

Factors Influencing the Shear Rate Acting on Silicone Oil to Cause Silicone Oil Emulsification

Yau Kei Chan,^{1,2} Ning Cheung,^{1,3,4} and David Wong¹

¹Department of Ophthalmology, Li Ka Shing Faculty of Medicine, University of Hong Kong, Pokfulam, Hong Kong

²Department of Mechanical Engineering, Faculty of Engineering, University of Hong Kong, Hong Kong

³Singapore Eye Research Institute, National University of Singapore, Singapore

⁴Centre for Eye Research Australia, University of Melbourne, Melbourne, Australia

Correspondence: David Wong, Department of Ophthalmology, Li Ka Shing Faculty of Medicine, University of Hong Kong, Pokfulam, Hong Kong; shdwong@hku.hk.

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PURPOSE. The shear force between silicone oil (SO) bubble and aqueous during eye movements may underlie the development of SO emulsification. This study examines factors that may affect such shear force induced by eye movements.

METHODS. A surface-modified model eye chamber was put under large-amplitude eye movements (amplitude 90°, angular velocity 360°/s, and a duration 300 ms). Agarose-made indentations were introduced to mimic the effect of encircling scleral buckle. Two SOs (1300 and 5000 centistokes [cSt]), three volumes (3, 4, and 5 mL), and two eye chambers (with and without indentation) were tested. Video recording was used to capture the movements of SO inside the model chamber under various conditions.

RESULTS. The presence of indentation within the eye chamber significantly reduced the velocity of SO movements relative to the eye chamber movements ($P < 0.001$). To a lesser extent, an increase in viscosity also had a significant effect in reducing the relative movements. No significant effect was observed for the extent of SO fill in the chamber.

CONCLUSIONS. Our experimental model suggests indentation within an eye, such as that created by scleral buckling, may have the greatest influence in reducing shear force induced by eye movements. Therefore, using an encircling scleral buckle may be similarly or more effective than using SO with higher viscosity in lowering the propensity to SO emulsification.

Keywords: eye movements, vitreoretinal surgery, retina

Polydimethylsiloxane (PDMS)-based silicone oil (SO) has been introduced as a long-term intraocular tamponade agent since 1962¹ and it is effective in treating complicated retinal detachment,² giant retinal tear,³ ocular trauma,⁴ and proliferative vitreoretinopathy.⁵ However, postoperative complications, such as glaucoma,⁶ and toxicity to retina⁷ and optic nerve,⁸ were reported commonly after the use of SO as the endotamponade. These complications were associated with the emulsification of SO in vivo. Kinetic energy from eye movements induces the shear force between the SO bubble and aqueous, and, therefore, may contribute to the onset of SO emulsification. Other factors also have been implicated in the propensity of SO to emulsify. The physical properties of SO, such as its shear viscosity,^{9,10} surface tension,¹¹ and the homogeneity of its molecules,¹¹ all have been investigated previously. In addition, the presence of emulsifiers, like proteins and phospholipids,^{12,13} which reduces surface tension, also may affect the stability of the emulsified oil droplets in aqueous phase.¹⁴ However, little is known about the potential effect of the physical environment of the eye cavity, such as the geometry and the portion of oil fill, on SO emulsification.

Only one experimental study reported the potential effects of scleral buckling and the extent of SO fill on emulsification¹⁵ by using shaking as the mechanical agitation. The study demonstrated that encircling scleral buckle and a more complete fill of SO could reduce the number of emulsified SO

droplets formed after mechanical agitation. The investigators proposed that the results could be due to a reduction of the relative movement, or shear force, between the SO bubble and aqueous.

We previously have found that the SO viscosity was an important determinant for the peak velocity of the relative movement at the oil-aqueous interface and, thus, the maximum shear stress exerted at the interface during eye movements.¹⁶ This study also showed that our model was capable of estimating the shear rate during physiological eye movements. In the current study, we used the same model to investigate the effects of scleral indentation and oil fill on shear rate, and, thus, propensity for SO emulsification. We compared these two factors with the shear viscosity to find the optimal parameters in reducing emulsification of SO due to shear stress inside the eye.

MATERIALS AND METHODS

Silicone oil 5000 centistokes (cSt; Fluoron GmbH, Ulm, Germany) and silicone oil 1300 cSt (Arcadophtha, Toulouse, France) were used. SeaKem LE Agarose (Lonza, Rockland, ME, USA) was dissolved in Milli-Q water (Millipore Corporation, Billerica, MA, USA) at 100°C to achieve a 3% agarose solution. It then was allowed to cool down in room temperature to form gel. The gel then could be modified to the desired shape as the indentation.



FIGURE 1. Snapshots during a 90° rotation in the (a) absence of indent and (b) presence of indents. The *yellow line* indicated the slope of the chord of the oil bubble. The chamber started to rotate at *frame 1* and reached the constant speed at *frame 2*. The chamber then decelerated at *frame 9* and stopped at *frame 10*.

Eye Chamber Model

We used a similar approach for the eye model as published recently.^{17–21} The eye chamber, made of polymethylmethacrylate, has a volume approximately to 6.3 mL. Its inner surface was coated with protein to achieve a hydrophilic surface property. Two agarose-made indents then were glued onto the inner surface of the eye model chamber by α -cyanoacrylate. The SO was injected into the two chambers (with or without indentation) with three different volumes (3, 4, and 5 mL) under trypan blue-colored PBS so to avoid the influx of air into the chamber. The remaining space was filled with the colored PBS.

Simulation of Eye Movements

We used the mechanical system as described in our previous study¹⁶ to simulate large-amplitude eye-like movements (amplitude 90°, angular velocity 360°/s, duration 300 ms). The eye chamber was filled first with SO and then mounted onto the shaft of the stepper motor. A preset program was used to control the motor to undergo motion repetitively. The shaft encoder together with the data acquisition device provided information of the actual executed motion, such as the angular displacement, velocity, and acceleration.

Measurements of Angular Displacement and Angular Velocity

We used a digital camera with a recording speed of 30 frames per second to capture the movements of the SO contained within the eye chamber during motion. We measured the angular displacement of the SO bubble between successive frames using Image J software (National Institutes of Health [NIH], Bethesda, MD, USA; Figs. 1a, 1b). The velocity of SO was calculated by the difference of angular displacement between two successive frames divided by time per frame (0.033 seconds), and the relative velocity between the wall of the model eye chamber and the oil bubble then could be calculated using the velocity of the eye chamber from the shaft encoder subtracted by the velocity of SO movement.

Statistical Method

All statistical tests were performed by SPSS 16.0.1 software (SPSS, Inc., Chicago, IL, USA). The MANOVA tests were used to compare the difference between different velocity profiles. The independent variables were the extent of SO fill, viscosity of SO, and presence or absence of indentations. The dependent variables were the 14 time points started from 0.033 to 0.467 seconds (time interval = 0.033 seconds). The ANOVA test was used to study the differences of peak relative velocity between different situations. The Bonferroni test was used as the post hoc test of ANOVA test. *P* values <0.05 were considered to be statistically significant. Sample size $n = 8$ for all groups. All values in the graphs were shown as mean \pm SD.

RESULTS

Effect of Indentation

Statistically significant difference was observed in all cases in the comparison between the presence and absence of indentation (Table 1), and a reduction in the average relative velocity of the SO was observed in the presence of indentation when compared to those without (Fig. 2). In addition, it also showed that the presence of indentation significantly reduced the peak relative velocity in all the cases (Fig. 3).

Effect of Extent of SO Fill

In the experiments with SO 1300 cSt, significant differences of the velocity profiles were observed in all the cases except in

TABLE 1. Statistical Results of MANOVA to Study the Effect of the Presence of Indentation on the Relative Velocity Profile of SO

	Effect of Indents, With or Without Indents		
	3 mL	4 mL	5 mL
1300 cSt	$P < 0.001$	$P < 0.001$	$P < 0.001$
5000 cSt	$P < 0.001$	$P < 0.001$	$P < 0.001$

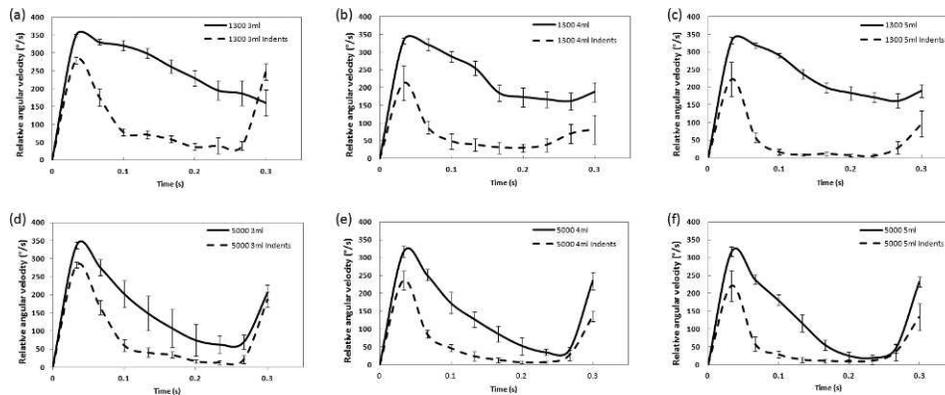


FIGURE 2. The relative velocity profiles of SO in the presence and absence of indents. (a-c) The SO used was 1300 cSt. (d-f) The SO used was 5000 cSt.

the comparison between 4 and 5 mL fill in the absence of indentation (Table 2). In the experiments using SO 5000 cSt, significant differences of the velocity profiles were observed in all the comparisons except in the case between 4 and 5 mL fill in the presence of indentation (Table 2). There was a trend indicating that the increase in the extent of oil fill decreased the average relative velocity in all the cases (Fig. 4). No significant reduction in peak relative velocity was observed in relation to variable SO fill without indentation (Fig. 5). However, in the presence of the indentation, the peak relative velocity in the 4 and 5 mL fills was significantly lower than that of the 3 mL fill in both SO groups (Fig. 5).

Effect of Viscosity

Statistically significant differences of the velocity profiles between SO 1300 and 5000 cSt were observed in all the cases except in the case of 5 mL fill in the presence of indentation (Table 3). The SO 5000 cSt group had an observable reduction in relative velocity than the SO 1300 cSt group without indentation (Fig. 6). On the other hand, no significant differences were seen in the peak relative velocity between SO 5000 and SO 1300 cSt in all the cases (Fig. 7).

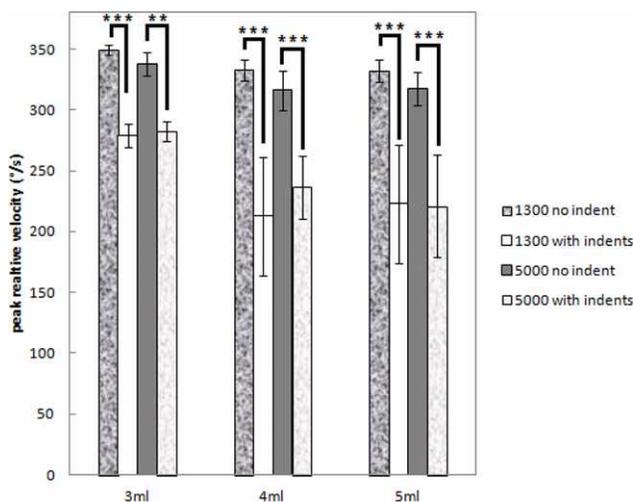


FIGURE 3. The comparison of the peak relative velocity of SO between the presence and absence of indents. Bonferroni test: ** $P < 0.01$, *** $P < 0.001$. Error bar: \pm SD.

DISCUSSION

Currently, surgeons have limited choice in long-term tamponade. Most choose SO between 1000 and 5000 cSt. One of the main considerations is that SO with higher viscosity might be less prone to emulsify. This belief stems from a number of in vitro experiments that involve different forms of mechanical agitation,^{13,22} which might not mimic the condition of SO inside the human eye. The force causing the dispersion of SO is derived from eye movement and is typically a shear force. Previously, our group had demonstrated the effect of viscosities (shear and extensional) of the SO on the shear rate. We showed that the shear viscosity determined the maximum shear rate at the interface between SO and the eye wall. It was, however, unexpected that the shear rate was only slightly decreased by 10% despite the shear viscosity of the SO had been increased from 5 to 12,500 cSt.¹⁶ In other words, shear viscosity, which previously was considered to be the major determinant for propensity for SO to emulsify, might not be as important as once thought. In this study, the effect of the presence of buckle indent and the extent of SO fill on the shear rate were investigated and compared to the effect of shear viscosity of the SO.

As shear rate depends on the relative velocity and the thickness of the aqueous film between the oil phase and the eye chamber wall, herein we assumed that the agarose indents did not make changes on the thickness of this aqueous film. In other words, the thickness of the aqueous layer was constant in all the experimental situations. Our results showed that the presence of indentation was the most significant factor that

TABLE 2. Statistical Results of MANOVA to Study the Effect of Fill of SO on the Relative Velocity Profile of SO

	3 vs. 4 mL	3 vs. 5 mL	4 vs. 5 mL
1300 cSt			
Effect of fill without indents oil	$P = 0.012$	$P = 0.008$	$P = 0.378$
Effect of fill with indents oil	$P < 0.001$	$P < 0.001$	$P = 0.001$
5000 cSt			
Effect of fill without indents oil	$P = 0.012$	$P = 0.029$	$P = 0.019$
Effect of fill with indents oil	$P < 0.001$	$P < 0.001$	$P = 0.073$

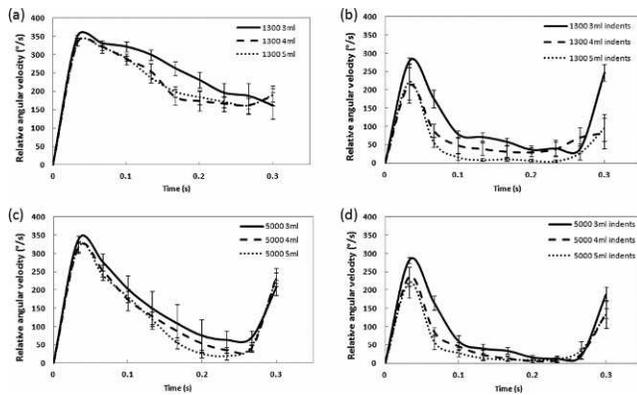


FIGURE 4. The relative velocity profiles of SO with different volumes of SO fill. (a–b) Amount SO used: 1300 cSt. (c–d) Amount SO used: 5000 cSt.

could reduce the average relative velocity of the oil phase and the chamber wall during eye-like motion (Fig. 2). In addition, the peak relative velocity had been reduced significantly by 16% to 36% within six different comparisons (Fig. 3). Such reduction would lead to a reduction on the maximum shear rate.¹⁶ Thus, our data suggested that the presence of indentation could effectively reduce the shear rate at the interface between oil phase and eye wall, and, hence, may reduce the propensity of SO to emulsify.

The effect of the extent of oil fill on the shear rate also was investigated in our study. A greater SO fill was shown to reduce the average relative velocity (Fig. 4). However, the reduction in the relative peak velocity was only significant in the cases in the presence of indents (Fig. 5). Moreover, there were no statistical differences in the relative peak velocity between 4 and 5 mL fill in the SO 1300 and 5000 cSt groups. The reduction was significant only in comparisons between 3 and 4 mL fill, and also between 3 and 5 mL fill. These observations suggested that increasing SO fill beyond a certain extent would not further reduce shear rate.

As expected, our study also showed that the effect of viscosity on the reduction of relative velocity was significant. The average relative velocity in SO 5000 cSt was much lower than that in SO 1300 cSt (Fig. 6), and this effect was observed

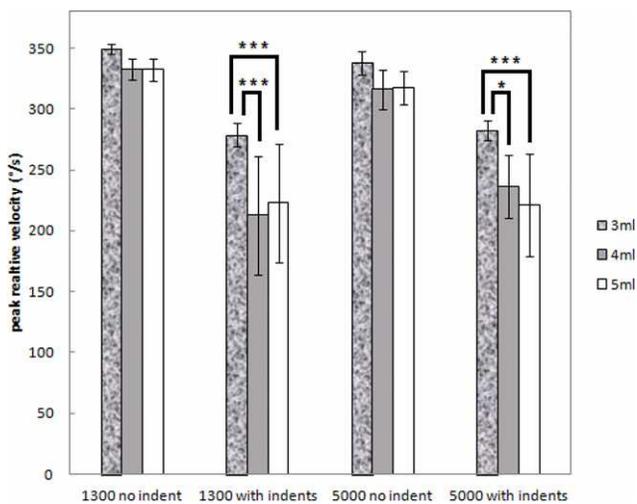


FIGURE 5. The comparison of the peak relative velocity of SO with different volumes of SO fill. Bonferroni test: * $P < 0.05$, *** $P < 0.001$. Error bar: \pm SD.

TABLE 3. Statistical Results of MANOVA to Study the Effect of the Viscosity of SO on the Relative Velocity Profile of SO

	1300 vs. 5000		
	3 mL	4 mL	5 mL
Effect of viscosity, without indents	$P < 0.001$	$P < 0.001$	$P < 0.001$
Effect of viscosity, with indents	$P < 0.001$	$P < 0.001$	$P = 0.053$

even in the absence of indentation. However, the reductions of the peak relative velocity were not significant in all comparisons given that the shear viscosity had been increased up to four times (Fig. 7). This finding also is consistent with our previous study.¹⁶

Apart from our study group, other investigators also have suggested that by changing the geometry of the eye globe using encircling scleral buckle, emulsification rate would decrease because of the reduction of relative motion between the SO bubble, aqueous, and eye wall.¹⁵ This particular study used two identical artificial eye chambers to show that the presence of encircling buckle significantly reduced the number of SO bubbles after mechanical agitation. In the presence of an encircling band, fewer emulsified bubbles were found in the higher portion of SO fill (90% vs. 75% filled), but no significant difference was observed when comparing different SO fill without the encircling band. These results are in keeping with our current study, although we studied the propensity of SO emulsification in terms of relative velocity, a measure of shear rate at the SO-aqueous interface. In other words, our dynamic eye model chamber was able to visually explain how indentation could have reduced SO emulsification. Of note, our dynamic eye model is considered to be more physiological than the model of de Silva et al.¹⁵ Firstly, the inner surface of our eye model was coated with protein on the surface to render hydrophilic properties. Importantly, this would prevent SO adhering onto the surface of the chamber. The SO is hydrophobic and the chamber, if made of plastic or glass, also would be hydrophobic. If the chamber was not surfaced modified to mimic the retina, SO might stick to the chamber, which yields misleading and different results. Secondly, our set up is designed to mimic physiological eye-like movement in that the axis of rotation virtually goes through the middle of the eye. The previous study used a rotational shaker in which the axis of rotation did not go through the chamber. Therefore, there almost certainly would be less relative movement. Thirdly, the velocity profile of our simulated eye model was designed to mimic actual physiological measurements obtained by recordings of saccadic eye movements from a large number of human subjects.¹⁶ All these improvements make our model more valid in understanding the formation of SO emulsification.

We believe that our results may have clinical relevance. The SO is an important tamponade agent used in vitreoretinal surgery, especially in complex retinal detachment repair. In some cases, SO cannot be safely removed due to the risk of retinal redetachment. However, SO tends to emulsify over time, leading to undesirable ocular complications, such as inflammation and glaucoma.⁶ Currently, the only strategy to limit emulsification is to choose SO of high viscosity with high purity. Most surgeons believe that 5000 cSt SO to be more emulsification-resistant than 1000 cSt SO. However, it is true to say that surgeons are divided, some opting to use 1000 cSt SO for one or more reasons. The evidence that 5000 cSt SO is more resistant stems mainly from in vitro study involving

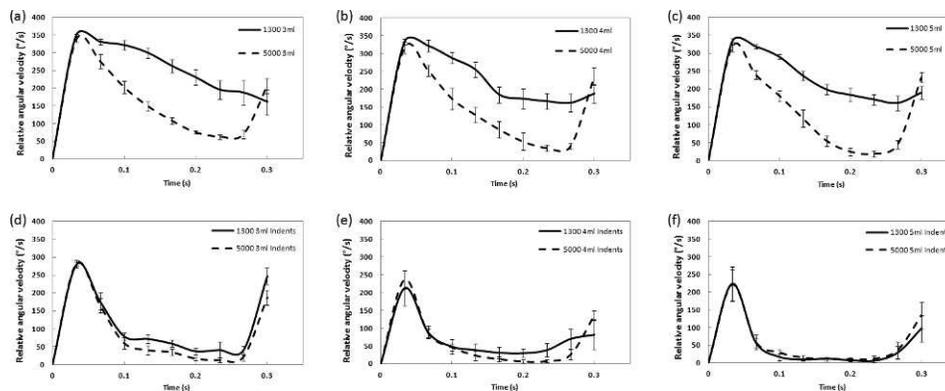


FIGURE 6. The relative velocity profiles of SO with different shear viscosity in (a-c) absence of indents, (d-f) presence of indents.

mechanical agitation in the form of ultrasound or shaking. Such mechanical forces, however, do not normally occur in the eye. Most agree that in patients, both SOs emulsify in time. The difference in the propensity to emulsify might not be so great in patients than in vivo for two important reasons. The SO in situ in patients is acted on mainly by shear force as the eyes rotate during saccades. The shear force, however, is a product of shear rate and viscosity. If the saccadic eye movements were stereotypical, moving with the same angular speed, then there may be a greater shear force acting on a 5000 cSt SO than 1000 cSt. Additionally, SO would tend to shear thin during high shear rate, which is a phenomenon that the apparent shear viscosity would decrease. This might also diminish the actual difference in shear viscosity and, thus, the shear force acting on the two types of SO.

The limitation of this study also should be noted. Clearly, we have not tested indents of all shapes and sizes. In addition, any internal structures, such as the iris and lens, are indentations that also could cause and may impede on the relative freedom of movement. Any indentation would depart from a near spherical oil bubble inside a near spherical eye cavity, a situation that gives the maximum freedom for the movement between SO and eye wall.

Many studies on emulsification of SO are hampered by the difficulties in controlling for individual patient factors, such as the extent of inflammation, breakdown of the blood ocular barrier, and presence of blood-derived potential surfactants. To

date, to our knowledge there is no conclusive evidence from a randomized clinical trial that favored 5000 vs. 1000 cSt SO in reducing rate of emulsification.²³ We think our current study, using an experimental eye model, contributes to the understanding of how shear stress might be influenced by the shape of the eye cavity, the viscosity of the SO used, as well as the degree of SO fill in the eye. Of these three factors, changing the eye shape, in the form of indentation, may exert the greatest effect in reducing shear stress on the SO bubble. Nonetheless, despite our study result, the evidence is likely not sufficient to recommend routine application when one is not otherwise indicated, to reduce risk of SO emulsification. In fact, a previous clinical study,²⁴ based on retrospective review of medical records, did not find any correlation between the use of encircling band and onset of SO emulsification. Thus, additional studies to clarify the role of scleral buckling are needed. Nonetheless, we could consider retaining the indent in revision surgery where the eye had encirclement or segmental explants.

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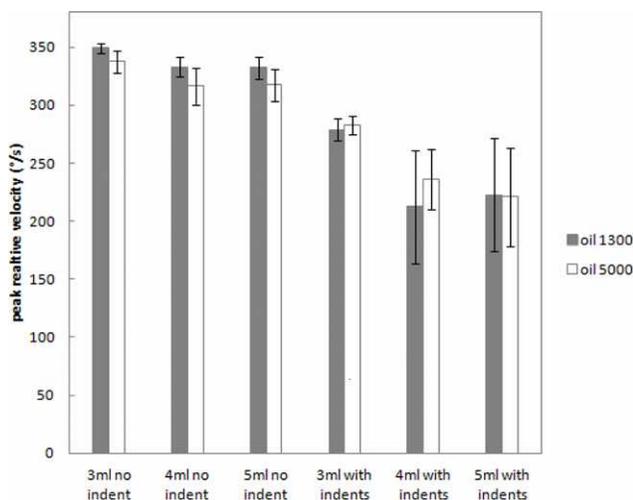


FIGURE 7. The comparison of the peak relative velocity of SO between SO 1300 and 5000 cSt. Bonferroni test. Error bar: \pm SD.

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