

BEACON (BEAVRS case collection initiative) study outline form

Full Title: Spontaneous clearance of sub-macular perfluorocarbon liquid study

Acronym: SCALPEL study

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What you are studying: Spontaneous clearance of sub-macular perfluorocarbon liquid (PFCL) previously retained after retinal detachment repair.

What is your primary research question:

What are the clinical features of eyes in which PFCL retained following previous retinal detachment repair, subsequently, spontaneously resolves? What are the functional and anatomical outcomes on these eyes following spontaneous clearance of the PCFL?

Background and importance:

PFCL is a very useful tamponade agent in the management of complex vitreoretinal pathology. Retained sub-macular PFCL is a recognised complication of its use.

Despite its inert chemical structure¹, sub-macular PFCL is thought to be toxic to the retina as anatomical changes have been noted on OCT and fundal imaging². In addition, functional deficits have been displayed on electroretinography³ and via microperimetry⁴ testing.

Although the mechanism of toxicity remains controversial, hypotheses have been proposed^{5,6} Firstly, inflammatory response to retained PFCL has been suggested with histopathological evidence of macrophages with intracellular vacuoles of PCFL⁵. Secondly, in a porcine model, it has been proposed PCFL leads to disruption to retinal buffering thus leading to an accumulation of potassium and subsequent neurodegeneration and reactive gliosis⁶.

Alternatively, it has been suggested that the associated damage of sub-macular PFCL may relate to a disruption of the normal transport of nourishing substances between retinal pigment epithelium (RPE) and photoreceptor cells, due to the physical barrier newly created by the presence of the PFCL between these two layer⁷. In this vein, removal of sub-macular retained PFCL often leads to visual acuity improvement, even after long periods of retention⁸, which may question its "toxicity"⁸⁻¹².

Although the preferred management strategy for retained submacular PFCL is surgical intervention, at least four cases of spontaneous resolution of sub-macular PFCL, with associated VA improvement, have been reported in the literature¹³⁻¹⁶. The authors of these reported cases hypothesised that the PFCL extruded through a retinal hole that developed in the thinned overlying retina, and subsequently closed spontaneously. Recently, it is been hypothesised that due “Laplace’s law”, a relatively small subretinal PFCL droplet if connected to a relatively larger supra-retinal PFCL droplet in the vitreous could be attracted to join the larger droplet thus facilitating spontaneous resolution¹⁷. The authors remarked the importance of further studies using high resolution OCT images are required to investigate this hypothesis further.

It is unclear how often spontaneous clearance of sub-macular PFCL occurs. SCALPEL aims to investigate clinical and optical coherence tomography characteristics and outcomes of eyes in which PFCL resolved spontaneously. This may help determining when observation may be considered for these cases.

Case definition:

Spontaneous clearance of sub-macular perfluorocarbon liquid (PFCL) is defined as the disappearance of previously retained PFCL from beneath the macula without surgical intervention.

Inclusion criteria:

- Retained PFCL as a consequence of previous retinal detachment repair and subsequently spontaneous clearance without any intervention
- Retained PFCL after any type of retinal detachment surgery
- Any type of retinal detachment: rhegmatogenous, tractional or traumatic.
- Any age of the patient

Exclusion criteria:

- Any previous treatment for retained PFCL
- Any retained sub-macular tamponade agent which is not PFCL
- Retained subretinal PFCL not affecting the macular area

Likely incidence:

It is difficult to estimate the incidence of spontaneous clearance of retained sub-macular PFCL. Due to the hypothesised toxicity of sub-retinal PFCL, prompt surgical intervention is often sought. There are at least four cases of spontaneous resolution of PFCL published recently¹³⁻¹⁶. NL witnessed spontaneous resolution of PFCL in one of her patients and presented this case at the last meeting of the Club Jules Gonin.

Prospective/Retrospective data collection?:

Retrospective data collection will be sought.

If Retrospective:

Eligible study period: 1st June 2011 to 1st June 2021 (10 years)

Target completion for end of data collection: 1st November 2021 (6 months)

If Prospective:

Case collection period:

Follow up duration:

Primary outcome measure: Anatomical clearance of sub-macular perfluorocarbon liquid (PFCL) without intervention, as determined using spectral domain optical coherence tomography (SD-OCT).

Secondary Outcome measures: Best corrected visual acuity (BCVA) at final follow up; change in BCVA from when PFCL was first noted; at the visit just prior to resolution of PFCL; at the time when PFCL was noted for the first time that it had resolved; and at last follow up in clinic following resolution of PFCL; follow up duration; time to clearance; patient demographics and baseline characteristics, including SD-OCT features at baseline; information on the original retinal detachment surgery that led to sub-macular PFCL retention; and SD-OCT features upon resolution of the PFCL at above time points.

We plan to obtain SD-OCT videos for each of the cases reported, from when the PFCL was first noticed; from the last visit when retained PFCL was observed; from the first visit when PFCL was noted to have resolved spontaneously; and from last follow up. This will allow us to analyse them as a group in order to discern, as best as possible, potential characteristics that may be shared among cases.

Pre-planned analysis outline: Simple statistical analysis will be undertaken to present means with ranges and SD of the outcomes of interest. Descriptive analysis will be undertaken when statistical analysis is not appropriate.

Data collection form(s): Pre-formatted excel data collection sheets will be available online via BEACON webpage and via email to the study team (pmccullough17@qub.ac.uk). Please remember to anonymise any data before imputing it into the data collection sheet.

Images required: SD-OCT videos are required for each of the cases reported. SD-OCT videos are required for the clinical visit from when the PFCL was first noticed; from the last visit when PFCL was observed (prior to being noted to have spontaneously resolved); from the first visit when PFCL was noted to have resolved spontaneously; and at last follow up. Guidance for extracting SD-OCT videos can be found in data extraction guidance document. If further assistance is required, please contact the study team (pmccullough17@qub.ac.uk). Please submit SD-OCT to our Google Drive account. Please consult the data extraction guidance for more information and for the link to the Google Drive. Data and images must not contain any patient identifiers.

References:

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