

## The Emerging Role of Heavy Silicone Oil as a Tamponade Agent



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Intraocular tamponade agents have been in use by vitreoretinal surgeons for nearly a century. Traditional agents, still widely used, include long acting gases such as perfluoropropane ( $C_3F_8$ ) and sulphur hexafluoride ( $SF_6$ ), and silicone oil. What these so called 'lighter than water' substances have in common is that they float upwards in the aqueous, on account of their specific gravity being lower than that of water. A consequence of this is that in the upright position the superior retina is very well supported, leaving the inferior retina less well so. In the past, investigation into the use of fluorinated silicone oils as a heavy tamponade revealed high complication rates, with the development of intraocular inflammation and promotion of proliferative vitreoretinopathy (PVR) development.<sup>1,2</sup> Subsequently, a second group of even heavier substances, the perfluorocarbon liquids (PFCL), have gained an important role as an intraoperative tool to manipulate the retina. However, they are not suited to long-term internal tamponade either, as they cause histological damage to the retina.<sup>3</sup> More recently, there has been renewed interest in the development of 'heavier than water' long-term tamponade agents that sink in the eye. The liquid semi-fluorinated alkanes are a group of substances which have a specific gravity greater than water, but less than PFCL. A pilot study into the use of one such substance, perfluorohexyloctane ( $F_8H_8$ ), as a long-term tamponade in humans with complicated retinal detachments, demonstrated favourable re-attachment rates, but was associated with early and extensive emulsification with dispersion of oil droplets into the anterior and posterior segments (Figure 1).<sup>4</sup> And so, to date, we are yet to find one single agent that satisfies the requirements of a long-term inferior tamponade.



**Figure 1:** Extensive dispersion of emulsified  $F_8H_8$  droplets in the anterior chamber.

### The physical properties of a good tamponade agent

The effectiveness of an internal tamponade agent depends on how well it displaces aqueous from the surface of the retina. This ability is a function of the following physical variables:

#### 1. Specific gravity (SG)

This governs whether a vitreous substitute will sink or float in aqueous. The SG of water is  $1.00g/cm^3$ ; the SG of aqueous fluid or liquid vitreous is a little higher than this. As already mentioned, the SG of silicone oil is slightly lower than that of water at  $0.97g/cm^3$ . Conversely, the SG of  $F_8H_8$  is higher at  $1.35g/cm^3$ . The SG is also the main determinant factor for the shape of any intraocular bubble (see below).

#### 2. Buoyancy

Archimedes states that the buoyant force exerted on a submerged object is equal to the weight of the displaced fluid (aqueous). An intraocular bubble of tamponade agent is acted upon by two opposing forces: buoyancy (an upward force) and the weight of the bubble (a downward force). The net result is the force with which the bubble 'presses' against the retina. For silicone oil, this 'pressing' force is relatively small, as the SG is close to that of aqueous. This also applies to heavy silicone oil. The force is greatest with air or gas as the SG is very low at  $0.001g/cm^3$ .

#### 3. Interfacial tension

For any agent to be effective as a tamponade, it must be immiscible with water. For example, a cohesive viscoelastic (e.g. Healon) cannot act as a tamponade even though it does possess some necessary qualities such as high viscosity and cohesiveness. If an agent is immiscible with water, it will form an interface with it and the term 'interfacial tension' refers to the surface free energy between the agent and water. An agent with a high interfacial tension will have a greater tendency to stay as one large bubble and will resist dispersion into small bubbles. Such an agent will not readily pass through small gaps (e.g. retinal holes) because to do so it would need to deform its surface and this too is resisted by a high surface energy. Air (or any of the gases) has the highest interfacial tension against water at around  $80mN/m$ , whereas PFCL and silicone oil are lower at around  $40-45mN/m$  and  $35mN/m$  respectively.

#### 4. Viscosity

The tendency of a substance to emulsify and disperse into droplets over time is also dependant on its viscosity. The less viscous a substance, the lower the energy required to disperse a large bubble of the substance into small droplets. For example,  $F_8H_8$  has a low viscosity of  $2.5mPas$ , close to that of water ( $1.00mPas$ ), in contrast to the high viscosity of silicone oil ( $5000mPas$ ). Once dispersed, the small droplets will tend to re-coalesce back as a large bubble. However, once coated by surfactants the small droplets become stable. In other words, the liquid is emulsified. Once emulsified, the tamponade effect is lost and the small droplets can pass through retinal breaks. Furthermore, there is evidence to suggest that this dispersion causes inflammation.

### What is heavy silicone oil?

Heavy silicone oil (HSO) is a transparent, homogenous solution of two substances used as a single tamponade agent with improved properties. There are currently two products licensed for use in Europe. Namely, Densiron® (F<sub>6</sub>H<sub>8</sub> + silicone oil) and Oxane HD® (fluorinated and hydrocarbonated olefin + silicone oil). The combination of different substances, each with unique physical properties, allows the desirable properties of the individual components to be used to maximum advantage, and their limitations to be overcome to a greater or lesser extent. One such HSO, Densiron®, has been designed to take advantage of the high specific gravity of F<sub>6</sub>H<sub>8</sub> and the high viscosity of silicone oil. The resulting solution has a specific gravity of 1.06g/cm<sup>3</sup> (higher than water), and a viscosity of 1400mPas (substantially higher than F<sub>6</sub>H<sub>8</sub>). Experiments using model eye chambers designed to replicate the vitreous cavity have shown that Densiron® behaves rather like an inverted silicone oil bubble, in that it sinks inferiorly and exerts pressure on the inferior retina (Figure 2).<sup>5</sup> The solution also shares certain limitations with silicone oil, such as the inability to fit into small recesses and make uninterrupted contact with the retina. However, this relatively poor contact with the retina is not wholly disadvantageous as it allows a thin film of aqueous to remain in contact with the retinal surface, thought to be important for retinal health.<sup>5</sup>

### Why do we need heavy silicone oil?

The basic role of any tamponade agent is to make contact with the retina and prevent passage of aqueous through the break. Another important role is to displace aqueous from the vicinity of the break, as aqueous contains a pro-inflammatory milieu that is responsible for the development of PVR. It is thought unlikely that direct pressure against the retina plays any great part in break closure.<sup>7</sup> It is logical to assume that a floating tamponade would be most effective for pathology of the upper fundus, and a sinking tamponade most effective for that of the inferior fundus.

The gravitational limitations of current 'lighter than water' agents means that they make poor contact with the inferior retina, particularly in an under-filled eye. In fact, some would argue that a sustained total fill can never really be achieved. This makes a floating tamponade less useful for the closure of inferior retinal breaks, and especially given the limitations of postoperative posturing. A 'heavier than water' agent should be a more effective tamponade in the management of inferior retinal breaks, and would allow for more patient-friendly posturing regimes. PVR has a predilection for the inferior retina and when silicone oil is used, there is a tendency for aqueous fluid to accumulate beneath the bubble. This exposes the inferior retina to the proliferative 'soup'. The



Figure 2: Two large droplets of heavy silicone oil in the lower part of the anterior chamber.

inferior retina is the prime site for harbouring tractional breaks as a result of PVR, and makes the inferior retina the most common site for re-detachment following internal tamponade with silicone oil. A sinking tamponade for long-term use would have the advantage of displacing aqueous upwards and away from the retinal breaks, and this may confer a big advantage in the management of PVR.

### Potential indications for the use of heavy silicone oil

The prime indication for the use of HSO is in the treatment of inferior rhegmatogenous retinal detachments complicated by PVR. The results of a pilot study into the use of Densiron® (F<sub>6</sub>H<sub>8</sub> + silicone oil) have recently been published.<sup>8</sup> This prospective non-controlled study describes the use of Densiron® in 42 consecutive patients with retinal detachment resulting from inferior breaks and PVR. The mean duration of tamponade was 72 days. Anatomical success was achieved in 81% (34 patients) after one operation, and 93% (39 patients) with further surgery. This favourable success rate concurs with other, smaller pilot studies utilising slightly different compounds.<sup>9,10</sup>

Recently, the management of inferior breaks with pars plana vitrectomy, air tamponade and without postoperative posturing has been advocated and received with enthusiasm.<sup>11</sup> The technique puts emphasis on the suggestion that adhesion and sealing with photocoagulation may be instant. It asserts that tamponade is not necessary. However, even if the tamponade is not directly displacing aqueous away from the retinal break, it may act as a stent and prevent sufficient intraocular fluid currents from impinging on the break. Such intraocular currents are thought to be a causal factor in retinal detachment in vitrectomised eyes in the presence of an open break. Whilst this strategy may work for rhegmatogenous retinal detach-

ment without any PVR or static traction, no one is suggesting that it would be effective in cases associated with PVR. In cases where postoperative posturing is deemed necessary and the patient is unable to adopt a face down position, then HSO may have a role to play. Another potential role for HSO might be in macular hole surgery, in cases where traditional vitrectomy and gas tamponade have failed.

Giant retinal tears (GRT) managed with traditional floating tamponade agents are associated with high re-detachment rates as a consequence of their predilection for PVR development. PFCL is well established as an intraoperative tool in the management of GRT. Despite the aforementioned concerns about retinal toxicity, this role has been successfully extended to short-term postoperative tamponade, with reduced re-detachment rates.<sup>12,13</sup> A less retinotoxic heavy tamponade agent might also be advantageous in this setting.

### Complications

There are several well recognised complications associated with the use of conventional silicone oil including cataract, glaucoma, uveitis and emulsification into droplets. In their pilot study into the use of Densiron®, Wong et al. found that all phakic patients in their pilot study developed slight nuclear sclerotic cataract, with posterior subcapsular changes in the early postoperative period similar to that seen with conventional silicone oil. An intraocular pressure (IOP) >30 was noted in 14% (six patients) in the early postoperative period, and persisted at three months post Densiron® removal in 5% (two patients). In every case, the raised IOP was successfully managed with medical therapy. Moderate anterior chamber activity was noted in 7% (three patients) at week one following initial surgery. Another group reported intraocular inflammation (granulomatous keratic precipitates and anterior chamber activity) in seven of nineteen eyes

(37%) with Oxane HD® *in situ*, which resolved completely on removal of the tamponade agent.<sup>14</sup> Retrolental and epiretinal membranes were a prominent feature of F<sub>6</sub>H<sub>8</sub> use;<sup>15</sup> this was not observed with Densiron®. The relatively high viscosity and stability of the solution formed by mixing F<sub>6</sub>H<sub>8</sub> with silicone oil make it much less prone to dispersion. We think that this is the main reason for the lack of inflammation seen with Densiron®.

### Conclusion

A safe and effective long-term inferior tamponade agent would make a welcome addition to the vitreoretinal surgeon's armamentarium. The forte of HSO may well lie in the sequential use of a light and then heavy tamponade agent in succession for eyes with retinal detachment and PVR, where conventional agents such as silicone oil or gas have failed and resulted in inferior re-detachment.<sup>16</sup> In this situation, the superior retina and macular region are often well attached, and replacement of the conventional agent with HSO would displace the aqueous superiorly to where the retina is most secure, and provide tamponade to the detached retina and, critically, the macula. Whether early optimism regarding HSO is realised depends on whether its safety and efficacy are sustained

across larger numbers and longer follow-up. A multicentred randomised control study, the 'Heavy Silicone Oil' study, is currently underway. ■

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### Declaration of Conflicting Interests:

**Roxane J Hillier:** None declared.

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