publication.  
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27 research. No authors have any financial/conflicting interests to disclose.  
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30 **Ethics approval** Zhongshan Ophthalmic Center Ethics Committee.  
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32 **Provenance and peer review** Not commissioned; externally peer reviewed.  
33

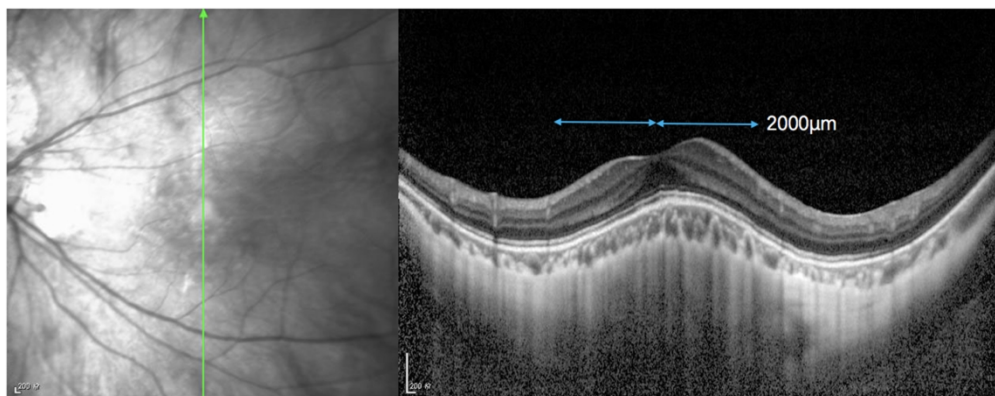
34 **Data sharing statement** Extra data can be accessed via the Dryad data repository at  
35 <http://datadryad.org/> with the doi: 10.5061/dryad.h544560.  
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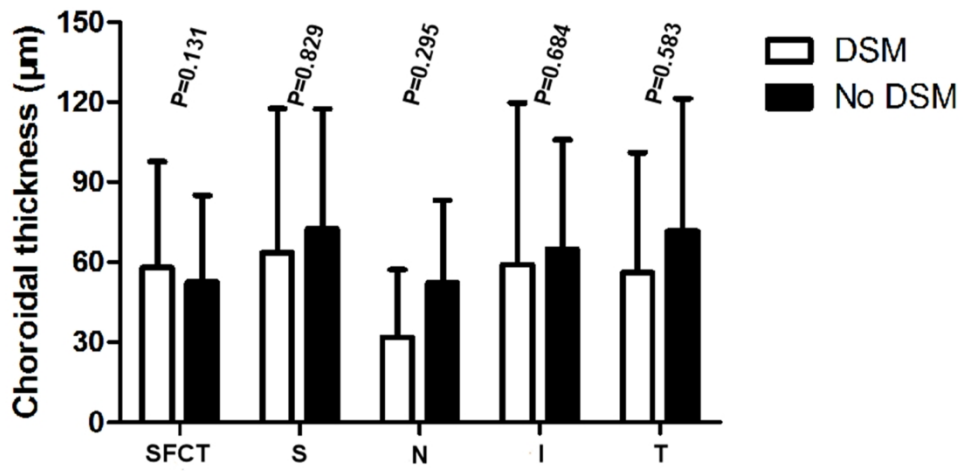
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Measurement protocol from horizontal and vertical scans obtained with spectral-domain optical coherence tomography (SD-OCT) in eyes with dome-shaped macula (DSM) configuration. The retinal and choroidal thickness were measured at subfoveal and at point 2000  $\mu\text{m}$  superior, nasal, temporal and inferior to the fovea.

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Comparison of dome-shaped macula (DSM) and non-DSM choroidal thickness in highly myopic eyes without macular complications.

168x90mm (300 x 300 DPI)



STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (page 1) (b) Provide in the abstract an informative and balanced summary of what was done and what was found (page 3)
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported (page 4)
Objectives	3	State specific objectives, including any prespecified hypotheses (page 4)
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper (page 4)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (page 4)
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants (page 4)
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable (page 4)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group (page 4)
Bias	9	Describe any efforts to address potential sources of bias (page 4)
Study size	10	Explain how the study size was arrived at (page 4)
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why (page 5)
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (page 5) (b) Describe any methods used to examine subgroups and interactions (page 5) (c) Explain how missing data were addressed (d) If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (page 5) (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (page 5) (b) Indicate number of participants with missing data for each variable of interest
Outcome data	15*	Report numbers of outcome events or summary measures (page 5)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (page 6) (b) Report category boundaries when continuous variables were categorized (page 6) (c) If relevant, consider translating estimates of relative risk into absolute risk for a

		meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses (page 6)
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives (page 6)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias (page 8)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence (page 8)
Generalisability	21	Discuss the generalisability (external validity) of the study results (page 8-9)
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based (page 15)

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at [www.strobe-statement.org](http://www.strobe-statement.org).