Clinical Research 

# Densiron 68 heavy silicone oil in the management of inferior retinal detachment recurrence: analysis on functional and anatomical outcomes and complications

Tomaso Caporossi, Fabrizio Franco, Lucia Finocchio, Francesco Barca, Fabrizio Giansanti, Ruggero Tartaro, Gianni Virgili, Stanislao Rizzo

Department of Translational Surgery and Medicine, Ophthalmology, University of Florence, Azienda Ospedaliero-Universitaria Careggi, Florence 50134, Italy

**Correspondence to:** Lucia Finocchio. Department of Translational Surgery and Medicine, Ophthalmology, University of Florence, Azienda Ospedaliero-Universitaria Careggi, Florence 50134, Italy. luciafinocchio@gmail.com Received: 2018-08-23 Accepted: 2019-02-22

## Abstract

• AIM: To assess the efficacy and safety of a heavy silicone oil (Densiron 68) in the management of inferior retinal detachment recurrence.

• METHODS: A retrospective non-comparative consecutive case series study. Forty-nine cases of complex inferior retinal detachment were treated using Densiron 68 heavy silicone oil (HSO) as the endotamponade. Our main purpose was anatomic reattachment following Densiron 68 removal. Functional outcomes, rate of recurrences, the presence of inflammatory complications and intraocular pressure alterations were evaluated.

• RESULTS: Forty-nine patients affected by complex retinal re-detachment were recruited. The mean follow-up was 7.6 (±1.5) mo. The mean best corrected visual acuity after Densiron 68 removal was 0.95 logMAR, standard error (SE: 0.068). Retinal reattachment was 61.2% after first surgery and 81.6% after second surgery. Nineteen cases (38.8%) had recurrences when intraocular heavy silicon oil was *in situ*, 26.3% (5 cases) of which involved the inferior retina.

• CONCLUSION: Densiron 68 efficiently fills the inferior retinal periphery and might lower the risk of inferior proliferative vitreoretinopathy development, in particular after a standard silicon oil tamponade that reduces the proliferative process in the upper quadrants of the retina.

• **KEYWORDS:** vitrectomy; complex retinal detachment; proliferative vitreoretinopathy; ocular endo-tamponade; heavy silicone oil; Densiron 68

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# INTRODUCTION

he treatment of inferior retinal detachment (RD) with proliferative vitreoretinopathy (PVR) in the lower retinal periphery represents a challenge for vitreoretinal surgeons. PVR is the most relevant complication associated with RD surgery and the main cause of poor anatomical and functional outcomes<sup>[1-4]</sup>. Pars plana vitrectomy (PPV) and silicone oil tamponade associated with scleral buckling are considered the treatment of choice of advanced PVR. Lighter-than-water tamponades allow the support of the superior retinal periphery and the posterior pole in the upright position. Nevertheless the surface of the lower retinal periphery is not efficiently covered by the silicon oil tamponade, hence allowing a mixture of aqueous humor and growth factors ("PVR soup") to concentrate here. The "PVR soup" moves to the pre-macular area, enhancing the risk of formation of pre-macular epiretinal membranes, cystoid macular edema and recurrence of inferior RD<sup>[2,5-7]</sup>. Havier-than-water intraocular tamponades have been developed to resolve this problem, thanks to their many advantages over conventional tamponades. Indeed a heavy silicone oil (HSO) can efficiently tamponade breaks and areas of retinotomy in the lower retinal periphery in the upright position. It displaces the "PVR soup" away from the lower retina and the posterior pole, leading to a quicker and durable reattachment of the macula. Re-detachments are likely to occur mainly in the superior periphery where they can be easily treated with gas tamponade<sup>[1]</sup>.

Densiron<sup>®</sup> 68 (Fluoron Co, Neu-Ulm, Germany) is a solution of perfluorohexyloctane (F6H8) and 5000 cSt silicone oil<sup>[4]</sup>, characterized by an increased viscosity of F6H8 (from 2.5 to 1387 mPa) and a resulting reduction of the tendency to disperse<sup>[8-9]</sup>. Several studies, including the "Heavy Silicone Oil Study" (HSO Study), evaluated the efficacy and safety of Densiron 68, mainly on patients with complex RD<sup>[10-16]</sup>.

The main purpose of our study was the anatomic reattachment of the retina following Densiron 68 removal and to evaluate functional outcomes, the rate of recurrences, the presence of inflammatory complications and intraocular pressure alterations.

## SUBJECTS AND METHODS

**Ethical Approval** This was a consecutive, retrospective, nonrandomized case review. The study was performed in accordance with the current version of the Declaration of Helsinki (52<sup>nd</sup> WMA General Assembly, Edinburgh, Scotland, October, 2000) and written informed consent was obtained from all patients prior to participation in the study. Institutional Review Board/Ethics Committee approval was obtained.

We reviewed the records of 49 eyes of 49 patients affected by complex inferior RD who underwent PPV at Careggi University Hospital, Florence, Italy, between November 2014 and February 2017 with a follow-up of at least 6mo. All the patients had undergone only one vitreoretinal procedure before. The surgical procedures were performed by 4 experienced surgeons (Rizzo S, Caporossi T, Barca F, Giansanti F). Twentyfive or 23-gauge PPV were selected and no encircling buckling was combined. In eyes tamponed with standard silicone oil (SSO) in previous surgery the oil was then removed; in patients who underwent scleral buckling in previous surgery, the buckling was not removed. Peripheral vitreous remnants were checked and shaving vitrectomy was extended when needed. Vital dye (Dual Blue, DORC, The Neederlands) was injected into the vitreous chamber on the retinal contraction area to evidence epiretinal PVR. Perfluorodecalin (F Decalin, Fluoron, Germany) was injected in order to flatten the retina up to the periphery to stabilize detached retinal movement during PVR peeling. If the retina contraction did not relax sufficiently after the peeling, a retinectomy was performed. In all the cases a 360° endolaser was performed. Every case was tamponed with Densiron<sup>®</sup> 68 (Fluoron Co, Neu-Ulm, Germany) HSO. A 23-gauge PPV was selected to remove Densiron 68. After silicone oil extraction dyeing of the epiretinal membrane remnants was performed and eventually laser treatment was applied over any new retinal breaks. Finally, an endotamponade (gas, SSO or HSO) was chosen depending on the retinal status.

The main outcome measures were the mean change in best corrected visual acuity (BCVA; logMAR, Snellen ratio), the anatomic reattachment of the retina following Densiron 68 removal, the rate of recurrences, the mean time of Densiron 68 intraocular tamponade, the presence of inflammatory complications and intraocular pressure alterations. The data also included the state of the lens and the kind of surgery performed. Statistical analyses were performed by means of Stata 12.1 software (StataCorp, College Station, TX, USA). The results were expressed as the mean±standard deviation of the mean (standard error, SE). Paired samples *t*-tests were used to compare preoperative and postoperative logMAR visual

acuities. A *P* value of 0.05 or less was considered statistically significant.

#### RESULTS

Forty-nine eyes of 49 patients (M:F=38:11) affected by pathologic complex retinal re-detachment were included. The characteristics of all patients are presented in Table 1.

The mean age of patients was 58.9y ( $\pm$ 8.7); 17 patients previously underwent PPV with gas endotamponade or scleral buckling and 32 patients were tamponed with SSO at first surgery. Forty-three eyes were pseudophakic, 6 cases had been made aphakic during previous surgery and in 4/6 cases an intraocular lens (IOL) was implanted during the first surgery. In 26 cases we performed 25-G vitrectomy and in the remaining 23 cases a 23-G PPV was selected. In 2 cases a penetrating keratoplasty was combined to solve corneal opacization which can occur during SSO persistence. We did not perform vitrectomy and scleral buckling together in any case. In all cases we found the presence of PVR (grade C1-3-D), in 3 cases there was a macular hole and in 1 case there was a choroidal detachment. Eleven cases (22.4%) were traumatic RD; 8 cases (16.3%) were high myopic eyes (over 7 diopters); 3 cases (6.1%) were already being treated for glaucoma.

The mean BCVA before surgery with Densiron 68 was 1.9 logMAR (20/2000; SE:0.064). The mean BCVA after Densiron 68 removal was 0.95 logMAR (20/200; SE:0.068). The mean follow-up was 7.6mo (±1.5). Rate of retinal reattachment after first surgery was 61.2% (30 eyes). In 19 cases (38.8%) we had recurrences with Densiron 68: in 26.3% (5 cases) the recurrence involved the inferior retina. In patients who underwent PPV with gas endotamponade or scleral buckling (17 patients) there were 11 recurrences of RD (64.7%). In patients with SSO at previous surgery (32 patients), 8 eyes (25%) had recurrences with Densiron 68 (4 cases in the superior retina). The Chi-square statistic test showed a statistically significant difference between the two groups (P<0.05). All re-detachment cases underwent vitrectomy with gas tamponade in 2 cases and SSO tamponade in 16 cases. In one eye HSO was used again to solve complicated inferior RD with wide inferior retinectomy. Final retinal reattachment rate was 81.6% (40 eyes; Table 2).

After a mean time of 3.5mo Densiron 68 was removed, according to the clinical retinal status. In 13 cases (26.5%) we had inflammatory complications: emulsion and inflammation in the anterior chamber. In 17 (34.7%) cases we found ocular hypertension with Densiron permanency that needed medical treatment; after Densiron 68 removal, ocular pressure returned to a normal value in 4 cases (23.5%), the remaining 13 cases continued with the medical treatment. No eyes needed incisional glaucoma surgery. Two cases of corneal opacification and 1 case of phthisis occurred. In 6 cases we had anterior chamber inflammation and ocular hypertension at

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 Tel:
 8629-82245172
 8629-82210956
 Email:
 ijopress@163.com

ID	Age (y)	Gender	Eye	Comorbidity	Previous surgery	PVR	BCVA
1	53	М	L	High myopia	Scleral buckling	Yes	20/20000
2	54	F	L	Post-traumatic	PPV+SSO	Yes	20/20000
3	25	F	R	Post-traumatic	PPV+SSO	Yes	20/80
4	60	М	R	/	PPV+SSO	Yes	20/80
5	78	F	R	/	PPV+SSO	Yes	20/250
6	85	М	R	/	PPV+SSO	Yes	20/20000
7	54	F	L	/	PPV+SSO	Yes	20/20000
8	70	М	R	/	Scleral buckling	Yes	20/250
9	72	F	L	High myopia	PPV+SSO	Yes	20/100
10	52	М	R	/	PPV+SSO	Yes	20/20000
11	49	М	L	/	PPV+SSO	Yes	20/20000
12	42	М	R	High myopia	PPV+SSO	Yes	20/80
13	75	М	L	/	PPV+SSO	Yes	20/200
14	69	М	R	/	Scleral buckling	Yes	20/20000
15	37	М	R	/	PPV+SSO	Yes	20/20000
16	43	М	L	/	PPV+SSO	Yes	20/250
17	86	F	R	Post-traumatic	PPV+gas	Yes	20/20000
18	49	М	L	Post-traumatic	PPV+SSO	Yes	20/20000
19	82	М	R	/	PPV+gas	Yes	20/20000
20	80	М	R	/	PPV+SSO	Yes	20/20000
21	29	М	L	/	PPV+gas	Yes	20/20000
22	73	М	R	/	PPV+SSO	Yes	20/400
23	58	М	R	/	PPV+SSO	Yes	20/20000
24	69	М	L	Post-traumatic	PPV+SSO	Yes	20/20000
25	52	М	R	/	PPV+SSO	Yes	20/200
26	30	М	R	Post-traumatic	PPV+SSO	Yes	20/2000
27	19	М	R	/	PPV+SSO	Yes	20/20000
28	66	М	R	/	Scleral buckling	Yes	20/200
29	50	F	R	/	PPV+gas	Yes	20/32
30	80	М	L	Post-traumatic	PPV+gas	Yes	20/100
31	24	F	L	Post-traumatic	Scleral buckling	Yes	20/20000
32	71	М	R	/	Scleral buckling	Yes	20/400
33	52	М	R	/	PPV+SSO	Yes	20/100
34	53	М	R	/	PPV+SSO	Yes	20/200
35	38	F	L	Post-traumatic	PPV+SSO	Yes	20/100
36	89	М	R	High myopia	PPV+SSO	Yes	20/20000
37	45	М	L	/	PPV+gas	Yes	20/400
38	64	М	R	/	PPV+gas	Yes	20/200
39	54	М	L	/	PPV+gas	Yes	20/20000
40	76	М	L	/	PPV+SSO	Yes	20/250
41	67	М	R	Post-traumatic	PPV+SSO	Yes	20/20000
42	57	F	R	High myopia	PPV+SSO	Yes	20/20000
43	81	M	L	/	PPV+SSO	Yes	20/20000
44	57	М	L	Post-traumatic	PPV+SSO	Yes	20/80
45	60	M	R	/	PPV+gas	Yes	20/20000
46	75	F	R	, /	PPV+SSO	Yes	20/20000
47	70	M	R	. /	PPV+SSO	Yes	20/200
48	61	M	R	, /	Scleral buckling	Yes	20/250
49	53	M	L	, ,	Scleral buckling	Yes	20/200

PPV: Pars plana vitrectomy; SSO: Standard silicon oil; PVR: Proliferative vitreoretinopathy.

## Densiron 68 in inferior retinal detachment recurrence

#### Table 2 Anatomic and functional outcomes

ID	RrD	Position	Tamponade	Result	Final BCVA	Complications
1	Yes	Inferior	Gas	Favourable	20/20000	ACE
2	Yes	Posterior pole	SSO	Unfavourable	20/20000	/
3	No			Favourable	20/40	ACE
4	No			Favourable	20/32	/
5	No			Favourable	20/200	OHT, G
6	Yes	Inferior	SSO	Unfavourable	20/20000	Phtisis
7	No			Favourable	20/2000	OHT, G
8	No			Favourable	20/200	/
9	No			Favourable	20/70	ACE
10	No			Favourable	20/20000	/
11	No			Favourable	20/2000	OHT, G
12	No			Favourable	20/50	OHT, G
13	No			Favourable	20/200	/
14	No			Favourable	20/20000	OHT, G, corneal opacity
15	No			Favourable	20/20000	/
16	Yes	Superior, nasal	SSO	Favourable	20/200	ACE
17	Yes	Inferior	SSO	Unfavourable	20/20000	Corneal opacity
18	No			Favourable	20/2000	/
19	Yes	Total	SSO	Unfavourable	20/2000	/
20	Yes	Inferior	SSO	Unfavourable	20/20000	OHT, G
21	Yes	Total	SSO	Unfavourable	20/20000	ACE
22	No	Totur	550	Favourable	20/200	/
23	Yes	Superior	SSO	Unfavourable	20/20000	/
24	No	Superior	550	Favourable	20/2000	ACE
25	No			Favourable	20/200	
26	No			Favourable	20/2000	OHT, G
27	Yes	Total	SSO	Unfavourable	20/2000	/
28	Yes	Superior	SSO	Favourable	20/125	OHT, ACE, G
29	Yes	Superior	SSO	Favourable	20/200	/
30	No	Superior	550	Favourable	20/200	OHT
31	Yes	Inferior	HSO	Favourable	20/20000	
32	No	menor	1150	Favourable	20/200	/
33	No			Favourable	20/200	OHT, ACE
34	No			Favourable	20/40	OHT, ACE
35	No			Favourable	20/123	
35 36	No			Favourable	20/80	/
30 37	Yes	Superior	Gas	Favourable	20/200	ACE
38		Superior	Gas	Favourable	20/200	ACE /
	No	Destarian mala	880			,
39	Yes	Posterior pole	SSO	Favourable	20/20000	OHT, ACE
40 41	Yes	Superior	SSO	Favourable Favourable	20/200	OHT, ACE, G
	No	C	880		20/20000	OHT OUT ACE
42	Yes	Superior	SSO	Unfavourable	20/20000	OHT, ACE
43	No			Favourable	20/20000	OHT, G
44	No		660	Favourable	20/200	/
45	Yes	Inferior	SSO	Unfavourable	20/2000	/
46	No			Favourable	20/200	OHT, G
47	No			Favourable	20/100	/
48	No			Favourable	20/125	/
49	No			Favourable	20/50	/

RrD: Retinal re-detachment after Densiron 68 removal; SSO: Standard silicon oil; HSO: Heavy silicon oil; ACE: Anterior chamber emulsification; OHT: Ocular hypertension with densiron; G: Glaucoma after PDMS removal.

the same time. In 1 case we registered a central vein occlusion during the silicone tamponade.

## DISCUSSION

Treating a complex RD is a very interesting and difficult challenge. However in severe PVR, especially in patients with previous multiple vitreous surgery and persistent RD of the inferior quadrants, the outcome can be discouraging even with silicone oil. Silicone oil limits, but does not exclude, the diffusion of proliferative cells and inflammatory mediators through the vitreous cavity. If the silicon does not completely fill the eye, it may lead to an incomplete tamponade in the inferior retina, exposed breaks and an accumulation of fluid containing proliferative cells. Therefore, in patients with complex inferior RD a tamponade with heavier-thanwater density could be useful<sup>[17]</sup>. In our series we had retinal attachment after the first surgery in 61.2% of the patients and recurrences in 38.7%; 32 patients had SSO at first surgery. Densiron removal was performed after an average of 3.5mo  $(\pm 0.8)$ . Most of our recurrences were in the superior retina, in agreement with the "HSO versus SSO study" by Joussen et  $al^{[16]}$ . In patients with gas or scleral buckling at the first surgery (17 patients), we had 11 recurrences (64.7%). In patients with SSO at the first surgery (32 patients), 8 had recurrences with Densiron 68 (25% of 32 patients). Wong *et al*<sup>[18]</sup> showed good anatomical and functional results: in his case series no patients developed macula-off detachments once Densiron 68 was used, even though a percentage of patients underwent re-operations involving gas or silicone oil injection; re-attachment in a single operation using Densiron 68 occurred in 81% (34 of 42) of patients, and after additional surgical interventions it became 93% (39 of 42 patients); silicone oil remained in situ in 4 of the 42 patients; re-attachment without any tamponade occurred in 86% (36 of 42) of patients<sup>[18]</sup>. In Auriol et al<sup>[10]</sup> case series, total anatomic success at the last follow-up visit was achieved in 25 of the 27 patients (92.5%) who had inferior complex RD treated with Densiron 68. In his series Sandner *et al*<sup>[19]</sup> treated 12 patients with complex inferior RD with Densiron 68: he achieved retinal attachment in all eyes at the end of the first surgery. However both when Densiron 68 was in situ and during follow-up after removal, only in four of the 12 patients (30%) the retinal condition was stable; 8 eyes developed redetachment. Nevertheless, after re-intervention in 9 out of the 12 patients (75%) a re-attachment was achieved; in 10 of the 12 patients (83.3%) the macula had re-attached (in 7 without endotamponade) at the 1-year follow up. We also evaluated the functional result: final mean visual acuity was 0.95 logMAR. Wong *et al*<sup>[18]</sup> registered visual acuity improvement from a</sup>mean logMAR of 1.41 to a mean of 0.94 after surgery. In Sandner's series the mean post-operative logMAR visual acuity increased to 1.87 logMAR<sup>[19]</sup>. Significant initial anatomical success and a mean final visual acuity of 1.52

logMAR were reported by Tognetto et al<sup>[20]</sup>. However visual function results are not easy to compare due to differences in previous retinal conditions. In other studies complications after HSO tamponade include severe inflammation, HSO emulsification/dispersion, new retinal tears in the superior retina, retinal vascular changes, cataract, ocular hypertension and hypotension. Inflammatory reactions, including exudation and membrane formation are quite common complications<sup>[21]</sup>. In our series, ocular hypertension was found in 17 patients (34.7%; mean value 25 mm Hg) and was treated with glaucoma drugs. Three of these patients had pre-existing medicallycontrolled glaucoma before surgery. After Densiron 68 removal did ocular pressure returned to normal values only in 4 of the 17 cases (23.5%) while the other cases continued with the glaucoma therapy. Tognetto *et al*<sup>[20]</sup> observed 5 cases of ocular hypertension after Densiron 68 tamponade; 3 were easily controlled by medication and 2 were resolved after Densiron 68 removal. Wong et al<sup>[18]</sup> reported that 6 patients had an IOP higher than 30 mm Hg at the 5-week follow-up after heavy oil surgery and 3 patients had an IOP higher than 30 mm Hg at the last follow-up (3mo after oil removal). All cases of high IOP were successfully treated medically. Sandner *et al*<sup>[19]</sup> found an increased IOP during Densiron 68 tamponade in 4 patients: it persisted after silicone oil removal in 3 cases and in all eyes it was treated successfully with topical anti-glaucoma medication. In 13 cases (26.5%) we had inflammatory complications such as emulsion and inflammation in the anterior chamber: a few drops of silicone oil adhered to the posterior capsule and to the iris and/or in the inferior part of the anterior chamber. We found 2 cases of corneal opacification but it is important to remember that the corneal condition was already complex prior to surgery. In 6 cases we had both anterior chamber inflammation and ocular hypertension. Wong *et al*<sup>[18]</sup> reported 3 cases of moderate anterior chamber inflammatory activity at 1wk after the initial operation and a minor dispersion of silicone oil detected postoperatively in 3 patients at 1wk and in 6 patients at 1mo follow-up. They had a few drops attached to the posterior capsule and/ or in the inferior part of the anterior chamber; none had any retrolental membranes or epiretinal membranes which had been previously observed in case series with F6H8<sup>[16]</sup>. Sandner et al<sup>[19]</sup> did not observe chronic inflammatory reaction in the anterior segment or endothelial precipitates in his series but in 3 patients they found a progression of intra-retinal gliosis; this was suspected during the Densiron 68 endotamponade. They also found epiretinal membrane development, probably due to the F6H8 component which activated an inflammatory response and resulted in a considerable intra-retinal gliotic reaction associated with additional retinal shortening, leading to a tractional re-detachment<sup>[19]</sup>. In contrast to Tognetto et  $al^{[20]}$  and Wong *et al*<sup>[18]</sup>, Sandner *et al*<sup>[19]</sup> noted the dispersion

of Densiron in 2 eyes with notable pseudohypopyon after 33d and 56d, respectively. Recently Dresp and Menz<sup>[22]</sup> observed that the tendency of silicone oil to emulsify might be triggered by impurities derived from remnants of heavy liquids used intraoperatively or from residual silicon oil particles located on the vitreoretinal devices.

In conclusion, the retinal re-attachment rate after one surgical operation in our case series is slightly inferior compared with literature but we have to consider the complexity of the cases we selected: 11 eyes (22.4%) had post traumatic RD. We usually use Densiron 68 as a second choice for inferior RD recurrence in eyes which have already undergone PPV with lighter-thanwater gas or SSO endotamponade, which should contrast upper retinal PVR development. Densiron 68 efficiently tamponades the inferior retinal periphery during second surgery for inferior RD recurrence and may lower the risks of PVR in the inferior quadrant. The displacement of the mixture of aqueous humor and growth factors away from the lower retina and the posterior pole to the upper quadrants had been used to contrast PVR and cystoid macular edema development. The purpose of our study was to evaluate the efficacy and safety of Densiron 68 in the treatment of complex retinal redetachments, especially those treated with SSO during the first surgery. In these cases we have found a 25% recurrence rate after Densiron 68 removal with a final re-attachment rate of 81.2%. We believe that Densiron 68 is a useful surgical tool to manage inferior complex RD, as a second step for eyes which have already undergone PPV with a SSO tamponade to contrast inferior PVR development. Further studies are needed to evaluate its use.

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