·Clinical Research·

New technique for removal of perfluorocarbon liquid related sticky silicone oil and literature review

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Received: 2021-02-26 Accepted: 2021-06-01

Abstract
● **AIM:** To investigate the safety and efficacy of sticky silicone oil (SSO) removal using a 22-gauge vein detained needle and inner limiting membrane (ILM) wrap-and-peel technique.

● **METHODS:** This retrospective consecutive case series reviewed the records of patients with a history of retinal detachment who had received silicone oil and perfluorocarbon liquid (PFCL) as intraocular tamponades. Patients were included in the analysis if they exhibited SSO remnants during silicone oil removal. The aspiration of most of the SSO remnants was performed by a 22-gauge vein detained needle. The small amounts of droplets adhered to the macula and epi-macular membrane were subsequently removed by the ILM warp-and-peel technique. The anatomical and functional outcomes, and postoperative complications were recorded. *In vitro* experiments were performed to simulate the formation of SSO remnants in four groups.

● **RESULTS:** Of 711 patients who underwent silicone oil removal during the study period, 9 patients exhibited SSO remnants and underwent follow-up for at least 3mo. Seven eyes (78%) underwent the ILM wrap-and-peel technique to completely remove small droplets of SSO that were glued to the macula and epi-macular membrane. No obvious complications occurred. Postoperative optical coherence tomography revealed normal retinal structure in all patients. *In vitro* analyses showed that balanced salt solution and prolonged vibration (for 1wk) had the strongest effects on silicone oil and PFCL compound opacities.

● **CONCLUSION:** SSO remnants could be removed in an intact manner and without complications, using a vein detained needle-assisted and ILM wrap-and-peel technique. The findings suggest that PFCL and infusion fluid should be completely removed before silicone oil injection to prevent SSO formation.

● **KEYWORDS:** sticky silicone oil; perfluorocarbon liquid; silicone oil removal; inner limiting membrane peel; *in vitro* analysis

DOI:10.18240/ijo.2021.12.14

Citation: Lin HS, Tang YP, Zhang L, Liu EZ, Ye LY, Xu MN, Wu RH, Hu ZX. New technique for removal of perfluorocarbon liquid related sticky silicone oil and literature review. *Int J Ophthalmol* 2021;14(12):1903-1908

INTRODUCTION

Perfluorocarbon liquid (PFCL), which is widely used to flatten a detached retina during surgery, is routinely removed at the end of the procedure[1-3]. Remnant PFCL in the vitreous cavity reportedly can induce retinal damage and vitreous emulsion, because PFCL has high density and low viscosity[4]. However, in some instances, PFCL is intentionally maintained at the end of vitreoretinal surgery; it serves as a temporary tamponade in eyes with a giant retinal tear or retinal hole in the inferior quadrant[5-6]. Silicone oil is used as an essential vitreous substitute in the treatment of complicated retinal detachment (RD), which is injected after PFCL removal[7-8]. The attachment of PFCL and silicone oil are presumably unavoidable in vitreoretinal surgery. Dissolved small amounts of PFCL, impurities of perfluoro-octane (PFO) or perfluorodecalin (PFD), and/or the biological environment of the vitreous cavity may promote formation of specific liquids[9-10]. Prolonged intraocular coexistence of PFCL and silicone oil could lead to complications involving sticky silicone oil (SSO) formation[11-12].

SSO, first reported in the Netherlands in 2000, is a hyper-viscous, gel-like liquid; its specific gravity is heavier than the specific gravity of water[13]. SSO, sometimes called "heavy silicone oil" or "sticky oil," mostly adheres to the macular area, after macroscopically apparent silicone oil has been removed intraoperatively. Previous reports indicated that small amounts of PFCL, an impurity of PFO, dissolved in the biological environment of the vitreous cavity could promote SSO formation[9,14]. Furthermore, the opacity and shear viscosity of SSO could change because of temperature variations[9]. The adhesion of SSO remnants to the retina can lead to photoreceptor toxicity and vision impairment[15]. Cases of retained PFCLs dissolved in silicone oil have been reported sporadically in the literature[16]. In the past, the main treatment of SSO remnants was observation[17]. The removal of SSO has been difficult[18-19] and can lead to serious iatrogenic complications such as choroidal hemorrhages and peripheral retinal tears[13].

Herein, we present a series of cases in which PFCL was retained in a silicone oil-filled eye; the amount of SSO ranged from a small amount to very large remnants. During the removal of silicone oil, 22-gauge vein detained needles and the inner limiting membrane (ILM) wrap-and-peel technique were used to remove SSO from the macula completely and safely. We reproduced the intraocular SSO by mixing different conditions (proportion, temperature, and vibration) of silicone oil-and-PFCL mixtures *in vitro*.

SUBJECTS AND METHODS

Ethical Approval This non-comparative, case series protocol adhered to the principles in the Declaration of Helsinki. The informed consent was obtained from the patients.

Study Population We retrospectively examined the records of 711 patients who underwent silicone oil removal after the use of silicone oil tamponade, for various vitreoretinal indications, during the period of January 2016 and December 2017. Complete ophthalmic examinations [*e.g.*, best-corrected visual acuity (BCVA), intraocular pressure (IOP) measurement, fundus photography, and spectral-domain optical coherence tomography (SD-OCT)] were performed before surgery and at the final follow-up after SSO removal.

Surgical Technique All eyes underwent 23-gauge standard three-port pars plana vitrectomy. A 22-gauge vein detained needle (Tuoren Inc., Hebei Province, China) with the steel needle core removed, was attached to a Luer slip needle-free connector (NIPRO Inc., Osaka, Japan), which interfaced the vein detained needle through the extrusion tubing of the vitrectomy machine (Figure 1). Active aspiration was controlled using the foot pedal of the vitrectomy machine that had a maximum suction of 600 mm Hg. The catheter of the vein detained needle was cut to produce a beveled tip that could penetrate through the scleral incision. The surface of the SSO was carefully touched with the catheter, under controllable suction power (online supplementary Video 1).

The ILM wrap-and-peel technique was used when small droplets of SSO remained glued to the macula. When necessary, indocyanine green was used to stain the ILM. The

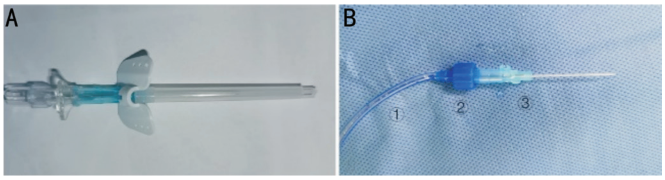

Figure 1 Structure of this combined instrument A: 22-gauge vein detained needle; B: Modified vein detained needle consisting of a Luer slip lock (2) interface with a 22-gauge vein detained needle (3) connected to the vitrectomy machine through active aspiration tubing (1).

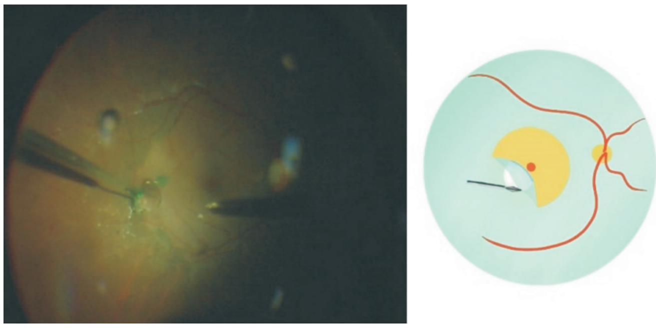

Figure 2 ILM wrap-and-peel technique The free ILM flap was used to wrap all SSO droplets, which were then removed with the ILM.

ILM was peeled in circles around the SSO droplets, and the free ILM flap was used to wrap all SSO droplets, thus releasing the retinal adhesion (Figure 2). The ILM was then removed together with the SSO droplets.

***In Vitro* Experiments** The samples were divided into four groups. Groups A and B were kept at a constant temperature in a shaking incubator set to 37°C (*i.e.*, body temperature). Sample vibration was adapted to mimic eye movements. Group A was exposed to vibration (100 vibrations/min), and group B was not exposed to vibration. Groups C and D were kept at constant temperature in a shaking incubator set to 22°C (*i.e.*, room temperature), with and without vibration (100 vibrations/min), respectively.

Each group consisted of two vials: subgroup one, 2.5 mL of 5000-mPas viscosity silicone oil (RT SIL-OL, Zeiss; Berlin, Germany) and 2.5 mL of PFD (RT DECALIN, Zeiss); subgroup two, 1 mL of additional balanced salt solution (BSS) combined with 1 mL of PFD and 1 mL of silicone oil to mimic residual infusion fluid.

RESULTS

Among 711 operations, SSO was encountered in 9 eyes (1.3%) of 9 patients (4 men and 5 women; mean age, 52±11.4y, range: 28-67y). Patients and procedural factors investigated in this study are listed in Table 1. Patients underwent active removal of SSO using the vein detained needle-assist, most with the ILM wrap-and-peel technique. The mean interval from the silicone oil tamponade surgery to SSO removal was 3.5±1.6mo (range: 0.1-6mo). There were no intraoperative or postoperative complications. In the follow-up exams, no

Table 1 Demographics, diagnosis, surgical interference and follow-up of patients with SSO

No.	Age (y)	Sex	Eye	Pre-SOR, BCVA	PFCL type	Diagnosis	Duration (mo)	Epiretinal membrane	Operation	Post-SOR, BCVA	Follow up (mo)
1	28	M	OD	0.53	PFO	RRD	4	Yes	VDN-assist+ILM W&P	0.70	10
2	49	M	OS	0.80	PFO	RRD	4	Yes	VDN-assist+ILM W&P	1.00	5
3	47	F	OS	1.30	PFO	RRD	4	Yes	VDN-assist+ILM W&P	1.00	4
4	48	F	OS	0.70	PFO	RRD	3	Yes	VDN-assist+ILM W&P	0.15	5
5	53	F	OS	0.80	PFO	RRD	4	Yes	VDN-assist+ILM W&P	0.22	6
6	52	F	OS	2.00	PFD	Recurrent RRD	0.1	Yes	VDN-assist+ILM W&P	0.05	5
7	63	M	OS	1.30	PFO	RRD	6	No	VDN-assist	1.00	4
8	61	F	OS	1.00	PFO	RRD	4	Yes	VDN-assist+ILM W&P	1.00	6
9	67	M	OD	1.70	PFO	RRD	3	No	VDN-assist	0.40	9

BCVA: Best-corrected visual acuity; SOR: Silicone oil removal; RRD: Rhegmatogenous retinal detachment; W&P: Wrap and peel; VDN-assist: Vein detained needle -assist; ILM: Inner limiting membrane; PFCL: Perfluorocarbon liquid.

SSO was found on fundus ophthalmoscopy, and no patients reported any floaters or visual disturbance. OCT examination showed normal retinal structure in all patients. The mean BCVA improved from 1.09±0.43 to 0.51±0.63 logarithm of the minimum angle of resolution (logMAR) at the final visit. Retinal reattachment was achieved in all patients (100%) after tamponade removal. Among the patients with SSO, different batches of PFO or PFD and silicone oil were used. These batches were also used in patients with normal silicone oil outcomes.

In 7 of the 9 operations, the ILM wrap-and-peel technique was used to remove small SSO droplets, after the vein detained needle-assisted technique was used to aspirate the majority of the silicone oil. In the rest 2 cases, the SSO could be cleared completely using only the vein detained needle.

In one patient (case No.6), a large amount of residual PFCL was evident (Figure 3). During surgery, after macroscopic silicone oil had been aspirated, a hypo-viscous, pink, opaque liquid was observed in the button of the vitreous cavity. To aspirate the compound, a modified 22-gauge vein detained needle was used (Figure 1A). At the end of the aspiration, after most turbid compound had been removed, a few transparent droplets were removed using the ILM wrap-and-peel technique (Figure 2). Sterilized air was used to fill the vitreous cavity at the end of surgery.

***In Vitro* Experiments** After 7d of incubation, the silicone oil and PFCL mixture was macroscopically turbid in both vibration Groups A and C (Figure 4). The contents of the vials in group A, which were mixed with BSS, appeared milkier white than did the two-component mixture in the PFD portion. There were "bubbles" in the silicone oil portion, similar to the findings in case No.6. Group C showed a mildly turbid layer between the PFD-silicone oil layer and the BSS layer. In the non-vibration groups (B and D), all vials remained clear at the border between the layers.

DISCUSSION

Findings of a mixture of PFCL and silicone oil in eyes after vitreoretinal surgery have been reported sporadically in recent decades (Table 2). Veckeneer *et al*[13] reported this result in 28 of 234 silicone oil removal procedures in Rotterdam Eye Hospital. Ghoraba *et al*[20] reported this finding in eight of 796 procedures. In most patients, a similar compound was detected: a sticky, transparent, gel-like substance that strongly adhered to the retina. Gas chromatography-coupled mass spectroscopy analyses showed partially fluorinated carbons in the PFO and PFD[17,20]. In contrast to these earlier reports, only one of our patients with substantial PFCL exhibited a mixture with large volume, opaqueness, and less stickiness, compared with SSO, as demonstrated in our *in vitro* experiment.

Romano *et al*[9] demonstrated that interactions of PFCL with heavy silicone oil, as well as variations in temperature, were responsible for the increased oil opacity. Their compound (5 mL heavy silicone oil and 250 μL of PFCL) became turbid when cooled from 36°C to 22°C. A similar turbid compound was observed in case No.6 in our study. These findings suggest that surgeons should remove most PFCL and infusion fluid (as much as possible) before silicone oil injection to prevent sticky silicone formation. The extensive remnants of PFCL combined with silicone oil formed a large amount of "turbid" SSO. To explain this, we assume that the liquid temperature decreased because of our perfusate, which was at a lower temperature compared with the intraocular fluid. However, we could not rule out as other contributing factors: the large amount of remnant PFCL (which altered the mixture ratio) and eye movements causing the turbid liquid.

In our *in vitro* experiment, we found that vibration and the presence of BSS could increase the macroscopic opacity of the compound. These findings suggest that patients should reduce eye movement to prevent sticky silicone formation. In addition, the bubble in the turbid layer of group A vials was similar to the results in our case No.6. In group A, we presume that the turbid liquid was caused by numerous small bubbles and the BSS mixture (Figure 5). However, we only used PFD and

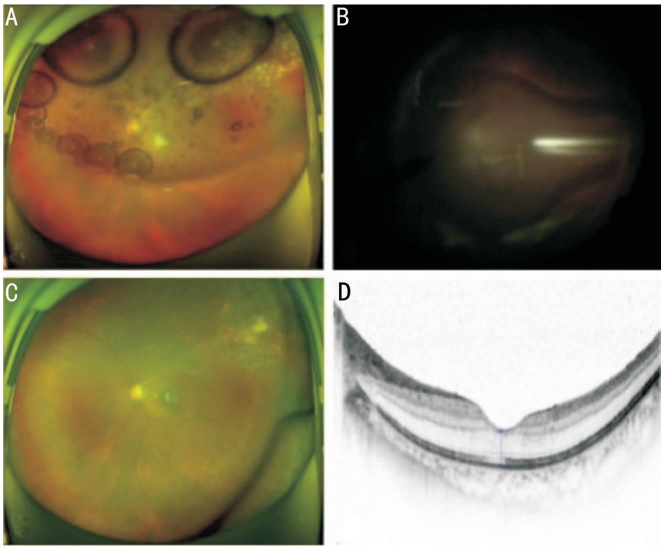

Figure 3 Fundus examination of the left eye of a 52-year-old female patient (case No.6) A: Fundus color photograph obtained at the first examination. Silicone oil-PFCL borderline is evident, along with various sizes of "bubbles" mixed in the silicone oil; B: Turbid compound coating the translucent SSO; C: After removal of PFCL and silicone oil compound, the retina remained attached at the 1-month follow-up; D: OCT examination showed normal retinal structure at the 1-month follow-up.

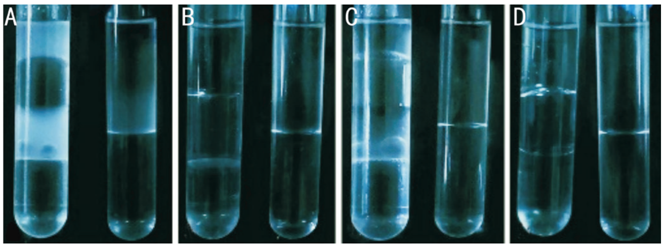

Figure 4 *In vitro* analysis results A: Group A (37°C with vibration); B: Group B (37°C without vibration); C: Group C (22°C with vibration); D: Group D (22°C without vibration). In the presence of BSS, vibration (groups A and C) led to the greatest opacity. Each group consisted of two subgroups: left, viscous silicone oil, and PFD; right, viscous silicone oil, PFD, and additional BSS.

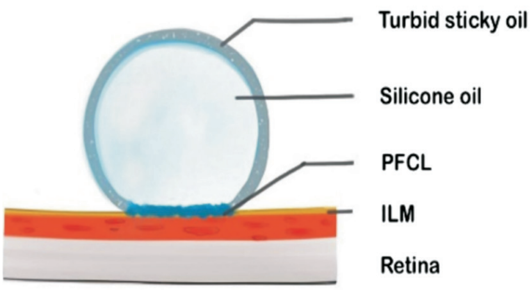

Figure 5 Schematic drawing of "SSO" with turbid liquid The turbid compound coating the translucent silicone oil which adhering to retina though thin PFCL layer.

5000-mPas viscosity silicone oil, which could not represent the full composition of PFCL.

Table 2 Summaries of clinical findings in selected studies concerning SSO

Study	No. cases	Indication of vitrectomy	Type of PFCL	Method of SOR	SO viscosity	Interval since the SO injection	ILM peeling	Complication	VA improvement or without visual disturbance (pre- & post-SOR)
Veckeneer *et al*	28/234	PVR related RRD (majority)	PFO	Retained	1000CS	94.3±60.0d	Not mentioned	Iatrogenic injury (3) Moderate (4) Mild (2)	SO migrated out of macula (2) at 2 and 4wk
Wang *et al*	2	RRD	PFD	Retained	Not mentioned	2 and 3mo	Not mentioned	Moderate (1) ERM&mild (1)	SO migrated out of macula (1) at 4mo
Ghoraba *et al*	8/796	RRD 1y (7) Trauma (1)	PFO	Retained	5000CS (6) 5500CS (2)	5.1±2.5mo	Yes (2) No (6)	Severe (2) Moderate (6)	SO released from retina (1) after 8mo
Fukumoto *et al*	1	RRD	Not mentioned	Aspiration of the PFCL layer underneath the SO	Not mentioned	During the first surgery	No	None	No symptoms
Present study	9	RRD	PFD (1) PFO (8)	ILM W&P (7) VDN-assist (9)	5000CS		Yes (7) No (2)	None	VA improvement (6), without visual disturbance (3)

Severe: Sticky oil at fovea, marked diminution of vision, central scotomata; Moderate: Sticky oil at parafovea, moderate visual disturbance; Mild: Sticky oil migrates out of macula, mild visual disturbance. SOR: Silicone oil removal; SO: Silicone oil; PFO: Perfluoro-octane; PFD: Perfluorodecalin; RRD: Phegmatogenous retinal detachment; PFCL: Perfluorocarbon liquid; ILM: Inner limiting membrane; ERM: Epiretinal membrane.

Dresp and Menz[21] and Zewar and Lochhead[22] suspected that the "stickiness" phenomenon was caused by reduction of the silicone oil surface tension by surrounding aqueous material, PFCL contamination, and organic materials, which led to lower substance cohesion compared with its adhesion to the underlying surface. Furthermore, Winter *et al*[23] demonstrated that total PFCL removal during surgery was very difficult and that a small amount of PFCL might remain as a transparent layer on the retinal surface. These results indicated the critical need to remove the PFCL layer between the retina and SSO. We presumed that ILM peeling could successfully resolve this problem.

The options for managing SSO remnants on the macula must be considered. SSO remnants may have various effects on visual prognosis. For instance, central relative scotomata, diminished vision, and mild or moderate visual disturbance have been reported[20]; OCT examinations have revealed no membrane underneath or around the SSO. Spontaneous release from the retina occurred in 4 of 38 eyes (10.5%) within 2wk to >8mo. Fukumoto *et al*[24] reported one case of SSO removal with aspiration of the PFCL layer underneath the silicone oil. The patient's visual acuity improved and no postoperative visual disturbance was noted. In our study, all nine patients underwent complete removal of the sticky oil and showed improved final vision. Therefore, patients benefit from the removal of silicone oil droplets adhering to the macular area, which improves visual acuity and eliminates visual disturbances.

Ensuring safety and avoiding iatrogenic injury are the highest priorities when removing SSO. Veckeneer *et al*[13] reported two choroidal hemorrhages and one peripheral retinal tear after forceful attempts. Fukumoto *et al*[24] successfully removed SSO by aspiration of the PFCL layer between the silicone oil and the retina. However, this method requires placement of the vitreous cutter very close to the retina where the PFCL layer is located. Furthermore, the SSO described by Fukumoto *et al*[24] had formed during the surgery; thus, it had only a short contact time, which might have limited SSO adhesion to the retina. In contrast, our approach involved a modified ILM peeling operation, whereby a vein detained needle was used to aspirate most of the SSO, and the "ILM wrap-and-peel" technique was used (when necessary) to remove tiny droplets of remnant oil. To remove the SSO, backflush instruments made by MedOne or Alcon and vein detained needles without steel needle cores have been considered. Compared with backflush instruments, a vein detained needle has a larger oblique suction inlet and lower cost. The larger vein detained needle opening could remove the "sticky compound" with greater efficiency and suction power. Thus, we used vein detained needles to aspirate the SSO. Because our vein detained needle-assisted technique allowed control of the aspiration power and the vein detained needle had a larger bore opening, compared with a vitreous cutter (allowing maintenance of a safe distance from the macula), our method reduced the risk of iatrogenic injury. ILM peeling might have provided additional benefit because one of our patients showed a tendency for epiretinal membrane growth in the nasal macula at the 1-month follow up; ILM peeling might have helped to avoid further intervention.

In summary, we have demonstrated a safe and effective technique for complete SSO removal. The technique appears to yield greater BCVA improvement and visual disturbance elimination, compared with an observational approach. Moreover, we found that the addition of BSS and vibration caused increased SSO opacity *in vitro*. Further studies are required to confirm the clinical relevance of our findings.

ACKNOWLEDGEMENTS

We thank Claire Barnes, PhD, and Ryan Chastain-Gross, PhD, from Liwen Bianji, Edanz Editing China (www.liwenbianji.cn/ac), for editing the English text of a draft of this manuscript.

Foundation: Supported by the Wenzhou Basic Scientific Research Program (No.20211003).

Conflicts of Interest: Lin HS, None; **Tang YP,** None; **Zhang L,** None; **Liu EZ,** None; **Ye LY,** None; **Xu MN,** None; **Wu RH,** None; **Hu ZX,** None.

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