THE MANAGEMENT OF POSTERIOR VITREOUS DETACHMENT

BY AN OPTOMETRIST

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A thesis submitted for the requirements of Doctor of Optometry,

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Thesis Summary

Acute posterior vitreous detachment (PVD) is the most common cause of retinal detachment. The management of this condition can be variable and often undue reliance is placed upon associated signs and symptoms which can be a poor indicator of pathology. Optometrists undertake a number of extended roles, however involvement in vitreo-retinal sub-specialities appears to be limited. One objective was to directly compare an optometrist and ophthalmologist in the assessment of patients with PVD, for this a high level of agreement was found (95% sensitivity, 99% specificity, 0.94 kappa).

A review of 1107 patients diagnosed with acute PVD that were re-evaluated in a PVD clinic a few weeks later was undertaken to determine whether such reviews are necessary. One-fifth of patients were found to have conditions undiagnosed at the initial assessment, overall 4% of patients had retinal breaks when examined in the PVD clinic and a total of 7% required further intervention. The sensitivity of fundus examination with +90D and 3-mirror lenses was 85-88% for detecting retinal breaks and 7-85% for pigment in the anterior vitreous for the presence of retinal breaks. Therefore patients with acute PVD should be examined by indirect ophthalmoscopy with indentation at the onset of PVD and 4-6 weeks later.

The treatment of retinal breaks with laser retinopexy is performed by ophthalmologists with a primary success rate 54-85%. In a pioneering development, an optometrist undertaking this role achieved a comparable primary success rate (79%).

Mid-vitreous opacities associated with PVD are described, and noted in 100% of eyes with PVD. The recognition of this sign is important in the diagnosis of PVD and retinal breaks. The importance of diagnostic imaging is also demonstrated, however the timing in relation to onset may be vital.

Keywords: Competency, optometrist, retinal breaks, vitreous opacities

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Chapter One: Posterior Vitreous Detachment and Retinal breaks

1.1 Introduction

The human eye is a fascinating organ owing to its unique structure and function. The vitreous humour is a major component of the eye; it is a transparent gel composed of approximately 98% water, with a volume of approximately 5ml and occupies the posterior segment of the eye between the crystalline lens and the retina (Bishop 2000; Le Goff & Bishop 2008). Despite the predominance of the vitreous within the eye, it appears to have received less interest in the literature than other structures of the eye (Kičová *et al.* 2012; Duker *et al.* 2013). Although there is substantial information regarding the structure there still remain limitations in understanding the function of this avascular, relatively acellular body (Le Goff & Bishop 2008; Duker *et al.* 2013).

1.2 Anatomy of the vitreous

The main constituent of the vitreous is known to be water, other components include collagens, glycosaminoglycans, proteins and other macromolecules. Collagen type II comprises around 60-75%, type IX up to 25% and type V/XI approximately 10% of the total collagen (Bishop *et al.* 1994; Bishop 2000; Bos *et al.* 2001; Le Goff & Bishop 2008), Glycosaminoglycans (GAGs) are extracellular matrix polysaccharides that contain repeating disaccharide units. Hyaluronan is the major GAG of the human vitreous, chondroitin sulphate and heparin sulphate are also present but in a smaller capacity (Le Goff & Bishop 2008). The proteins predominantly consist of fibrillin and opticin. The collagen fibres are suspended in the GAG matrix and the proteins maintain the inter-fibril space of the collagen and stabilize the structure (Sebag 1992; Bishop 2000; Los *et al.* 2003; Le Goff & Bishop 2008).

Histological studies of the vitreous have been instrumental in our understanding of the vitreous (Worst 1976; Jongebloed & Worst 1987; Sebag & Balazs 1989; Kishi & Shimizu 1990; Sebag 2002 and 2008a), with advances in imaging complementing our knowledge (Uchino *et al.* 2001; Mojana *et al.* 2010; Pang *et al.* 2014; Schaal *et al.* 2014; Stanga *et al.* 2014). Anatomically the vitreous consists of three entities; the cortex, vitreous base, and central vitreous. The vitreous cortex is a thin membrane that encapsulates the central vitreous body. The anterior-most portion of the cortex is termed the anterior hyaloid face and is in contact with the posterior surface of the crystalline lens and aqueous humour. The central vitreous consists of collagen fibrils that are arranged in an antero-posterior fashion, perpendicular to the crystalline lens and merge directly with the ciliary body and anterior retina. This region is termed the vitreous base, an organised area of annular adhesion between the vitreous and retina with an almost indestructible bond. The posterior portion of

the collagen fibrils of the central vitreous attach to the vitreous cortex. The posterior cortex orientates parallel to the surface of the retina and is adherent to the internal limiting membrane of the retina (Worst 1976; Jongebloed & Worst 1987; Sebag & Balazs 1989; Le Goff and Bishop 2008). Histological examination of the vitreous cortex has revealed it is the thinnest in the macula region and absent in the region of the optic disc (Sebag & Balazs 1989) (Figs 1.2.1 and 1.2.2). As the collagen fibres of the posterior vitreous do not insert directly into the retina or other structures, the bond with the retina is weaker (Le Goff & Bishop 2008). However, the cortex is strongly adherent to the optic nerve head (Fig 1.2.3) known as Martegiani's ring, the posterior lens capsule; Wiegerts ligament with moderate adhesion, and also to the macula and blood vessels (Bishop 2000; Hayreh & Jonas 2004; Chen *et al.* 2006).

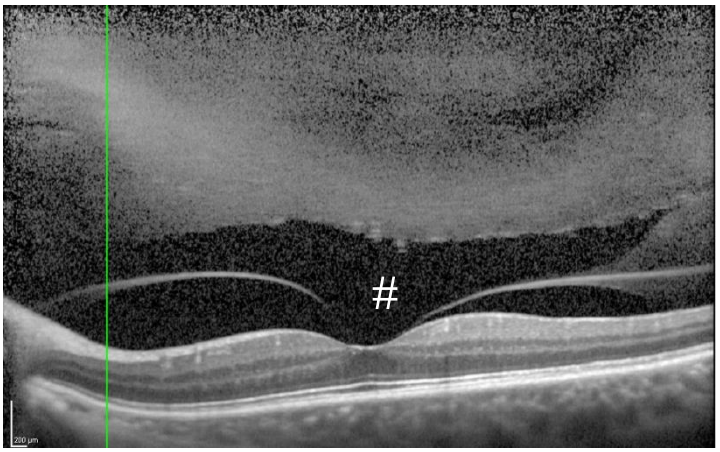

Fig 1.2.1 An OCT image portraying the anatomical attachment of the vitreous to the fovea
Premacular bursa

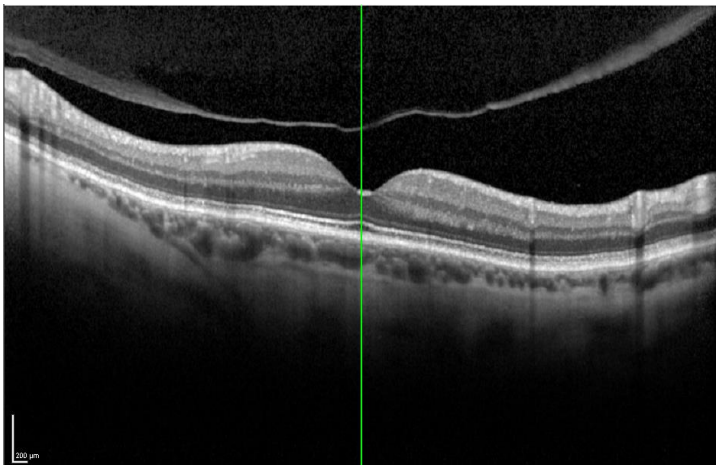

Fig 1.2.2 An OCT image demonstrating the variation in thickness of the vitreous cortex

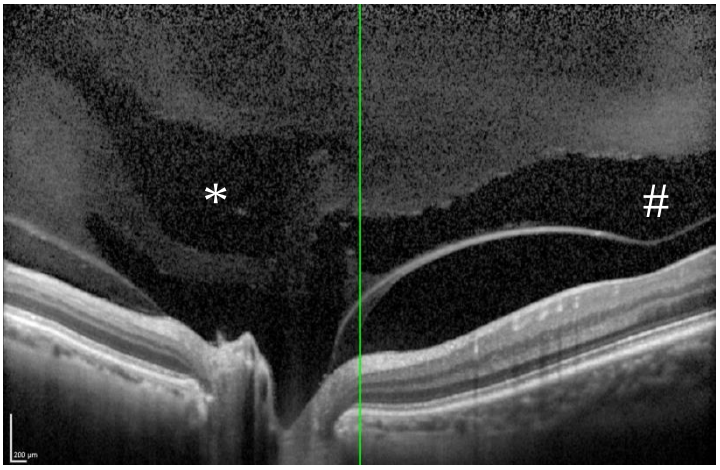

Fig 1.2.3 An OCT image portraying the anatomical attachment of the vitreous to the optic nerve head
* Cisternal space within the vitreous
# Premacular bursa

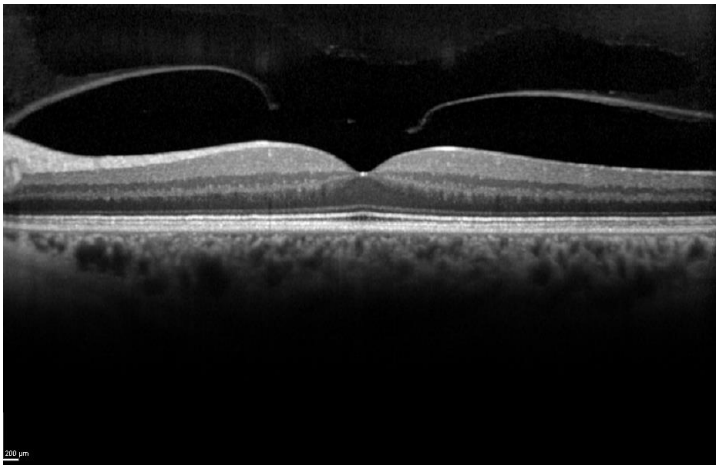

Fig 1.2.4 An OCT image depicting an opening in the posterior vitreous cortex and separation of the cortex from the retinal surface

1.3 Ageing of the vitreous

The primary function of the vitreous is to transmit light to the retina, other functions include protection of the internal structures of the eye from trauma and eye movements, maintain the volume of the globe and internal tamponade of the retina to underlying structures (Foulds 1987). The vitreous, as other structures of the body and the eye are subjected to ageing, this process results in alterations of the vitreous structure and subsequently the function. It is recognised during this degenerative change two processes occur; liquefaction of the vitreous (synchisis) and coagulation of fibrils (syneresis) (Sebag 1987a and 1987b). Liquefaction simply describes the vitreous becoming less gel-like and more liquid in state. Interestingly liquefaction and syneresis of the vitreous occurs with age and has been documented to occur from approximately four years of age, and with increasing age the vitreous further progressively liquefies (Balazs & Delinger 1982). In conjunction with liquefaction there is a progressive weakening in the adhesion of the posterior vitreous cortex to the retina (Balazs

& Delinger 1982). The monumental studies by Worst (1976) highlighted the cisternal structure of the vitreous and the presence of a liquefied area anterior to the macula termed the premacular bursa or a pre-cortical vitreous pocket by Kishi and Shimizu (1990) (figs 1.2.1, 1.2.2 and 1.2.3). This presence of liquefied vitreous in this region may contribute to the progressive weakening of adhesion of the posterior cortex to the retina to such a degree it permits the entry of liquefied vitreous into the space between the vitreous and retina (the retrohyaloid space) (Sebag 1989). The passage of liquefied vitreous into the retrohyaloid space accelerates the process of vitreo-retinal separation (fig 1.2.4). Once the vitreous has separated from the retina this is termed a posterior vitreous detachment (PVD) (Balazs & Delinger 1982; Hayreh & Jonas 2004; Johnson 2010; Stalmans *et al.* 2012; Duker *et al.* 2013). Thus it appears liquefaction is one of the most important processes involved in the process of PVD (Los *et al.* 2003; Johnson 2010; Duker *et al.* 2013). It has been recognised that separation of the vitreous from the retina is a gradual process and may take months and potentially years to complete (Uchino *et al.* 2001; Sharma *et al.* 2004; Carvounis & Holz 2006; Duker *et al.* 2013). A landmark prospective study by Uchino *et al.* (2001) evaluated the evolutionary process of PVD with optical coherence tomography. This study demonstrated the vitreous begins to separate in the paracentral retina and this feature may be absent on clinical examination with biomicroscopy. Furthermore this study enhanced knowledge pertaining to the natural history of PVD and exhibited the process may in fact take years to progress without symptoms.

1.4 Diagnosis of posterior vitreous detachment

Posterior vitreous detachment is diagnosed on the basis of history and clinical findings (Novak & Welch 1984; Yonemoto *et al.* 1996; Coffee *et al.* 2007; Johnson 2010; Schweitzer *et al.* 2011). A common finding in PVD is a Weiss ring, this represents the area of adhesion that was present between the vitreous and optic disc prior to detachment of the vitreous. Once the vitreous separates from the optic disc, this area of vitreous condensation can be seen on clinical examination (Akiba *et al.* 2001). It is often assumed a posterior vitreous detachment is present if a Weiss ring is visible (Carrero 2012; Kuhn & Aylward 2014; Blindbæk & Grausland 2014), however this may be incorrect as a Weiss ring exhibits detachment of the vitreous from the optic disc only, and the vitreous may be attached elsewhere. (Kakehashi *et al.* 1997; Sebag 2004; Kakehashi *et al.* 2014). Furthermore it has been reported this annular opacity may be absent or difficult to detect in 7-13.5% of cases (Tanner *et al.* 2000; Akiba *et al.* 2001)

Detailed examination of the posterior hyaloid membrane may be of greater accuracy in confirming the presence of a posterior vitreous detachment (Snead *et al.* 1994). The

posterior hyaloid membrane can be visible when examining the vitreous with the slit-lamp biomicroscope; the illumination is obliquely directed through the pupil with the observation directly in front. The posterior hyaloid membrane may be visible as a condensed opacity in the posterior aspect of the vitreous cavity with, or using a high powered condensing lens focussed anterior to the retina when the membrane is located further posteriorly (Pischel 1952; Snead *et al.* 1994; Kakehashi *et al.* 1997). Kakehashi *et al.* (1997) devised a clinical classification for the variations of PVD from their study of 400 eyes based on the clinical appearance of the vitreous on the slit-lamp with a condensing lens. They classified PVD into four types, the first of which is associated with increasing age and myopia termed PVD with collapse. In this type of PVD a Weiss ring is present together with a large retrocortical space and there is smooth movement of the detached vitreous on eye movements. The other three types of PVD are encountered in retinal vascular disease:

- PVD without collapse in which a Weiss ring is present, however there is minimal vitreous liquefaction and hence limited movement of the detached vitreous
- Partial PVD with a thickened posterior vitreous cortex (TPVC) in which the posterior vitreous cortex is attached at two of the following points; vitreous base, optic disc, along the vascular arcade, a neovascular complex or the macula
- Partial PVD without TPVC in which the posterior vitreous cortex is not thickened

Recently, this classification has been refined to include the use of optical coherence tomography as an adjunct to facilitate an accurate diagnosis (Kakehashi *et al.* 2014) as some cases of retinal tears have no evidence of PVD on slit-lamp, but Optical Coherence Tomography (OCT) may reveal a shallow peripheral PVD.

1.5 Variants of posterior vitreous detachment

A further entity of vitreoretinal separation that is recognised is vitreoschisis. Although the vitreous cortex is thinnest in the macular region it may be strongly adherent, and as such during posterior vitreous detachment the vitreous may effectively split anterior to the vitreous cortex. In vitreoschisis, remnants of the posterior vitreous cortex remain attached to the retinal surface (Kishi *et al.* 1986; Snead *et al.* 2008a; Kuhn & Aylward 2014), and the remaining vitreous body migrates anteriorly in accordance with the natural progression of posterior vitreous detachment. In such cases the inner wall of a vitreoschisis cavity may be misinterpreted as the posterior hyaloid membrane, additionally there will be an absence of a Weiss ring as the outer wall of the vitreous will still be attached to the retinal surface. Hence there may be a discrepancy between the figures quoted in the literature for prevalence of

posterior vitreous detachment compared to observations in clinical practice (Sebag 2008b; Kuhn & Aylward 2014).

During the process of posterior vitreous detachment, the vitreous may still have areas of strong adherence to the retina. This has been described as anomalous PVD and arises when the degree of vitreous liquefaction is greater than the degree of weakening of the posterior vitreous cortex adhesion to the retina. Anomalous PVD with concurrent vitreoretinal traction is the fundamental cause of complications in PVD and can result in a plethora of untoward complications (Sebag 2004; Johnson 2005). The initial stages of PVD often are asymptomatic (Uchino *et al.* 2001) however where anomalous PVD exists complications can affect both the central and peripheral retina and result in symptoms (Sebag 2008b; Johnson 2010).

1.6 Symptoms

Photopsia and floaters are the two most common symptoms associated with PVD and become most evident when vitreous separates from its attachment at the optic nerve head, however identical symptoms may be experienced when a retinal break develops (Novak & Welch 1984; Diamond 1992; Hikichi & Trempe 1994; Dayan *et al.* 1996; Yonemoto *et al.* 1996*;* Tanner *et al.* 2000; Hikichi & Yoshida 2004; Coffee *et al.* 2007; Johnson 2010; Schweitzer *et al.* 2011). The literature suggests a combination of photopsia and floaters are the most frequently presenting symptoms in PVD with approximately 50% of patients, with approximately 40% experiencing floaters and 10% photopsia in isolation (Novak & Welch 1984; Byer 1994; Hikichi & Trempe 1994; Dayan *et al.* 1996; Hikichi & Yoshida 2004; Tanner *et al.* 2000; Al-Asadi 2013). Consequently Hikichi & Trempe (1994) noted approximately 5% of eyes with floaters as the sole symptom and 10% of eyes with photopsia with or without floaters harboured a retinal break. A loss of vision or reduced visual field in combination with these symptoms can be a symptom of retinal detachment (Goodfellow *et al.* 2010; Hurst *et al.* 2015).

1.6.1 Floaters

Liquefaction of the vitreous body and aggregation of collagen fibrils results in the scattering of light and the perception of floaters (Byer 1994; Kakehashi *et al.* 1998; Roufail & Polkinghorne 2006; Sebag 2011). Floaters can also arise if during the evolution of a PVD there is avulsion of a retinal blood vessel, releasing red blood cells and other blood vessel constituents into the vitreous, resulting in a vitreous haemorrhage. Similarly if retinal pigment epithelium (RPE) cells are released into the vitreous by virtue of a retinal break floaters may be perceived (Roufail & Polkinghorne 2006; Law & Sternberg 2007).

1.6.2 Photopsia

Photopsia is commonly referred to as flashing lights and these are usually in the temporal field of vision, often lasting momentarily (Byer 1994; Goodfellow *et al.* 2010). One of the first detailed reports of photopsia was described by Moore in 1935. In this account he provides excerpts from twenty-six cases of photopsia, and in summary Moore felt there was no underlying sinister cause of these symptoms. Verhoeff (1941), then uninformed of the work by Moore, shortly himself later developed photopsia and provided a detailed account of his symptoms. In this account he describes photopsia occurring in all quadrants and not solely the temporal field, an observation previously not encountered by Moore. Furthermore Verhoeff was able to elicit photopsia voluntarily by virtue of eye movements, concluding eye movement was necessary for photopsia to arise. Although Moore suggested photopsia usually disappear within a few weeks, Verhoeff accounted his photopsia was still present over three years later. Interestingly it appears Verhoeff, unlike Moore, correctly attributed photopsia to be vitreoretinal in origin. However, Verhoeff concurred with Moore that photopsia are of no real significance. An adjunctive description of photopsia was given by Moore in 1947 when he himself also developed photopsia a short time later. In summary his descriptions were similar to Verhoeff and he felt further confirmed his original suggestion that photopsia are of little significance. Contrary to the notion of Moore and Verhoeff that photopsia is innocuous, Berens *et al*. (1954) published a series of 36 cases where photopsia was attributed to other systemic and ocular conditions. Essentially traction on the retina was the most frequent cause of photopsia, however retinal detachment, ocular melanoma, vascular occlusion and infection were also cited as a cause of photopsia. In summary they recommend any report of photopsia warrants a detailed examination through dilated pupils including scleral indentation.

Photopsia are thought to arise due to traction on the retina from the vitreous, this stimulates the retinal photoreceptors resulting in the perception of flashing lights (Novak & Welch 1984; Law & Sternberg 2007; Kuhn & Aylward 2014). Anomalously, photopsia arise in the temporal field regardless of the area of vitreo-retinal separation (Moore 1935; Boldrey 1983). One pathophysiological postulation for this could be due to the gradual progression of PVD affecting the superior and temporal quadrants initially, and often is asymptomatic in the early stages particularly in the absence of significant vitreoretinal traction (Uchino *et al.* 2001; Johnson 2010; Shunmugam *et al.* 2014). However acute photopsia only arise once vitreopapillary separation occurs, furthermore as the vitreoretinal separation progresses nasally then symptoms are projected into the temporal field. An insightful paper by Goodfellow *et al.* (2010) prospectively collated specific details from 77 patients with photopsia diagnosed with either PVD, retinal tear or retinal detachment, of which almost

three-quarters of patients had photopsia in the temporal field. Photopsia affecting any field other than temporal was associated with a retinal detachment, with a specificity of 95% and sensitivity of 48%. Almost half of the patients described the shape as a line, the other most common descriptions were crescentic and star shapes, in combined proportion this was reported by approximately one-quarter of patients. The orientation of photopsia was interesting in that the majority of patients with PVD described vertical photopsia, whereas patients with retinal tear or detachment most often described oblique or horizontal photopsia. These findings were both statistically and clinically significant. Another important finding of this study was over 90% of patients reported each episode of photopsia lasted a second or less regardless of the aetiology.

Byer (1994) noted identical symptomology in patients with retinal breaks and PVD; 54% had both photopsia and floaters with an additional 40% experiencing floaters alone. Paradoxically 6% of eyes with photopsia alone had PVD, whereas only 2% of eyes with retinal breaks experienced photopsia. Similar findings have been found by others reporting on symptoms in PVD and retinal breaks (Tanner *et al.* 2000; Al-Asadi 2013). It is therefore evident that unfortunately, neither floaters nor photopsia as symptoms alone can be relied upon as predictors of retinal breaks (Novak & Welch 1984; Dayan *et al.* 1996; Hollands *et al.* 2009; Goodfellow *et al.* 2010; Schweitzer *et al.* 2011). This has been substantiated by a very recent publication by Hurst and colleagues (2015) that found photopsia and floaters in conjunction or in isolation to be present in 62% of eyes with acute onset PVD, 15% had a retinal break or detachment, almost 10% had other retinal pathology with the remainder having no abnormality detected. Therefore overall in over three-quarters (77%) of patients with photopsia with or without floaters the symptoms are vitreoretinal in origin.

In the process of PVD, once the vitreous separates and the traction resolves the photopsia subside (Law & Sternberg 2007; Goodfellow *et al.* 2010). This process generally takes between four and twelve weeks (Snead *et al.* 2008a), conversely floaters can have a longer duration and be more bothersome (Kakehashi *et al.* 1998; Sebag 2011). The duration of symptoms can be indicative of the presence of a retinal break as Dayan *et al.* (1996) 99% and 95% of patients with serious pathology presented within six and four weeks respectively; Richardson *et al.* (1999) 91% of eyes with breaks had symptoms for 30 days or less Sharma *et al.* (2004) found 93% of eyes with retinal breaks had symptoms for less than one month. However Schweitzer *et al.* (2011) report that an improvement in initial symptoms does not exclude the presence of retinal breaks.

1.7 Aetiology of retinal breaks and retinal adhesion

The most serious consequence of PVD is the development of a break in the structural integrity of the retina with subsequent development of retinal detachment (Novak & Welch 1984; Akiba 1993; Byer 1994; Ghazi & Green 2002; Mitry *et al.* 2010b; Kuhn & Aylward 2014). This primarily arises due to tractional forces exerted on the retina from the vitreous, ultimately resulting in loss of visual function (Sigelman 1980; Novak & Welch 1984; Hikichi *et al.* 1995; Dayan *et al.* 1996; Yonemoto *et al.* 1996; Sharma *et al.* 1999; Tanner *et al.* 2000; Coffee *et al.* 2007; Sebag 2008b; Shechtman & Calderon 2008; Qureshi & Goble 2009; Mitry *et al.* 2010b; Johnson 2010; Schweitzer *et al.* 2011; Kuhn & Aylward 2014). The development of a retinal break is a complex interaction in the relationship of the retina, vitreous and associated structures (Machemer 1984; Foulds 1985 & 1987; Ghazi & Green 2002; Mitry *et al.* 2010b; Kuhn & Aylward 2014). Retinal breaks primarily arise due to persistent adhesion between the retina and vitreous, hence in this area the retina remains attached to the vitreous and instead detaches from the RPE, an underlying pigmented layer beneath the neurosensory retina. The RPE is a pigmented layer and plays an instrumental role in the transport of fluid from within the retina, thus maintaining its coherence against the retina. Between the neurosensory retina and RPE a medium described as the interphotoreceptor matrix exists, this is a glycosaminoglycan based compound and it has been suggested it may have a role in the apposition of the neurosensory retina to the RPE (Bermab 1969; Hollyfield *et al.* 1989). In addition there appears to be a biological interaction between the microvilli of the RPE and the outer segments of the photoreceptors that assist in the adherence of the RPE to the neurosensory retina (Hollyfield *et al.* 1989; Finneman & Chang 2008). Furthermore retinal oxygenation is also recognised as an entity implicated in the adhesion of the retina to the RPE (Kim & Yao 1993).

The two most common entities of a retinal break that occur as part of PVD are operculated holes and horseshoe tears (Sharma *et al.* 2004). Operculated holes develop when there is a localised area of vitreoretinal adhesion surrounded by weaker adhesion. Hence in this scenario an area of retinal tissue detaches fully from the surrounding retina and remains in contact with the vitreous, consequently relieving the tractional forces previously exerted upon the retina. Operculated breaks as a result of PVD comprise approximately one-third of all breaks. Conversely horseshoe tears constitute approximately two-thirds of all retinal breaks as a consequence of PVD, and are a partial discontinuity of the retina of which the open end of the horseshoe shape invariably is orientated to the vitreous base, often there is no detachment of the vitreous from the retina in this region (Foos & Allen 1967; Bishop 2000; Ghazi & Green 2002; Sharma *et al.* 2004). The risk of a retinal break occurring during the acute phase of PVD has been found to be in the order of 6-46% (Kanski 1975; Boldrey

1983; Byer 1994; Hikichi & Trempe 1994; Dayan *et al.* 1996; Sharma *et al.* 1999; Hikichi & Yoshida 2004), with a meta-analysis by Coffee and colleagues (2007) reporting an incidence of 22%. Once a retinal break forms, the subretinal space is exposed to liquefied vitreous and dynamic interactions of intraocular currents due to ocular movements together with vitreoretinal traction are pertinent factors for the progression of a retinal break to a detachment (Sigelman 1980; Pederson *et al.* 1982; Machemer 1984; Foulds 1987; Ghazi & Green 2002; Mitry *et al.* 2010b; Kuhn & Aylward 2014). These altered dynamics can result in lifting of the retina and accumulation of intraocular fluid which is termed a retinal detachment. The risk of a retinal detachment associated with a retinal break secondary to PVD has been reported to 28-36% (Colyear & Pischel 1956; Davis 1974; Byer 1994). Nevertheless it is important to appreciate that not all retinal breaks associated with PVD will ultimately result in retinal detachment (Machemer 1984; Foulds 1987; Ghazi & Green 2002; Byer 1998; Mitry *et al.* 2010b; Kuhn & Aylward 2014).

1.7.1 Prognosis of retinal breaks

There are a number of relevant prognostic factors to consider whether a retinal break will result in a subsequent retinal detachment. The most significant relate to the configuration, location and size of the retinal break together with symptoms and each of these are discussed in further detail

1.7.1.1 Configuration

A primary factor that governs the prognosis of a retinal break is the configuration of the retinal break. In operculated breaks, it is assumed the tractional forces exerted on the retina are no longer present and thus only a limited amount of (if any) fluid will enter the subretinal space. In such cases the interphotoreceptor matrix and RPE may be able to stabilise further progression of the retinal separation (Pederson *et al.* 1982; Machemer 1984; Foulds 1987; Bishop 2000; Ghazi & Green 2002; Mitry *et al.* 2010b; Kuhn & Aylward 2014). Although some degree of vitreoretinal traction may be relieved, there may still be persistent traction at the edge of the retinal break and the risk of an operculated retinal break associated with PVD progressing to a retinal detachment has been reported to be in the order of 11-16% (Colyear & Pischel 1956; Davis 1974). Conversely, in the presence of a horseshoe tear this risk is significantly greater 31-57% due to the continual traction at the anterior margin (Colyear & Pischel 1956; Davis 1974).

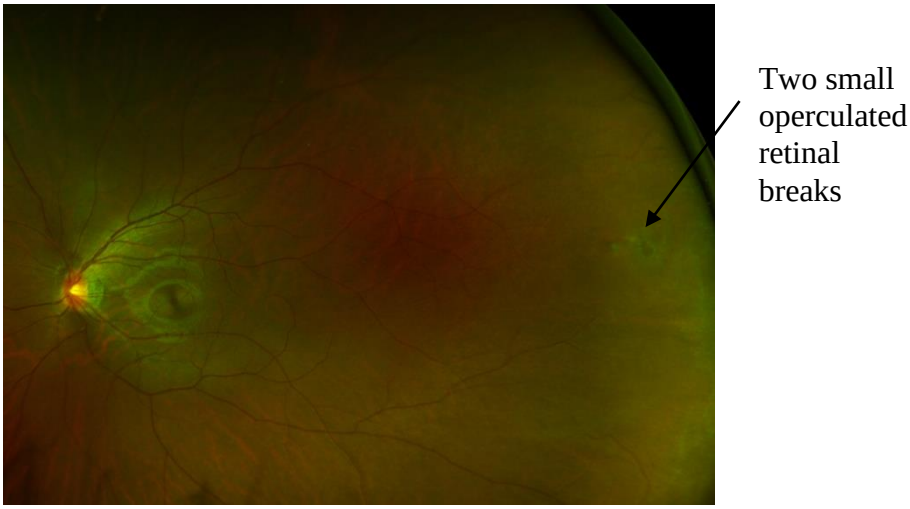

Fig 1.6.1 A widefield retinal photograph of two operculated retinal breaks

1.7.1.2 Size

The size of the retinal break also appears to be directly correlated to whether retinal detachment will ensue. Retinal breaks larger than approximately 1500µm are associated with a greater likelihood of progression to retinal detachment (31%) compared to smaller retinal breaks (5%) (Davis 1974). Fundamentally in smaller retinal breaks the interphotoreceptor matrix and RPE are often able to expel the incoming intravitreal fluid, additionally the effect of intraocular currents is less thus a retinal detachment may not necessarily arise. Finally the vitreous cortex can be highly influential and it has been demonstrated if the vitreous cortex overlies a retinal break this can provide an internal tamponade against intraocular currents and prevent the access of liquefied vitreous into the subretinal space (Pederson *et al.* 1982; Machemer 1984; Foulds 1987).

1.7.1.3 Pigmentation

Another factor that has been implicated in the prognosis of a retinal break is the presence of pigmentation. Pigment adjacent to the location of a retinal break does not imply adhesion of the retina and does not offer any protective value against progression to retinal detachment, it merely signifies chronicity and that the break has been present for a period of at least three months, but does not obviate the need for treatment (Morse & Eagle 1975; Sigelman 1980).

1.7.1.4 Symptoms

The presence of symptoms is positively correlated with a greater incidence of development of retinal breaks and detachment. Recent reviews of the literature have found 31-57% of eyes with symptomatic retinal breaks advance to retinal detachment, whereas it has been found 0-14% of asymptomatic retinal breaks will progress to retinal detachment (Carvounis & Holz 2006; Blindbæk & Grausland 2014). One of the most notable studies evaluating the

natural history of asymptomatic retinal breaks was undertaken by Byer (1998). In this study he assessed 235 eyes over a period of at least twelve months, with 102 eyes being studied for at least 10 years. The majority of these breaks (55%) were located in the inferior hemisphere. Of a total of 45 horseshoe tears, 3 (7%) developed into operculated breaks which did not require intervention. Reassuringly 32 of 32 operculated breaks did not progress or require intervention. The largest group observed were those with round holes harboured within lattice degeneration consisting of 158 eyes. Three of these eyes developed new retinal breaks secondary to PVD, all of which were symptomatic and treated. Lattice degeneration was also noted in 95% of eyes with subclinical retinal detachment. The outcome of this study was only 1 eye developed retinal detachment requiring intervention. In summary this study found asymptomatic retinal breaks in phakic eyes rarely progress and no intervention is necessary. Although PVD did not influence pre-existing retinal breaks in 22 eyes, 3 (13.6%) of these eyes did develop new breaks. This finding is however limited due to the small number of eyes determined to have PVD. Of greater relevance is that all of the three eyes harboured lattice degeneration, suggesting eyes with such lesions are at greater risk of developing new breaks secondary to PVD. Prophylactic treatment of symptomatic retinal breaks dramatically reduces this figure by approximately 5- to 10-fold, with only 1-11% of treated eyes continuing to retinal detachment (Carvounis & Holz 2006; Blindbæk & Grausland 2014). Although these reviews clarified some observations, the authors do acknowledge its limitations, primarily the lack of controlled studies (Blindbæk & Grausland 2014).

1.7.1.5 Location

Theoretically a retinal break can occur in any location however the overwhelming majority of retinal breaks affect the peripheral retina. This may in part be due to the peripheral retina being anatomically thinner; the thickness of the centre point of the retina, the fovea, to be 0.10mm, the thickness then increases dramatically to 0.23mm at the foveal margin, gradually tapering to 0.11mm at the ora serrata (Straatsma *et al.* 1969). There appear to be numerous additional contributing factors, one such factor is the variation in strength of vitreoretinal adhesion at different locations; the adhesion of the vitreous to the retina is strongest peripherally, whereas the vitreous cortex is thinner over the macula region. Furthermore vitreous detachment begins in the central retina relieving this region of traction and thus reducing the risk of a retinal break. (Sebag & Balazs 1989; Bishop 2000; Uchino *et al.* 2001; Sebag 2004; Johnson 2005; Kampik 2012). Another contributing anatomical factor is that the RPE and interphotoreceptor matrix that aid the adhesion of the retina are less effective in the peripheral retina (Hollyfield *et al.* 1990). Additionally vitreoretinal abnormalities are present in the peripheral retina and devoid centrally (Dunker *et al.* 1997);

there is a lack of supporting tissue and vasculature in the periphery in comparison and these can support the retina even in the presence of a retinal break (Anderson 1932) coupled with the fact the peripheral retina is essentially ischaemic in comparison (Michaelson 1948; Combs & Welch 1982) are all causative in the predilection for the peripheral retina in developing retinal breaks.

Similar to the variation in the central and peripheral retina, there are disparities between different locations of the peripheral retina for the development of retinal breaks with the superior and temporal hemispheres more frequently afflicted (Linder 1966; Jaffe 1968; Tasman 1968; Kanski 1975; Combs & Welch 1982; Novak & Welch 1984; Byer 1994; Sharma *et al.* 2004; Shunmugam *et al.* 2014). Retinal breaks arising secondary to PVD are most frequent in the superotemporal quadrant (40-60%) followed by inferotemporal (20-30%) and superonasal (15-30%) with the inferonasal quadrant being least frequently involved (5-10%) (Romem & Singer 1978; Combs & Welch 1982; Byer 1994; Sharma *et al.* 2004). Gravitational forces may be expected to influence the development of retinal breaks and their location, and this would be a reasonable explanation as to the greater preponderance of retinal breaks in the superior hemisphere, however the last region in which the vitreous detaches is inferiorly. The vitreous in conjunction with gravity can therefore provide a tamponade to the inferior retina reducing the risk of a retinal break (Pederson *et al.* 1982; Machemer 1984; Foulds 1987; Shunmugam *et al.* 2014). Gravity alone however does not explain why the temporal retina has a greater predisposition to the formation of retinal breaks. The increased susceptibility of the temporal retina to the formation of retinal breaks secondary to vitreous traction may in fact be multifactorial. The first of these is possibly due to the underlying anatomical differences between the nasal and temporal regions. The nasal retina extends further anteriorly to approximately 6mm behind the limbus, conversely the temporal retina lies approximately 7mm behind the limbus (Straatsma *et al.* 1968). Histological studies have confirmed the thickness of the ora serrata is relatively constant in all quadrants, however the nasal retina has a greater number of extensions of the retina that insert into the ciliary body, (Straatsma *et al.* 1968), whereas in the temporal retina cystoid degeneration is prominent. Cystoid degeneration represents areas of intraretinal separation and may be due to the avascularity of the ora resulting in premature senescence (Anderson 1932; O'Malley & Allen 1967; Foos *et al.* 1969). It has long been recognised through embryological studies of the development of retinal vasculature, the temporal retina is the last to become vascularised. By month 8 of gestation, the vasculature is almost at the ora nasally but only reaches the equator temporally. The temporal retina becomes fully vascularised at around birth, but overall has larger ischaemic areas in comparison and this may be attributable to blood vessels of the temporal periphery being finer due to the greater

distance from the optic disc (Michaelson 1948; Shunmugam *et al.* 2014). This difference in vascular development and supply may indeed be a fundamental factor that predisposes the temporal retina to the development of a variety of degenerations and retinal breaks. In addition retinal blood vessels may also offer resistance to the development of retinal breaks and they remain intact across retinal breaks, as the temporal retina is more devoid of vasculature there is a distinct lack of surrounding support to the retina (Anderson 1932). The temporal retina is also more exposed to trauma and as such may develop structural damage predisposing this region to the formation of retinal breaks (Anderson 1932). Furthermore, anatomically the vitreous base extends approximately 1.8mm temporally, whereas nasally it reaches approximately 3mm. As mentioned earlier, it is recognised the vitreous base has an almost indestructible bond with the retina, therefore the periphery of the nasal retina in comparison is somewhat protected against the development of retinal breaks as it is straddled by the vitreous base (Kampik 2012). Recently measurements of retinal thickness using optical coherence tomography have confirmed the temporal retina is thinner compared to the nasal retina (Wenner *et al.* 2014).

The results of a prospective study, with duration of over 10 years, evaluating the distribution of retinal breaks in retinal detachment have recently been published (Shunmugam *et al.* 2014). This highly informative study of 844 patients with rhegmatogenous retinal detachment has consolidated findings of previous research whilst further enhancing insight. The first of these notable findings is that the superior retina is most frequently involved in the development of retinal breaks, furthermore confirming the notion that the superotemporal quadrant has the greatest predilection. Interestingly, only 39% had a solitary break, and in over 50% of cases this was located in the superotemporal quadrant. Conversely, although the inferonasal quadrant was found to be least frequently involved, breaks located here had an increased probability for the presence of breaks in other quadrants. Another factor predictive of break multiplicity was the size of the break detected; in eyes with large breaks (greater than 2 disc diameters) there was a decreased likelihood for multiple breaks to be present, whereas there was a greater tendency for the presence of multiple breaks in eyes with smaller breaks. Overall, 59% of eyes had breaks involving more than one quadrant. The findings of this study further add credence to the concept that the vitreous detaches in a progressive manner, in which the superotemporal region is affected first, followed by superonasal, then inferotemporal and finally inferonasal. Notably 92% of retinal breaks in the superotemporal quadrant were within an area of detached retina compared to 60% of inferonasal breaks. Inferior breaks were less likely to be detached as gravitational effects and tractional forces exerted upon the retina would be less, indeed the detached vitreous may in fact provide a tamponade hence maintaining adhesion of the neurosensory retina to

the RPE, thus preventing the development of retinal detachment. A landmark paper by Lincoff and Geiser in 1971 devised a system to identify the location of the retinal break depending upon the configuration and location of the retinal detachment it produced. This is highly relevant as a retinal break may not be identified in all cases, and undetected breaks are the primary cause of treatment failure (Shunmugam *et al.* 2014)

1.8 Significance of haemorrhage

Traction on a retinal blood vessel can result in avulsion and subsequent haemorrhage which may be retinal, pre-retinal or extend into the vitreous (Novak & Welch 1984, Spraul & Grossniklaus 1997; Goff *et al.* 2006). Haemorrhages can masquerade as and conceal retinal breaks, and the incidence of a retinal break in the presence of vitreous haemorrhage associated with PVD has been reported to be in the order of 45-79% (Linder 1966; Jaffe 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Hikichi & Trempe 1994; Sharma *et al.* 1999; van Overdam *et al.* 2005; Coffee *et al.* 2007). Furthermore, haemorrhages may signify concurrent traction and impending retinal breaks (Tasman 1968). Therefore in such cases caution must be exercised as there is an increased likelihood an underlying retinal break exists (Byer 1994; Hikichi & Trempe 1994; Sharma *et al.* 1999; Goff *et al.* 2006).

1.9 Other complications of posterior vitreous detachment

The majority of retinal breaks occur at the onset of symptoms in PVD, however numerous studies have demonstrated delayed retinal breaks can develop in up to 4% of eyes within the first few weeks of acute PVD (Jaffe 1968; Tasman 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Dayan *et al.* 1996; Richardson *et al.* 1999; van Overdam *et al.* 2001 and 2005; Coffee *et al.* 2007; Hollands *et al.* 2009; Schweitzer *et al.* 2011; Williams *et al.* 2011).

In conjunction the onset of PVD can result in a plethora of macular pathology including epiretinal, macular hole, choroidal neovascularisation and vitreomacular traction, all of which may produce symptoms together with visual loss and necessitate intervention (Johnson 2005; Sebag 2008b; Carrero 2012).

1.10 Prevalence and influencing factors

A complete posterior vitreous detachment occurs when the vitreous separates as far as the border of the vitreous base where the vitreoretinal adhesion is recognised as being resilient and indissoluble (Le Goff & Bishop 2008). A variety of risk factors predispose individuals to the development of PVD and potentially retinal breaks, most of which are non-modifiable.

1.10.1 Age

The primary cause of PVD is increasing age (Foos & Wheeler 1982; Hikichi *et al.* 1995; Yonemoto *et al.* 1996), refractive error, trauma and intraocular surgery are also other recognised causes (Novak & Welch 1984; Yonemoto *et al.* 1996; Schweitzer *et al.* 2011). An autopsy study of 4,492 eyes by Foos & Wheeler (1982) found 27% of eyes in the seventh decade and 63% of eyes in the eighth decade exhibited PVD. The mean age for the onset of PVD has been reported as 57-64 years (Jaffe 1968; Tasman 1968; Novak & Welch 1984, Diamond 1992). A study by Akiba (1993) of 220 emmetropic eyes found the prevalence of PVD to increase with age and the findings are summarised in table 1.1.

Decade	Prevalence
5th	8%
6th	23%
7th	44%
8th	74%
9th	86%

Table 1.10.1.1 The prevalence of PVD per decade in emmetropic eyes as found by Akiba 1993

Yonemoto and colleagues (1994) noted eyes with features of peripheral retinal degeneration developed PVD at slightly earlier age (2.2 years) compared to eyes without peripheral retinal degeneration. However this was not statistically significant, but may be clinically significant as eyes with peripheral retinal abnormalities are predisposed to the development of retinal breaks due to the altered anatomical relationship (Anderson 1932; O'Malley & Allen 1967; Foos *et al.* 1969; Hollyfield *et al.* 1990; Dunker *et al.* 1997). The mean age of eyes with retinal breaks has been reported to be 60.4 years by Combs & Welch (1982) and 59.0 years by Smiddy *et al.* (1991). In contrast both Goldberg & Boyer (1980) and Sharma *et al.* (2004) have reported the mean age to be less at 52.7 and 54.6 years respectively. The distribution of retinal breaks as documented by Combs and Welch (1982) is represented in table 1.10.2

Decade	Prevalence
4th	2%
5th	6%
6th	28%
7th	56%
8th	7%
9th	1%

Table 1.10.1.2 Distribution of retinal breaks per decade (Combs & Welch 1982)

Expectedly the majority of retinal breaks developed in the sixth and seventh decades, coinciding with the onset of PVD. The overall incidence of retinal detachment is in the order of approximately 1 per 10,000 and the prevalence of retinal detachment increases with age

and. The incidence of retinal detachment is greatest in the seventh decade attributable to the onset of PVD (Mitry *et al.* 2010a).

1.10.2 Laterality

It has been reported the onset of PVD is a sequential rather than simultaneous event between the two eyes (Novak & Welch 1984; Byer 1994; Hikichi & Yoshida 2004). Novak and Welch (1984). Novak and Welch (1984) reported 88% of seventeen patients that developed sequential PVD did so within two years. Interestingly this study found in three-quarters of second affected eyes the behaviour of the second affected eye was remarkably similar to the first eye, in that if the first eye developed a haemorrhage or retinal break this was again a feature in the contralateral eye. It is important to note however that their observations were of only seventeen patients and may not be statistically significant. Nevertheless the landmark prospective study by Byer (1994) found PVD developed in the fellow eye within 2 years of the initial eye in 80% of such individuals, a similar finding to Novak & Welch (1984) despite the difference in the size of the studies (50 patients and 17 patients, respectively). Byer (1994) also commented on the asymmetry of involvement with the right eye being involved in 55% of cases. A prospective study by Hikichi & Yoshida (2004) evaluating this particular subject documented the development of PVD in the contralateral eye in one-quarter (24%) within 12 months, 65% within 2 years and 90% of subjects within 3 years. Patients older than 60 were more likely to develop PVD in the second eye compared to younger counterparts, although this was not quite statistically significant. An interesting finding of this study was that second affected eyes were more likely to develop a retinal break (13% vs 10%). A prospective observational study by Hayreh and Jonas (2004) found right and left eyes were affected equally, however PVD was found more often bilaterally (27.5%) rather than unilaterally (9.7%). The mean age of eyes with unilateral PVD was 68.7 years and were 4 years younger than those with bilateral PVD.

1.10.3 Refractive error

Refractive error is another significant influencing factor and a number of studies have found myopic eyes developing PVD at an earlier age in comparison to non-myopic eyes. Both Jaffe (1968) and Novak & Welch (1984) report the mean age of onset of PVD in myopia to be 56 years, with non-myopes developing PVD at 66 and 61 years of age respectively in each study. Novak & Welch (1984) found twice as many low myopes (-1.00 to -3.00) and 13 times as many high myopes (-3.00 and above) with PVD compared to an age-matched population Akiba (1993) formally studied the prevalence of PVD in high myopia (greater than six dioptres) and found the greater the degree of myopia the earlier the onset of PVD. The findings of this study are summarised in Table 1.10.3.1.

Decade	Prevalence
4th	23%
5th	29%
6th	44%
7th	72%
8th	100%

Table 1.10.3.1 The prevalence of PVD in myopic eyes per decade (Akiba 1993)

In essence, compared to emmetropic eyes PVD developed approximately 10 years earlier in myopic counterparts (tables 1.1 and 1.2). In the study conducted by Byer (1994) almost half (47%) of eyes with PVD were myopic, compared to 37% of the control population being myopic. Furthermore in this study the mean age at which PVD developed in myopes was 56.1 years, whereas in non-myopes PVD developed later at a mean age of 62.5 years. An eloquent study by Yonemoto *et al.* (1994) further expanded on the relationship between the age of onset of PVD and refractive error. In agreement with Byer (1994) myopes were noted to develop PVD earlier than non-myopes, however Yonemoto *et al.* (1994) were able to formulate this relationship in a sophisticated manner utilising linear regression. Essentially the mean age of onset of PVD in emmetropic eyes was 61 years, the influence of refractive error was such that for each dioptre of mean spherical equivalent refractive error the age of onset altered accordingly by one year (approximately); increasing in hyperopia and reducing in myopia. A relatively recent study by Chuo *et al.* (2006) found myopes were four times more likely to develop PVD in comparison to non-myopes, further consolidating the impact of myopia.

Myopia is known to induce changes to the vitreous, retina, choroid and vasculature resulting in structural changes that may alter the dynamics of retinal apposition (Pierro *et al.* 1992; David *et al.* 1998; Logan *et al.* 2004; Repetto *et al.* 2005; Fujiwara *et al*. 2009; Ikuno & Tano 2009; Ikuno *et al*. 2013). In myopic eyes there is an increased vitreous volume and this predisposes the retina to greater shearing forces induced by eye movements (David *et al.* 1998; Repetto *et al.* 2005). Recent fourth generation optical coherence tomography studies have demonstrated the choroid is thinner in the nasal retina compared to the temporal retina in high myopia (Fujiwara *et al*. 2009; Ikuno & Tano 2009; Ikuno *et al*. 2013), further suggesting abnormalities of the choroid may be implicated in the development of retinal pathology associated with myopia. Cheng *et al* (2010) measured peripheral retinal thickness in both myopic and non-myopic eyes with third generation optical coherence tomography and were able to assess locations 40 degree eccentrically. This study found the retina thickness to be consistently thinner in the temporal quadrant in both myopic and non-myopic eyes. This was further corroborated by a more recent study by Wenner *et al.* (2014) and provides comprehensive data with regard to the retinal thickness in peripheral locations,

confirming the temporal retina is thinner in comparison to the nasal retina. This was a consistent finding in these randomly selected participants and exhibited some correlation with axial length measurements. This may be a further contributory factor for the greater predisposition of the temporal retina to develop retinal breaks.

A number of studies have documented a greater incidence of retinal breaks and detachment in myopic eyes with PVD (Linder 1966; Jaffe 1968; Romem & Singer 1978; Combs & Welch 1982; Novak & Welch 1984; Eye Disease Case-Control Study Group 1993; Byer 1994). Both Linder (1966) and Jaffe (1968) reported on this specific observation. Of 106 eyes with acute PVD, Linder (1966) found 16 eyes with retinal breaks (15%) of which over one-quarter of breaks (31%) were in eyes with 3 dioptres or more of myopia. Similarly Jaffe (1968) found 9 retinal breaks from 84 eyes (11%) of which 66% developed in eyes with myopia of more than 3 dioptres. Overall both studies found similar incidences of retinal breaks in myopes; 28% in the former and 33% in the latter compared to 13% and 5% respectively in eyes with less than 3 dioptres of myopia. These findings have further been established by poignant observations of the Eye Disease Case-Control Study Group (1993) which found that 55% of rhegmatogenous retinal detachments occurred in myopes. In low myopes (-1 to -3) there was a four-fold increase in risk and in myopia greater than 3 dioptres the risk was increased ten-fold in comparison to non-myopic eyes.

1.10.4 Gender

Yonemoto *et al.* (1994) found the mean age of onset in males was marginally greater than in females, 61.1 years compared to 59.7 years. On the contrary Tanner *et al.* (2000) found the mean age of females to be 62.2 years and in males to be 60.9 years at the time of occurrence of PVD. The disparity in these studies is likely to be multifactorial, firstly the figures by Yonemoto *et al.* (1994) are reported from 930 eyes, whereas the study by Tanner *et al.* (2000) was significantly smaller of 200 patients (of which 25 had retinal breaks). Secondly refractive error differences are likely to have contributory, unfortunately Tanner *et al.* (2000) did not report on the refractive error distribution, whereas 75-80% of were emmetropic, with only 2-3% hypermetropic, and the remainder with varying degrees of myopia in the study by Yonemoto *et al.* (1994). Nevertheless neither study found the difference in mean age between males and females to be statistically significant. A further observation from both studies and others is that the PVD appears to occur more frequently in females than males, with a male to female ratio in the order of approximately 2:3 (Linder 1966; Jaffe 1968; Tasman 1968; Novak & Welch 1984; Diamond 1992; Gutteridge 1993; Byer 1994; Richardson *et* al. 1999; Hayreh & Jonas 2004). The nature of this disparity has been elusive to a number of individuals (Linder 1966; Jaffe 1968; Tasman 1968; Novak &

Welch 1984), however Byer (1994) compared this ratio to a control group of new patients in his practice and found no statistically significant difference, thus suggesting gender was not an influential factor for PVD. Chuo *et al.* (2006) found PVD was twice as likely to occur in females compared to males and this was attributable to a higher intake of vitamin B6 and menopause.

Of significance however is the greater incidence of retinal breaks and detachments in males compared to females (Linder 1966; Jaffe 1968; Goldberg & Boyer 1980; Novak & Welch 1984; Byer 1994; Tanner *et al.* 2000; Sharma *et al.* 2004; Mitry *et al.* 2010a). The incidence of retinal breaks in males secondary to PVD has been reported to be 16-23% whereas in females this is in the order of 4-10%. Therefore males appear to have a 2-4 times greater predisposition to the development of retinal breaks associated with PVD. Similar to eyes with uncomplicated PVD, Combs and Welch (1982) did not find a significant difference in the mean ages of males and females with retinal breaks (61.1 in males, 59.5 in females).

1.10.5 Ethnicity

Although myopia has become epidemic in East Asia (Morgan *et al.* 2012; Dolgin 2015), ethnicity does not appear to influence the age of onset of PVD (Hikichi *et al.* 1995; Chuo *et al.* 2006). Furthermore this observation is reciprocated in cases of retinal detachment (Mitry *et al.* 2010a)

1.10.6 Phakic status

Removal of the crystalline lens can result in alterations in the vitreous resulting in PVD with subsequent retinal breaks and detachment. The precise underlying mechanism is yet be identified, however a number of plausible explanations have been submitted. The first of these is that anterior movement results following removal of the lens, thus inducing traction at the vitreous base resulting in a retinal break (Lois & Wong 2003). Byer (1994) noted the incidence of retinal tears due to PVD was 37% in aphakic eyes compared to 13% in phakic eyes, with an odds ratio of 3.84 which was statistically significant. Furthermore only 18% of retinal breaks in phakic eyes advanced to retinal detachment whereas in contrast 86% of tears in aphakic eyes progressed to retinal detachment, again a statistically significant finding. Although removal of a cataract may improve fundus visualisation, it can inadvertently impede peripheral retinal examination due to poor mydriasis, cortical remnants and posterior capsular opacification. In rhegmatogenous retinal detachment retinal breaks are not identified in 2-4% of phakic eyes, 7-16% pseudophakic eyes and 5-23% of aphakic eyes and are the primary cause of failure of treatment (Salicone *et al.* 2006). As Shunmugam *et al.*

(2014) identified it is of the highest importance that all retinal breaks in retinal detachment are located as unidentified breaks are the most frequent cause of failed surgical repair**.**

1.10.7 Pre-existing abnormalities

Gutteridge (1993) conducted a prospective study of 1600 consecutive patients presenting to an optometric practice, and found a prevalence of 20-25% (depending upon the conditions included) of ocular conditions identified in this sample, specifically 6% had retinal degenerations. Byer (1994) recorded 22% of patients in his study had co-existing lattice degeneration or retinoschisis. The presence of coexisting vitreo-retinal pathology such as retinal degeneration and vitreo-retinal tufts can also have a significant influence in the pathophysiological development of retinal breaks and subsequent retinal detachment (Ghazi & Green 2002, Mitry *et al.* 2010a). Lattice degeneration is such a degeneration of the peripheral retina that may represent a predisposition to the development of retinal breaks. Histologically the findings are of focal retinal thinning with overlying liquefaction and abnormal vitreoretinal adhesions along the border. Notably lattice degeneration can be associated with 60% of retinal detachments (Byer 1974). Despite this observation, the evidence currently does not advocate prophylactic treatment for such lesions as there is no significant risk reduction (Carvounis & Holz 2006).

1.10.8 Trauma

The pathogenesis of trauma to the eye has been described by Weidenthal and Schepens (1966) and Delori *et al.* (1969). Contusion from blunt trauma results in compression of the globe with subsequent compensatory distension of the ocular structures including the retina and concomitant traction at the vitreous base, this is subsequently followed by decompression of the globe in which there can be further tractional forces exerted upon the retina (Weidenthal & Schepens 1966; and Delori *et al.* 1969). As a consequence this may result in avulsion of the vitreous from the retina (premature PVD) or retinal breaks may form with or without associated retinal detachment (Cooling 1986). Penetrating trauma can result in direct perforation of the retina and may also induce abnormal vitreo-retinal traction with consequential retinal detachment (Ruiz 1969; Cooling 1986). It therefore appears such trauma induces premature vitreo-retinal separation and associated complications, as such the mean age of patients with traumatic retinal detachment has been found to be 28 years whereas in eyes without traumatic retinal detachment the mean age was older at 58 years (Youssri & Young 2002). Furthermore males appear to have a greater predisposition to trauma due to differences lifestyle in contrast to their female counterparts (Tasman 1972).

1.11 Examination

It is recommended all patients with symptoms of acute PVD have dilated fundoscopy to exclude the presence of retinal breaks (Royal College of Ophthalmologists 2010; American Academy of Ophthalmologists 2014; College of Optometrists 2014). A number of studies have demonstrated that retinal breaks may not be evident at the onset of PVD when symptoms arise, however may develop in 2-4% of patients shortly afterwards (Jaffe 1968; Tasman 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Dayan *et al.* 1996; Richardson *et al.* 1999; van Overdam *et al.* 2001 and 2005; Coffee *et al.* 2007; Hollands *et al.* 2009; Schweitzer *et al.* 2011; Williams *et al.* 2011). Nevertheless as a result of these studies there are inconsistencies as to whether further examination of patients with acute PVD is necessary if the initial examination was uneventful. All do however agree, should there be any progression of symptoms or new symptoms develop then re-examination should be prompted. The American Academy of Ophthalmology (2014) have published extensive guidelines with reference to the examination of patients presenting with PVD and these have been adopted by the International Council of Ophthalmology (2011).

The clinical history should include details of the symptoms, family history, previous eye trauma, myopia and history of ocular surgery. It is recognised indirect ophthalmoscopy with scleral indentation is the gold standard examination for the identification of retinal breaks (Ruiz 1969; Sharma *et al.* 1999; Natkunarajah *et al.* 2003), however not all are proficient in the technique (Tanner *et al.* 2000; Qureshi & Goble 2009) and thus various adjunctive examinations are recommended. Complimentary examinations may include assessment of pupil reactions, intraocular pressure, anterior vitreous examination and visual field assessment. In cases where the peripheral fundus cannot be visualised B-scan ultrasonography is recommended (American Academy of Ophthalmologists 2014).

1.11.1 Pupil reactions

Previous studies have demonstrated a relative afferent pupillary defect can arise in the presence of retinal detachment (Bovino & Burton 1980; Thomson *et al.* 1982; Folk *et al.* 1987). These studies have shown a relative afferent pupillary defect will be present if at least one quadrant of the retina is detached. Thomson and colleagues in 1982 further validated the observation that the pupil defect correlated with extent of visual field loss and effectively the magnitude of the retinal defect. This was further substantiated by Folk *et al.* (1987) found the extent of the detachment was proportional to the depth of the pupil defect, and was further enhanced to a greater degree if the macula was affected.

1.11.2 Intraocular pressure

In 1963, a study by Dobbie revealed that the cause of ocular hypotension in an eye with retinal detachment was the result of reduced aqueous humour production. Dobbie (1963) found the difference in intraocular pressure was not significant in small detachments, despite a long duration of the detachment. Furthermore, the intraocular pressure did not alter significantly in the early phase of detachment. This observation of reduced intraocular pressure was only found to be substantial when more than one quadrant of the retina was detached, the mean reduction in intraocular pressure was found to be 22% These findings were further validated by Langham and Regan in 1969, however they further speculate an insufficiency of the vascular supply to the anterior uvea may be a precipitating factor in vitreoretinal degeneration and subsequent decrease in intraocular pressure associated with retinal detachment. Although low intraocular pressure can be associated with retinal detachment, Schwartz-Matsuo syndrome is an entity which exists in which the intraocular pressure may actually be elevated. In this condition it has been found the trabecular meshwork is obstructed by photoreceptor outer segments thus resulting in the elevation in intraocular pressure (Netland *et al.* 1994).

1.11.3 Pigment in the anterior vitreous

First described by Shafer in 1965, was the presence of pigment cells in the anterior vitreous to be a pathognomonic finding in eyes with retinal detachment. This observation has been validated by numerous studies that have unequivocally demonstrated presence of pigment cells in the anterior vitreous to be highly specific and sensitive for the presence of a retinal break and/or detachment. In this examination the illumination of the slit-lamp biomicroscope is set off-axis to the observation system. The slit-lamp is then focussed to the anterior vitreous and the patient is asked to make vertical and horizontal movements of the eye to enable dynamic assessment of the vitreous enabling visualisation of pigment cells (Brod *et al.* 1991; Tanner *et al.* 2000). One of the earliest studies to assess the sensitivity of pigment in the vitreous for the presence of a retinal break was undertaken by Hamilton and Taylor (1972). In this study of 63 eyes with retinal holes the sensitivity was found to be 82.5% with a specificity of 100%. The authors also speculate the pigment originates from the RPE and note the pigment is most frequently located in the anterior vitreous. Almost twenty years later, Brod *et al.* (1991) determined the sensitivity to be 93.8% for the presence of pigment in the anterior vitreous existing in conjunction with a retinal break. Similar to Hamilton & Taylor (1972); Brod *et al.* (1991) determined a specificity of 100% and also suggest the pigment cells enter the tear vitreous cavity once a discontinuity forms in the retina during the process of a retinal break. Importantly they recognise the pigment cells settle in the inferior aspect of

the vitreous and are only visualised when the vitreous is agitated with vertical eye movements.

In view of the fact retinal breaks are invariably located anteriorly, this may be the underlying explanation as to why pigment cells are visualised more frequently in the anterior vitreous. Sharma *et al.* (1999) determined a sensitivity and specificity of 88% for this examination in their multicentre cross sectional study of 59 patients with acute PVD. They conclude patients with pigment or red blood cells in the vitreous are 52 times more likely to have a retinal break compared to those without pigment cells in the vitreous. In a similar prospective study of 200 eyes, Tanner *et al.* (2000) found the sensitivity of pigment cells in the vitreous to be 92% for the detection of retinal breaks. Similarly, a prospective study in 2013 by Al-Asadi found the sensitivity of this sign to be 86% for the presence of retinal breaks. Although this feature is considered pathognomonic for the presence of a retinal break, it must be remembered this is only applicable to eyes that have not previously been subjected to intraocular disturbance such as surgery, inflammation or trauma. Therefore, in pseudophakic eyes, which may be of a similar age group to patients with symptoms of PVD, the sensitivity of this test will be negatively affected. Furthermore, media opacity may also hinder accurate observation, and therefore it is advisable not to unduly rely upon the lack of visibility of pigment in the anterior vitreous as a diagnostic indicator for the absence of a retinal break. In addition the experience of the examiner will invariably influence the outcome of this observation

This was demonstrated in a noteworthy study by Qureshi and Goble (2009) to assess the interobserver variability between different levels of ophthalmic staff. In this study the vitreo-retinal consultant found both the sensitivity and specificity of pigment cells in the vitreous for the presence of a retinal break to be in the order of 94% with a kappa coefficient of 0.86, suggesting excellent correlation. However less experienced staff, a junior doctor and an optometrist, were less reliable than the consultant. The percent agreement between the doctor and consultant was 78% with a kappa coefficient of 0.55 suggesting moderate agreement, the percent agreement between the optometrist and consultant was 62% with a kappa coefficient of 0.28 suggesting fair agreement (Viera 2005). In this study the false negative error by the less experienced ophthalmic staff was the largest source of error, and in conclusion there may be undue reliance on the detection of pigment cells in the vitreous for inexperienced ophthalmic professionals. Furthermore it has been suggested that pigment and red blood cells may become less pigmented over time and therefore discernible characteristics may become less discrete (Boldrey 1983). Henceforth it would be unwise to rely upon an absence of pigment in the vitreous to exclude the presence of a retinal break. This was demonstrated by Coffee *et al.* (2007) in which pigment was absent from the

anterior vitreous of one of two eyes that went on to develop a retinal break secondary to PVD. Conversely if pigment is identified in the vitreous in a patient then further investigation would be obligatory, primarily to exclude the presence of a retinal break.

1.11.4 Fundus examination

Although there is no doubt these adjunctive assessments described can be insightful, they are not specific for the presence of retinal breaks. In fact the evidence suggests the results of such examinations may be entirely normal in the presence of retinal breaks and/or small detachments. Binocular indirect ophthalmoscopy with scleral indentation is the recommended examination for the identification of retinal breaks (Ruiz 1969, Sharma *et al.* 1999; Natkunarajah *et al.* 2003). Binocular indirect ophthalmoscopy involves the examiner directing a bright light source into the eye of the subject, a condensing lens such as a +20D lens is introduced into the path of the light beam. This produces an indirect image of the retina which the examiner is able to view. To examine the extremities of the retina, an indenter is applied to the eye externally producing a depression, consequently elevating the far periphery of the retina which can then be visualised. There are numerous advantages of this binocular indirect ophthalmoscopy in comparison to other methods of viewing the peripheral retina. Firstly the field of view is larger owing to the fact the condensing lens is physically larger and has less positive power. Secondly, as the illumination system is portable and not restricted, it permits a more superior dynamic assessment of the far periphery. Although poor pupillary dilation and media opacities can diminish the view whichever method is used to view the fundus, scleral indentation allows visualisation of the retina that would otherwise be not be possible. In essence, as scleral indentation manipulates the globe and retina, it greatly assists in the differential diagnosis of retinal pathology. An example of this is the differential diagnosis of degenerative retinoschisis. Degenerative retinoschisis is a condition of the peripheral retina in which there is a split within the retinal layers, fluid accumulates within this area and this elevation can masquerade as a retinal detachment. With scleral indentation the cavity in retinoschisis persists, however in retinal detachment the cavity can be collapsed (Byer 1982, Ip *et al.* 1999). Furthermore scleral indentation will result in blanching of the outer leaf which will not occur in a retinal detachment (Blach 1967). An alternative method of fundus examination utilises a 3-mirror contact lens. For this technique, a special contact lens which has mirrors incorporated within it, is placed on the front of the eye and the illumination beam from the slit-lamp biomicroscope is directed towards the mirror designed for peripheral fundus examination, the image of the retina is seen in the mirror (Yanoff & Duker 2003).

Richardson *et al.* (1999) in their study found the 3-mirror contact lens had a sensitivity of only 33% for detecting retinal breaks, and all breaks anterior to the equator were missed by this method of examination. Natkunarajah *et al.* (2003) undertook a prospective study of patients presenting with retinal breaks to compare the sensitivity of slit-lamp examination together with a condensing lens against indirect ophthalmoscopy with scleral indentation. The findings of this study were almost 90% of retinal breaks were identified using the slit-lamp examination compared to examination with scleral indentation. Adjunctively, for the breaks not identified by the slit-lamp examination, they undertook a 3-mirror contact lens assessment to identify the breaks. However, this technique also failed to identify all of the breaks missed by the slit-lamp examination, suggesting 3-mirror examination was of no additional benefit. There were however limitations of this study; only a small number of patients, a total of 17 eyes, were recruited to the study due to the selective inclusion criteria; and there were only a limited number of examiners. These factors would inevitably have introduced bias which the authors recognise and imply artificially improved the sensitivity of the slit-lamp examination. Nevertheless they conclude indirect ophthalmoscopy with scleral indentation should be utilised in the examination when there is a suspicion of retinal break. In contrast to this study previous studies have suggested the 3-mirror examination was superior to indirect ophthalmoscopy with scleral indentation (Jaffe 1968; Chapman-Davies & Lazarevic 1996). Jaffe (1968) detected an additional three retinal breaks with the 3-mirror lens compared to indirect ophthalmoscopy with indentation which detected six breaks. However, the proficiency of the author with the techniques was stated as a factor. Similarly Chapman-Davies and Lazarevic (1996) found the Goldmann 3-mirror lens to be superior or the detection of retinal breaks in compared to the indirect ophthalmoscope. It must be borne in mind however only four eyes were found to have a retinal break in 26 patients with symptoms of acute PVD. It is highly unusual for retinal breaks to be missed with indirect ophthalmoscopy with scleral indentation as this is considered the gold standard (Sharma *et al.* 1999, Natkunarajah *et al.* 2003). The authors' state in their methodology scleral indentation was not employed in all cases. Unfortunately they do not specify if scleral indentation was employed in the cases in which retinal breaks were missed with indirect ophthalmoscopy, therefore the validity of their study is questionable. Furthermore neither study provides additional details such as patient co-operation or features of the breaks that may have contributory factors explaining the superiority of one technique over the other.

1.12 Imaging

Due to its very nature of transparency, the vitreous has been notoriously difficult to study and indeed image in detail. A review by Sebag (2002) acknowledges at the time there has been no single technique that enabled accurate non-invasive examination of the vitreous and the most accurate studies of the vitreous have been in vitro histological examinations.

1.12.1 Ultrasonography

An imaging modality that has been successfully employed to image the vitreous and the ocular structures is ultrasonography. Ultrasonography is an imaging technique that utilises the properties of sound waves; a transducer is used to convert electrical energy to a high frequency sound wave (ultrasound). The transducer is placed in contact with the eye and the ultrasound wave is transmitted into the eye, and is reflected back from the ocular structures. The reflected ultrasound wave is captured by the transducer, converted and displayed on a screen as series of spots. As each ocular structure has a different density, the reflected ultrasound wave can be used to produce two-dimensional images of the eye and its structures. The main advantage of ultrasonography in evaluating is that it is independent of physical factors such as pupil dilation and media opacities that can impede fundus examination.

A novel study by Lorenzo-Carrero *et al.* (2009) evaluated the accuracy of B-scan ultrasonography in the detection of retinal breaks in acute posterior vitreous detachment. In this prospective study of 239 patients, ultimately 28 retinal breaks were detected. All patients were originally examined by a general ophthalmologist in an emergency clinic. From these 239 patients, 25 retinal breaks were detected by fundoscopy, equating to a sensitivity of 89%. Subsequent to this, all patients had B-scan ultrasonography the next working day, the results of the fundus examination from the day prior were masked from the ultrasonographer. Ultrasonography detected 27 retinal breaks, a sensitivity of 96%. There were a total of seven patients in which there was disagreement between the two examinations, this was resolved by a scleral indentation examination by a vitreo-retinal specialist. Thus the vitreo-retinal specialist examined only seven eyes in total. Although it appears from this study ultrasongraphy was superior to fundoscopy for the detection of retinal breaks, it is important to note that not all patients had examination by scleral indentation when examined by the general ophthalmologist, and thus retinal breaks may have gone undetected. Secondly as the ultrasound examination was performed the next day, it is reasonable to speculate retinal breaks could have developed in the 2 eyes that were not detected at the initial examination. Finally only those patients where there was discordance between the two methods of examination were reassessed by a vitreo-retinal

specialist with scleral indentation. Scleral indentation by a retinal specialist was the reference standard against which the two examination techniques were compared. However, less than 3% of the study sample was assessed in this manner and thus the sensitivity analysis may be flawed. Hence the results overall highlight the need for scleral indentation being performed in patients presenting with acute symptoms of photopsia and/or floaters.

A recent study has demonstrated ultrasonography is less accurate than determining the presence of PVD by surgical methods. In a small cohort, preliminary study of Ocriplasmin, a vitreolytic agent developed to induce vitreoretinal separation, there was discrepancy between ultrasonography and surgical findings for the presence of PVD such that surgical fewer patients were found to have PVD (de Smet *et al. 2009*). Although this was in a relatively small study population, Kuhn and Aylward (2014) concur there is significant disproportion between findings surgically and on ultrasonography, in that PVD is less frequently present intraoperatively. Overall the resolution of ultrasonography does not permit an accurate detailed examination of the vitreous, and hence it has been suggested the diagnosis of PVD cannot be made with a great deal of accuracy by this technique (Sebag 2002)

Studies in recent years have assessed the sensitivity of ultrasonography for the detection of retinal breaks in the presence of vitreous haemorrhage preventing adequate visualisation of the fundus. One such study was a small prospective case study of eight non-diabetic patients with fundus obscuring vitreous haemorrhage conducted by Nischal *et al.* (1995) found 50% of their study group had retinal breaks on ultrasonography which was later confirmed on clinical examination once the haemorrhage cleared. Probably the most notable study was a retrospective study by DiBernardo *et al.* (1992), in which they managed to correctly identify 10 of 11 eyes with retinal breaks with ultrasonography in eyes with dense vitreous haemorrhage. In a recent study by Rabinowitz *et al.* (2004) the sensitivity of ultrasonography was 44% compared to clinical examination. Although ultrasonography is an extremely useful aid, particularly when the fundus cannot be visualised (Kakehashi *et al.* 2014), the literature confirms it should not be used as a diagnostic tool to exclude the presence of retinal breaks as an alternative to clinical examination.

1.12.2 Optical Coherence Tomography

Optical coherence tomography (OCT) is similar to ultrasonography and is non-invasive. It utilises the properties of light to generate high resolution images of the retina and has greatly enhanced our understanding of posterior vitreous detachment and the vitreoretinal interface (Uchino *et al.* 2001). With further developments in OCT technology there has been a greater

improvement in the imaging quality and understanding of the vitreous (Mojana *et al.* 2010; Liu *et al.* 2014; Pang *et al.* 2014; Stanga *et al.* 2014; Kolb *et al.* 2015). Further details regarding this technology are discussed in Chapter 5.

1.12.3 Widefield retinal imaging

Another imaging modality that has been employed in the management of posterior vitreous detachment is widefield retinal imaging. Widefield retinal imaging employs scanning laser technology to produce a digital colour image of the retina. A recent study (Khandhadia *et al.* 2009) has assessed the sensitivity of widefield imaging in the detection of retinal breaks. This study demonstrated widefield imaging was able to detect retinal detachments and had a sensitivity of 100%, however it was not accurate in the detection of retinal breaks in patients presenting with photopsia and/or floaters to an eye casualty environment. The sensitivity of widefield imaging for the detection of retinal breaks was found to be less than half in comparison to clinical assessment by an eye casualty officer. In essence, widefield imaging is not suitable to exclude the presence of pathology of the peripheral retina in patients presenting with symptoms of PVD.

Despite advances in imaging modalities and technology, no single imaging technique currently exists which permits adequate study of the vitreous and subsequently posterior vitreous detachment (Sebag 2002 and 2008a; Mojana *et al.* 2010; Duker *et al.* 2013)

1.13 Treatment of posterior vitreous detachment

The mainstay of treatment for eyes with PVD is conservative as in the majority symptoms improve without any significant visual consequence. If the symptoms of PVD are chronic and troublesome or produce visual loss then surgical intervention may be appropriate. In this procedure, termed vitrectomy, the vitreous is removed, the effect of this is twofold; firstly the traction upon the retina is relieved, and secondly the vitreous opacities responsible for the floaters are removed. Nevertheless, vitrectomy is not recommended as a routine procedure for the treatment of PVD. This is primarily due to the fact that once the acute phase of PVD has transpired, symptoms often improve spontaneously without intervention. In addition, vitrectomy, due its very nature of being an invasive surgical intervention is invariably accompanied with potential complications, which could in fact result in loss of visual function (Tan *et al.* 2011). Needless to say this would be highly undesirable, and therefore vitrectomy is not considered as a first line treatment for PVD. Recently a less invasive therapeutic option has become available which can relieve vitreo-retinal traction. Ocriplasmin is a pharmacologic agent that cleaves the bonds between the retina and vitreous through enzymatic proteolysis thus relieving the tractional forces exerted upon the retina from the

vitreous (Song & Smiddy 2014; Stefani *et al.* 2014). At present Ocriplasmin is not approved as a treatment for chronic symptoms of posterior vitreous detachment, nor have any studies been formally published in this context. Nonetheless, it would be reasonable to conceptualise the use of Ocriplasmin for cases of persistent, symptomatic, gradually evolving PVD or in eyes with a high risk of developing retinal breaks secondary to vitreous traction. Licensing studies of Ocriplasmin have revealed successful treatment, defined as the resolution of vitreo-macular traction, is in the order of 27-41% (Stalmans *et al.* 2012). Extrapolating the results of these studies to PVD and vitreo-retinal traction may demonstrate equally disappointing and ineffective results. Additionally the potential risks of intravitreal Ocriplasmin may significantly outweigh the benefits and therefore this may not be an appropriate intervention (Song & Smiddy 2014; Stefani *et al.* 2014). Paradoxically the most significant risk would be that a retinal break with concurrent retinal detachment develops, the very condition one would be trying to avoid.

1.14 Treatment of retinal breaks

If a retinal break is detected in a patient with symptoms then current clinical guidelines recommend treatment (American Academy of Ophthalmologists 2014; Makhzoum *et al.* 2014). The treatment of retinal breaks can be undertaken in a variety of methods with the purpose of creating adhesion between the retina and the underlying structures to prevent further migration of fluid under the retina which would progress to retinal detachment (Machemer 1984; Smiddy *et al.* 1991; Lock & Fong 2011). Such treatment can be performed with an Argon laser, and primary success is in the order of 15-46%, reducing the risk of progression to retinal detachment by up to ten-fold (Smiddy *et al.* 1991; Ghosh *et al.* 2005; Carvounis & Holz 2006; Levin *et al.* 2009; Khan 2013; Petrou & Lett 2014). Although successful treatment reduces the risk of progression to retinal detachment, additional breaks may develop and hence further review of such patients is recommended (Sharma *et al.* 2004).

The study by Goldberg & Boyer (1980) highlighted the need to schedule further reviews for eyes treated for retinal breaks. In their study of 83 eyes, 8 eyes (9.6%) went on to develop 20 additional retinal breaks of which 95% (19 breaks) developed within the first 3 months of the initial break. Smiddy *et al.* (1991) also noted 24 of 171 eyes (14%) treated for retinal breaks developed additional retinal breaks. Similarly the retrospective study by Sharma and colleagues (2004) of 155 eyes treated for retinal breaks due to posterior vitreous detachment, found 12% of these treated eyes developed additional retinal breaks. Almost half of these new breaks developed within one month of identifying the original break, and over three-quarters were identified within 12 months. A significant point of note from this

study is that only 40% of eyes with new retinal breaks were symptomatic and the majority of breaks were asymptomatic. The authors attribute the lack of symptoms to inadequacy of subjective ability to detect new symptoms in the presence of pre-existing symptoms. Both studies therefore recommend patients treated for retinal breaks should be examined at regular intervals. Furthermore the development of subsequent retinal breaks has been suggested to arise due to the evolving nature of posterior vitreous detachment and this is supported by the fact that approximately half of eyes with PVD is actually incomplete and there is continual dynamic vitreous traction.

1.15 Synopsis

Four chapters are subsequently presented which essentially describe of the development and progression of an optometrist from acquiring skills of examination to evolving into an interventional clinician, with the final chapter presenting a new finding within the context of posterior vitreous detachment. The first of these four chapters describes the process undertaken by the optometrist to acquire the appropriate examination expertise in order to correctly evaluate patients with symptoms of PVD. There has been significant progression of the extended roles of optometrists and a number of studies have demonstrated substantial agreement between optometrists and ophthalmologists (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Marks *et al.* 2012). There is however no evidence of such studies directly evaluating the outcome of fundus examination performed by an optometrist and an ophthalmologist in patients with acute posterior vitreous detachment with or without retinal breaks. The primary focus of this chapter was to validate the optometrist against a vitreoretinal consultant ophthalmologist to ensure the optometrist was able to assess patients in the required manner.

The next chapter is a retrospective evaluation of patients assessed by the optometrist in a dedicated posterior vitreous detachment review clinic over a 3 year period. Currently in the UK there is no agreed consensus as to whether all patients with acute PVD require further review, indeed there are contrasting views in the literature (Jaffe 1968; Tasman 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Dayan *et al.* 1996; Richardson *et al.* 1999; van Overdam *et al.* 2001 and 2005; Coffee *et al.* 2007; Hollands *et al.* 2009; Schweitzer *et al.* 2011; Williams *et al.* 2011; Blindbæk & Grausland 2014). The aim of this evaluation was to decipher a definitive management plan for patients diagnosed with acute PVD.

The treatment of retinal breaks with laser retinopexy is a procedure performed by ophthalmologists and there are no accounts of any other clinician undertaking this role either in the UK or worldwide. An account of a pioneering development is illustrated in the following

chapter in which the optometrist performs laser retinopexy for the treatment of retinal breaks. Once again the process of knowledge and skill acquisition is detailed followed by a direct evaluation of the outcomes of breaks treated by the optometrist compared to those reported in the literature and against a prior retrospective audit at the same institution.

The penultimate chapter describes mid vitreous opacities in PVD not previously reported upon in detail. Clinical examination is the fundamental factor to determine whether PVD has occurred or not, however the signs may be confounding and therefore the diagnosis and potential prognosis may be inaccurate. Diagnostic imaging can be a useful adjunct, however this can be inconsistent or inconclusive also (Sebag 2002 and 2008a; Mojana *et al.* 2010; Duker *et al.* 2013; Kuhn & Aylward 2014). This finding described may improve the accuracy of diagnosis without the need for imaging. Furthermore recognising the features as described is of paramount importance in order to be able to distinguish them from other potentially sight-threatening signs.

The final chapter presents a summary of the findings together with an analysis of the cost of reviewing patients with PVD.

Chapter Two: The reliability of an Optometrist in the Examination of eyes with Posterior Vitreous Detachment and Retinal Breaks

2.1 Introduction

The first of the four aforementioned chapters is essentially a preliminary study to validate the clinical competency of an optometrist to undertake autonomous assessment of patients referred to the vitreo-retinal service posterior vitreous detachment clinic for routine assessment after presenting to the eye casualty service with signs and symptoms of posterior vitreous detachment. The General Optical Council has provided the following definition of an optometrist:

'An optometrist examines eyes, tests sight and prescribes spectacles or contact lenses for those who need them. They also fit spectacles or contact lenses, give advice on visual problems and detect any ocular disease or abnormality, referring the patient to a medical practitioner if necessary'

Although optometrists are formally trained and assessed to be clinically competent for their role, optometrists may diversify and progress to become involved in roles that were traditionally undertaken by ophthalmologists (Hawley *et al.* 2010; Parkins *et al.* 2014; Creer *et al*. 2014). The following is a definition of an ophthalmologist, as per the Royal College of Ophthalmologists:

'An ophthalmologist is a medically trained doctor who commonly acts as both physician and surgeon. (S)he examines, diagnoses and treats diseases and injuries in and around the eye'

Hospital optometry is the largest sector in the UK in which optometrists are involved in traditional ophthalmology based services (Creer *et al*. 2014). At University Hospital Coventry and Warwickshire optometrists have been involved in a variety of extended roles including pre- and post-cataract surgery assessment, eye casualty, medical retina, glaucoma, anterior segment and general ophthalmology services. In order to be involved in these services, the optometrists undergo rigorous training and assessment to ensure patient care is paramount and a safe, effective is service is provided. In accordance with clinical governance, the services are continually monitored by an ongoing audit process and development of the service.

Margo *et al.* (2002) have provided their observations of inter-observer variability in a number of different ophthalmological situations and have found there is significant variability among clinicians, ranging from poor to excellent agreement depending upon the scenario. The

interpretation of a fluorescein angiogram for the characteristics of choroidal neovascularisation can be likened to the interpretation of a fundus examination for retinal breaks, in both cases if the pathological features are undetected this could result in visual loss to the patient in a relatively short space of time if the appropriate measures are not undertaken. The inter-observer variability for the interpretation of fluorescein angiography for choroidal neovascularisation subtype was fair to moderate (kappa = 0.29 - 0.64) by retinal specialists (Friedman & Margo 2000; Holz *et al.* 2003; Zayit-Soudry *et al.* 2007)

Previous studies have compared the ability of optometrists in comparison to consultant ophthalmologists to ascertain whether optometrists are able to perform to a suitable standard in order to deduce an accurate diagnosis. One such study by Hau *et al.* (2007) compared the diagnosis of two optometrists against one consultant ophthalmologist for patients presenting to the emergency eye clinic. The optometrists examined the patient first after which the ophthalmologist was masked to the findings of the optometrist. Notably this study found the agreement between the optometrists and ophthalmologist was in the order of 90%, with a weighted kappa of 0.82. From a clinical and statistical perspective this would be considered to a high level of agreement (Viera 2005) and demonstrated the autonomous ability of optometrists in the assessment of such patients.

The diagnostic performance of accredited optometrists was evaluated by Azuara-Blanco *et al.* in a study in 2007, in which optometrists were trained to participate in glaucoma clinics. For this study 100 patients were recruited and assessed in optometric practice, with a decision made regarding the status of glaucoma in each patient. Patients were then seen in a hospital outpatient clinic and had undergone repetition of the same assessment as done by the optometrist, followed by a clinical decision regarding glaucoma status. The percent agreement between the optometrist and consultant ophthalmologist for diagnosis of glaucoma was 89% with a weighted kappa of 0.70, indicating significant agreement. The sensitivity of the optometrist for the detection of glaucoma compared to the consultant was 0.76 with a specificity of 0.93. The lower degree of sensitivity was for cases at the lower end of the severity scale, with the implication that further continual training and revised guidelines would improve this figure. Nevertheless the level of agreement and capabilities of the optometrist were high and found to be suitable for the purpose.

In more recent years, Marks and colleagues (2012), undertook a similar study in which glaucoma patients were assessed both by accredited optometrists and consultant ophthalmologists separately and independently. A direct comparison was then made to evaluate the performance of the optometrists against the ophthalmologists. For the 96

patients included in this study, who were seen by one of four optometrists and one of two ophthalmologists, the agreement specifically for optic disc assessment was found to be 64.5% with a weighted kappa of 0.17-0.31. Although for this feature a low kappa statistic was found, the percent agreement for partial or complete agreement of disc stability was 95%.

A recent review of extended roles of optometrists has revealed optometrist involvement in vitreo-retinal conditions is limited compared to other conditions (Hawley *et al.* 2011; Creer *et al.* 2014). One study comparing optometrists and ophthalmologists in a vitreoretinal setting was by Qureshi & Goble (2009). This study compared the agreement between observers for the detection of pigment cells in anterior vitreous in eyes with retinal breaks. In this study the agreement between the consultant ophthalmologist and optometrist for this feature was 62% with a kappa coefficient of 0.28, suggesting some degree of correlation. It is important to note that only the consultant had previous vitreoretinal experience and the optometrist did not, the low degree of agreement was primarily attributable to this factor.

A significant proportion of referrals to the vitreo-retinal clinic originate from the eye casualty service, with the majority of these patients diagnosed with recent, uncomplicated posterior vitreous detachment. According to the University Hospital Coventry and Warwickshire ophthalmology protocol these patients are seen in a vitreo-retinal clinic approximately four weeks after presentation to the eye casualty. The fundamental rationale for this is the experience of clinicians in eye casualty can vary tremendously as can the ability to examine the peripheral retina, and secondly as described in the first chapter, it been recognised in the literature delayed retinal breaks may occur in patients with acute posterior vitreous detachment (Carvounis & Holz 2006; Coffee *et al.* 2007; Blindbæk & Grausland 2014). Historically there were no optometrists directly involved in the vitreo-retinal service. However, over recent years there has been an increased demand for vitreo-retinal clinic appointments with limited increase in ophthalmology resources. By virtue of the previous development and extended roles of the optometrists it was deemed appropriate to incorporate an optometrist into the vitreo-retinal service. The aim of this study was therefore to determine the reliability of an optometrist in examining the eyes of patients with possible posterior vitreous detachments (PVD) and retinal breaks.

2.2 Methods

The optometrist selected for this role had over five years of experience in hospital and community optometric services. During this time in the hospital eye service this optometrist developed a high degree of ability in a variety of services and had become integrated as a specialist clinician in a diverse range of ophthalmological services including medical retina clinics (assessing and managing patients with vascular and inflammatory conditions of the retina), eye casualty, general ophthalmology and performing Yttrium-Aluminium-Garnet (YAG) laser procedures for capsular opacification secondary to cataract surgery. To develop the role of the optometrist, an initial period of training took place over a period of three months where the optometrist was required to undertake further theoretical and practical training to consolidate and develop knowledge and practical skills. Following this a formal assessment was undertaken by a vitreo-retinal consultant ophthalmologist to validate the optometrist.

For the purpose of this validation study a direct comparison of 100 consecutive eyes examined by both a consultant vitreoretinal surgeon and the optometrist was undertaken during November 2008 and July 2009. The patients were recruited primarily from eye casualty either as an acute presentation on the day or as those seen previously and diagnosed with PVD then referred to the vitreo-retinal clinic for re-assessment 4-6 weeks later as per current clinical practice within the department. However practitioners in eye casualty had been instructed to inform the vitreo-retinal consultant if eyes with retinal breaks, retinal/vitreous haemorrhage or retinal degenerations were encountered during the sessions in which this study was due to be taking place so that they could be included in this study. The purpose of this was to increase the exposure of the optometrist to the various presentations of retinal breaks and to develop the skills of the optometrist in detecting retinal pathology. The decision to study 100 eyes was based upon natural history studies of eyes with acute PVD and it was envisaged of these at least 20 eyes would harbour retinal breaks either at some point between the acute presentation or when reviewed (Carvounis & Holz 2006; Coffee *et al.* 2007; Blindbæk & Grausland 2014). Ethics approval was not obtained for this as this was a clinical audit of the performance of an optometrist compared to a consultant vitreoretinal ophthalmologist. This audit was however approved and supported by the clinical lead for ophthalmology and departmental manager.

All patients initially had their habitual monocular visual acuity assessed by a nurse or ophthalmic technician, if the visual acuity was found to be worse than 0.20 logMAR (6/9.5 Snellen) then a pinhole test was used to determine the potential visual acuity of the eye. If there were any ambiguous results, patient concerns, or if there were any contraindications to

pupillary dilation, the patient was examined by an ophthalmologist to address these issues. This was followed by instillation of 1% Tropicamide and 2.5% Phenylephrine eyedrops into both eyes of the patient. Once sufficiently dilated, the patient was examined by the consultant ophthalmologist who undertook a detailed examination of the patient and recorded his findings and management plan in the medical notes. Once the consultant had finished his examination he explained the validation process to the patient and if the patient agreed they were then instructed to withhold all information from the optometrist including current and past ocular and medical history. Furthermore the optometrist was masked to the findings of any previous examinations and did not have access to any prior knowledge or medical records relating to the patient.

The optometrist proceeded with fundoscopy of the right eye, followed by left, using a +90 dioptre condensing lens in conjunction with the slit-lamp as conventionally performed. With the slit-lamp illumination coupled, the height of the slit beam was increased to maximum (8mm) with a width of approximately 1mm (dimensions of the slit-beam were adjusted according to the light intensity tolerability levels of the patient as necessary) with the illumination and observation system coaxial. The magnification was set at 6x, and the slit-lamp was focused on the central cornea followed by introduction of a +90D condensing lens in to the line of the illumination beam, whilst retracting the focus of the slit-lamp until the fundus was clearly visualised. Although other condensing lenses are commercially available, the +90D lens is the most widely available in the clinic and used for peripheral retinal examination and hence it was employed for this purpose in this study.

Firstly the posterior vitreous was examined specifically to identify the presence of a Weiss ring, signs of vitreous syneresis and separation of the posterior hyaloid membrane from the retina (Pischel 1952; Kakehashi *et al* 1997; Snead *et al.* 2008a). This was followed by a detailed examination of the fundus of both eyes in nine positions of gaze (primary position, up, up-left, left, down-left, down, down-right, right and up-right). Subsequently the patient was then reclined to a supine position (or near supine position as the patient could comfortably tolerate) and the fundus examination was repeated using head-mounted binocular indirect ophthalmoscopy with a +20D condensing lens and scleral indentation in eight positions of gaze. Although a variety of condensing lenses are available for this purpose, in the clinic the +20D is most frequently available and therefore was the lens of choice for this study.

The technique of scleral indentation has been described in detail previously (Shuey 1995; Townsend 1992), however a summary of the procedure is described. Firstly the indirect

ophthalmoscope was focussed with the largest aperture of the illumination beam in place. The illumination was then directed towards the dilated pupil of the patient and the patient was asked to look down. A thimble indentor was then applied to the upper lid crease. The patient was then instructed to look up whilst advancing the indentor into the orbit with the indentor tangential to the globe with the illumination directed towards the dilated pupil. A +20D lens was then introduced into the illuminated beam to obtain an image of the fundus. The angle of illumination, lens tilt and position of the indentor was adjusted as necessary to examine the retina up to and including the ora serrata or lesions on the retina requiring further assessment. This procedure was then repeated with the gaze of the patient directed in different positions to complete a 360 degree examination of the ora serrata. The optometrist recorded the clinical findings, diagnosis and proposed management plan on to a proforma.

Once the optometrist completed the examination the vitreo-retinal consultant was informed who verified whether the findings, diagnosis and management determined by the optometrist were correct or not. If the consultant agreed with the optometrist this was documented on the proforma. If any discrepancy was found between the optometrist and ophthalmologist, the opinion of the ophthalmologist was assumed to be correct, and a correct entry with any additional comments was made on the proforma. The optometrist then re-examined the area(s) of disagreement within direction from the consultant as a learning opportunity and to further consolidate development.

2.2.1 Statistical analysis

The primary objective of this study was to determine whether an optometrist could safely undertake assessment of patients with recent PVD and identify retinal breaks appropriately. The findings of the optometrist and consultant were analysed to determine the percent agreement, sensitivity and specificity of the optometrist in comparison to the consultant for the detection of retinal breaks. The following formulae were used to determine these measures:

$$\text{Sensitivity} = \frac{\text{No. of breaks detected by optometrist}}{\text{No. of breaks detected by optometrist + No. of breaks missed by optometrist}}$$

$$\text{Specificity} = \frac{\text{No. without breaks (optometrist)}}{\text{No. falsely classified with breaks (optometrist) + No. without breaks (optometrist)}}$$

Although no figures currently exist as acceptable level of agreement for this specific feature, a level of 90% minimum agreement was assigned. This was based on findings from previous studies assessing the correlation optometrists and ophthalmologists for diagnosis (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Marks *et al.* 2012), and also from a clinical safety perspective. Furthermore, it would be unrealistic to expect two clinicians to have 100% sensitivity when the experience of the clinicians is vastly different (Margo *et al.* 2002).

In addition the inter-examiner agreement was calculated, using the weighted kappa coefficient. It is accepted that a kappa of 0.81 or greater is regarded as almost perfect agreement, a kappa of 1 indicating perfect agreement (Viera 2005), and in this situation would be acceptable.

Furthermore the mean ages together with standard deviations were calculated for eyes with PVD alone and independently for eyes with retinal breaks. Unpaired 2-tailed t-tests were used to investigate differences in age between the male and female groups for laterality of PVD and retinal breaks. Chi-squared analysis was employed to determine odds ratio for comparative differences within each gender and between the gender groups. A p-value greater than 0.05 was not considered to be statistically significant. Furthermore specific features were analysed for eyes with retinal breaks, including distribution according to gender, laterality, location and type of retinal break. With regard to location of retinal breaks, they were classified according to the following:

Clock hour (nearest)	**Location**
1200	Superior (S)
1330 LE / 1030 RE	Superotemporal (ST)
0300 LE / 0900 RE	Temporal (T)
0430 LE/ 0730 RE	Inferotemporal (IT)
0600	Inferior (I)
0730 LE / 0430 RE	Inferonasal (IN)
0900 LE / 0300 RE	Nasal (N)
1030 LE / 1330 RE	Superonasal (SN)

Table 2.2.1 Classification and annotation of retinal break according to location

2.3 Results

A total of ninety patients had been referred from eye casualty, with the remainder referred from other ophthalmology clinics, community optometrists and general practitioners. Almost three-quarters of patients (72%) of patients in this process had been referred from the eye casualty diagnosed with acute posterior vitreous detachment without retinal complications in the preceding six weeks. Of note however was that this group of patients examined included those with vitreous haemorrhage secondary to posterior vitreous detachment, but the severity did not preclude fundus examination with slit-lamp biomicroscopy.

Of the 100 eyes examined, 23 retinal breaks were detected in 20 eyes by the consultant ophthalmologist, whereas the optometrist detected 21 breaks in 20 eyes. Two breaks were missed by the optometrist in 2 eyes of 2 separate individuals. In the first case a subtle retinal break was masked by a vitreous haemorrhage which the optometrist failed to detect, but was identified by the consultant ophthalmologist. In a second case a round hole was overlooked by the optometrist. The hole was flat and adjacent to a large horseshoe tear, which was noted correctly by the optometrist. Additionally in one eye an enclosed oral bay was misdiagnosed by the optometrist as a retinal hole, which was confirmed by the ophthalmologist.

	Gender	Age	Consultant	Optometrist
1	M	73	RE I horseshoe	RE Vitreous haemorrhage
2	M	71	LE S operculated	LE S operculated
3	F	44	LE ST operculated	LE ST operculated
4	M	63	RE ST operculated	RE ST operculated
5	M	69	LE N horseshoe	LE N horseshoe
6	F	55	LE SN operculated	LE SN operculated
7	F	56	RE IN horseshoe	RE IN horseshoe
8	F	65	LE S operculated	LE S operculated
9	F	72	RE ST operculated	RE ST operculated
10	F	57	RE N horseshoe	RE N horseshoe
11	F	61	RE S operculated	RE S operculated
12	F	59	RE S operculated	RE S operculated
13	F	46	LE S round hole	LE S round hole
14	F	64	RE SN operculated	RE SN operculated
15	F	62	LE S horseshoe	LE S horseshoe
16	M	37	LE N horseshoe	LE N horseshoe
17	M	71	RE ST horseshoe RE ST hole	RE ST horseshoe
18	F	69	RE ST horseshoe RE ST operculated hole	RE ST horseshoe RE ST operculated hole
19	M	58	RE ST horseshoe x2	RE ST horseshoe x 2
20	F	66	RE ST operculated	RE ST operculated
21	M	64	LE enclosed oral bay	LE I round hole

Table 2.3.1 Summary of the eyes with retinal breaks as identified by the optometrist and consultant

		Consultant	
		Breaks	No breaks
Optometrist	Breaks	21	1
	No breaks	2	0

Table 2.3.2 Cross-tabulation of the retinal breaks identified by the two examiners

		Consultant	
		Eyes with breaks	Eyes without breaks
Optometrist	Eyes with breaks	19	1
	Eyes without breaks	1	79

Table 2.3.3 Cross-tabulation of the eyes found to harbour retinal breaks and those with isolated PVD

The percent agreement between the optometrist and ophthalmologist was 98% for the detection of eyes with retinal breaks with a sensitivity of 95%, and specificity of 99%. The weighted kappa coefficient for inter-observer variability was 0.94 (SE 0.044, 95% CI 0.852-1.00) suggesting excellent correlation between the two examiners. For the eyes with retinal breaks, the sensitivity of the optometrist of correctly identifying all retinal breaks was 91%.

2.3.1 Characteristics of eyes with PVD

In total there were 80 eyes with uncomplicated PVD, with almost equal distribution between right and left eyes (38 right eyes, 42 left eyes). The mean age of eyes with uncomplicated PVD was 62.6 years of age (SD 11.0, range 22-84). In the male subgroup the mean age was slightly higher at 65.0 years (SD 11.2, range 27- 84) and in the female subgroup was slightly lower at 61.3 years (SD 10.8, range 22-79). Females comprised approximately 60% of all eyes, thus a male to female ratio of 2:3. The mean difference in age between males and females with PVD was not found to be statistically significant (p = 0.16). When assessing age against laterality, the p-value was 0.69 and 0.51 for the male and female subgroups respectively, and was not statistically significant in either group. Table 2.4 summarises the number and laterality of eyes affected according to gender.

	Male	**Female**
Right	15	23
Left	14	28

Table 2.3.1.1 A matrix table representing eyes with PVD according to gender and laterality

2.3.2 Characteristics of eyes with retinal breaks

The mean age of eyes with retinal breaks was 60.9 years (SD = 9.6, range 37-73). For males, there were a total of nine retinal breaks in seven eyes, of which six breaks affected the right eye and the remaining three were in left eyes. The mean age of the male subgroup with retinal breaks was 63.1 years (SD = 11.7, range 37-73), with a mean age of 59.0 years for right eyes affected and 66.3 for left eyes affected. There was no statistically significant

difference in age with respect to laterality of retinal breaks in males (p=0.58). Furthermore, although there were twice the number of breaks in right eyes compared to left eyes, with an odds ratio of 1.9 (95% CI 0.4 – 8.9), this was not found to be statistically significant (p= 0.48).

Conversely for the females with retinal breaks the mean age was slightly less at 59.7 (SD = 7.9, range 44-72), but there was no statistically significant difference in age between the male and female subgroups with retinal breaks (p= 0.47). There were a total of fourteen retinal breaks in thirteen eyes of the female subgroup with nine breaks involving the right eye with five in the left. Similar to the male subgroup, right eyes were more frequently afflicted with retinal breaks with almost twice the number of breaks with an odds ratio of 2.2 (95% CI 0.6 – 7.5), however this was not statistically significant significance (p=0.24). The mean age of right eyes with retinal breaks was 63.0 years and for left eyes was 54.4 years, but this difference did not reach statistical significance (p=0.11). Table 2.5 summarises the findings for gender and laterality for eyes with retinal breaks.

	Male	**Female**
Right	6	9
Left	3	5

Table 2.3.2.1 A matrix table representing retinal breaks according to gender and laterality

Overall the mean age for eyes with retinal breaks was approximately 1.5 years less in comparison to eyes with PVD alone, however again this was not statistically significant (p = 0.52), nor was it statistically significant for either the male subgroups (p= 0.71) or the female subgroups (p = 0.62). Males were marginally more likely to harbour a retinal break in comparison to their female counterparts with an odds ratio of 1.1 (95% CI 0.4 – 2.9) however this was not statistically significant (p=0.81). Overall the right eye was twice as likely to be affected with an odds ratio of 2.1 (95% CI 0.8 – 5.4), again however this was not statistically significant (p=0.16)

Figure 2.3.2.1 A box and whisker plot to demonstrate the age distribution according to gender and pathology
There were a total of 11 outliers, the following points refer to the same patients:
1 and 139; 21 and 101; 22 and 102, 50 and 137; 51 and 138;
52 and 139; 53 and 140; 54 and 141; 100 and 200

With respect to location in which retinal breaks occurred, 78% of the 23 breaks were in the superior hemisphere. Females were found to have a greater likelihood of developing breaks in the superior quadrants (between 10 and 2 o'clock) compared to males with an odds ratio of 3.0 (0.95% CI 0.4 – 23.1), but was not statistically significant p=0.34. The superotemporal quadrant was the most frequently affected, with 43% of eyes having breaks in this quadrant. Specifically in the male subgroup 55% of breaks were in the superotemporal quadrant, whereas in the female subgroup 36% of breaks were in this quadrant. The odds ratio for this quadrant for males compared to females was 2.25 (0.95% CI 0.4 - 12.4), but was not statistically significant (p=0.42). The superior quadrant was the next most frequently affected with 36% of all breaks arising in this region. Unexpectedly, the temporal and inferotemporal quadrants were unaffected by retinal breaks in this study. Furthermore in the males, the superior quadrant was less frequently affected than the nasal quadrant, and in the females

was equally involved as the superotemporal quadrant. These findings may however be a confounding factor attributable to the relatively small number of eyes with retinal breaks in this study.

Almost half of the breaks were of the horseshoe variety, with 43% of breaks being operculated. Round holes were least frequently encountered with less than 10% of all breaks being of this variety. Subgroup analysis according to gender revealed in the male group the majority of retinal breaks were horseshoe in nature with two-thirds being of this variety. Conversely in the female group, almost two-thirds of breaks were operculated with less than one-third being horseshoe in nature.

	All	Male	Female
Horseshoe	10 (43%)	6	4
Operculated	11 (48%)	2	9
Round	2 (9%)	1	1

Table 2.3.2.2 A summary table of retinal breaks according to gender and configuration

Location	All	Males (HS/O/R)	Females (HS/O/R)
Superior	6 (26%)	1 (0/1/0)	5 (1/3/1)
Supero-temporal	10 (43%)	5 (3/1/1)	5 (1/4/0)
Temporal	0	0 (0/0/0)	0 (0/0/0)
Infero-temporal	0	0 (0/0/0)	0 (0/0/0)
Inferior	1 (4%)	1 (1/0/0)	0 (0/0/0)
Infero-nasal	1 (4%)	0 (0/0/0)	1 (1/0/0)
Nasal	3 (13%)	2 (2/0/0)	1 (1/0/0)
Supero-nasal	2 (9%)	0 (0/0/0)	2 (0/2/0)
Total	**23**	**9**	**14**

Table 2.3.2.3 A summary table of retinal breaks according to gender, anatomical location and type of configuration
HS = Horseshoe O = Operculated R = Round

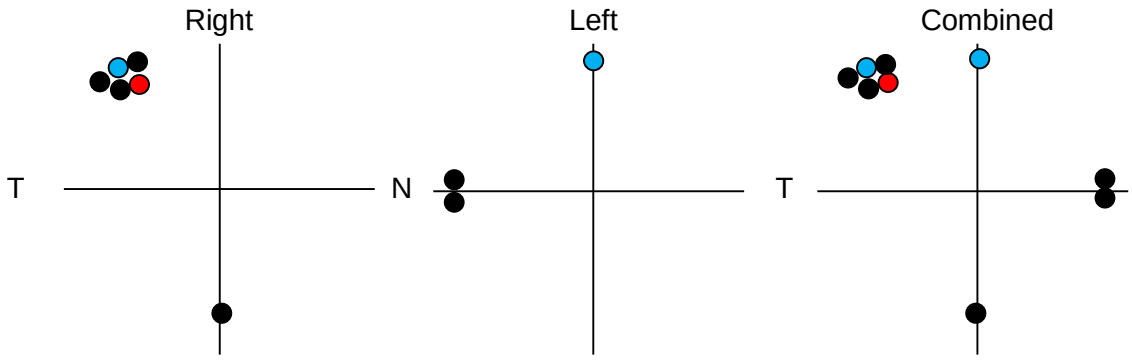

Fig 2.3.2.2 Diagrams to represent retinal breaks in males according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes
Key: Horseshoe ● Operculated ● Round ●

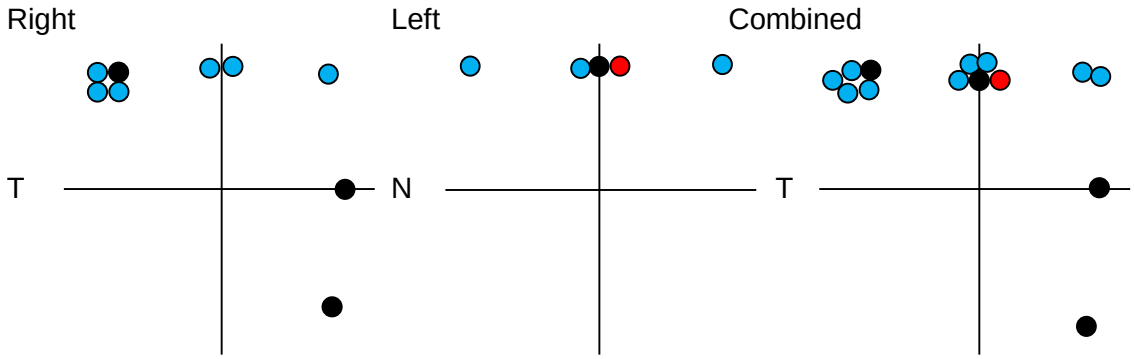

Fig 2.3.2.3 Diagrams to represent retinal breaks in females according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe ● Operculated ● Round ●

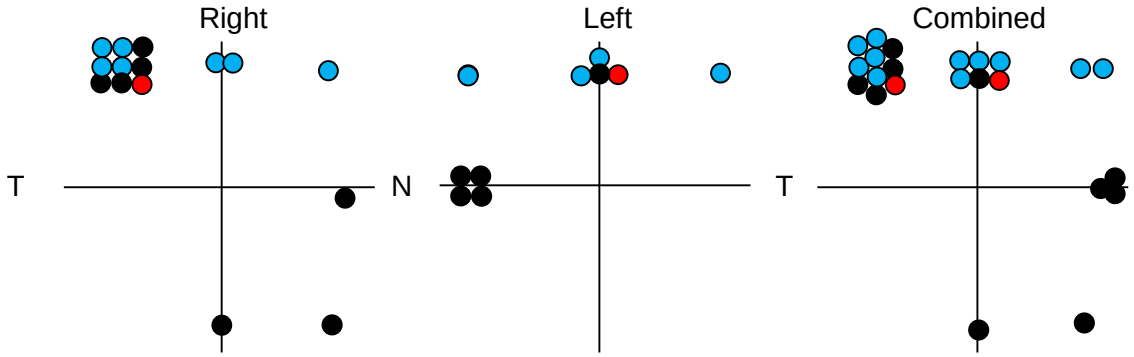

Fig 2.3.2.4 Diagrams to represent retinal breaks according to type of break and location in all eyes. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe ● Operculated ● Round ●

2.4 Discussion

To the best of knowledge this has been the first study to compare the findings of an optometrist against the findings of a vitreoretinal consultant ophthalmologist in the examination of patients reviewed for recent onset PVD and for the detection of retinal breaks in such eyes. It was originally estimated approximately one-third of eyes in the study would have a retinal break, a higher figure than actually occurred. This discrepancy is likely to be multifactorial; it was expected a greater number of eyes with vitreous haemorrhage would have been encountered. This was not the case as although the eye casualty practitioners had been alerted to refer patients with such pathology to the vitreo-retinal clinic on the day for the purpose of this study, this instruction was not always adhered to. Also the optometrist was not in all vitreo-retinal clinics and thus a number of patients with retinal breaks/vitreous haemorrhage may have been seen and not been included in this study.

In this study percent agreement was 97% indicating almost perfect correlation and this was reflected in the kappa coefficient of 0.91. Although not statistically significant, there was disagreement in three cases. In the first case where a horseshoe break was missed by the optometrist as it was obscured by an overlying vitreous haemorrhage. In cases of vitreous haemorrhage where the fundus cannot be adequately visualised it is recognised there is a high prevalence of underlying retinal breaks and hence short term review is advised (Linder 1966; Jaffe 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Hikichi & Trempe 1994; Sharma *et al.* 1999; van Overdam *et al.* 2005; Coffee *et al.* 2007). In this particular case, the patient would have been scheduled to return for further examination on a one to two weekly basis with the advice to return should there be any exacerbation of symptoms. It is therefore unlikely there would be any detriment to the patient as it would be expected the retinal break would be identified with subsequent treatment once the visualisation improved. In the second case where a round hole was overlooked adjacent to a horseshoe break, this alone is unlikely to have been detrimental to the patient due to the nature of the defect (Sigelman 1980; Machemer 1984; Ghazi & Green 2002; Kuhn & Aylward 2014). Firstly there was no accompanying subretinal fluid and secondly there was no coexisting vitreoretinal traction, the two primary causes of progression (Sigelman 1980; Machemer 1984; Ghazi & Green 2002; Kuhn & Aylward 2014). Furthermore treatment for round holes alone is not advocated (Carvounis & Holz 2006; American Academy of Ophthalmologists 2014), however in this case due to the close proximity of the two lesions it was felt appropriate to encompass both with retinopexy. Otherwise the hole would lie within the laser barrier and may result in inadequate treatment for the horseshoe break. Finally the optometrist misdiagnosed an enclosed oral bay as a flat round hole. As mentioned treatment for round holes with the absence of other factors is not advocated and thus in this case whether the defect was a

round hole or an oral bay the outcome for the patient would be identical. Although there was no detriment to these patients the findings do demonstrate the need for meticulous examination in such cases and the value of prior clinical experience and knowledge.

Compared to previous studies (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Qureshi & Goble 2009; Marks *et al.* 2012), the percent agreement and weighted kappa values were higher in this study. These previous studies have found percent agreement between optometrists and ophthalmologists to be in the order of 62-90%, with weighted kappa values ranging from as low as 0.17 to as high as 0.82. One explanation for this is there were only two examiners whereas in others studies some contained multiple examiners. Another potential contributing factor is that each examiner used two complementary techniques to examine each patient, whereas in previous studies only one technique has been used to assess the structure under observation. This study further confirms the notion of other studies (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Marks *et al.* 2012) that dedicated training generally results in greater agreement between findings of optometrists and ophthalmologists. In the Qureshi & Goble (2009) study, the agreement between the optometrist, who had no specific vitreoretinal training, and the vitreoretinal consultant was 62% with a weighted kappa of 0.28. In contrast, of the studies described earlier in which optometrists have undertaken additional training, the percent agreement is generally in the order of approximately 90% with weighted kappa of 0.65 to 0.82.

Although one-fifth of eyes exhibited one or more retinal breaks, this is not representative of the incidence of retinal breaks secondary to PVD. It is known the incidence of retinal breaks due at the time of symptomatic PVD is approximately 15-22%, and that around a further 2-4% of eyes will develop retinal breaks within a period of a few weeks after the event (Carvounis & Holz 2006; Coffee *et al.* 2007; Blindbæk & Grausland 2014). In this study eyes with both acute and delayed retinal breaks were assessed. Furthermore it is recognised eyes with vitreous haemorrhage secondary to PVD are more likely to harbour retinal breaks and these eyes were also included (Jaffe 1968; Kanski 1975; Boldrey 1983; Novak 1984; Byer 1994; van Overdam *et al.* 2005; Coffee *et al.* 2007; Blindbæk & Grausland 2014). It is probable the combined characteristics of the study eyes contributed to a higher number of retinal breaks observed than may have otherwise been expected. It is interesting to note that although there were only 23 retinal breaks in total, the frequency of location of these breaks was in general agreement with previous studies (Combs & Welch 1982; Sharma *et al.* 2004; Shunmugam *et al.* 2014). The superotemporal quadrant was most frequently involved in 43%, and overall, more than three-quarters of the breaks were in the superior hemisphere. Unexpectedly there were no breaks in the inferotemporal quadrant despite the presence of

inferonasal breaks. It is likely the relatively small number of eyes with retinal breaks is the underlying element for this result.

The mean age in eyes with PVD and in eyes with retinal breaks is relatively similar to prior studies assessing this demographic (Jaffe 1968; Kanski 1975; Combs & Welch 1982; Boldrey 1983; Novak & Welch 1984; Byer 1994; Chuo *et al.* 2006). Additionally in both groups females were the larger in representation, in parallel with previous studies (Jaffe 1968; Kanski 1975; Boldrey 1983; Novak & Welch 1984; Byer 1994; Chuo *et al.* 2006). The overwhelming majority of retinal breaks were of the operculated variety in the female group, whereas in males over half of the breaks were horseshoe in nature. The reason for this variance is unlikely to be due to gender difference, rather the small number of retinal breaks in this study is the most likely cause. In addition this is likely to be the underlying explanation as to the predilection for retinal breaks to occur in the right eye, as almost twice as many breaks occurred in the right eye compared to the left. In contrast, for eyes with PVD alone the laterality difference was much less marked and in males there was almost equal distribution of right and left eyes. Irrespective of the diagnosis, when combining the eyes according to gender, as expected there is almost equal distribution of right and left eyes involved in both males and females. These findings reflect the fact this study was not designed to evaluate these features and that some of these results are incidental and erroneous in nature due to the inherent design of this study.

A number of improvements could have been made to this study in order to enhance the significance of the findings, as the majority of the findings were not statistically significant. The foremost is the most obvious and this would have been to include a larger number of eyes, naturally this would have improved the statistical and potentially clinical significance of the findings as the margin of standard error would be further reduced. Secondly, although the consultant was accepted as the reference standard, adjunctive diagnostic procedures such as dynamic imaging in the form of optical coherence tomography and/or B-scan ultrasonography would have provided an objective means of assessment. This would provide an additional measure against which the findings of the optometrist could be corroborated, further enhancing the validation process.

Additionally, complementary examinations could have also been assessed such as the presence of Shafer's sign and use of a 3-mirror contact lens. Although scleral indentation is the gold standard for the examination of eyes with recent onset PVD, the aforementioned complementary examinations can be useful particularly when there is ambiguity or difficultly in examination using traditional methods. Finally, it would have been ideal to include a

greater number of observers, preferably another vitreoretinal ophthalmologist to verify the findings and also to arbitrate on any disagreements of which there were three in this study.

2.5 Conclusion

The primary aim of this study was to assess the clinical competency of an optometrist to detect retinal breaks in eyes with recent onset PVD in comparison to a consultant vitreoretinal ophthalmologist. Due to the high level of agreement found, the optometrist was deemed clinically competent to undertake independent assessment and management of patients referred to the vitreo-retinal clinic diagnosed with posterior vitreous detachment. The fundamental assumption of course is that the vitreo-retinal consultant is the ‘gold standard’ and made the correct diagnosis in all cases. Needless to say, to attain the position of ophthalmic consultant one has to undergo rigorous and extensive training and essentially be proficient in their subspecialty. In this case the patients examined had vitreo-retinal conditions, by virtue of the above it is accepted, as has been done in other studies, the consultant was the reference standard.

Chapter Three: The Posterior Vitreous Detachment Clinic

3.1 Introduction

As alluded to in chapter one, the management of patients with acute posterior vitreous detachment can be variable. Furthermore, from the preliminary study (chapter two) a number of observations were made. The first of these notable observations was a significant number of patients were identified with retinal breaks. One hypothesis is that there may have been the development of new retinal breaks since the initial examination in eye casualty. Nevertheless, it is also feasible to speculate these breaks may have been overlooked at the initial examination in eye casualty. The issue of PVD is an important one due to the potential of sight-threatening complications, and as such there have been numerous studies in the literature that have examined the risk of developing retinal breaks secondary to PVD.

Dayan *et al.* (1996) conducted a study over a period of twelve months during which time 295 patients with floaters and/or flashes due to PVD were assessed. The patients were examined by a senior house officer in the casualty department with a 90D or 3 mirror followed by scleral indentation. They found 188 patients (64.0%) had PVD alone at presentation, 49 had retinal detachment (17%), and a further 33 had retinal breaks (11%). Out of the 188 patients with PVD, 169 patients were a given follow up appointment, from which 157 patients attended and at this follow-up visit 3 patients were found to have retinal breaks (1.9%). On this basis they concluded patients presenting with PVD should be reviewed 6-weeks after the initial examination.

Richardson *et al.* (1999) conducted a similar study in which 107 patients were patients were reviewed in the PVD clinic who were diagnosed with a PVD in eye casualty. In eye casualty all patients were examined by an ophthalmic doctor using a +78D lens, 3-mirror contact lens and indirect ophthalmoscopy using a +20D condensing lens. Scleral indentation was not reported in all cases. Notably only one retinal break was documented from the 107 patients examined in eye casualty. Patients were then referred to the PVD clinic, and seen within 8 days, in which all patients had examination with an indirect ophthalmoscopy using a +20D and scleral indentation. They found at the first visit 6 patients had round holes, 2 had horseshoe tears and 1 had lattice degeneration with holes, a total of 9 patients requiring treatment (8.4%). This is a highly important finding recognised by the authors as it demonstrates either eight additional breaks developed within as many days between the visits to eye casualty and PVD clinic, or these were missed at the initial visit. In the former situation this demonstrates PVD is evolutionary rather than instantaneous, in the later the importance of detailed examination is evident. Fundamentally there is significant risk of

developing breaks during this phase necessitating the need for detailed examination. Following this, 96 patients were given an appointment for another further review, from which a total of 86 attended. From these 86, 2 required treatment (2.3%). At the first visit, both of these patients had vitreous haemorrhage which obscured the examination. Despite a higher incidence than Dayan *et al.* (1996), the authors of this study were of the opinion in the absence of vitreous haemorrhage and increasing symptoms, if a thorough examination has been performed, further follow-up may not be necessary.

From a group of 280 patients studied, van Overdam *et al.* (2001) found an incidence of 10.7% of retinal breaks/detachment at first presentation when examined with a slit-lamp and 3-mirror lens. Forty of the 250 patients without a retinal break/detachment were given an appointment 2 weeks later due to the presence of haemorrhage at the initial examination, and five of these patients developed a retinal break (12.5%). Of the remaining 210 patients who were later reviewed 6 weeks after the initial assessment, 8 were found to have developed a retinal break (3.8%). The authors suggest only patients with photopsia in conjunction with multiple floaters or a cloud or curtain in their vision require scheduled follow-up examination. This is in contrast to the findings of Richardson *et al.* (2009) where patients with symptoms of 'net' like floaters did not further develop a retinal break.

The follow-up study by van Overdam *et al.* (2005) in which they studied 270 patients, found an incidence of 3.7% of new breaks at follow-up visits, in which 80% of these eyes had a haemorrhage at presentation. Combined data from the studies by van Overdam *et al.* (2001 and 2005) found 15.7% of patients with haemorrhage at presentation ultimately developed a retinal break and 2.3% of patients without haemorrhages at presentation developed retinal breaks, an overall incidence of 4.4%.They conclude follow-up examination is only needed for patients with haemorrhage and/or multiple/large floaters. It is important to note however in both these studies scleral indentation was not performed, neither was the anterior vitreous assessed for pigment cells. Therefore it is possible there may have been an under-detection retinal breaks and undue reliance may have been emphasised upon symptoms.

Coffee *et al.* (2007) retrospectively reviewed of 219 patients diagnosed with an acute PVD, which they defined as the new onset of symptoms (flashes and floaters) within one month of presentation and the presence of a Weiss ring, to determine the incidence of delayed retinal breaks in patients with symptomatic PVD. All of the patients were examined and managed by one of two vitreo-retinal specialists. They found the median age to be 62 years, with around 18% of patients having undergone previous cataract surgery. At initial presentation they found 8% of patients had retinal breaks. From the remaining 201, 65 patients did not

return for a follow-up examination, the other 136 were re-examined within four weeks and a further two retinal breaks were identified (1.5%). Both of these patients had horse-shoe tears and were myopic, of which one had no new symptoms, haemorrhage or vitreous cells. In addition they undertook a meta-analysis of the literature which totalled 1568 patients from ten studies. They found the incidence of retinal breaks at presentation to be 22% (range 8%-48%) and at follow-up an incidence of 1.8%. It is important to note over 80% of these patients with delayed retinal breaks had new symptoms or a haemorrhage. They conclude in the absence of risk factors follow-up is not necessary. However they recognise the limitations in this meta-analysis primarily the retrospective nature of some of the studies included and the variation in clinical information collated.

Hollands *et al.* (2009) also reviewed the literature relating to this topic and found a prevalence of retinal tear associated with onset of PVD to be 14%, a significantly smaller figure than reported by Coffee *et al.* (2007). The variance in the incidence reported is due to the inherent difference in nature between to the reviews and the inclusion criteria of each. The meta-analysis by Coffee *et al.* (2007) was specific to observational follow-up studies and essentially included only those in which the incidence of delayed retinal breaks was reported, whereas the meta-analysis by Hollands *et al.* (2009) was not restricted to those studies with follow-up data. With regard to gender it was found men were slightly more likely to have a retinal break. Age, whether older or younger, as a factor was not found to be correlated with an increased risk of developing a retinal break. Interestingly, the presence of myopia was not found to be correlated with an increased probability of developing a retinal break. However, a subjective reduction in vision together with either photopsia or floaters was found to increase the probability of developing a retinal break to 45%. Conversely if there is no subjective vision loss the likelihood reduces to 8.9%. If a vitreous haemorrhage was present then the probability of a retinal break was 62%, and if pigment in the vitreous is detected then the probability increased to 88%, however the confidence interval ranged from 27%-97%. They concluded the 6-week incidence of developing a retinal break was 3.4%, and that patients who experience an increase in floaters or subjective loss of vision are predictive factors for the development of a retinal tear and should be re-examined by an ophthalmologist.

A prospective study by Schweitzer *et al.* (2011) studied 99 patients in Canada who were diagnosed with an acute PVD. They excluded patients who had retinal breaks at presentation, previous ocular disease, less than 40 years of age who had symptoms for more than one month or anyone with a history blunt trauma. All patients were seen by an ophthalmology resident and also by either a staff physician, vitreoretinal fellow or a

vitreoretinal consultant. Each patient had a full ophthalmological examination including slit-lamp examination, indirect ophthalmoscopy and scleral indentation, Goldmann 3-mirror examination was used as required. Patients were then given a Queen's University Posterior Vitreous Detachment Patient Diary and instructions. The diary was used to document the patient symptoms on a weekly basis. All patients were then examined 6 weeks later unless haemorrhage or anterior vitreous pigment was detected, this group of high risk patients were re-examined 2 weeks after the initial examination. A total of 2 patients developed a retinal break of which one patient had vitreous and retinal haemorrhage and had been reviewed at 2 weeks. This patient had noted a decrease in floater frequency but also had persistent, stable symptoms of photopsia. The other patient had a large number of floaters on presentation, which did not alter and only had photopsia for the initial 6 days. Although they recognise the limitation of this study; a small number of delayed breaks, they concur with the finding of van Overdam *et al.* (2005) that patients with 10 or more floaters, a curtain or cloud, haemorrhage require further review. They suggest the addition of high floater frequency may increase the predictive value of follow-up criteria.

A recent study by Williams *et al.* (2011) prospectively studied 354 patients with an acute PVD. All patients were examined with fundus viewing contact lens. They found an incidence of 3.95% of delayed retinal breaks, over 90% of the breaks exhibited one or more of the following; haemorrhage, pseudophakia, myopia, or symptoms less than 14 days. The presence of vitreous haemorrhage was found to be the most statistically significant risk factor for developing a delayed retinal break. The authors conclude patients presenting with symptomatic PVD should be followed up regardless of characteristics.

Owing to the findings of the preliminary validation study, a posterior vitreous detachment clinic evolved, in which patients were to be examined by the validated optometrist. The sole purpose of this clinic was to review patients referred to the vitreo-retinal service from eye casualty diagnosed with uncomplicated acute posterior vitreous detachment. The primary objective of this chapter was to determine whether patients seen in eye casualty that had been diagnosed with uncomplicated posterior vitreous detachment required further review or could be safely discharged without further review; in essence the incidence of retinal breaks in the PVD clinic.

3.2 Methods

A retrospective review of the medical records of patients attending the optometrist PVD clinic from 1st December 2010 until 31st December 2013 with was undertaken. The inclusion criterion was a provisional diagnosis of PVD in one or both eyes referred to the PVD clinic after examination in an outpatient ophthalmology clinic or the eye casualty at University Hospital Coventry and Warwickshire NHS Trust for symptoms of acute PVD. This study was registered with both University Hospital Coventry and Warwickshire NHS Trust and by Aston University and was approved.

For each patients the following details were collected:

1- Age
2- Gender
3- Date of presentation to eye casualty
4- Source of referral when the patient presented to eye casualty
5- Duration of symptoms when the patient presented to eye casualty
6- Presence of floaters when the patient presented to eye casualty
7- Presence of photopsia when the patient presented to eye casualty
8- Presence of reduced vision when the patient presented to eye casualty
9- Presence of anterior vitreous pigment when the patient presented to eye casualty
10- Presence of associated pathology when the patient presented to eye casualty
11- If the patient underwent scleral indentation and/or 3 mirror examination in eye casualty
12- Diagnosis in eye casualty
13- Date of outpatient clinic appointment
14- Presence/change in floaters when the patient was examined in the PVD clinic
15- Presence/change in photopsia when the patient was examined in the PVD clinic
16- Presence/change in reduced vision when the patient was examined in the PVD clinic
17- Refractive error. The refractive status had been determined in the PVD clinic using one of the following methods:
    a) From the most recent spectacle prescription which they had been asked to bring to the appointment
    b) If this was not available then neutralisation/focimetry of the distance spectacles was used to determine the refractive status
    c) If the patient had neither the spectacle prescription, spectacles nor any knowledge of their refractive status they were questioned as to how they perceived their vision for different tasks. If the patient responded by having good vision for the distance and near, with a visual acuity of 0.20 logMAR or better in

the worst eye then they were presumed to be emmetropic/near emmetropic. In the event the patient responded the near vision was significantly worse than the distance without correction and had visual acuity of 0.20 logMAR or better in the worst eye, it was presumed the patient was emmetropic/near emmetropic. If the same subjective response was obtained with visual acuity of 0.22 logMAR or worse, then they were presumed to be hypermetropic. Finally if the patient responded in having good near vision but poor distance vision without correction, they were presumed to be myopic

18- Previous ocular history, specifically surgery or interventions
19- Presence of anterior vitreous pigment when the patient was examined in the PVD clinic
20- Presence of associated pathology when the patient was examined in the PVD clinic
21- If a peripheral retinal pathology was present, whether it was visible on +90D examination and whether it was visible on 3-mirror examination, or if only visible on scleral indentation
22- Diagnosis in the PVD clinic
23- Clinical management e.g. discharge, follow-up, refer to another clinic or to undertake treatment

Fundamentally, as there was no alteration to the clinical pathway of the patient, it was deemed ethical approval was not necessary. In addition, as the data was to be collected retrospectively this further negated the need for ethical approval. For this study, all patients were examined in an identical manner as in the preliminary study (see methods in Chapter 2), except the vitreo-retinal consultant did not examine all patients and a separate proforma for recording the findings of the examination was not employed. Moreover the consultant only re-examined those patients in whom an abnormality was detected by the optometrist. The reasons for this were twofold, firstly the validation study demonstrated a high degree of correlation in the assessment and management of this group of patients between the optometrist and the vitreo-retinal consultant and therefore continued validation of optometrist was not considered necessary for patients who were found to have no vitreo-retinal pathology. Secondly due to time and resource constraints within the clinic it was not practical for the consultant to examine each patient in conjunction with the optometrist. There were two further modifications to the methodology employed in the validation study, the first of which was if a peripheral retinal abnormality was detected then examination with a 3-mirror fundus contact lens was also undertaken to ascertain whether the abnormality was visible using this method of fundoscopy by the optometrist alone. The technique to assess for pigment in the anterior vitreous was the same as employed by Brod *et al.* 1991; Tanner *et al.*

2000). Similarly the technique of fundus examination with a 3-mirror contact lens has previously been described (Yanoff & Duker 2003)

3.3 Statistical methods

As reported in the literature the incidence of delayed retinal breaks in this group of patients is in the order of 1.5-4.4%, thus in order to have a statistically significant study population with and acceptable margin of error the magnitude a sample size calculation was undertaken using the following formula:

$$(Z^2 \times p(1-p))/e^2$$

Z= value from standard normal distribution corresponding to desired confidence level (1.96 for 95%)
p= estimated incidence
e= margin of error

For a confidence level of 95% with a 5% margin of error, with an expected incidence of 4.4% delayed breaks a minimum sample size of 59 would be required; whereas for an incidence of 1.5% a minimum sample size of 23 would be required.

Additional secondary objectives of this study were to determine the presence of other and/or co-existing pathology in the patients referred to the PVD clinic. Finally demographics of the sample were to be analysed namely age, gender, refractive status, laterality, symptomology profile and source of referral. Although the sample size was calculated to detect the statistical significance of retinal breaks detected in the PVD clinic, a similar sample size calculation was undertaken using data from the from chapter two described to determine whether the potential numbers recruited would be sufficient to address the secondary objectives. From chapter two, a mean age difference between males and females with PVD was almost 5 years, and for those with retinal breaks almost 2 years, whereas Combs & Welch (1982) report the difference in age between males and females to be 1.6 years in those with retinal breaks.

Therefore a sample size calculation comparing two means was undertaken using the following:

$$(Z\alpha + Z\beta)^2 \times 2 \times \sigma^2 / d^2$$

Zα = critical value from standard normal distribution corresponding to desired confidence level (1.96 for 95%)
Zβ = critical value from standard normal distribution corresponding to desired power (0.84 for 80%)
σ = population variance
d = difference to be detected

In order to detect a difference of 1 year in age for any variable e.g. gender, laterality, for a 95% confidence interval with a power of 80%, with a population variance of 100, a minimum of 1570 patients would be required in each group. Needless to say this was not compatible with the original sample size calculation, as these variables were secondary objectives and a 40/60 male/female split was expected, the figures were adjusted so that for a difference of 2 years to be detected 393 patients would be required in each group. From previous data it was estimated 1.5-4.4% of patients of the 998 would have retinal breaks i.e. 15 - 40 patients. Therefore, for the aforementioned statistics, a minimum sample of 33 patients would be required in each group in order to detect a 7 year difference between the means of any two groups.

A further objective of this chapter was to refine the assessment and management of patients with posterior vitreous detachment, specifically the sensitivity and specificity of the following:

1- Presence of pigment in the anterior vitreous associated with retinal breaks
2- Examination of the fundus with +90D non-contact fundus lens for the detection of peripheral retinal abnormalities including retinal breaks compared to head mounted binocular indirect ophthalmoscopy with scleral indentation
3- Examination of the fundus with a 3-mirror Goldmann contact lens for the detection of peripheral retinal abnormalities including retinal breaks compared to head mounted binocular indirect ophthalmoscopy with scleral indentation

3.4 Results

During the period 1st December 2010 until 31st December 2013 data was collected for 1107 patients. Of these 1107 patients, 851 were diagnosed with posterior vitreous detachment alone and did not warrant any further investigation or intervention, equating to 76.9% of the study population. A total of 50 (4.5%) were found to have retinal breaks of which half required treatment. The remaining 206 (18.6%) patients were found to have additional abnormalities of which 55 (5.0%) required further investigation and/or intervention. The findings of each of these subgroups has been categorised to evaluate specific characteristics:

- 3.4.1 PVD alone
- 3.4.2 PVD and additional findings not requiring further assessment/intervention
- 3.4.3 PVD and additional findings requiring further assessment/intervention
- 3.4.4 Retinal breaks
    - 3.4.4.1 Retinal breaks not treated
    - 3.4.4.2 Retinal breaks requiring treatment

A detailed analysis of each subgroup has been undertaken however a summary of the findings complied in section 3.6

3.4.1 Eyes with uncomplicated posterior vitreous detachment

Of the 851 patients with uncomplicated PVD, 262 (31%) were male and 589 (69%) were female, a male to female ratio of approximately 1:2. The characteristics of those with uncomplicated posterior vitreous detachment are represented in table 3.4.1.

	Total 851	Male 262	Female 589
Age			
Mean (SD)	65.8 (8.7)	66.0 (9.3)	64.2 (8.8)
Range	25-92	27-92	25-92
Refractive error			
Emmetropia	347 (41%)	104 (40%)	243 (41%)
Hyperopia	236 (27%)	70 (27%)	166 (28%)
Myopia	268 (31%)	88 (33%)	180 (31%)
Laterality			
Bilateral	298 (35%)	93 (35%)	205 (35%)
Left	251 (30%)	76 (30%)	175 (30%)
Right	302 (35%)	93 (35%)	209 (35%)
Source of referral			
GP	71 (8%)	30 (11%)	41 (7%)
Community optician	164 (19%)	45 (17%)	119 (20%)
HES clinic	17 (2%)	4 (2%)	13 (2%)
Self referral	599 (70%)	183 (70%)	416 (71%)
Symptoms			
Floaters alone	299 (35%)	106 (40%)	193 (33%)
Photopsia alone	41 (5%)	13 (5%)	28 (5%)
Floaters and photopsia	509 (60%)	142 (54%)	367 (62%)
Floaters/photopsia & reduced vision	2 (<1%)	1 (<1%)	1 (<1%)
Duration of symptoms (days)			
Mean (SD)	11.0 (18.7)	13.4 (22.0)	10.0 (16.8)
1-7	516 (61%)	154 (59%)	362 (61%)
8-14	106 (12%)	20 (8%)	86 (15%)
15-21	54 (6%)	16 (6%)	38 (6%)
22-28	36 (4%)	17 (6%)	19(3%)
>28	45 (5%)	21 (8%)	24 (4%)
Not documented	94 (11%)	34 (13%)	60 (10%)
Method of initial examination			
3 mirror	17 (2%)	3 (1%)	14 (2%)
Indentation	476 (56%)	144 (55%)	332 (56%)
Both	6(1%)	1(<1%)	5 (1%)
Neither	94 (11%)	25 (10%)	69(12%)
Not documented	258 (30%)	89 (34%)	169 (29%)
Time until follow-up (days)			
Mean (SD)	37.8 (16.6)	38.3 (13.5)	37.5 (17.8)
Range	5-219	6-84	5-219
Change in symptoms from presentation to follow-up			
Floaters at initial examination	**810 (95%)**	**249 (95%)**	**561 (95%)**
Resolved	58 (7%)	22 (9%)	36 (6%)
Improved	450 (55%)	135 (54%)	315 (56%)
Stable	301(37%)	92 (37%)	209 (37%)
Worse	5* (1%)	2* (<1%)	3* (<1%)
Photopsia at initial examination	**552 (65%)**	**156 (60%)**	**396 (67%)**
Resolved	231 (42%)	64 (41%)	167 (42%)
Improved	260 (47%)	73 (47%)	187 (47%)
Stable	60 (11%)	19 (12%)	41 (10%)
Worse	4 (<1%)	0	4[#] (1%)

*2 eyes that had photopsia only at presentation went on to develop floaters

[#] 3 eyes went on to develop photopsia after the initial examination

Table 3.4.1.1 Demographic profile of the patients with posterior vitreous detachment

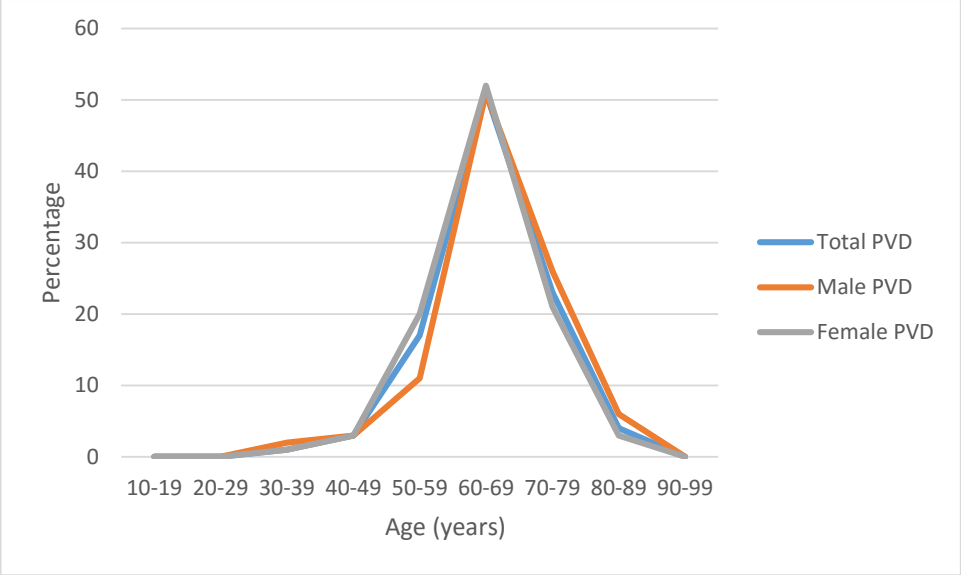

Fig. 3.4.1.1 A line graph of the age distribution of patients with PVD

Over half of patients with PVD were in their seventh decade (fig 3.4.1.1), in the females approximately 20% were in the sixth decade with a further 20% in the eighth decade. In males one-tenth were in their sixth decade with a quarter in their eighth decade.

The mean age collectively for males was almost two years greater than the age at which PVD occurred in women and this was found to be statistically significant (p=0.02). Interestingly PVD occurred in myopes at approximately three and eight years earlier in both males and females compared to their emmetropic and hypermetropic counterparts respectively (table 3.4.1.2), and this was found to be statistically significant (table 3.4.1.3).

	Myope	Emmetrope	Hyperope
Male			
Mean	62.3	65.7	70.1
SD	11.4	8.6	8.5
Range	27-80	36-82	43-92
Female			
Mean	60.8	63.8	68.5
SD	9.0	8.3	7.5
Range	32-87	25-92	48-91

Table 3.4.1.2 Mean age at which posterior vitreous detachment occurred according to gender and refractive status

	p-value
Male myope vs Male hyperope	<0.001
Male myope vs Male emmetrope	0.009
Male hyperope vs Male emmetrope	0.002
Female myope vs Female hyperope	<0.001
Female myope vs Female emmetrope	<0.001
Female hyperope vs Female emmetrope	<0.001
Female myopes vs Male myopes	0.22
Female emmetropes vs Male emmetropes	0.053
Female hyperopes vs Male hyperopes	0.17

Table 3.4.1.3 Results of 2-tailed unpaired t-tests between the subgroups for age at which PVD occurred with respect to refractive status and gender

There was no statistically significant difference ($p>0.05$) in the mean age between males and females dependent upon refractive error alone (table 3.4.1.3). In both males and females the right eye was affected in 5% more cases compared to the left, and a similar number of patients had bilateral involvement as those presenting with only the right eye affected. The mean age was greater in males compared to females in cases of unilateral involvement (table 3.4.1.4), however this was only statistically significant when the right eye alone had been affected (table 3.4.1.5). Conversely, in cases of bilateral involvement, females were slightly older but this was not statistically significant.

	RE	LE	BE
Male	66.1 (9.3)	65.5 (8.9)	65.6 (11.8)
Female	62.9 (8.2)	63.8 (8.3)	66.0 (9.6)
Total	63.9 (8.7)	64.3 (8.5)	65.6 (11.8)

Table 3.4.1.4 Age profile of patients with PVD according to gender and laterality

	p-value
Male right eye vs left eye	0.64
Male right eye vs bilateral	0.71
Male left eye vs bilateral	0.93
Female right eye vs left eye	0.27
Female right eye vs bilateral	0.0004
Female left eye vs bilateral	0.002
Male right eye vs Female right eye	0.0004
Male left eye vs Female left eye	0.16
Male bilateral vs Female bilateral	0.77
Right eye vs left eye	0.56

Table 3.4.1.5 Results of 2-tailed unpaired t-tests evaluating mean age and laterality within and between the two gender groups

In the male subgroup there was no statistically significant difference between the age at which unilateral or bilateral involvement occurred, whereas in the female subgroup patients with bilateral involvement were older and this was a statistically significant finding. In both groups there was no statistically significant difference in the age at which PVD occurred when there was unilateral involvement irrespective of laterality.

A further subgroup categorisation according to refractive status, gender and laterality, and this is represented in table 3.4.1.6, statistical analyses of this data have been tabulated in tables 3.4.1.7 and 3.4.1.8.

	Myope			**Emmetrope**			**Hyperope**		
	RE	**LE**	**BE**	**RE**	**LE**	**BE**	**RE**	**LE**	**BE**
Male (age)	63.0	61.7	62.3	66.0	66.0	66.0	69.7	70.3	72.0
SD	8.9	14.6	10.3	9.2	8.2	7.8	8.4	7.6	10.2
N	27	2	38	38	30	35	31	23	24
Range	27-76	37-80	41-80	36-82	48-82	39-80	43-92	51-82	48-84
Female (age)	59.5	61.0	62.2	63.0	64.0	66.0	67.0	67.0	71
SD	8.5	6.5	10.6	7.5	9.3	7.9	7.4	6.4	8.0
N	60	47	71	94	79	71	53	50	63
Range	34-79	43-75	32-87	37-81	25-81	42-92	50-85	48-77	51-91

Table 3.4.1.6 Subgroup classification according to gender, mean age, refractive status and laterality

	Male (p-value)			**Female (p-value)**		
	RE	LE	BE	RE	LE	BE
Myope vs Hyperope	0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Myope vs Emmetrope	0.19	0.07	0.09	<0.01	0.06	0.03
Hyperope vs Emmetrope	0.09	0.05	0.02	<0.01	0.01	<0.01

Table 3.4.1.7 Results of 2-tailed unpaired t-tests for each gender according to refractive status and laterality

	Male vs Female (p-value)		
	RE	LE	BE
Myopia	0.09	0.70	0.95
Emmetropia	0.05	0.25	0.79
Hyperopia	0.16	0.17	0.61

Table 3.4.1.8 Results of 2-tailed unpaired t-tests between males and females for refractive status and laterality

The findings of 2-tailed unpaired t-tests for males and females dependent on refractive state (table 3.4.1.7) validate the finding that myopes were younger than hyperopes in both the male and female populations. The age at which PVD occurred in emmetropes was less than that of hyperopes and greater than that of myopes, however this was only statistically significant in cases of bilateral involvement between the hyperopic and emmetropic males. Conversely for the female population, the general trend was PVD occurred in myopes in the early 60s followed by emmetropes in the mid-60s and finally in hyperopes in the late 60s. This was statistically significant, except when myopic left eyes were compared against emmetropic left eyes where this did not quite reach statistical significance.

Essentially there was no statistically significant difference in the mean age at which PVD occurred between males and females regardless of laterality and refractive state. The exception to this was emmetropic right eyes, in which the male subgroup were older, however the number of females were almost 2.5 times greater than the males.

Symptoms

Floaters were the predominant symptom with 95% of the patients examined experiencing floaters at presentation. A combination of floaters and photopsia were experienced by over half of males and females, 54% and 62% respectively.

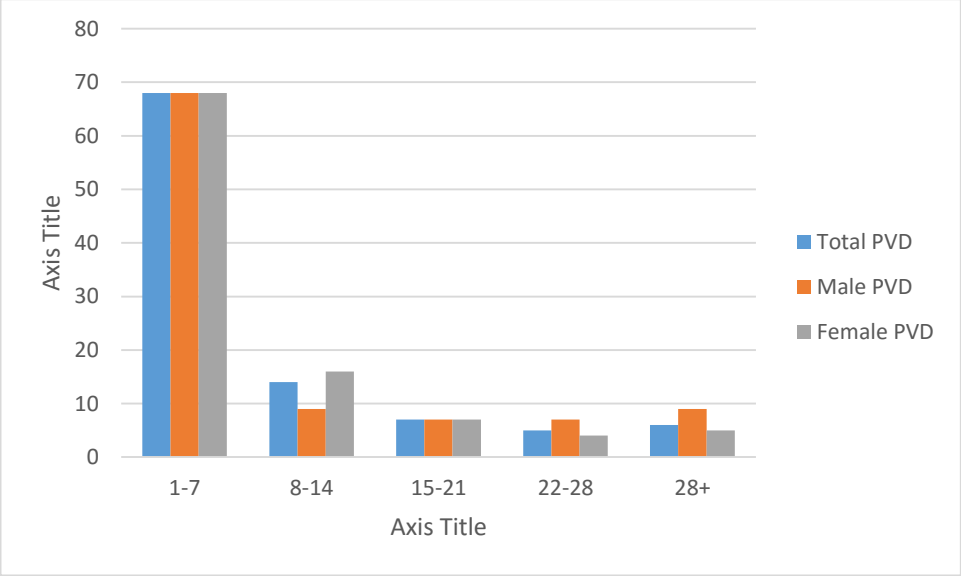

Fig 3.4.1.2 Duration of symptoms prior to examination in eye casualty in patients with PVD
Note: patients in whom duration of symptoms was not documented have been excluded

Of the patients with PVD, over two-thirds of patients had symptoms for seven days or less, and approximately 80% had symptoms for 2 weeks or less prior to their initial examination in eye casualty (table 3.4.1.1). The duration of symptoms was slightly longer in males than females by almost one day and this was found to be statistically significant (p=0.04) (tables 3.4.1.9, 3.4.1.10 and 3.4.1.11).. A subgroup analysis revealed hyperopic females and indeed hyperopes overall had symptoms for a longer duration than their emmetropic equivalents and this was a statistically significant finding (table 3.4.1.10). Interestingly however this was not replicated in the male or myopic subgroups.

	Males	Females	Combined
Myopes			
Mean	13.0	9.5	10.7
SD	21.5	14.8	17.4
Range	1-90	1-100	1-100
Emmetropes			
Mean	12.2	8.4	9.5
SD	23.9	12.0	16.3
Range	1-180	1-90	1-180
Hyperopes			
Mean	15.9	13.2	14.0
SD	19.8	24.0	22.9
Range	1-90	1-180	1-180

Table 3.4.1.9 Mean duration of symptoms subcategorised according to refractive error and gender

	Males	Females	Combined
Myopes vs Hyperopes	0.43	0.11	0.10
Myopes vs Emmetropes	0.81	0.48	0.43
Hyperopes vs Emmetropes	0.30	0.03	0.02

Table 3.4.1.10 Results of unpaired 2-tailed t-tests for refractive error and duration of symptoms

	p-value
Myopes	0.21
Emmetropes	0.15
Hyperopes	0.42
Total	0.04

Table 3.4.1.11 Results of unpaired 2-tailed t-tests for refractive error between males and females

Patients were seen in the PVD clinic at approximately 5 ½ weeks after their initial assessment in the eye casualty, and there was no statistically significant difference in this timescale between the male and female subgroups as expected (p=0.51).

In eyes with floaters, more than half experienced improved by the time they were seen in the PVD clinic. A small proportion of between 5-10% had resolution of their floaters, and just over one-third had no change in this time period. The improvement of photopsia was significantly more prompt in comparison to floaters with almost 90% of patients experiencing improvement or resolution in the same timescale.

3.4.2 Eyes with posterior vitreous detachment and additional findings not requiring further assessment/intervention

A total of 151 patients were identified with in the PVD clinic with additional findings that did not require further intervention in conjunction with posterior vitreous detachment. Similarly to the eyes with posterior vitreous detachment alone, the ratio of females to males was in the order of approximately 2:1. The conditions identified are shown in table 3.4.2.1 together with the number and percentage of each identified in eye casualty.

	Total		Males		Females	
Condition	**N**	**Identified at 1st exam**	**N**	**Identified at 1st exam**	**N**	**Identified at 1st exam**
Age-related maculopathy	5	0	1	0	4	0
Amaurosis fugax	2	0	2	0	0	0
Anxiety-related	1	0	0	0	1	0
Cataracts	3	0	2	0	1	0
Choroidal naevus	9	2 (22%)	5	1 (20%)	4	1 (25%)
Chorioretinal scar	7	3 (43%)	3	1 (33%)	4	2 (50%)
CHRPE	3	1 (33%)	2	1 (50%)	1	0
Epiretinal membrane	10	3 (30%)	2	1 (50%)	8	2 (25%)
Lattice	18	4 (22%)	6	3 (50%)	12	1 (8%)
Macular hole	1	0	0	0	1	0
Meridional fold	1	0	1	0	0	0
Microcystoid degeneration	2	0	1	0	1	0
Migraines	8	1 (13%)	1	0	7	1 (17%)
Myelination	3	0	2	0	1	0
Optic atrophy	1	0	1	0	0	0
Pars plana cyst	3	0	1	0	2	0
Pavingstone degeneration	26	3 (12%)	9	2 (22%)	17	1 (6%)
Reticular degeneration	12	4 (33%)	5	1 (20%)	7	3 (43%)
Retinoschisis	18	6 (33%)	4	2 (50%)	14	4 (29%)
Snowflake degeneration	5	2 (40%)	1	1 (100%)	4	1 (25%)
Vitreo-retinal traction	4	1 (25%)	2	1 (50%)	2	0
Vitreous haemorrhage	1	0	1	0	0	0
White without pressure	8	1 (13%)	1	1 (100%)	7	0
Total	**151**	**28 (19%)**	**53**	**15 (28%)**	**98**	**16 (16%)**

Table 3.4.2.1 Conditions identified in the PVD clinic

Of the 151 patients, a total of 89 (59%) had retinal degenerative conditions, and in this subgroup the male to female ratio remained approximately 1:2. The retinal degenerative conditions identified are tabulated in table 3.4.2.2 according to gender and the frequency of

each identified at the first visit in eye casualty. In the male subgroup, 27 patients were found with retinal degeneration with just over one-third of these being identified at the first visit. Remarkably even though the female subgroup was more than twice the size of the male subgroup, retinal degenerative conditions were identified significantly less frequently at the first visit (see table 3.4.2.2).

	Total		Males		Females	
Condition	**N**	**Identified at 1st exam**	**N**	**Identified at 1st exam**	**N**	**Identified at 1st exam**
Lattice	18	4 (22%)	6	3 (50%)	12	1 (8%)
Microcystoid degeneration	2	0	1	0	1	0
Pavingstone degeneration	26	3 (12%)	9	2 (22%)	17	1 (6%)
Reticular degeneration	12	4 (33%)	5	1 (20%)	7	3 (43%)
Retinoschisis	18	6 (33%)	4	2 (50%)	14	4 (29%)
Snowflake degeneration	5	2 (40%)	1	1 (100%)	4	1 (25%)
White without pressure	8	1 (13%)	1	1 (100%)	7	0
Total	**89**	**20 (22%)**	**27**	**10 (37%)**	**62**	**10 (16%)**

Table 3.4.2.2 A table of retinal conditions identified in the PVD clinic with reference to how many of each were identified in eye casualty.

Condition	**N**	**90D**	**3 mirror**
Lattice	18	16 (89%)	16 (89%)
Meridional fold	1	0	0
Microcystoid degeneration	2	1 (50%)	1 (50%)
Pars plana cyst	3	1 (33%)	1 (33%)
Pavingstone degeneration	26	24 (92%)	24 (92%)
Reticular degeneration	12	11 (92%)	11 (92%)
Retinoschisis	18	16 (89%)	17 (94%)
Snowflake degeneration	5	3 (60%)	4 (80%)
White without pressure	8	6 (75%)	6 (75%)
Total	**93**	**78 (84%)**	**80 (86%)**

Table 3.4.2.3 Sensitivity of slit-lamp examination with 90D lens and 3 mirror contact lens compared to scleral indentation

The sensitivity of 90D lens examination and 3 mirror examination was almost identical, however examination with scleral indentation identified approximately 15% more lesions than either technique.

Methods of examination

At the initial assessment in eye casualty, indentation was employed in over 50% of males, however 11% less frequently in females. In approximately one-third of patients there was no documentation of adjunctive fundus assessment other than slit-lamp examination. Interestingly in males, there was no significant difference in the techniques employed for examination between the eyes with PVD alone and those analysed in this section (3.4.2) (tables 3.4.1.1 and 3.4.2.4). On the contrary, in females it appears that eyes with additional pathology identified in the PVD clinic were 10% less frequently examined with an adjunctive method compared to the eyes with PVD alone.

	Total 151	Male 53	Female 98
Age			
Mean (SD)	61.4 (12.4)	65.1 (10.2)	59.3 (13.0)
Range	22-87	26-85	22-87
Refractive error			
Emmetropia	52 (34%)	23 (43%)	29 (30%)
Hyperopia	34 (23%)	13 (25%)	21 (21%)
Myopia	65 (43%)	17 (32%)	48 (49%)
Laterality			
Bilateral	55 (36%)	17 (32%)	38 (39%)
Left	46 (30%)	18 (34%)	28 (28%)
Right	50 (33%)	18 (34%)	32 (33%)
Symptoms			
Floaters alone	48 (32%)	19 (36%)	29 (31%)
Photopsia alone	11 (7%)	4 (8%)	7 (7%)
Floaters and photopsia	89 (59%)	29 (55%)	60 (61%)
Floaters/photopsia & reduced vision	3 (2%)	1 (1%)	2 (1%)
Duration of symptoms (days)			
Mean (SD)	15.5 (20.6)	17.9 (25.7)	14.0 (17.0)
1-7	70 (46%)	26 (49%)	44 (45%)
8-14	18 (12%)	5 (9%)	13 (13%)
15-21	11 (7%)	6 (11%)	5 (5%)
22-28	6 (4%)	2 (4%)	4 (4%)
>28	17 (11%)	6 (11%)	11 (11%)
Not documented	29 (19%)	8 (15%)	21 (22%)
Method of initial examination			
3 mirror	3 (2%)	1 (2%)	2 (2%)
Indentation	75 (50%)	30 (57%)	45 (46%)
Both	2 (1%)	1 (2%)	1 (1%)
Neither	16 (11%)	4 (8%)	12 (12%)
Not documented	55 (36%)	17 (32%)	38 (39%)
Source of referral			
GP	11 (7%)	7 (13%)	4 (4%)
Community optician	34 (23%)	11 (21%)	23 (24%)
HES clinic	1 (<1%)	0	1 (1%)
Self referral	105 (70%)	35 (66%)	70 (71%)
Time until follow-up (days)			
Mean (SD)	38.4 (15.1)	41.3 (17.7)	36.8 (13.3)
Range	2-116	2-90	14-116
Change in symptoms from presentation to follow-up			
Floaters at initial examination	**141 (93%)**	**49 (92%)**	**93 (95%)**
Resolved	5 (4%)	0	5 (6%)
Improved	69 (49%)	25 (51%)	44 (47%)
Stable	73 (52%)	24 (49%)	44 (47%)
Worse	0	0	0
Photopsia at initial examination	**101 (67%)**	**33 (62%)**	**68 (69%)**
Resolved	27 (27%)	10 (31%)	17 (26%)
Improved	50 (50%)	16 (48%)	34 (52%)
Stable	22 (22%)	7 (21%)	15 (23%)
Worse	2 (2%)	0	2 (2%)

Table 3.4.2.4 Demographic profile of the patients with posterior vitreous detachment and additional pathology not requiring intervention

Although most patients in this category presented in the seventh decade, there was some disparity in the age distribution between males and females. In females approximately one-quarter were in the sixth decade and one-tenth in the eighth, whereas in males one-tenth were in the sixth decade and one quarter in the eighth (fig 3.4.2.1).

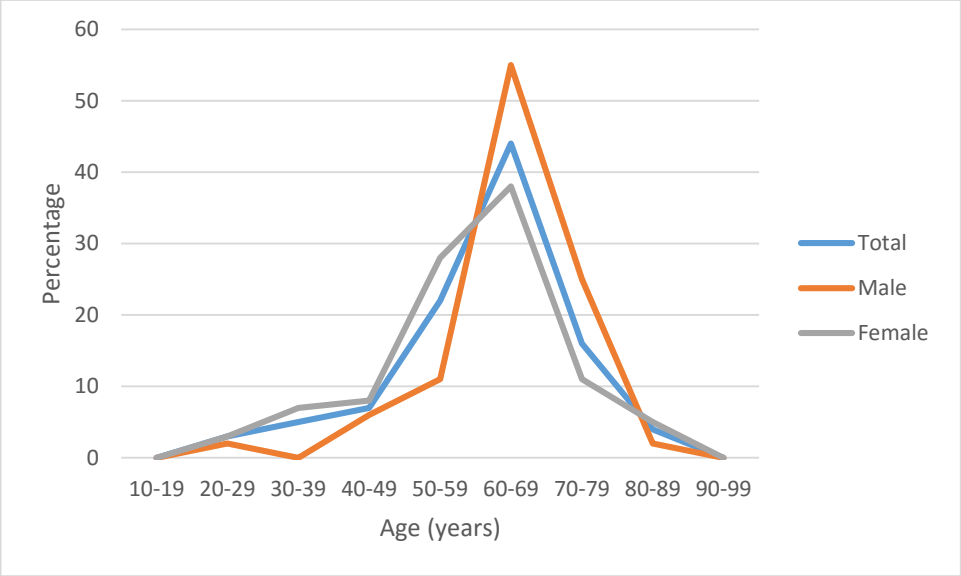

Fig 3.4.2.1 Age distribution of patients in category 3.4.2

Despite the number of individuals in this category was less than one-fifth of the eyes with PVD alone, the distribution of age at presentation across the spectrum of refractive error was comparable in that myopes presented at a younger age, subsequently emmetropes and finally hyperopes (table 3.4.2.5). Nevertheless, the mean difference in age between the three refractive states was not found to be statistically significant in males or when the male subgroup was compared to the female subgroup, however it was statistically significant in the female subgroup alone (table 3.4.2.6).

	Myope	**Emmetrope**	**Hyperope**
Male			
Mean	61.3	66.0	68.6
SD	13.8	8.0	6.4
Range	26-79	44-85	59-78
Female			
Mean	54.0	61.6	68.0
SD	12.3	13.7	7.4
Range	29-87	22-82	55-82

Table 3.4.2.5 Age profile of patients according to gender and refractive status

	p-value
Male myope vs Male hyperope	0.07
Male myope vs Male emmetrope	0.22
Male hyperope vs Male emmetrope	0.29
Female myope vs Female hyperope	<0.001
Female myope vs Female emmetrope	0.002
Female hyperope vs Female emmetrope	0.004
Female myopes vs Male myopes	0.07
Female emmetropes vs Male emmetropes	0.78
Female hyperopes vs Male hyperopes	0.16

Table 3.4.2.6 Results of 2-tailed unpaired t-tests evaluating mean age and refractive status within and between the two gender groups

	RE	LE	BE
Male			
Mean	68.7	65.0	62.4
SD	5.7	9.0	13.1
Range	59-85	44-79	26-74
Female			
Mean	59.3	57.5	61.4
SD	11.5	13.3	13.5
Range	33-78	22-88	31-87

Table 3.4.2.7 Age profile of patients according to laterality and gender

In males, unexpectedly bilateral PVD occurred at a younger age than unilateral PVD and occurred later in right eyes alone (table 3.4.2.7), however these findings were not statistically significant (table 3.4.2.8). Conversely in females bilateral PVD was present at a later age than unilateral PVD, however similarly to males the left eye appeared to be affected first and there was no statistical significance for these findings (table 3.4.2.8). Upon comparing the differences between males and females, unilateral PVD occurred earlier in females; 9.4 years for right eyes and 7.5 years for left eyes and was statistically significant. However there was no statistical significance between males and females when bilateral PVD was present (table 3.4.2.8).

	p-value
Male right eye vs left eye	0.14
Male right eye vs bilateral	0.09
Male left eye vs bilateral	0.51
Female right eye vs left eye	0.62
Female right eye vs bilateral	0.47
Female left eye vs bilateral	0.25
Male right eye vs Female right eye	0.005
Male left eye vs Female left eye	0.03
Male bilateral vs Female bilateral	0.81

Table 3.4.2.8 Results of 2-tailed unpaired t-tests evaluating mean age and laterality within and between the two gender groups

On comparing the mean age between the eyes with PVD alone from category 3.4.1 with the eyes in section 3.4.2, statistically there was no significant difference in the male population (table 3.4.2.9). In the females however, those in a category 3.4.2 presented at a younger age than those with PVD alone (right eye 3.6 years; left eye 6.3 years; bilateral 4.6 years). Although statistically significant in cases of bilateral involvement and when the left eye was affected, this was not the case when the right eye alone had been affected.

	p-value
Male right eye	0.12
Male left eye	0.84
Male bilateral	0.36
Female right eye	0.12
Female left eye	0.03
Female bilateral	0.045

Table 3.4.2.9 Results of 2-tailed unpaired t-tests evaluating mean age between category 3.4.1 and 3.4.2

A further subgroup analysis of gender, refractive status and laterality for this category of patients (table 3.4.2.10) revealed in males there was statistically no significance for age regardless of refractive status (table 3.4.2.11). In females however, myopes were younger than hyperopes and this was statistically significant independent of laterality. Furthermore emmetropic females with bilateral involvement were older than their myopic counterparts and this was statistically significant, however this was not applicable in cases of unilateral involvement. Although overall females were generally younger than their male equivalents in this category of patients, this was not a statistically significant observation (table 3.4.2.12).

	Myope			**Emmetrope**			**Hyperope**		
	RE	LE	BE	RE	LE	BE	RE	LE	BE
Male (age)	63.0	61.7	58.4	68.0	65.2	64.8	66.9	70.5	71.0
SD	14.2	9.3	16.7	3.3	10.7	7.4	6.0	8.6	4.2
N	4	5	8	7	10	6	7	4	2
Range	42-73	54-79	26-74	63-72	59-85	52-73	59-75	59-78	68-74
Female (age)	52.2	55.0	54.4	57.0	59.0	63.8	68.0	66.0	68.9
SD	11.3	11.0	14.3	17.0	6.7	13.7	7.4	8.7	7.4
N	14	14	20	7	4	18	8	5	8
Range	33-68	29-71	31-87	22-75	53-66	26-82	55-78	57-80	57-82

Table 3.4.2.10 Subgroup classification according to gender, mean age, refractive status and laterality

	Male (p-value)			**Female (p-value)**		
	RE	LE	BE	RE	LE	BE
Myope vs Hyperope	0.63	0.36	0.10	0.0009	0.054	0.002
Myope vs Emmetrope	0.53	0.91	0.35	0.50	0.38	0.04
Hyperope vs Emmetrope	0.67	0.36	0.23	0.15	0.23	0.24

Table 3.4.2.11 Results of 2-tailed unpaired t-tests for each gender according to refractive status and laterality

	Male vs Female (p-value)		
	RE	LE	BE
Myopia	0.23	0.10	0.57
Emmetropia	0.15	0.24	0.82
Hyperopia	0.69	0.47	0.63

Table 3.4.2.12 Results of 2-tailed unpaired t-tests between males and females for refractive status and laterality

Symptoms

The symptomology profile of the eyes at presentation in this subgroup was unequivocally similar to those eyes with PVD alone (table 3.4.1.1 and table 3.4.2.4). Floaters again were the predominant symptom with 95% of all patients in 3.4.2 afflicted with this symptom.

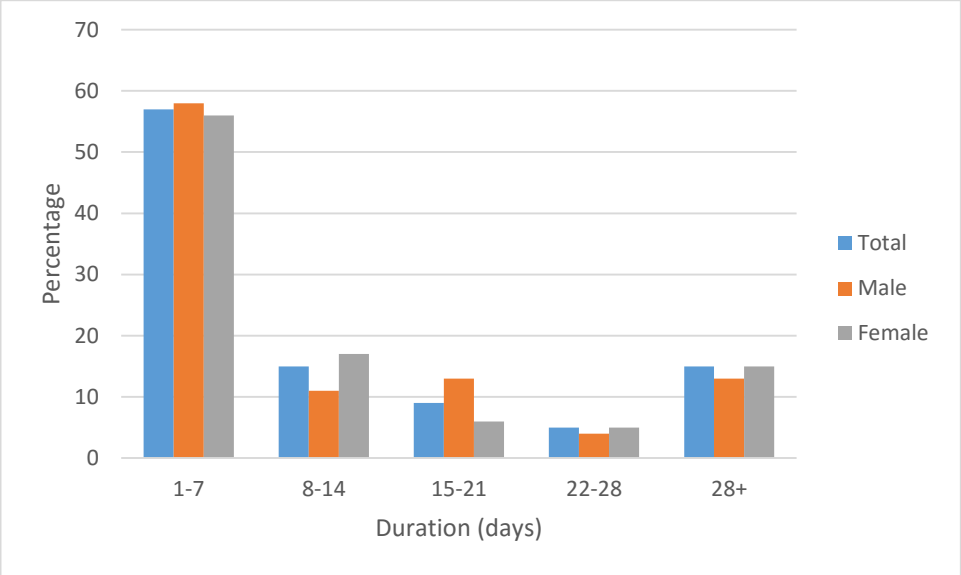

Fig 3.4.2.2 The duration of symptoms prior to examination in eye casualty in category 3.4.2

Although the majority of patient presented to eye casualty within the first week of symptoms, with a steady decline over the next three weeks, over 10% of patients had symptoms longer than four weeks (fig 3.4.2.2). Females presented 3.9 days earlier than males for the initial assessment, but this statistically was not significant (p=0.37). Male myopes had symptoms for more than twice as long as female myopes, however this was not statistically significant (tables 3.4.2.13 and 3.4.2.15). Similarly for the other refractive states there was a disparity in the duration of symptoms between males and females however there was no statistical significance in any category (tables 3.4.2.13 and 3.4.2.15).

	Males	Females	Combined
Myopes			
Mean	25.5	12.5	16.7
SD	32.5	14.2	22.1
Range	1-90	1-60	1-90
Emmetropes			
Mean	8.4	12.7	10.8
SD	8.3	17.4	14.0
Range	1-28	1-60	1-60
Hyperopes			
Mean	21.5	19.1	20.0
SD	30.0	21.9	24.7
Range	1-90	1-60	1-90

Table 3.4.2.13 Mean duration of symptoms subcategorised according to refractive error and gender

	Males	Females	Combined
Myopes vs Hyperopes	0.73	0.27	0.56
Myopes vs Emmetropes	0.04	0.97	0.12
Hyperopes vs Emmetropes	0.20	0.33	0.09

Table 3.4.2.14 Results of unpaired 2-tailed t-tests for refractive error and symptom duration

	p-value
Myopes	0.12
Emmetropes	0.31
Hyperopes	0.83
Total	0.37

Table 3.4.2.15 Results of unpaired 2-tailed t-tests for refractive error between males and females for symptom duration

Patients in this category were reviewed in the PVD clinic within the expected time frame. Compared to eyes with PVD alone, there was disparity in symptomology when the patients were reviewed in the PVD clinic. In both males and females, eyes with PVD alone were 10% more likely to have resolution or improvement in their symptoms compared to those in category 3.4.2.

3.4.3 Eyes with posterior vitreous detachment and additional findings requiring further assessment / intervention

In this category the ratio of females to males was in the order of 3:2, less disproportionate than the higher ratio of 2:1 seen in the previous two categories. Notably the number of patients overall was less as would be expected. The two most common conditions encountered were uveitis and a suspicion of glaucoma (table 3.4.3.1).

Condition	Total	Males	Females
Dry eyes	7	2	5
Glaucoma suspect	13	7	6
Maculopathy	6	0	6
Oculomotor abnormality	1	0	1
Retinal vascular anomalies	7	4	3
Suspicious choroidal naevus	4	1	3
Uveitis	17	7	10
Total	**55**	**21**	**34**
Age			
Mean (SD)	60.4 (16.5)	60.9 (15.1)	60.1 (17.5)
Range	19-90	19-77	21-90
Refractive error			
Emmetropia	25 (45%)	8 (38%)	17 (50%)
Hyperopia	17 (31%)	6 (29%)	11 (32%)
Myopia	13 (24%)	7 (33%)	6 (18%)
Laterality			
Bilateral	23 (42%)	13 (62%)	10 (29%)
Left	15 (27%)	5 (24%)	10 (29%)
Right	17 (31%)	3 (14%)	14 (41%)
Source of referral			
GP	6 (11%)	3 (14%)	3 (8%)
Community optician	11 (20%)	7 (33%)	4 (12%)
HES clinic	4 (7%)	2 (10%)	2 (6%)
Self referral	34 (62%)	9 (43%)	25 (74%)
Symptoms			
Floaters alone	20 (36%)	12 (57%)	8 (24%)
Photopsia alone	6 (11%)	1 (5%)	5 (15%)
Floaters and photopsia	26 (47%)	6 (29%)	20 (59%)
Asymptomatic	3 (5%)	2 (10 %)	1 (2%)
Duration of symptoms (days)			
Mean (SD)	26.8 (52.8)	17.3 (16.4)	31.5 (63.6)
1-7	17 (31%)	4 (19%)	13 (39%)
8-14	7 (13%)	4 (19%)	3 (9%)
15-21	3 (5%)	2 (10%)	1 (3%)
22-28	6 (11%)	1 (5%)	5 (15%)
>28	7 (13%)	2 (10%)	5 (15%)
Not documented	14 (25%)	8 (38%)	6 (18%)
Method of initial examination			
3 mirror	0	0	0
Indentation	20 (36%)	6 (29%)	14 (41%)
Both	1 (2%)	0	1 (3%)
Neither	10 (18%)	3 (14%)	7 (21%)
Not documented	24 (43%)	12 (57%)	12 (35%)
Time until follow-up (days)			
Mean (SD)	40.0 (18.6)	41.3 (25.8)	39.2 (12.8)
Range	18/128	18-128	21-80

Change in symptoms from presentation to follow-up			
Floaters at initial examination	**46 (84%)**	**18 (86%)**	**28 (82%)**
Resolved	3 (7%)	1 (5%)	2 (7%)
Improved	18 (39%)	7 (39%)	11 (39%)
Stable	22 (48%)	9 (50%)	13 (46%)
Worse	3 (7%)	1 (5%)	2 (7%)
Photopsia at initial examination	**32 (58%)**	**7 (33%)**	**25 (74%)**
Resolved	9 (28%)	4 (57%)	5 (20%)
Improved	15 (47%)	2 (29%)	13 (52%)
Stable	8 (25%)	1 (14%)	7 (28%)

Table 3.4.3.1 Demographic profile of the patients with posterior vitreous detachment and additional pathology requiring further management

The mean age for this category was 5.4 years younger than eyes with PVD alone, a statistically significant difference ($p<0.01$) and 1 year younger but not statistically significant ($p=0.68$) for eyes described in category 3.4.2. In males this figure was 5.1 years and 4.2 years younger respectively, but not statistically significant ($p=0.24$ and 0.16). In the females, they were 4.1 years younger and 0.8 years older for patients in categories 3.4.1 and 3.4.2 respectively, but again this was not statistically significant ($p=0.18$ and 0.82). Comparing mean age between males and females in this category, males were 0.8 years older than females a difference not found to be significant ($p=0.88$). The refractive error distribution in males was similar in this category to the two previous categories with emmetropia being the most common in approximately 40%, followed by myopia in one third and the remainder hyperopic. Conversely in the females, this trend was not consistent across the three categories; for eyes with PVD alone the trend was similar to males; whereas in category 3.4.2 myopes accounted for almost 50% and emmetropes almost one-third; finally in category 3.4.3. emmetropes accounted for almost 50%, hyperopes one-third with myopia being least common in less than 20% of eyes. Interestingly males were more likely to present with bilateral involvement, whereas there was a greater preponderance for the right eye to be affected in females.

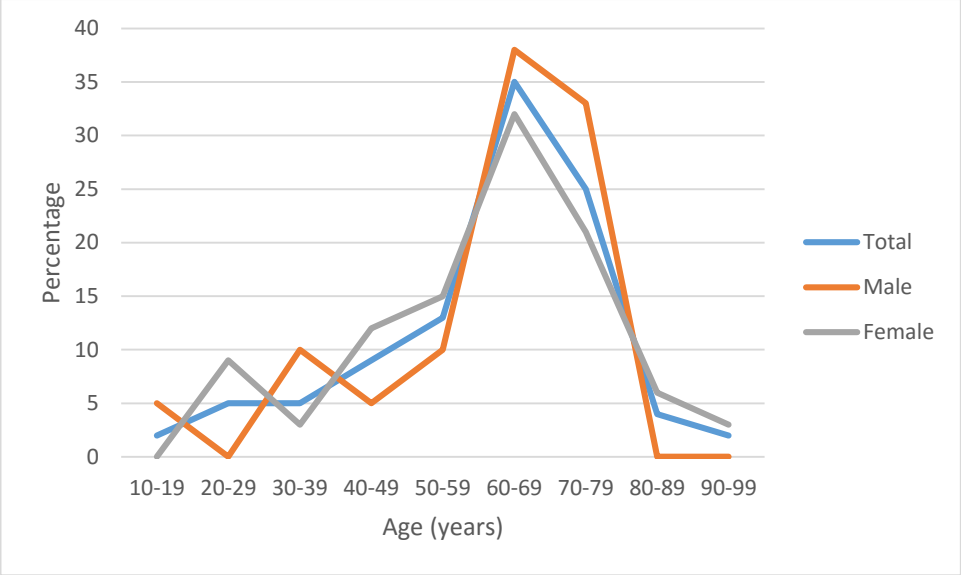

Fig 3.4.3.1 Age distribution of eyes in category 3.4.3

The seventh decade was still the most commonly affected as in the previous categories, however the proportion was significantly less (fig 3.4.3.1). One-third of males were in the eighth decade, a tenth in both the fourth and sixth decade and finally the remainder equally represented in the second and fifth decades. In comparison the females had greater representation in the younger decades and less representation in the older decades.

	Myope	Emmetrope	Hyperope
Male			
Mean	60.4	54.0	70.5
SD	13.1	18.7	5.2
Range	33-73	19-77	62-76
Female			
Mean	50.2	58.9	67.3
SD	13.2	15.4	20.6
Range	34-66	22-75	21-90

Table 3.4.3.2 The age profile of patients according to refractive status

	p-value
Male myope vs Male hyperope	0.10
Male myope vs Male emmetrope	0.45
Male hyperope vs Male emmetrope	0.04
Female myope vs Female hyperope	0.06
Female myope vs Female emmetrope	0.22
Female hyperope vs Female emmetrope	0.26
Female myopes vs Male myopes	0.19
Female emmetropes vs Male emmetropes	0.63
Female hyperopes vs Male hyperopes	0.53

Table 3.4.3.3 Results of 2-tailed unpaired t-tests evaluating mean age and refractive status within and between the two gender groups

The refractive status trend for females continued in parallel to the previous categories in that myopes were youngest, followed by emmetropes and finally the hyperopes (table 3.4.3.2). Although there was a 17 year difference between the mean age of the myopes and hyperopes, this did not quite achieve statistical significance (table 3.4.3.3). The mean difference in age between emmetropes and the other two refractive states was approximately eight years, but again this was not statistically significant (tables 3.4.3.2 and 3.4.3.3). Interestingly for the males, the emmetropes were youngest with the mean age of hyperopes 16.5 years greater, a statistically significant difference. Although the myopic males were on average 10 years younger in comparison to their hyperopic counterparts this was not statistically significant (tables 3.4.3.2 and 3.4.3.3) most likely to be attributable to the relatively small numbers in this group.

Symptoms

As depicted in fig. 3.4.3.2 approximately 60% of patients experienced symptoms for two weeks or less prior to their examination in eye casualty, this is in contrast to the previous two categories where a similar proportion of patients presented at or within one week of symptoms. Furthermore almost one-fifth of patients had symptoms longer than four weeks in duration, a greater proportion than seen in previous categories.

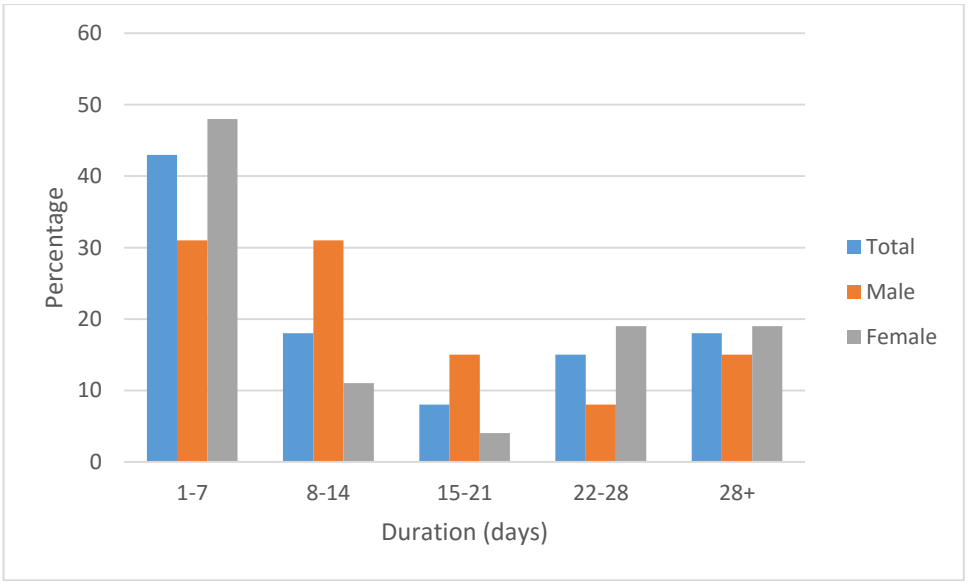

Fig 3.4.3.2 Duration of symptoms prior to examination in eye casualty in category 3.4.3

Overall the patients in this category were less symptomatic than the former two categories; 6-9% fewer males experienced floaters and only one-third of males experienced photopsia compared to 60-62%. The findings of the females exhibited greater disparity with 13% less experiencing floaters, however 5-8% were more troubled by photopsia. Although there were disparities between males and females, statistical significance was not achieved in any

category inter-or intra-gender dependent or independent of refractive error (tables 3.4.3.4, 3.4.3.5 and 3.4.3.6).

	Males	Females	Combined
Myopes			
Mean	17.0	41.2	29.1
SD	15.5	62.2	44.6
Range	2-42	3-150	2-150
Emmetropes			
Mean	19.0	41.3	34.7
SD	22.0	85.2	72.3
Range	1-56	1-300	1-300
Hyperopes			
Mean	15	13.2	13.7
SD	11.4	11.6	11.0
Range	7-28	3-28	3-28

Table 3.4.3.4 Mean duration of symptoms subcategorised according to refractive error and gender

	Males	Females	Combined
Myopes vs Hyperopes	0.84	0.37	0.31
Myopes vs Emmetropes	0.87	0.99	0.81
Hyperopes vs Emmetropes	0.84	0.28	0.25

Table 3.4.3.5 Results of unpaired 2-tailed t-tests for refractive error and symptom duration

	p-value
Myopes	0.44
Emmetropes	0.42
Hyperopes	0.83
Total	0.25

Table 3.4.3.6 Results of unpaired 2-tailed t-tests for refractive error between males and females for symptom duration

3.4.4.1 Eyes with retinal breaks

A total of fifty patients with retinal breaks were identified from the 1107 patients examined, a prevalence of 5%. The characteristics of fifty patients are tabulated in table 3.4.4.1. In contrast to the previous categories, the most obvious disparity was a greater proportion of males than females. Males were on average 8.4 years older than females, but this was not quite statistically significant (p=0.07). Overall eyes with retinal breaks were younger than eyes in all other categories, but only statistically significant when compared to eyes with PVD alone (p=0.04). The mean difference in age between males with breaks and the other three categories was not statistically significant. Females with breaks were almost a decade younger than their counterparts with PVD alone and this mean difference of 8.8 years was statistically significant (p=0.04). The distribution of refractive error for females was comparable with the eyes with PVD alone (tables 3.4.1.1 and 3.4.4.1), whereas in males there was a preponderance of myopia in eyes with retinal breaks. Interestingly the right eye was more frequently involved and bilateral involvement was present in less than 15% of cases.

	Total 50	Male 28	Female 22
Age			
Mean (SD)	60.1 (15.4)	63.8 (12.2)	55.4 (17.9)
Range	17-87	24-85	17-87
Refractive error			
Emmetropia	19 (38%)	9 (32%)	10 (45%)
Hyperopia	12 (24%)	7 (25%)	5 (23%)
Myopia	19 (38%)	12 (43%)	7 (32%)
Laterality			
Bilateral	6 (12%)	3 (11%)	3 (14%)
Left	18 (36%)	9 (32%)	9 (41%)
Right	26 (52%)	16 (57%)	10 (45%)
Source of referral			
GP	0	0	0
Community optician	13 (26%)	7 (25%)	6 (27%)
HE S clinic	5 (10%)	3 (11%)	2 (9%)
Self referral	32 (64%)	18 (64%)	14 (64%)
Symptoms			
Floaters alone	19 (38%)	11 (39%)	8 (36%)
Photopsia alone	1 (2%)	1 (4%)	0
Reduced vision alone	1 (2%)	1 (4%)	0
Floaters and photopsia	25 (50%)	12 (43%)	13 (59%)
Floaters/photopsia & reduced vision	0	0	0
Asymptomatic	4 (8%)	3 (11%)	1 (5%)
Duration of symptoms (days)			
Mean (SD)	11.7 (20.9)	12.3 (18.9)	10.5 (25.3)
1-7	23 (46%)	13 (52%)	10 (45%)
8-14	5 (10%)	4 (16%)	1 (5%)
15-21	1 (2%)	1 (4%)	0
22-28	3 (6%)	3 (12%)	0
>28	2 (4%)	1 (4%)	1 (5%)
Not documented	12 (24%)	3 (12%)	9 (40%)
Method of initial examination			
3 mirror	2 (4%)	2 (7%)	0
Indentation	23 (46%)	14 (50%)	9 (41%)
Both	0	0	0
Neither	11 (22%)	5 (18%)	6 (27%)
Not documented	14 (28%)	7 (25%)	7 (32%)
Time until follow-up (days)			
Mean (SD)	36.3 (15.6)	33.9 (11.0)	39.4 (19.9)
Range	4-92	16-54	4-92
Change in symptoms from presentation to follow-up			
Floaters at initial examination	**44 (88%)**	**23 (82%)**	**21 (95%)**
Resolved	3 (7%)	0	3 (14%)
Improved	22 (50%)	13 (57%)	9 (43%)
Stable	17 (39%)	8 (35%)	9 (43%)
Worse	3* (7)	3* (11%)	0
Photopsia at initial examination	**26 (52%)**	**13 (46%)**	**13 (59%)**
Resolved	10 (38%)	4 (31%)	6 (46%)
Improved	11 (42%)	8 (62%)	3 (23%)
Stable	5 (19%)	1 (8%)	4 (31%)
Worse	0	0	0

*1 patient developed floaters following the initial examination

Table 3.4.4.1 Characteristics of eyes with retinal breaks

The mean age of males with retinal breaks was similar to previous categories, whereas females with breaks were almost a decade younger than those with PVD alone and

approximately five years younger than those in categories 3.4.2 and 3.4.3 (tables 3.4.1.1, 3.4.2.1 and 3.4.3.1).

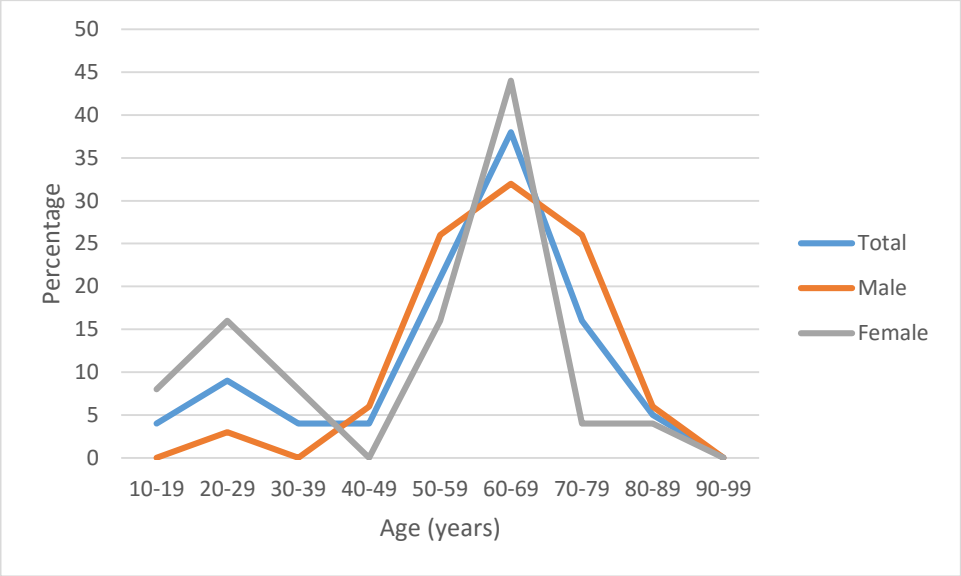

Fig 3.4.4.1 The age distribution of eyes with retinal breaks

The seventh decade was again the most involved similar to previous categories. For males there was an almost equal distribution either side of the seventh decade. In the females, one third of patients were below the age of forty and less than 10% in the eighth and ninth decades.

	Myope	Emmetrope	Hyperope
Male			
Mean	62.4	65.5	61.3
SD	8.2	15.3	11.5
Range	48-77	24-81	44-85
Female			
Mean	54.4	49.4	51.0
SD	14.1	23.4	22.6
Range	34-71	17-87	22-69

Table 3.4.4.2 The age profile of patients with retinal breaks according to refractive status

	p-value
Male myope vs Male hyperope	0.81
Male myope vs Male emmetrope	0.57
Male hyperope vs Male emmetrope	0.50
Female myope vs Female hyperope	0.76
Female myope vs Female emmetrope	0.57
Female hyperope vs Female emmetrope	0.89
Female myopes vs Male myopes	0.21
Female emmetropes vs Male emmetropes	0.06
Female hyperopes vs Male hyperopes	0.34

Table 3.4.4.3 Results of 2-tailed unpaired t-tests evaluating mean age and refractive status within and between the two gender groups

Table 3.4.4.2 represents the mean age profile according to refractive error, despite the differences statistical significance was not achieved in any category (table 3.4.4.3).

There were a total of 56 breaks in 56 eyes of fifty patients, of the fifty patients there were 2 females with round holes without PVD, all other eyes were found to have PVD on clinical examination. When reviewed in the PVD clinic, examination with indentation identified all 56 breaks, whereas examination with slit-lamp fundoscopy identified 48 breaks, and examination with 3-mirror identified 50 breaks; a sensitivity of 86% and 89% respectively.

The configuration of the breaks together with the absence or presence of tobacco dust is tabulated in table 3.4.4.4. In this series, tobacco dust was visible in only 15 eyes, a sensitivity of 27% with 100% specificity. When the analysis was limited to only horseshoe and operculated breaks this figure rose to 43%. Therefore in more than half of cases of retinal breaks associated with vitreo-retinal traction, tobacco dust was not a reliable indicator for the presence of a retinal break.

	Configuration of retinal break		
Presence of TD	Round	Horseshoe	Operculated
Y	0	10	5
N	21	7	13
Total	21	17	18

Table 3.4.4.4 Cross tabulation of retinal break configuration against the presence or otherwise of pigment in the anterior vitreous

The distribution of retinal breaks is represented in table 3.4.4.5 and figures 3.4.4.2 - 3.4.4.4. In males the supero-temporal quadrant was most frequently affected, the temporal, infero-temporal and inferior quadrants were similarly affected. The nasal retina was only involved in one eye (2%). The right eye was affected in 50% more cases than the left eye. In females the superior hemisphere was most frequently involved, with 15 breaks located superiorly and 7 located inferiorly. The superior quadrant harboured the most breaks, the inferior and supero-temporal quadrants contained a similar number of breaks. Overall, there was a greater preponderance for breaks in the temporal and superior hemispheres, the supero-temporal location being most frequently involved. The nasal retina was least frequently involved with less than 10% of breaks located in this region.

Location	All	Males (HS/O/R)	Females (HS/O/R)
Superior	9 (16%)	(1/0/0)	(1/1/6)
Supero-temporal	16 (29%)	(3/4/4)	(2/2/1)
Temporal	9 (16%)	(2/4/0)	(1/1/1)
Infero-temporal	6 (11%)	(0/3/2)	(0/1/0)
Inferior	12 (21%)	(3/0/3)	(1/0/5)
Infero-nasal	1 (2%)	(1/0/0)	(0/0/0)
Nasal	1 (2%)	(0/1/0)	(0/0/0)
Supero-nasal	2 (4%)	(0/0/0)	(1/1/0)
Total	**56**	**31**	**25**

Table 3.4.4.5 Distribution of retinal breaks according to location, gender and configuration

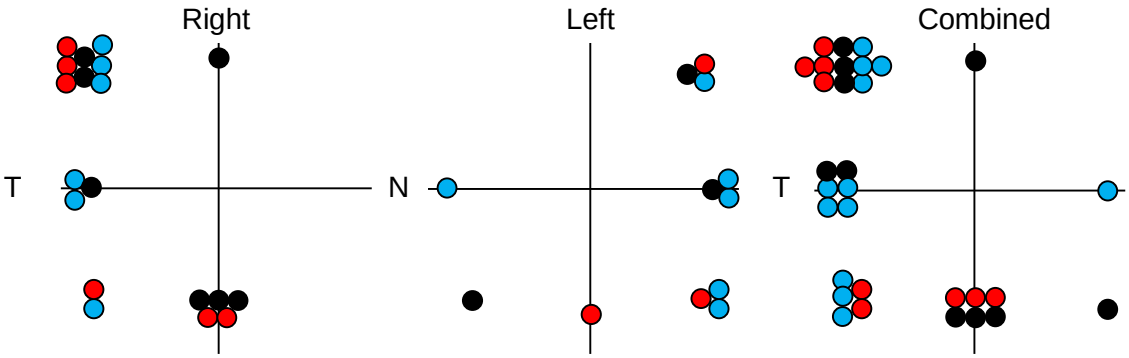

Fig 3.4.4.2 Diagrams to represent retinal breaks in males according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

For males there was an equal distribution of breaks in the superior and inferior hemispheres, with an odds ratio of 1 (p=1), whereas the temporal quadrant was nine times more likely to be affected than the nasal (OR 9.19, 95% CI 1.84 – 45.58) and this was highly statistically significant (p=0.005).

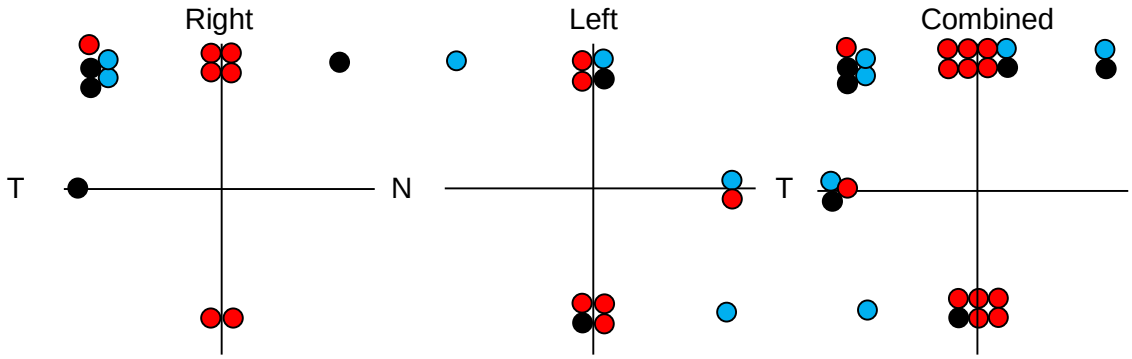

Fig 3.4.4.3 Diagrams to represent retinal breaks in females according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

For females the superior hemisphere was almost five times more likely to be affected than the inferior hemisphere (OR 4.75, 95% CI 1.41 – 16.05) and this was statistically significant (p=0.02). Similarly the temporal hemisphere was more than six times more likely to be affected than the nasal hemisphere (OR 6.47, 95% CI 1.23 – 34.01).

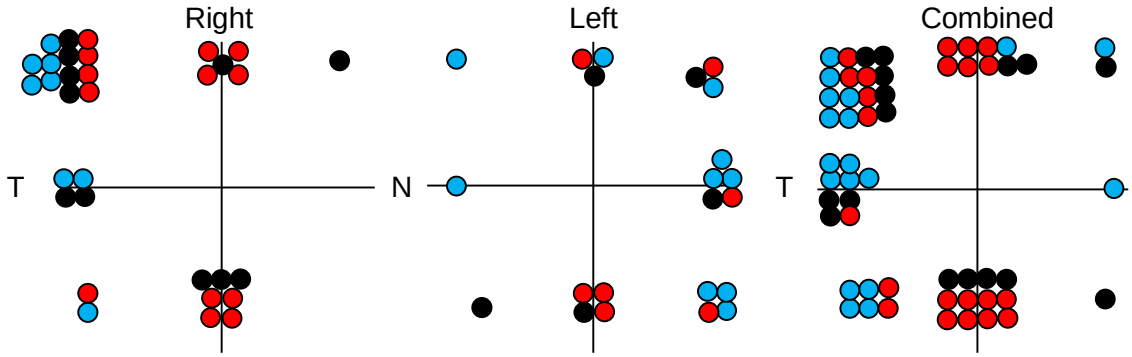

Fig 3.4.4.4 Diagrams to represent retinal breaks according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

Quadrant	Odds ratio (95% CI)	p
Superior	0.07 (0.01 - 0.62)	0.007
Supero-temporal	2.20 (0.65 - 7.50)	0.24
Temporal	1.76 (0.39 - 7.89)	0.50
Infero-temporal	4.62 (0.50 – 42.39)	0.21
Inferior	0.76 (0.21 – 2.73)	0.75
Infero-nasal	∞	1
Nasal	∞	1
Supero-nasal	0	0.19

Table 3.4.4.6 Odds ratio of each quadrant affected between males compared to females for all retinal breaks

Symptoms

Overall the duration of symptoms was similar compared to eyes with PVD alone in that two-thirds of patients had symptoms for one week or less prior to presenting to eye casualty (fig 3.4.4.5).

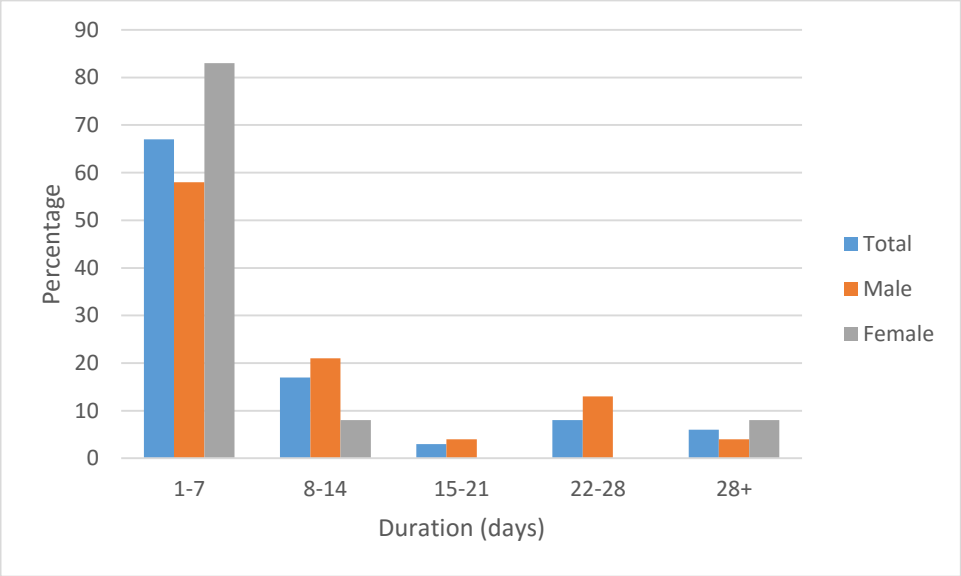

Fig 3.4.4.5 The duration of symptoms prior to presenting to eye casualty in eyes with retinal breaks

The length of symptom duration was not found to be significantly different between eyes with uncomplicated PVD nor with any other category. In comparison to other categories, the category of eyes with retinal breaks was the only category to contain asymptomatic patients. Similar to previous categories floaters were the predominant symptom with over 80% of males and almost all females afflicted, photopsia was experienced by just under half of males and over half of females (table 3.4.4.1). With regard to resolution of symptoms 57% of both males and females had improved or resolved floaters by the tie they were seen in the PVD clinic. Improvement in photopsia was more evident with over 90% of males and almost 70% of females attaining resolution or improvement in the same time period. Although there were disparities between males and females, statistical significance was not achieved in any

category inter-or intra-gender dependent or independent of refractive error (tables 3.4.4.8 and 3.4.4.9).

	Males	Females	Combined
Myopes			
Mean	8.6	4.6	7.3
SD	10.7	5.5	9.3
Range	1-28	1-14	1-28
Emmetropes			
Mean	9.1	1.6	6.2
SD	10.2	0.9	8.7
Range	1-28	1-3	1-28
Hyperopes			
Mean	22.5	47.5	28.8
SD	33.6	60.1	38.2
Range	1-90	5-90	1-90

Table 3.4.4.7 Mean duration of symptoms subcategorised according to refractive error and gender

	Males	Females	Combined
Myopes vs Hyperopes	0.37	0.50	0.16
Myopes vs Emmetropes	0.92	0.29	0.76
Hyperopes vs Emmetropes	0.38	0.48	0.14

Table 3.4.4.8 Results of unpaired 2-tailed t-tests for refractive error and symptom duration

	p-value
Myopes	0.36
Emmetropes	0.08
Hyperopes	0.66
Total	0.83

Table 3.4.4.9 Results of unpaired 2-tailed t-tests for refractive error between males and females for symptom duration

In order to appreciate the findings in greater detail the subjects with retinal breaks were further sub-divided into those requiring treatment and not requiring treatment. Remarkably in both males and females there was an equal distribution of each harbouring retinal breaks in each category for treatment or otherwise.

3.4.4.2 Eyes with retinal breaks not treated

Of the fifty patients with retinal breaks, it was not clinically necessary to treat 25 of these patients according to clinical guidelines as there was no subretinal fluid. Table 3.4.4.2.1 contains the demographical details of these retinal breaks.

	Total 25	**Male 14**	**Female 11**
Age			
Mean (SD)	57.9 (15.6)	61.7 (13.1)	53.0 (17.8)
Range	22-81	24-81	22-69
Refractive error			
Emmetropia	9 (36%)	4 (28%)	5 (45%)
Hyperopia	8 (32%)	5 (36%)	3 (27%)
Myopia	8 (32%)	5 (36%)	3 (27%)
Laterality			
Bilateral	5 (20%)	3 (21%)	2 (18%)
Left	8 (32%)	4 (29%)	4 (36%)
Right	12 (48%)	7 (50%)	5 (45%)
Source of referral			
GP	0	0	0
Community optician	7 (28%)	3 (21%)	4 (36%)
HES clinic	2 (8%)	1 (7%)	1 (9%)
Self referral	16 (64%)	10 (71%)	6 (54%)
Symptoms			
Floaters alone	7 (28%)	6 (43%)	1 (9%)
Photopsia alone	0	0	0
Floaters and photopsia	17 (68%)	8 (57%)	9 (82%)
Floaters/photopsia & reduced vision	0	0	0
Asymptomatic	1 (4%)	0	1 (9%)
Duration of symptoms (days)			
Mean (SD)	15.1 (19.4)	19.5 (23.1)	3.6 (4.1)
1-7	8 (33%)	4 (29%)	4 (36%)
8-14	4 (17%)	4 (29%)	0
15-21	2 (8%)	1 (7%)	1 (9%)
22-28	3 (13%)	3 (21%)	0
>28	1 (4%)	1 (7%)	0
Not documented	6 (25%)	1 (7%)	5 (45%)
Method of initial examination			
3 mirror	1 (4%)	1 (7%)	0
Indentation	11 (44%)	8 (57%)	3 (27%)
Both	0	0	0
Neither	9 (36%)	4 (29%)	5 (46%)
Not documented	4 (16%)	1 (7%)	3 (27%)
Time until follow-up (days)			
Mean (SD)	41.2 (18.4)	35.4 (12.1)	36.8 (22.8)
Range	16-92	16-54	31-92
Change in symptoms from presentation to follow-up			
Floaters at initial examination	**24 (92%)**	**14 (100%)**	**10 (91%)**
Resolved	2 (8%)	0	2 (20%)
Improved	12 (50%)	8 (57%)	4 (40%)
Stable	10 (42%)	6 (43%)	4 (40%)
Worse	0	0	0
Photopsia at initial examination	**17 (68%)**	**8 (57%)**	**9 (82%)**
Resolved	8 (47%)	3 (38%)	5 (56%)
Improved	6 (35%)	5 (62%)	1 (11%)

Stable	3 (18%)	0	3 (33%)
Worse	0	0	0

Table 3.4.4.2.1 Characteristics of eyes with retinal breaks not requiring treatment

Of these 30 breaks, only 8 were originally identified at the first assessment (27%). Six of these breaks were examined with indentation at the first assessment, the remaining two were identified by slit-lamp fundoscopy. Therefore an additional 22 breaks were identified when re-examined in the PVD clinic. These details are compiled in table 3.4.4.2.2

	Configuration of retinal break		
Identified at 1st examination	Round	Horseshoe	Operculated
Y	5	0	3
N	10	3	9
Total	15	3	12

Table 3.4.4.2.2 Cross tabulation of the breaks identified at the first visit and those identified in the PVD clinic

Interestingly 50% of breaks identified were flat round holes, 6 of the 15 were located within areas of lattice degeneration. Although there were 3 horseshoe breaks, treatment was not delivered as they were small, flat and the patients decided against treatment after discussion of the risks and benefits.

At the first assessment, pigment was recorded to be absent from the anterior vitreous of all 30 eyes. When examined in the PVD clinic only two of these eyes exhibited pigment in the anterior vitreous, the sensitivity of this test was therefore 7%. Although, limiting this to operculated and horseshoe breaks increases the sensitivity to 13% this remained a poor indicator for the presence of retinal breaks.

	Configuration of retinal break		
Presence of TD	Round	Horseshoe	Operculated
Y	0	0	2
N	15	3	10
Total	15	3	12

Table 3.4.4.2.3 Cross tabulation of retinal break configuration against the presence or otherwise of pigment in the anterior vitreous

	Myope	Emmetrope	Hyperope
Male			
Mean	60.6	62.3	60.2
SD	6.2	20.1	3.6
Range	55-73	24-81	57-66
Female			
Mean	51.3	49	45
SD	15.0	20.5	26.6
Range	34-60	23-68	22-69
Total			
Mean	60.1	50.0	56.8
SD	11.3	18.8	18.7
Range	34-73	23-81	22-69

Table 3.4.4.2.4 The age profile of patients according to refractive status

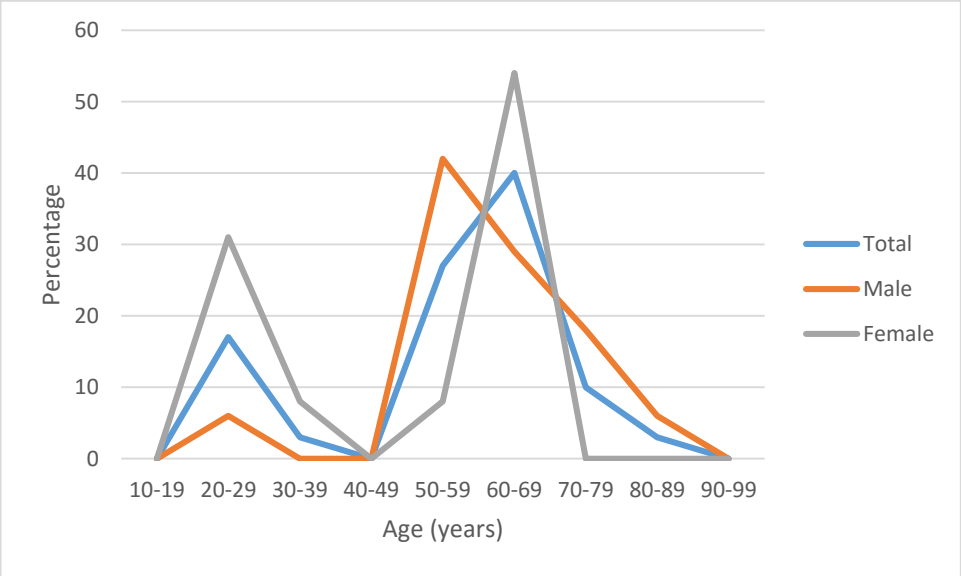

Fig 3.4.4.2.1 The age distribution of patients with retinal breaks that were not treated

Although the distribution was less regular in females, the seventh decade was still the most frequently involved with over 50% of affected females in this age group, of note almost one-third were in the third decade of life (fig 3.4.4.2.1). In males however, the sixth decade was most frequently involved, with the combined majority in older age categories.

Symptoms

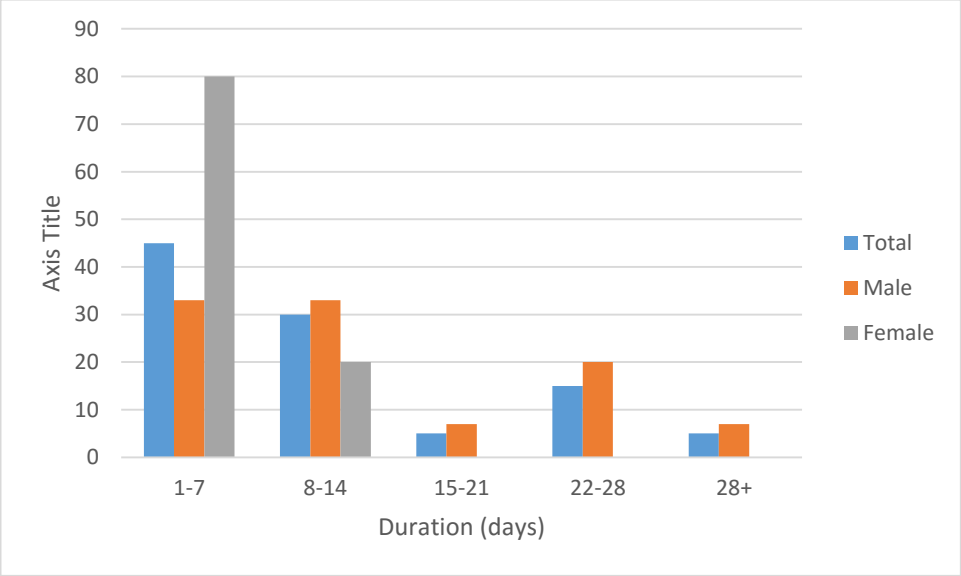

Fig 3.4.4.2.2 Duration of symptoms in patients prior to examination in eye casualty for eyes with retinal breaks that did not necessitate treatment

Interestingly in females 100% had symptoms for two weeks or less, with 80% experiencing symptoms for 7 days or less prior to attending eye casualty. This is in comparison to males in which around one-third had symptoms for 7 days or less and a further third for between one and two weeks (fig 3.4.4.2.2).

Location	**All**	**Males (HS/O/R)**	**Females (HS/O/R)**
Superior	3 (10%)	(0/0/0)	(0/0/3)
Supero-temporal	5 (17%)	(0/2/1)	(0/2/0)
Temporal	7 (23%)	(2/4/0)	(0/0/1)
Infero-temporal	5 (17%)	(0/2/2)	(0/1/0)
Inferior	8 (27%)	(0/0/3)	(0/0/5)
Infero-nasal	1(3%)	(1/0/0)	(0/0/0)
Nasal	0	(0/0/0)	(0/0/0)
Supero-nasal	1 (3%)	(0/0/0)	(0/1/0)
Total	**30**	**17**	**13**

Table 3.4.4.2.5 Distribution of retinal breaks according to location, gender and configuration

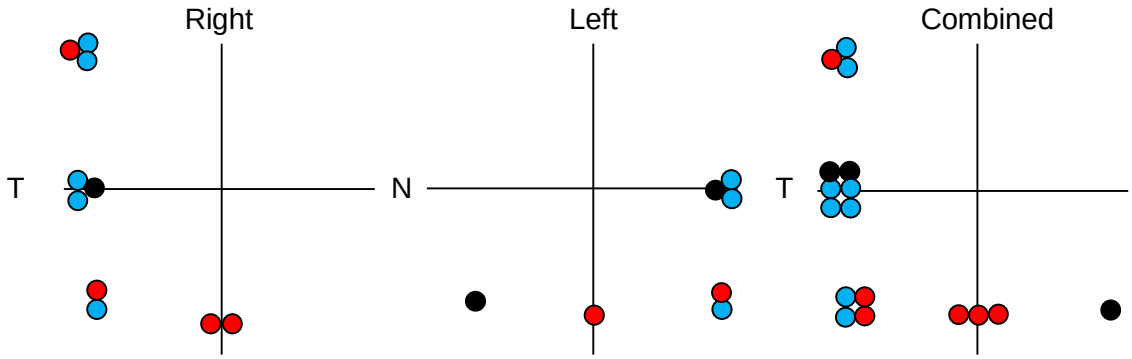

Fig 3.4.4.2.3 Diagrams to represent retinal breaks in males that did not require treatment according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

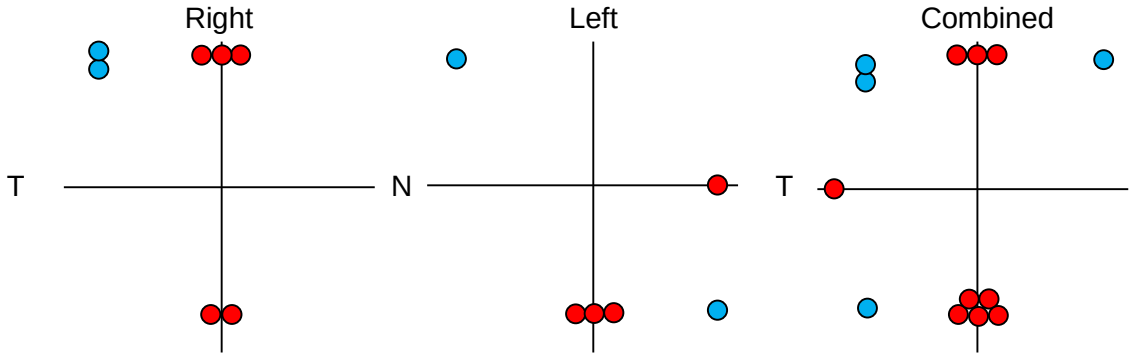

Fig 3.4.4.2.4 Diagrams to represent retinal breaks that did not require treatment in females according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

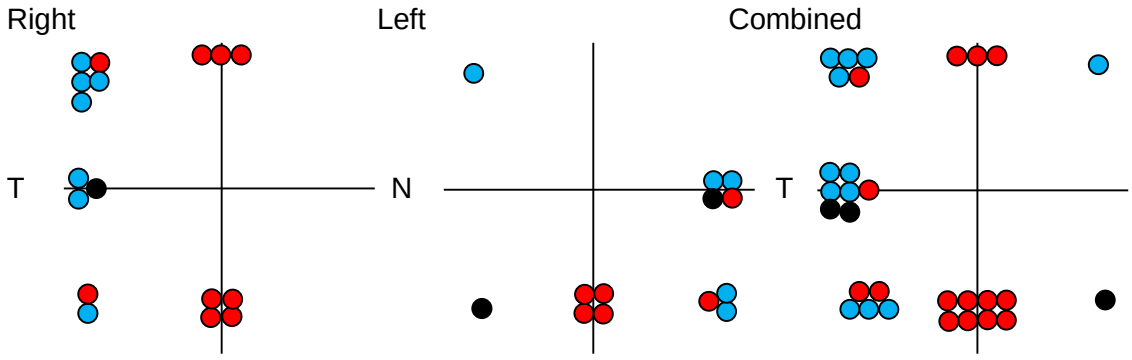

Fig 3.4.4.2.5 Diagrams to represent retinal breaks that did not require treatment according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

When reviewed in the PVD clinic, examination with indentation identified all 30 breaks, whereas examination with slit-lamp fundoscopy identified 26 of the 30 breaks, and examination with 3-mirror identified 27 of the 30 breaks; a sensitivity of 87% and 90% respectively.

3.4.4.3 Eyes with retinal breaks requiring treatment

	Total 25	Male 14	Female 11
Age			
Mean (SD)	62.2 (15.1)	65.8 (11.4)	57.7 (18.5)
Range	17-87	44-85	17-87
Refractive error			
Emmetropia	10 (40%)	5 (36%)	5 (45%)
Hyperopia	4 (16%)	2 (14%)	2 (18%)
Myopia	11 (44%)	7 (50%)	4 (36%)
Laterality			
Bilateral	1 (4%)	0	1 (9%)
Left	10 (40%)	5 (36%)	5 (45%)
Right	14 (56%)	9 (44%)	5 (45%)
Source of referral			
GP	0	0	0
Community optician	6 (24%)	4 (29%)	2 (18%)
HES clinic	3 (12%)	2 (14%)	1 (9%)
Self referral	16 (64%)	8 (57%)	8 (73%)
Symptoms			
Floaters alone	12 (48%)	5 (36%)	7 (64%)
Photopsia alone	0	0	0
Floaters and photopsia	8 (32%)	4 (28%)	4 (36%)
Floaters/photopsia/reduced vision	0	0	0
Asymptomatic	5 (20%)	5 (36%)	0
Duration of symptoms (days)			
Mean (SD)	8.3 (17.8)	2.7 (2.3)	15.4 (32.9)
1-7	15 (60%)	9 (64%)	6 (55%)
8-14	0	0	0
15-21	0	0	0
22-28	0	0	0
>28	1 (4%)	0	1 (9%)
Not documented	9 (36%)	5 (36%)	4 (36%)
Method of initial examination			
3 mirror	1 (4%)	1 (7%)	0
Indentation	12 (48%)	6 (43%)	6 (55%)
Both	0	0	0
Neither	2 (8%)	1 (7%)	1 (9%)
Not documented	10 (40%)	6 (43%)	4 (36%)
Time until follow-up (days)			
Mean (SD)	31.5 (10.4)	32.6 (10.0)	30.2 (11.4)
Range	4-50	22-50	4-46
Change in symptoms from presentation to follow-up			
Floaters at initial examination	**20 (80%)**	**9 (64%)**	**11 (100%)**
Resolved	1 (5%)	0	1 (9%)
Improved	10 (50%)	5 (56%)	5 (45%)
Stable	7 (35%)	2 (22%)	5 (45%)
Worse	3*(15%)	3* (33)	0
Photopsia at initial examination	**9 (36%)**	**5 (36%)**	**4 (36%)**
Resolved	2 (22%)	1 (20%)	1 (25%)

Improved	4 (44%)	3 (60%)	1 (25%)
Stable	3 (33%)	1 (20%)	2 (50%)

*1 eye with photopsia initially went on to develop floaters

Table 3.4.4.3.1 Characteristics of eyes with retinal breaks requiring treatment

There were a total of 26 breaks requiring intervention, as all had associated subretinal fluid. None of these breaks were identified at the initial visit, furthermore none of these eyes that developed breaks exhibited pigment in the anterior vitreous at the time. When reviewed in the PVD clinics, only thirteen of these eyes were noted to have pigment in the anterior vitreous, a sensitivity of 50% (table 3.4.3.2). However limiting this to horseshoe and operculated breaks improves the sensitivity to 68%.

	Configuration of retinal break		
Presence of TD	Round	Horseshoe	Operculated
Y	0	10	3
N	7	3	3
Total	7	13	6

Table 3.4.4.3.2 Cross tabulation of retinal break configuration against the presence or otherwise of pigment in the anterior vitreous

	Myope	**Emmetrope**	**Hyperope**
Male			
Mean	63.7	69.2	64.5
SD	9.6	6.9	29.0
Range	48-77	61-77	44-85
Female			
Mean	56.8	49.8	63
SD	15.2	28.1	2.83
Range	37-71	17-87	61-65
Total			
Mean	61.2	58.6	63.8
SD	11.7	22.7	16.8
Range	37-77	17-87	44-85

Table 3.4.4.3.3 The age profile of patients according to refractive status

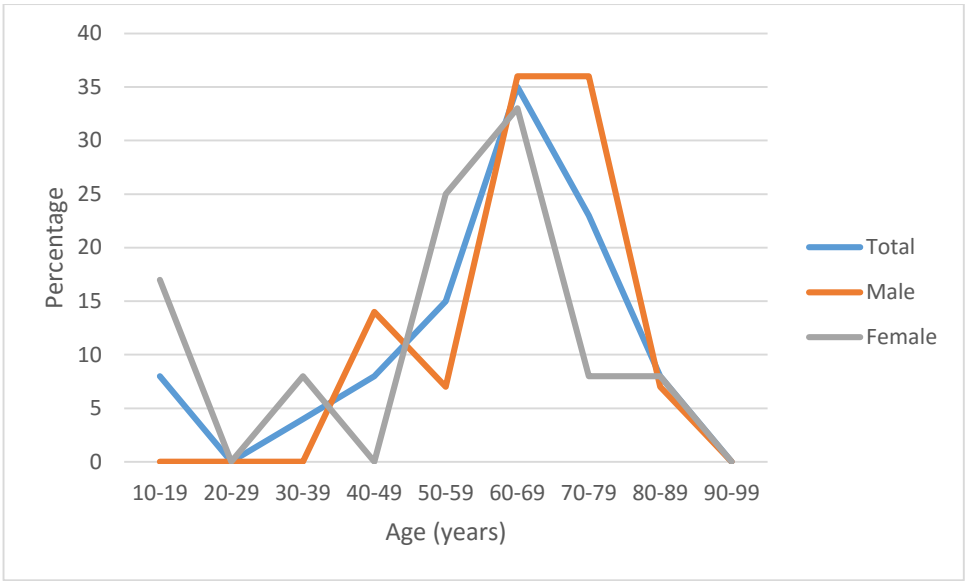

Fig 3.4.4.3.1 The age distribution of patients with retinal breaks that were treated

In males patients the seventh and eighth decade were equally affected and in combination contained almost three-quarters of patients in this category. Contrastingly in females one-third of patients were in the seventh decade and a further quarter in the sixth (fig 3.4.4.3.1)

Symptoms

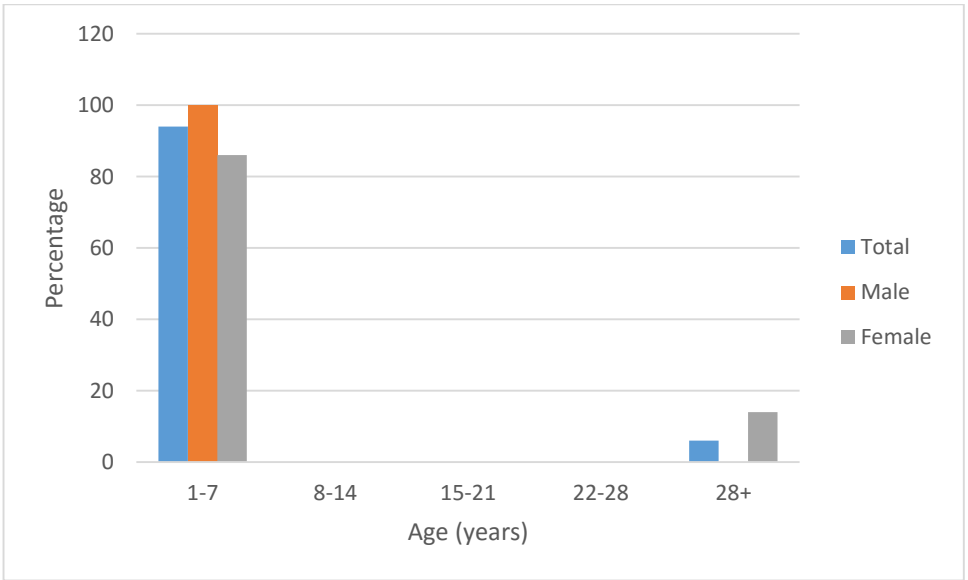

Fig 3.4.4.3.2 Duration of symptoms in patients prior to attending eye casualty in eyes with retinal breaks requiring treatment

In this category, strikingly all males and the significant majority of females with retinal breaks requiring treatment in the PVD clinic had symptoms for seven days or less prior to their initial presentation in eye casualty.

Location	All	Males (HS/O/R)	Females (HS/O/R)
Superior	6 (23%)	(1/0/0)	(1/1/3)
Supero-temporal	11 (42%)	(4/2/2)	(0/2/1)
Temporal	2 (8%)	(0/0/0)	(1/1/0)
Infero-temporal	1 (4%)	(0/1/0)	(0/0/0)
Inferior	4 (15%)	(3/0/0)	(1/0/0)
Infero-nasal	0	(0/0/0)	(0/0/0)
Nasal	1 (4%)	(0/1/0)	(0/0/0)
Supero-nasal	1 (4%)	(0/0/0)	(0/1/0)
Total	**26**	**14**	**12**

Table 3.4.4.3.4 Distribution of retinal breaks according to location, gender and configuration

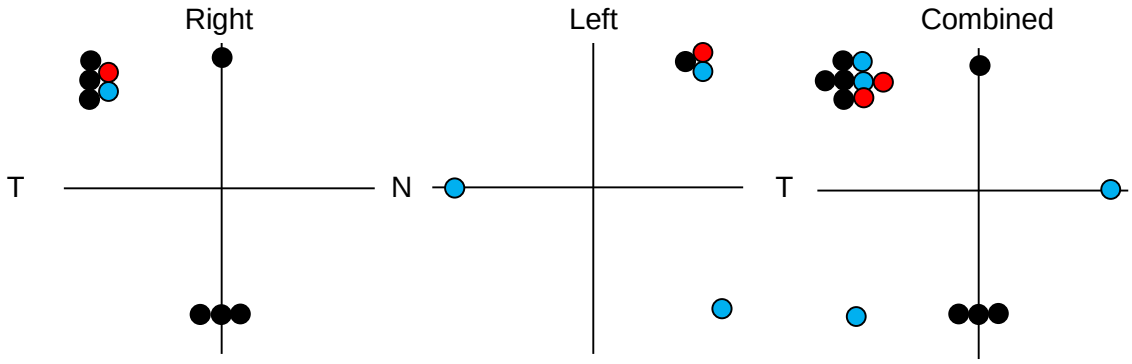

Fig 3.4.4.3.3 Diagrams to represent retinal breaks in males that were treated according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

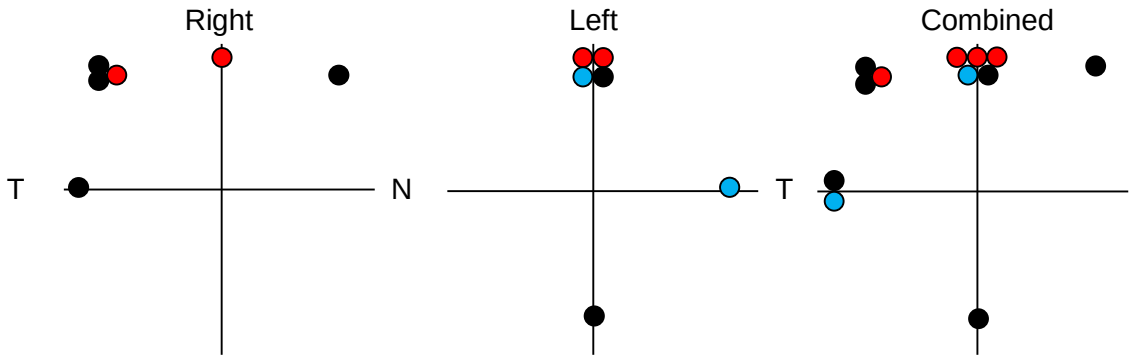

Fig 3.4.4.3.4 Diagrams to represent retinal breaks that were treated in females according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

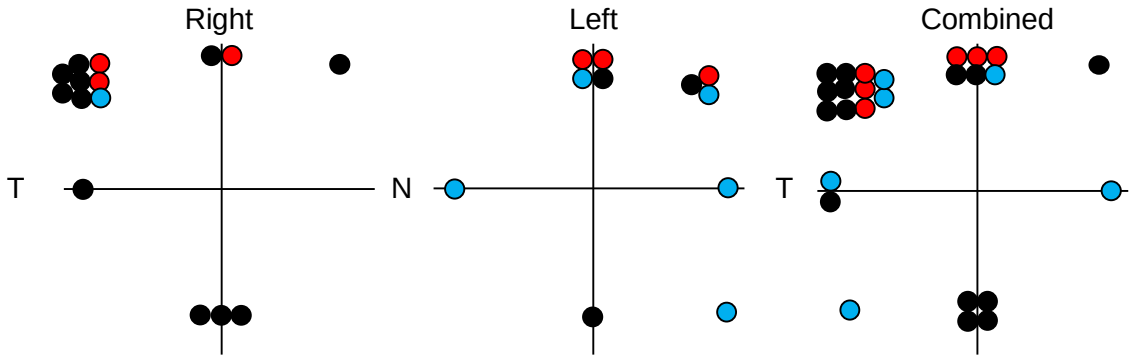

Fig 3.4.4.3.5 Diagrams to represent retinal breaks that were treated according to type and location. The left hand diagram represents the retinal breaks according to quadrantic distribution in the right eye, centre diagram left eye. The right diagram exhibits the distribution according to quadrantic location of both eyes

Key: Horseshoe● Operculated● Round●

When reviewed in the PVD clinic, examination with indentation identified all 26 breaks, whereas examination with slit-lamp fundoscopy identified 22 of the 26 breaks, and examination with 3-mirror identified 23 of the 26 breaks; a sensitivity of 85% and 87% respectively. Of all the eyes with retinal breaks only one had progressed to retinal detachment. This patient presented to the eye casualty with floaters and was documented to be pseudophakic with recent onset PVD following examination with slit-lamp fundoscopy with a condensing lens followed by examination with the BIO and scleral indentation. When re-examined in the PVD clinic, this patient had improvement in symptoms and did not develop any additional symptoms. An inferior macula-on retinal detachment was noted, the visual acuity at this point was recorded as 6/5. As expected the patient was scheduled for prompt surgical repair.

3.5 Comparison of treated and untreated breaks

The characteristics of eyes that were treated were compared with eyes that were not treated. Firstly with respect age, eyes that underwent treatment were almost 5 years older than eyes that were not treated (tables 3.4.4.2.1 and 3.4.4.3.1), however this was not found to be statistically significant (p=0.28). This trait was similar in both males and females also, the mean age was 4.1 and 4.7 years respectively greater in eyes that were treated, but again not statistically significant (p=0.78 for males and 0.47 for females)

A further analysis of age and refractive error between the treated and untreated group (tables 3.4.4.2.4 and 3.4.4.4.3) confirmed the notion across all refractive states treated eyes were older than eyes not requiring treatment. Nevertheless this was not found to be a statistically significant finding in the female subgroup (tables 3.5.3). Hyperopic males that did not require were 9 years younger than emmetropic male eyes that were treated and this was the only finding with statistical significance (table 3.5.2). Collectively, there was no statistically significant difference in the age of eyes that were treated compared to eyes that were not treated across the three refractive states (table 3.5.4)

		Treated breaks		
		Myopes	Emmetropes	Hyperopes
Not treated Breaks	Myopes	0.51	0.07	0.88
	Emmetropes	0.88	0.46	0.93
	Hyperopes	0.39	0.04	0.87

Table 3.5.2 Cross-tabulation of the p-value of 2-tailed t-tests for males comparing age for the three refractive states and whether treatment was performed

		Treated breaks		
		Myopes	Emmetropes	Hyperopes
Not treated Breaks	Myopes	0.66	0.92	0.31
	Emmetropes	0.51	0.95	0.16
	Hyperopes	0.48	0.79	0.27

Table 3.5.3 Cross-tabulation of the p-value of 2-tailed t-tests for females comparing age for the three refractive states and whether treatment was performed

		Treated breaks		
		Myopes	Emmetropes	Hyperopes
Not treated Breaks	Myopes	0.44	0.85	0.51
	Emmetropes	0.44	0.75	0.46
	Hyperopes	0.30	0.61	0.38

Table 3.5.4 Cross-tabulation of the p-value of 2-tailed t-tests comparing age for the three refractive states and whether treatment was performed

A similar analysis for the duration of symptoms revealed males that were not treated had symptoms for 16.8 days longer than eyes that harboured breaks necessitating treatment, a

statistically significant finding (p=0.02). This was in contrary to the females, in which eyes requiring treatment had symptoms for 11.8 days longer than eyes not treated, but not statistically significant (p=0.39). Collectively for males and females, eyes requiring treatment presented to the eye casualty almost 7 days prior to eyes not treated, but this was not statistically significant (p=0.39).

3.6 Analysis of results

A multivariate analysis of refractive error, mean age and gender between four categories of patients was undertaken. The p-value of 2-tailed t-tests are presented in table 3.6.1 and discussed below.

Age

The mean age of patients with in category 3.4.1 was approximately 5 years greater than all other eyes; 65.8 years compared to 60.1-61.4 years and this was statistically significant for eyes with retinal breaks (p=0.004) and for those in category 3.2 (p=0.002), however this was not quite statistically significant for eyes with other conditions requiring further intervention in category 3.4.3 (p=0.06). There was no statistically significant difference in age between categories 3.4.2, 3.4.3 and 3.4.4.1.

Fig 3.6.1 A box and whisker plot of the each category according to gender and age. There were a total of 54 outliers, with the following points referring to the same patients;
1 and 1108; 2 and 1109; 3 and 1110; 4 and 1111; 5 and 1112;
7 and 1114; 8 and 1115; 585 and 1692; 586 and 1693; 587 and 1694;
588 and 1695; 589 and 1696; 593 and 1700; 596 and 1703; 599 and 1706;
612 and 1719; 613 and 1720; 614 and 1721; 615 and 1722; 645 and 1752;
646 and 1753; 647 and 1754; 648 and 1755; 649 and 1756; 744 and 1851;
745 and 1852; 746 and 1853; 748 and 1855; 749 and 1856; 1005 and 2112;
1010 and 2117; 1035 and 2142; 1036 and 2143

A subgroup analysis of the males revealed males in category 3.4.1 were eldest, followed by those in 3.4.2 then 3.4.4.1 and finally those in 3.4.3, mean age differences of 0.9, 2.2 and 4.1 years younger respectively. There was no statistically significant difference in the mean age of males studied across the four categories. A similar analysis of the females revealed females in category 3.4.1 were again eldest, followed by those in 3.4.3, then those in 3.4.2 and finally in 3.4.4.1, mean age differences of 4.1, 4.9 and 8.8 years younger respectively. The mean age difference between category 3.4.1 compared to categories 3.4.2 and 3.4.4.1 was statistically significant, it was not statistically significant for category 3.4.3. The smallest difference in age was between eyes in categories 3.4.2 and 3.4.3, of only 0.8 years and was not statistically significant. Finally for categories 3.4.2 and 3.4.3 compared to 3.4.4.1 the mean age difference did not quite reach statistical significance p=0.07 and 0.09 respectively.

Overall males were older than females across all four categories of patients studied. The largest difference between males and females was found in eyes with retinal breaks a mean age difference of 8.4 years followed by eyes in category 3.4.2 with a mean age difference of 5.8 years, these differences were found to be statistically significant p=0.001 and 0.003 respectively. Females in category 3.4.1 were 1.8 years young than their male counterparts and this again was statistically significant p=0.02. For category 3.4.3, the mean age difference between males and females was only 0.8 years and not statistically significant (p=0.86).

Refractive error

The distribution of refractive error varied between each of the categories studied, however overall the majority of patients were emmetropic in the order of 40%, myopes constituted approximately 35% with hyperopes being least in number at around 25%.

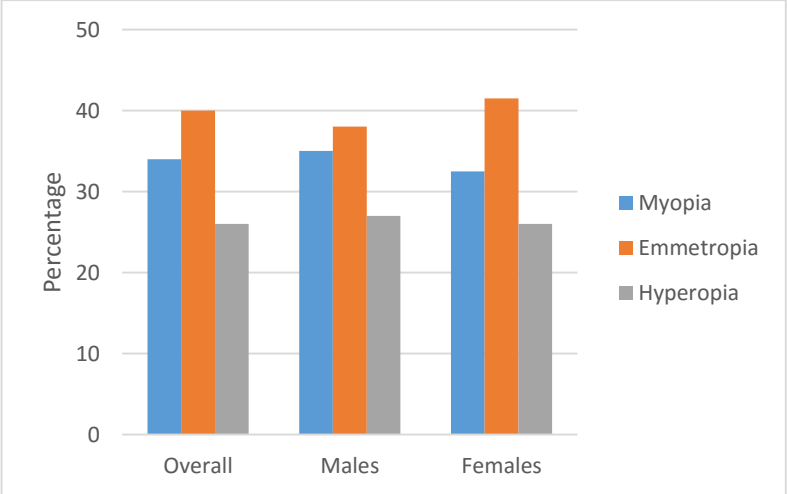

Fig 3.6.2 Refractive error distribution of all categories combined

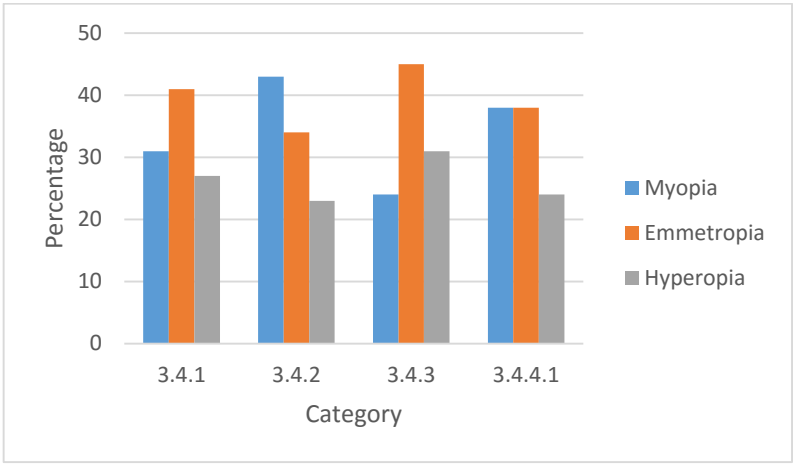

Fig 3.6.3 Refractive error distribution according to each category

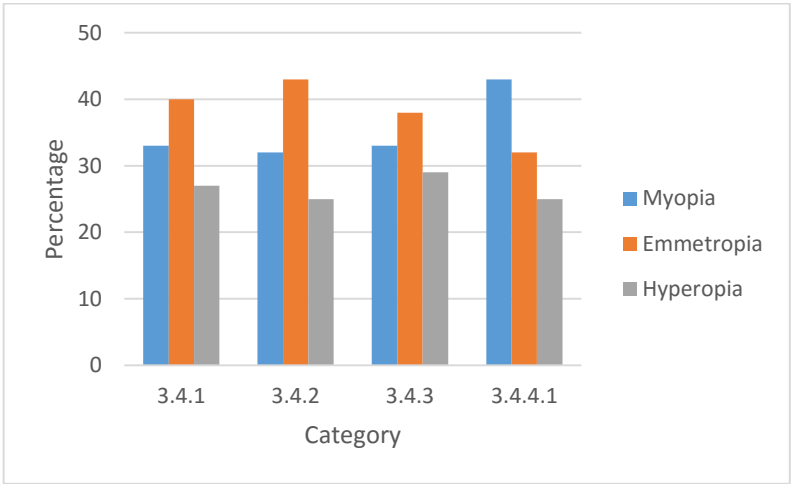

Fig 3.6.4 Refractive error distribution in males for each category

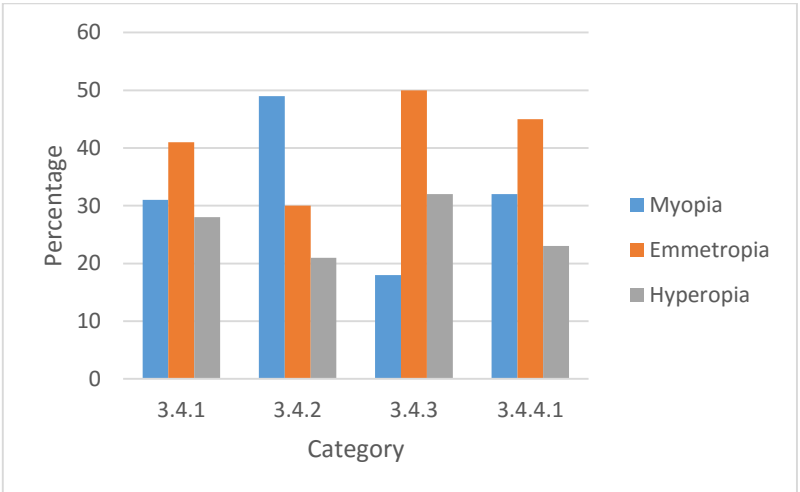

Fig 3.6.5 Refractive error distribution in females for each category

For males there was no statistically significant difference in age for any refractive state across the four categories or collectively. Conversely in females, patients with PVD alone were 4.9 and 8.8 years older than those in category 3.4.2 and 3.4.4.1 respectively, both of these were highly statistically significant. Specifically for the female myopes, eyes with PVD

were 6.8 years older than eyes in category 3.4.2 and this was a highly statistically significant observation.

	3.4.1 vs 3.4.2	3.4.1 vs 3.4.3	3.4.1 vs 3.4.4.1	3.4.2 vs 3.4.3	3.4.2 vs 3.4.4	3.4.3 vs 3.4.4.1
Male myopes	0.77	0.72	0.39	0.89	0.43	0.48
Male emmetropes	0.90	0.12	0.29	0.08	0.29	0.54
Male hyperopes	0.48	0.87	0.63	0.51	0.87	0.59
Males	0.67	0.16	0.41	0.24	0.62	0.48
Female myopes	0.0007	0.10	0.28	0.52	0.95	0.59
Female emmetropes	0.41	0.21	0.23	0.55	0.39	0.64
Female hyperope	0.76	0.85	0.26	0.92	0.28	0.36
Females	0.0004	0.18	0.004	0.82	0.07	0.09
Overall	0.002	0.06	0.004	0.68	0.59	0.92

Table 3.6.1 Results of 2-tailed unpaired t-tests evaluating mean age, gender and refractive between the different categories

To further refine the results categories 3.4.1 and 3.4.2 were combined to give an overall category (discharged) in which eyes did not require further evaluation, and those in 3.4.3 were combined with 3.4.4.1 to give an overall category (reviewed) in which further evaluation was deemed necessary. The age characteristics of these are shown in table 3.6.2 with reference to gender and refractive error. The p-values for t-tests to compare differences between the two groups are presented in table 3.6.3.

	Discharged	Reviewed
Male myopes		
Mean	62.1	61.7
SD	11.7	9.9
Range	26-80	33-77
Male emmetropes		
Mean	65.8	60.6
SD	8.4	17.3
Range	36-85	19-81
Male hyperopes		
Mean	69.9	65.2
SD	8.2	10.2
Range	43-92	44-85
Males		
Mean	65.6	62.3
SD	10.1	13.1
Range	26-92	19-85
Female myopes		
Mean	59.4	52.5
SD	10.1	13.3
Range	29-87	34-71
Female emmetropes		
Mean	63.6	54.7
SD	9.0	19.3
Range	22-92	17-87
Female hyperopes		
Mean	68.4	61.5
SD	7.5	33.1
Range	48-91	21-90
Females		
Mean	63.5	56.3
SD	9.7	19.1
Range	22-92	17-90
Overall		
Mean	64.2	59.1
SD	9.8	16.7
Range	22	17-90

Table 3.6.2 Age characteristics of eyes according to gender, refractive error and whether further assessment was deemed necessary in the PVD clinic

	Discharged vs Reviewed
Male myopes	0.85
Male emmetropes	0.22
Male hyperopes	0.13
Males	0.07
Female myopes	0.09
Female emmetropes	0.02
Female hyperope	0.22
Females	0.005
Overall	0.002

Table 3.6.3 Results of t-tests comparing the age in males and females together according to refractive error for the two groups

Collectively, the discharged group was 5.1 years older than the reviewed group and this was statistically significant. For the female population alone, the discharged group were 7.2 years older than the reviewed group and noted to be statistically significant. There was no statistically significant difference in the female hyperopes between the two groups, and the difference of 6.9 years in the myopic females did not quite reach statistical significance. However in the emmetropic females, the difference of 8.9 years between the two groups was statistically significant. In the male population, the discharged group were 3.3 years older than the reviewed group however this did not attain statistical significance.

Laterality

Similar to refractive error there was some degree of variability with regard to laterality. Collectively for all categories (3.4.1-3.4.4.1), the right eye appeared to be most often affected in 39% of cases, the left in 32% and bilateral involvement in 28% (fig 3.6.6 and 3.6.7). A similar pattern was observed in females; in 39% the right eye alone was affected, 32% with left eye involvement and 29% with bilateral involvement (fig 3.6.9). In males however, those with involvement of the right eye alone and bilateral involvement were identical 35%, 5% fewer of left eyes were affected (fig 3.6.8).

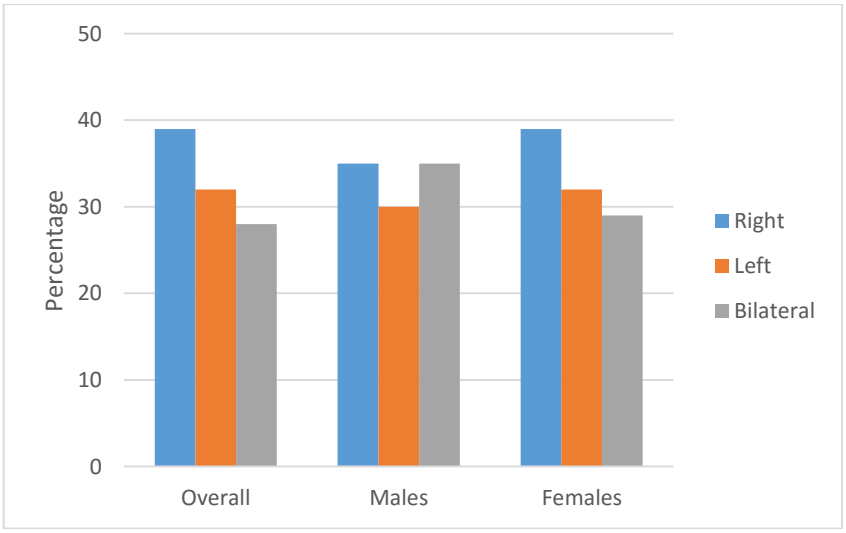

Fig 3.6.6 Affected eyes according to laterality across all categories

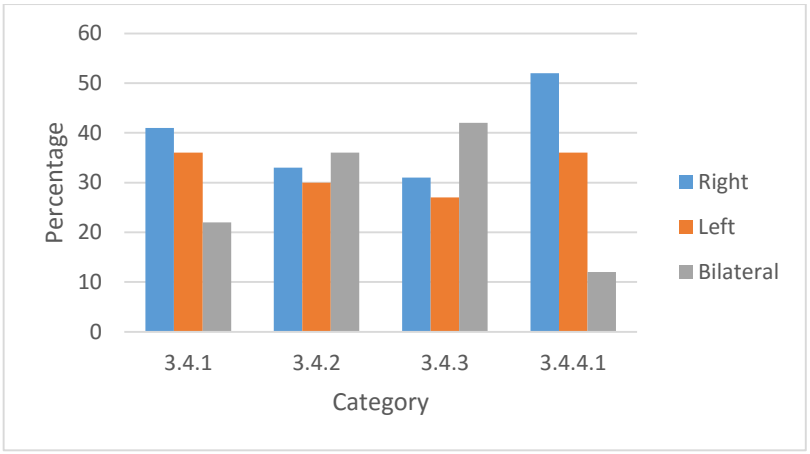

Fig 3.6.7 Affected eyes according to laterality across each category

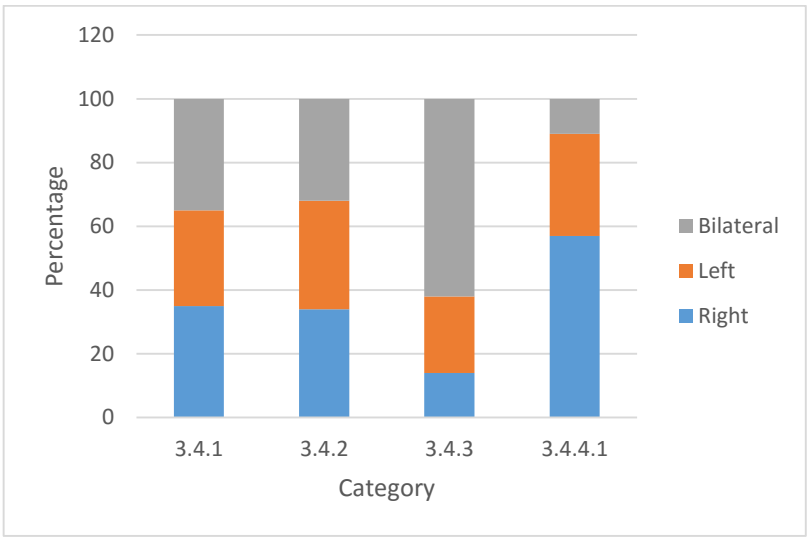

Fig 3.6.8 Affected eyes in males according to laterality across each category

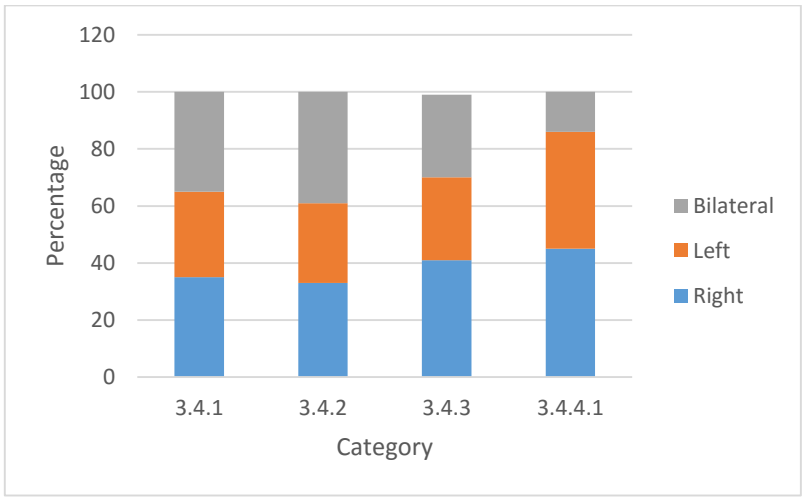

Fig 3.6.9 Affected eyes in females according to laterality across each category

Referral source

The overwhelming majority of patients presented without referral to the eye casualty (fig 3.6.10). Collectively for males and females in those that were not treated 70% were self-presentation, whereas in patients that required further evaluation this figure was marginally less at 62-64%. For the male subgroup, self-referrals accounted for 66-70% of the groups not treated, and for 43-64% of the groups requiring treatment. Similarly in the females, self-referrals accounted for 71% of those not treated, whereas this figure was in the order 64-74% for the patients requiring intervention. Overall between males and females there was no significant difference in the origin of referral except for those patients described in 3.4.3, males were 31% less likely to present of their own accord in comparison to females (fig 3.6.11 and 3.6.12).

Referrals initiated by community optometrists accounted for 19-26% of total referrals (fig 3.6.10). In males alone this figure was highest (33%) in patients described in 3.4.3 and lowest (17%) in eyes with PVD alone (fig 3.6.11). Conversely in females the lowest number of referrals by community optometrists was for those in 3.4.3 (12%), almost three times less than males (fig 3.6.12).

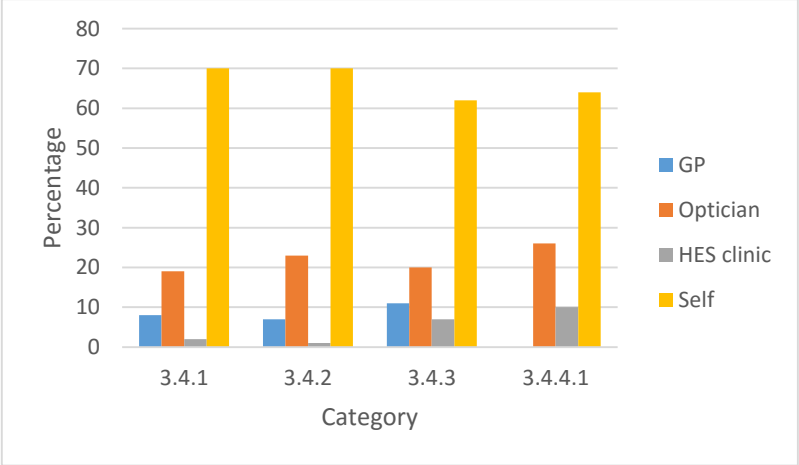

Fig 3.6.10 Source of referral for each category

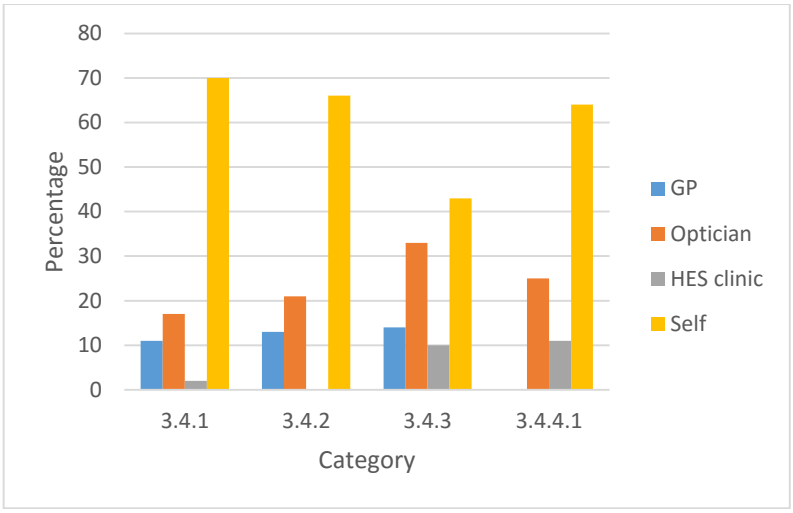

Fig 3.6.11 Source of referral for each category in males

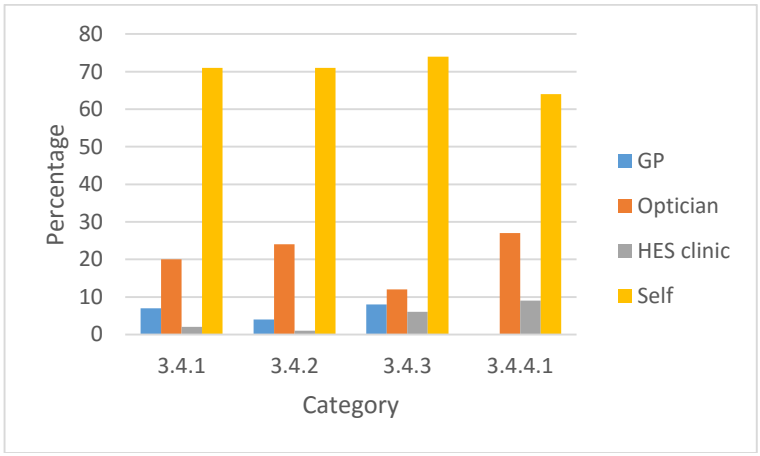

Fig 3.6.12 Source of referral for each category in females

Symptoms

The most common afflicting symptom was a combination of photopsia and floaters affecting over half (54%) of the sample, floaters in isolation were the next most common symptom in over one-third (35%), isolated photopsia occurred in a minority 6% (fig 3.6.13). Across the spectrum the findings were almost identical, however for males in category 3.4.3 the proportion of patients with photopsia and floaters was less than one-third (29%) whereas those with floaters alone represented over-half (57%) (fig 3.6.14, 3.6.15 and 3.6.16). This disproportion is likely to be attributable to the small number of patients in this category.

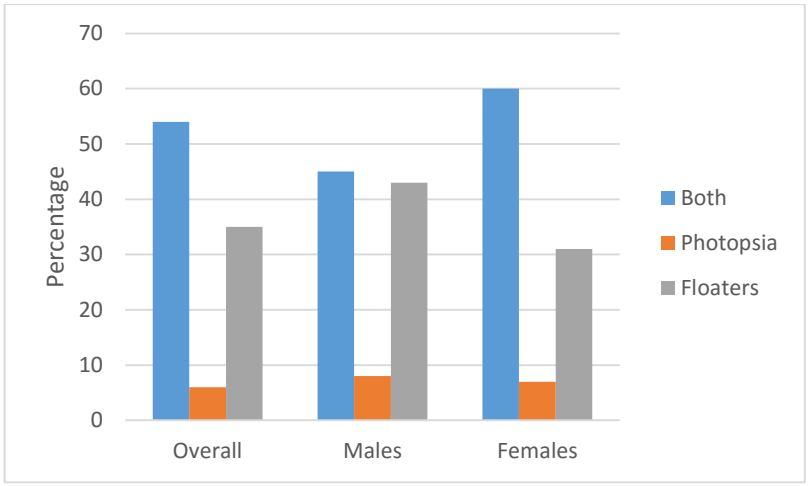

Fig 3.6.13 Nature of initial symptoms

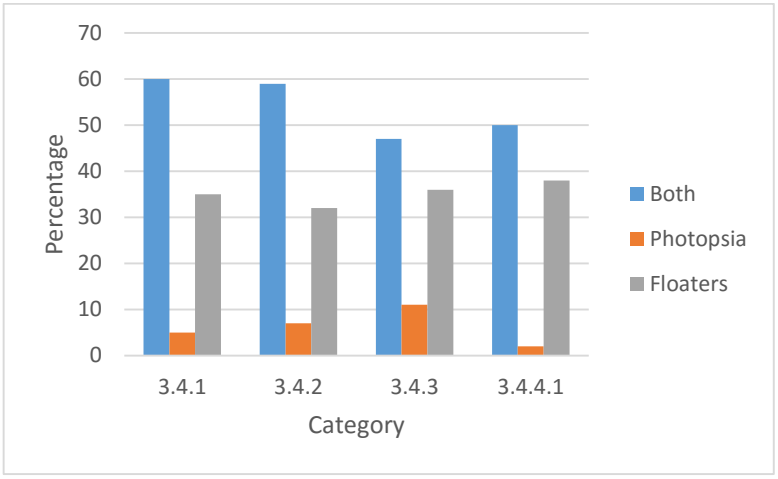

Fig 3.6.14 Nature of symptoms in each category

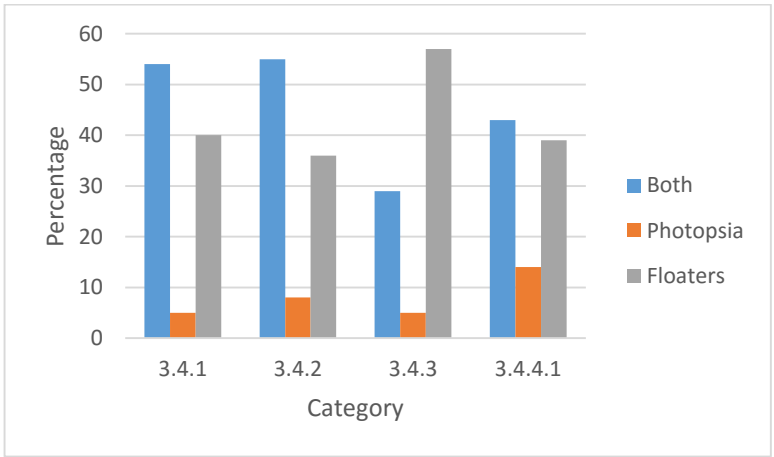

Fig 3.6.15 Nature of symptoms in each category in males

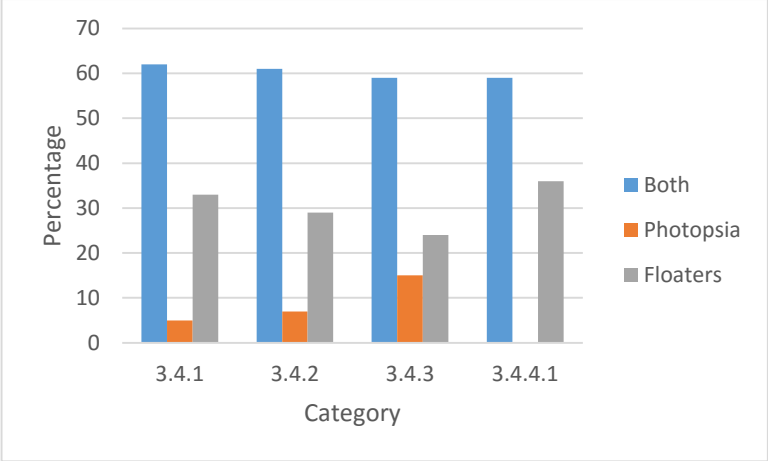

Fig 3.6.16 Nature of symptoms in each category in females

Duration of symptoms

From the onset of symptoms, 59% of patients presented to eye casualty within one week, and approximately three quarters presented within two weeks (fig 3.6.17). It was interesting to note in category 3.4.1 61% of patients had symptoms of seven days or less, for categories 3.4.2 and 3.4.4.1 this figure was less at 46%, for category 3.4.3 this further reduced to 31%. Unfortunately the duration of symptoms was not documented in the eye casualty records in 13% of cases. For eyes in category 3.4.1 documentation was missing in 11%, whereas this was significantly higher in the other categories 19-25%. This could potentially introduce bias and skew the results so these findings may not be totally representative.

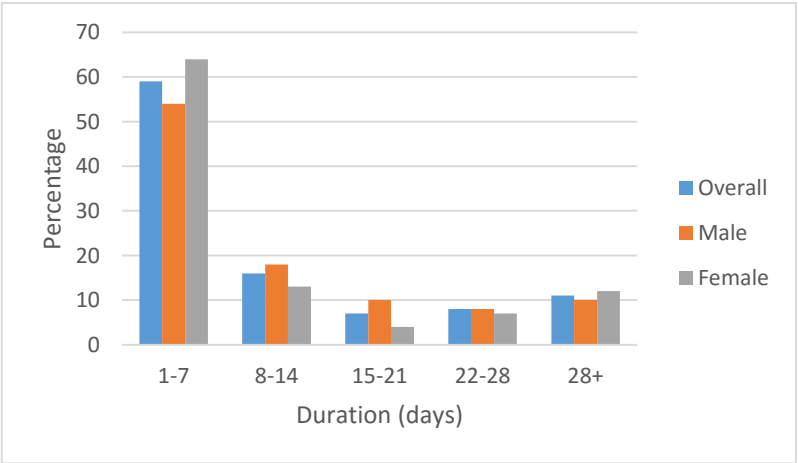

Fig 3.6.17 Duration of symptoms prior to examination in eye casualty for each gender and overall

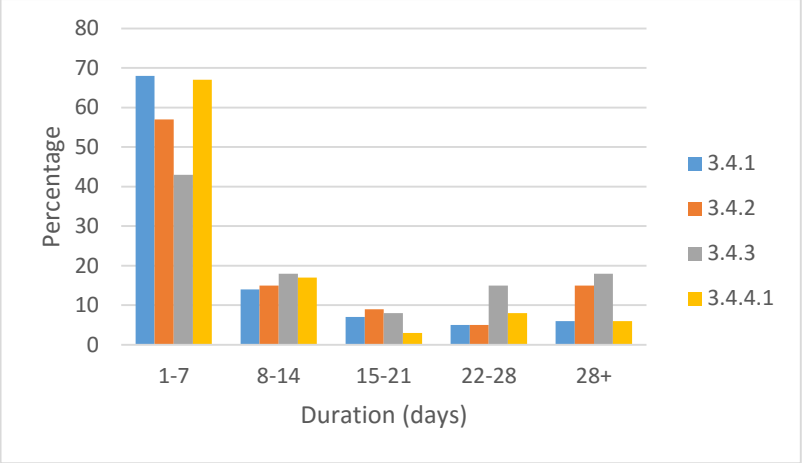

Fig 3.6.18 Duration of symptoms prior to examination in eye casualty for each category

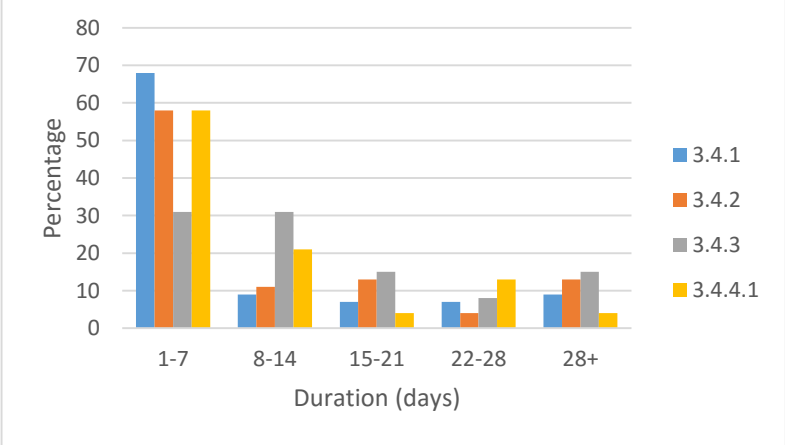

Fig 3.6.19 Duration of symptoms prior to examination in eye casualty for males for each category

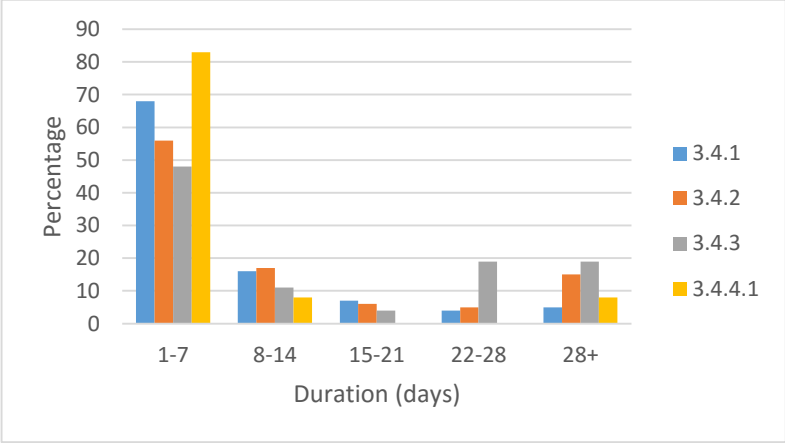

Fig 3.6.20 Duration of symptoms prior to examination in eye casualty in females for each category

For the patients with PVD alone the mean duration of symptoms prior to presenting in eye casualty was relatively similar across the four categories and (fig 3.6.15, 3.6.16, 3.6.17 and 3.6.18). The differences in duration of symptoms between the four categories were

compared with two-tailed unpaired t-tests to determine the significance of these results (table 3.6.4). The only statistically significant differences found were in the female population; eyes with retinal breaks had symptoms for half a day more than those with PVD alone and 3.5 days less than eyes in category 3.4.2. This is likely to be an erroneous result due the disproportion in the numbers in each group, and therefore this variance needs to be interpreted with caution.

	3.4.1 vs 3.4.2	**3.4.1 vs 3.4.3**	**3.4.1 vs 3.4.4.1**	**3.4.2 vs 3.4.3**	**3.4.2 vs 3.4.4.1**	**3.4.3 vs 3.4.4.1**
Male myopes	0.14	0.61	0.31	0.41	0.06	0.32
Male emmetropes	0.23	0.54	0.49	0.35	0.86	0.39
Male hyperopes	0.58	0.91	0.65	0.59	0.95	0.64
Males	0.28	0.43	0.78	0.92	0.30	0.40
Female myopes	0.25	0.32	0.13	0.36	0.04	0.26
Female emmetropes	0.27	0.21	<0.001	0.27	0.007	0.14
Female hyperopes	0.32	0.99	0.57	0.38	0.62	0.57
Females	0.06	0.10	<0.001	0.18	<0.001	0.15
Overall	0.03	0.07	0.86	0.20	0.34	0.10

Table 3.6.4 Results of 2-tailed unpaired t-tests evaluating duration of symptoms, gender and refractive between the different categories

	Discharged	Reviewed
Male myopes		
Mean	17.1	11.4
SD	25.8	12.6
Range	1-90	1-42
Male emmetropes		
Mean	11.1	12.9
SD	20.8	15.8
Range	1-180	1-56
Male hyperopes		
Mean	17.3	20
SD	22.5	27.4
Range	1-90	1-90
Males		
Mean	14.7	14.0
SD	23.2	18.0
Range	1-180	1-90
Female myopes		
Mean	10.1	22.9
SD	14.7	45.9
Range	1-100	1-150
Female emmetropes		
Mean	8.8	29.6
SD	12.5	73.1
Range	1-90	1-300
Female hyperopes		
Mean	13.8	19.5
SD	23.8	25.7
Range	1-180	3-90
Females		
Mean	10.5	23.1
SD	16.9	54.6
Range	1-180	1-300
Overall		
Mean	11.9	18.6
SD	19.4	40.7
Range	1-180	1-300

Table 3.6.5 Duration of symptoms according to gender, refractive error and whether further assessment was deemed necessary in the PVD clinic

The duration of symptoms was compared between the discharged and reviewed groups (table 3.6.5 and 3.6.6). Although there were differences between each category, statistical significance was not achieved in any category.

	Discharged vs Reviewed
Male myopes	0.18
Male emmetropes	0.71
Male hyperopes	0.78
Males	0.84
Female myopes	0.40
Female emmetropes	0.26
Female hyperope	0.50
Females	0.12
Overall	0.17

Table 3.6.6 Results of t-tests comparing the duration of symptoms in males and females together according to refractive error between eyes that were discharged and those further reviewed

Methods of examination

All patients were examined with slit-lamp fundoscopy at the initial examination and this was the only method of examination in 16% of the population studied. Adjunctive examination was performed in 50% of patients in the form of either scleral indentation in (47%) or 3-mirror contact lens (2%) or both methods (1%). It was not possible to determine the methods of adjunctive examination in 35% due to lack of documentation in the eye casualty notes (fig 3.6.21, 3.6.22, 3.6.23 and 3.6.24).

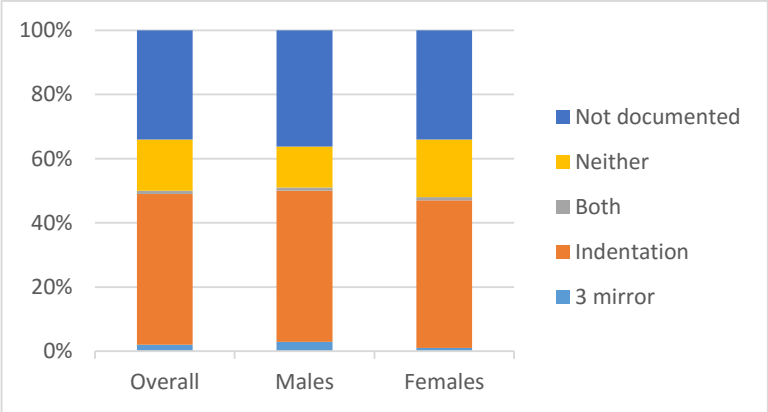

Fig 3.6.21 Examination techniques employed at the initial assessment

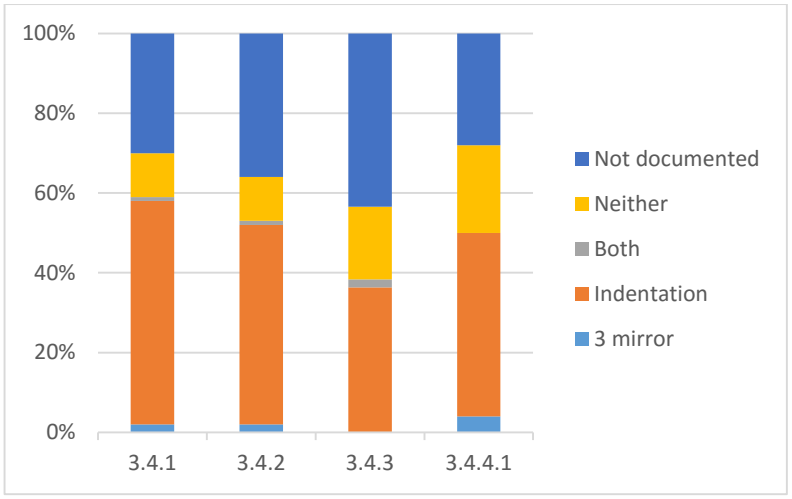

Fig 3.6.22 Examination techniques employed at the initial assessment in each category

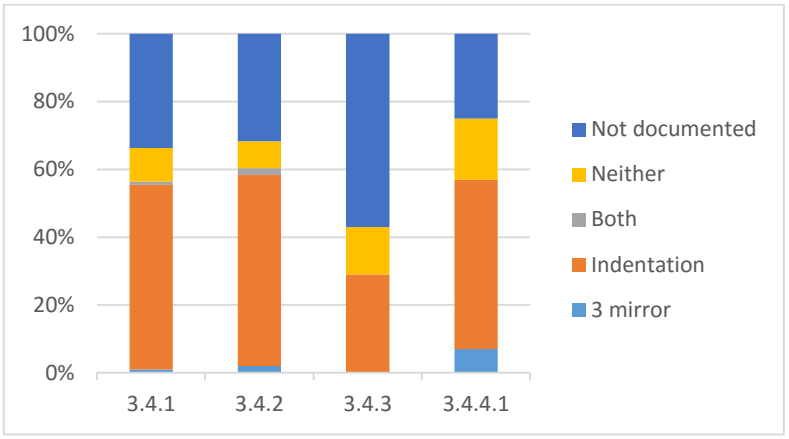

Fig 3.6.23 Examination techniques employed at the initial assessment in each category for males

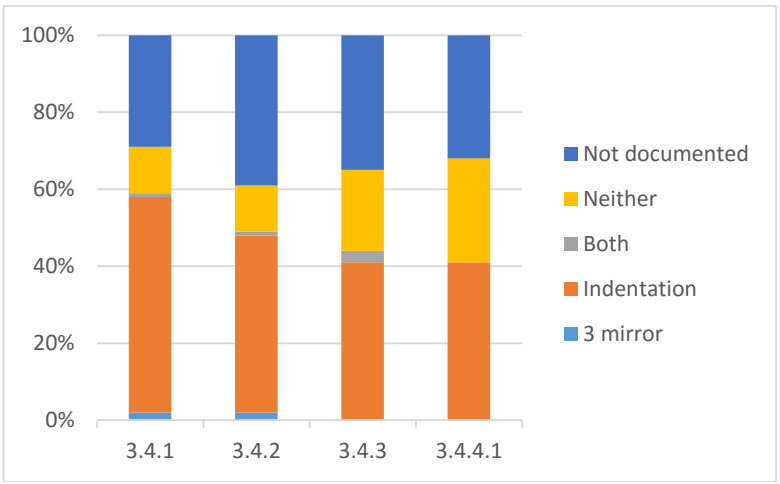

Fig 3.6.24 Examination techniques employed at the initial assessment in each category for females

Time until seen in PVD clinic

As envisaged the time until patients were seen in the PVD clinic was very similar across all categories, and any minor difference was not statistically significant (p= 0.36-0.86 across the categories). This was primarily due to the fact that all patients were assigned appointments according to the diagnosis made in eye casualty, which was essentially uncomplicated PVD. Although there were a significant proportion of eyes (19%) with other conditions identified (category 3.4.2), these conditions would not have warranted expediting the appointment for the outpatient clinic.

Change in symptoms

The discharged group (categories 3.4.1 and 3.4.2) were 10% more likely to improvement in floaters compared to the reviewed group (categories 3.4.3 and 3.4.4.1), 7% in both groups had resolution of floaters by the time they were reviewed in the PVD clinic. Importantly 7% of patients in the reviewed group had progression of floaters compared to less than 1% in the discharged group. Eight-seven percent of the discharged group had resolution or improvement in photopsia, this is in comparison to 78% of the reviewed group. Photopsia was likely to persist in 9% more of the reviewed group, notably there was no-one in the reviewed group with progression of photopsia. Males were overall more likely to have improvement in their symptoms compared to females (table 3.6.7) by the time they were seen in the PVD clinic however this was not statistically significant in any category.

Symptom improvement	**Category**	**Odds ratio (95% CI)**
Photopsia	3.4.1	1.16 (0.65 – 2.08), p=0.66
	3.4.2	1.09 (0.40 – 3.01) p= 1
	3.4.3	2.33 (0.24-23.04) p=0.65
	3.4.4.1	5.33 (0.51 – 56.24) p=0.32
Floaters	3.4.1	1.01 (0.74 – 1.38), p=0.94
	3.4.2	0.94 (0. 47 – 1.87), p=0.86
	3.4.3	0.89 (0.26 - 3.02), p=1
	3.4.4.1	1.22 (0.35 – 4.18) p=1

Table 3.6.7 A comparison of the improvement of symptoms in males compared to females for each category

Phakic status

Overall 14% of the eyes included were pseudophakic, for each category the percentage of pseudophakic eyes is represented in table 3.6.8.

	3.4.1	**3.4.2**	**3.4.3**	**3.4.4.1**
Male	11%	6%	24%	13%
Female	16%	6%	15%	12%
Total	14%	6%	18%	13%

Table 3.6.8 Percentage of pseudophakes in each category

Categories 3.4.1 and 3.4.4.1 had a similar distribution of phakic and pseudophakic patients, with category 3.4.2 containing the fewest pseudophakes. In females, with the exemption of category 3.4.2, all other categories had a similar percentage of pseudophakes. In males category 3.4.3 disparately contained the highest number of pseudophakes, however it must be borne in mind there were only a total of 21 males in this category. As result of the overall small number of pseudophakes a further subgroup analysis for refractive error or other variables was not undertaken.

3.7 Discussion

The literature suggests there is an incidence of retinal breaks of between 1.5-4.4% within the first few weeks after the onset of PVD, the current study found the incidence of delayed retinal breaks was 4.3%. One stark difference in the current study is eyes that exhibited retinal and/or vitreous haemorrhages at the initial examination were excluded as it is recognised these are more likely to harbour retinal breaks (Byer 1994; Hikichi & Trempe 1994; Dayan *et al.* 1996; Richardson *et al.* 1999; Sharma *et al.* 1999; van Overdam *et al.* 2001 and 2005; Williams *et al.* 2004; Schweitzer 2011). As the purpose of this study was to determine whether uncomplicated PVD required further review, patients with haemorrhage were excluded. Although this figure is higher than predicted, it may not necessarily be unexpected as from previous studies the general trend was the incidence of delayed breaks was proportional to the size of study in that larger studies found a greater incidence. Furthermore all patients in the PVD clinic had a complete retinal examination performed, whereas this was not the case in at least 10% of cases in whom fundoscopy was performed with one method only at the initial examination (in a further one-third there was no documentation of adjunctive examination). In addition to retinal breaks a further 178 patients (16.1%) had other pathology not documented at the initial presentation, therefore in total 226 (20.4%) patients had additional pathology of which 81 (7.3%) required intervention.

As expected the largest group of patients in this study had PVD without complications or additional pathology (76.9%). The total number of patients with PVD alone was 851 with a standard deviation of 8.7, for this sample a confidence level of 99% with a 1% margin of error a sample size of 502 patients would be required. Therefore this sample of 851 patients was sufficiently powered with respect to comment upon the age of onset of PVD. To evaluate whether there was a difference in the age of onset between males and females, the sample size was calculated as 420 in each group with a standard deviation of 9.3 (as found in the male population with PVD) for a confidence level of 95% with a power of 80%. Expectedly the male population was smallest and for a mean difference in age of 1.8 years found between males and females by this study a confidence level of 90% with a power 70% was achieved.

Age

The age of onset of PVD of eyes in category 3.4.1 was found to be approximately 65 years of age. For myopic eyes in this current study the mean age was found to be 59.7 and for non-myopic eyes to be 66.2 years. This is comparable to the findings of Byer (1994) who reported the mean age to be 56.1 in myopic eyes and 62.5 years for other refractive errors

pooled together. Although these figures are approximately 3.5 years greater than those reported by Byer (1994), interestingly the difference in the mean age between myopic and non-myopic subgroups was almost identical, and both found this mean age difference to be statistically significant. The mean age in the current study was approximately 5 years greater than the figure reported by Yonemoto *et al.* (1994) however the distribution of refractive error between the two studies is vastly different. In the former study approximately 2% were hypermetropic unlike the current study in which over one-quarter were hypermetropic.

The studies by Gutteridge (1993) and Hayreh & Jonas (1994) & Jonas found the mean age of patients to be older, approximately 70-73 years however patients in these prospective observational studies were not recruited as acute presentations of PVD. The very nature of the studies is likely to be the explanatory factor for the difference in mean age as the findings were similar between the current study and Byer (1994), both of which assessed acute presentations of PVD, whereas the findings between Gutteridge (1993) and Hayreh & Jonas (1994) were comparable.

The current study found patients in category 3.4.2 were approximately 4.5 years younger than those in 3.4.1 ($p=0.002$, see table 3.6.1). A further subgroup analysis of the 89 eyes with retinal degeneration in category 3.4.2 found a mean age of 60.1 years with a standard deviation of 11.7, compared to the eyes with PVD alone this group was still approximately 5 years younger and this was statistically significant ($p=0.001$). This is inconsistent with the findings of Yonemoto and colleagues (1994) as although they also found the mean age of eyes with retinal degeneration to be 2.2 years younger than eyes without, this was not a statistically significant finding. This is an interesting finding as both studies had a similar number of patients with and without retinal degeneration; the former study consisting of 818 eyes without retinal degeneration and 112 with retinal degeneration, and the current 851 and 89 respectively. One could postulate this difference could be due to the different ethnicities in the two studies; however this has been studied previously by Hikichi *et al.* (1995) and found there was no difference in age for the prevalence of PVD. Nevertheless this could be related to the difference in distribution of refractive errors between the two studies.

Patients in category 3.4.3 were 5.4 years younger than patients in 3.4.1, although not quite statistically significant. This is possibly due to the small number of patients in category 3.4.3 with a large standard deviation. In order to detect a difference, the sample size would need to contain approximately 150 patients with this standard deviation for a confidence level of 95% with a 5% margin of error and power of 80%.

The mean age of patients with retinal breaks was 5.7 years less than their counterparts with PVD alone (p=0.004), additionally when categories 3.4.1 and 3.4.2 were combined the mean age was 64.2 years, and were 4.1 years older than eyes with retinal breaks (p=0.008). Combs & Welch (1982) reported a mean age of 60.4 years (61.1 in males, 59.5 in females) in eyes with retinal breaks. The mean age of eyes with retinal breaks in the current study was 60.1 years, in males 63.8 and females 55.4. The mean age between the two studies correlates extremely well, however the difference in the studies when assessing for gender are likely to be attributable to two primary factors. Firstly the difference in the number of patients in each, the Combs & Welch (1982) study consisted of 248 patients, whereas the current study was approximately one-fifth in size. Secondly, Combs & Welch (1982) only reported on eyes with tractional breaks, whereas the current study included eyes with atrophic breaks also.

The results of unpaired two-tailed t-tests for age between the four categories are shown in table 3.6.1. Patients with PVD were approximately 4.5 years older than eyes with in other categories and this was statistically significant. There was no significant difference in mean age of eyes for the other categories, and one could speculate whether the presence of pathology initiates PVD at an earlier age. It is likely there are a number of factors that may have contributed to this result. One such factor is that the number of patients particularly in categories 3.4.3 and 3.4.4.1 were significantly smaller, for statistically significant results the size of each group would need to have consisted of at least 61 patients for a confidence level of 95% with a margin of error of 5%, assuming a standard deviation of 10. Therefore in order to confirm whether these findings are significant a further study incorporating an appropriate sample size calculation would be necessary

A further analysis of patients that were discharged compared to those that were reviewed revealed a 5.1 year difference in mean age, with the discharged group being older, this was a statistically significant finding, but was not consistent for gender or refractive error alone (table 3.6.3)

Laterality

Laterality was another factor evaluated in this study, for categories 3.4.1 and 3.4.2 the left eye was less frequently affected. The mean difference in the age at which PVD occurred was 0.4 years earlier in the right than left, with bilateral involvement occurring a further 1.3 years later, however this difference was not found to be statistically significant (p=0.56 for right vs left, p=0.06 for unilateral vs bilateral). Category 3.4.3 contained the highest proportion of patients with bilateral involvement, with category 3.4.4.1 containing the least.

Due to the small number of patients in these categories and the knowledge from previous categories regarding power, confidence level and sample size it was not statistically viable to assess for laterality in categories 3.4.3 and 3.4.4.1. Nevertheless figures 3.6.4, 3.6.5, 3.6.6 and 3.6.7 demonstrate a preponderance of right eye involvement compared to the left eye. Byer (1994) also documented a greater proportion of right eyes were involved compared to left eyes. One could speculate whether a difference in vascular dynamics could be an underlying factor. It is well recognised the temporal retina is less oxygenated in comparison to the nasal and this is contributes to the greater predisposition of retinal breaks in the temporal retina (Michaelson 1948; Shunmugam *et al.* 2014). It would interesting to see the findings of an appropriately designed study to assess this hypothesis.

Gutteridge (1993) reported the mean age of patients with bilateral PVD was 71.6 years for males and 72.1 for females, for those with unilateral PVD the mean age of males was 71.7 years and 72.4 for females. The current study found the mean age of males with bilateral PVD to be 65.6 years and 66.0 years in females (p=0.77), almost identical to the difference found by Gutteridge (1993). In contrast however the mean age of unilateral PVD in males was 65.0 and in females 63.3 (p=0.14). Hayreh & Jonas (1994) reported no difference between the age of onset of PVD between right and left eyes, however a difference of 4 years was noted between eyes with unilateral PVD and bilateral PVD. The mean age of unilateral PVD was 63.6 and for bilateral PVD 65.9 in the current study and this was statistically significant (p=0.001), compared to 68.7 for unilateral PVD and 72.7 for bilateral PVD found by Hayreh & Jonas (1994) and also found this to be statistically significant.

Refractive error

Although the determination of the refractive error was not strictly accurate as refraction was not performed at the time of assessment in the PVD clinic, the findings of this study concur with the findings of both Byer (1994) and Yonemoto *et al.* (1994). The results of this study suggest PVD occurs at approximately four years earlier in myopic eyes and four years later than hyperopic in comparison to emmetropes, and these results were statistically significant (table 3.4.1.6 and 3.4.1.7). It would have been useful to obtain axial length measurements together with an accurate refraction for the patients studied to further the relationship between the age of onset of PVD, gender, laterality and pathology, as a relationship between the age of onset of PVD has been found to reduce with increasing axial length (Morita *et al.* 1995). This was also a limitation acknowledged by Yonemoto *et al.* (1994) in their study. Despite a difference in the mean age of eyes in the categories, apart from female myopes in categories 3.4.1 and 3.4.2 there was no statistically significant difference in the mean age of patients for the refractive states (table 3.6.1)

Gender

A number of studies have noted a disparity in the representation of males and females with PVD (Diamond 1992; Gutteridge 1993; Byer 1994; Yonemoto *et al.*1994; Hayreh & Jonas (2004); Chuo *et al.* 2006). This disparity was reflected in the current study as the ratio of males to females was found to be 1:2 in categories 3.4.1 and 3.4.2, whereas there was less disparity in category 3.4.3 with a ratio of 2:3. Finally in eyes with retinal breaks there was a slight preponderance of males to females. Males were older than females in all four categories; category 3.4.1 males were 1.8 years older (p=0.02); category 3.4.2 males were 5.8 years older (p=0.003); category 3.4.3 males were 0.8 years older (p= 0.86); category 3.4.4.1 males were 8.4 years older (p=0.01). Yonemoto *et al.* (1994) report the age of onset of PVD in females to be 59.7 and 61.1 in males, a difference of 1.4 years which is almost equal to the difference found in category 3.4.1. Whereas Combs & Welch (1982) reported the mean age of males with retinal breaks was 1.6 years greater than that of females, the current study found a larger difference, however this is likely to be due to the significant difference in the size of the two studies.

Symptoms

The most frequent symptom reported at presentation was floaters, and was the sole symptom 32-35% of patients in categories 3.4.1 and 3.4.2. Photopsia was the sole symptom in 5-7%, with a combination of both reported by 59-60%. This is comparable to the findings of previous studies (Byer 1994; Hikichi *et al.* 1995; Dayan *et al.* 1996; Hikichi & Yoshida 2004). It is however accepted that symptoms of PVD do not necessarily correlate with presence of pathology (Dayan *et al.* 1996; Sharma *et al.* 2004; Hollands 2009; Kuhn & Aylward 2014). This finding is reflected in the results of this study (fig 3.6.12), there were 5-8% of asymptomatic patients in category 3.4.3 and those with retinal breaks. Interestingly, with regard to resolution of symptoms patients with PVD marginally more inclined to have improvement or resolution in their floaters compared to those with retinal breaks; odds ratio 1.15 (95% CI 0.61 – 2.16) however this was not statistically significant (p=0.74). Similarly for photopsia patients with PVD alone were almost twice as likely to have improvement compared to those with retinal breaks; odds ratio 1.95 (95% CI 0.71 – 5.36), but again this was not statistically significant (p=0.20). Additionally across the four categories there was no statistically significant difference between males and females for improvement of symptoms (p>0.05).

Pathological findings

Gutteridge (1993) reported a prevalence of 20-25% (depending upon the conditions included) of ocular conditions identified in his sample of 1600 patients, specifically 6% had retinal degenerations. In the current study, 23% of patients were identified to have ocular conditions in conjunction to or other than PVD, with 8% harbouring coexisting retinal degeneration. Despite the obvious differences in the two studies these figures are strikingly similar, suggesting the patients included in the current study are essentially an acceptable representative sample of the population. In contrast however, Byer (1994) also noted in his cohort of 350 patients, 22% were noted to have peripheral retinal degenerative conditions namely lattice degeneration and retinoschisis. In the current study 3.3% of eyes contained these abnormalities specifically. The variance between the studies could be attributable to the enrolment of patients in the studies, Byer's 350 patients were recruited over a twelve year period, compared to three years in the current study. The presiding factor is that a vitreo-retinal consultant or specialist would scrutinise the referrals from eye casualty for PVD, if peripheral retinal degenerations such as lattice degeneration or retinoschisis were documented then these would be given an appointment for the vitreo-retinal clinic in preference to the PVD clinic. Therefore the number of patients with PVD and peripheral retinal degenerations is likely to have been underestimated in this study.

Category 3.4.3 was an unexpected group of patients to have been discovered. Captivatingly almost one-third of this group were found to have uveitis (intermediate and/or posterior), with almost a further quarter with retinal vascular or macular abnormalities. Of particular note is that almost one-quarter of this group exhibited features of glaucoma that were not detected at the initial examination. This may presumably be due to the examination in eye casualty being focussed to exclude retinal breaks and address the presenting symptoms owing to the nature of the clinic. However in combination with categories 3.4.2 and 3.4.4.1 this does highlight the fact that abnormalities were detected in an additional 220 eyes in the PVD clinic (19.9%).

Retinal breaks

The incidence of delayed retinal breaks was 4.3%, this figure is greater than that reported previously. This is an interesting observation as previously studies have included eyes with haemorrhages and this has correlated with the presence of delayed breaks. Males were more likely to develop retinal breaks; 28 developed breaks from 364, an incidence of 7.7%; whereas in females 22 developed breaks from 743, an incidence of 3.0%. The odds ratio for males to females for the incidence of retinal breaks was 2.15 (95% CI 1.21- 3.79), and was statistically significant (p= 0.007). The temporal hemisphere was more than twice as likely to

be affected in males compared to females (OR 2.44, 95% CI 0.30 – 20.12) but this was not statistically significant (p=0.57). The superior hemisphere was less likely to harbour breaks in males compared to females (OR 0.47, 95% CI 0.14 – 1.55), however this was not statistically significant (p=0.24).

Of the breaks that required treatment 42% were located in the supero-temporal quadrant (table 3.4.3.4), a similar figure (42.9 - 47.7%) to that reported by Combs & Welch (1982). Sharma *et al.* (2004) report a larger figure (57%), however their study contained a significantly greater number of breaks requiring treatment (157 eyes). Overall the superior quadrant was affected in 78%, as similar figure to that reported from previous studies; Combs & Welch (1982) and Byer found this to be 70-71%; Sharma *et al.* (2004) found a marginally higher figure of 73%. The temporal hemisphere harboured a greater number of breaks compared to the nasal hemisphere (88% vs 12%) which is in agreement to previous studies; Combs & Welch (1982) reported 64 - 70% of breaks were found temporally; with Sharma *et al.* (2004) again reporting a greater figure of 81% in comparison. Furthermore, considering the breaks not treated, over half of breaks (61%) were in the inferior hemisphere which correlated reasonably with Byer (1994) who reported this to be 55%.

With regard to the configuration of retinal breaks, half of those treated were noted to be horseshoe in nature and when combined with the operculated breaks these two configurations accounted for almost three-quarters of breaks that were treated. With regard to the other seven round-hole type breaks, it is possible these breaks may have been present prior to the onset PVD, however may have been exacerbated by the PVD process resulting in accumulation of subretinal fluid.

So far it has been assumed breaks discovered in the PVD clinic were all fresh delayed onset breaks. However there is a possibility that at least some of these breaks may have been overlooked at the initial examination, a factor which has also been recognised by Sharma *et al.* (2004). Of the breaks that required treatment, adjunctive examination (3-mirror or binocular indirect ophthalmoscopy with scleral indentation) was documented as performed in only 50% of cases. This in itself may have resulted in under-detection of breaks. Conversely even if adjunctive examination had been performed, the interpretation of the findings is directly dependent upon the examiner. The fact that less than one-quarter of retinal degenerations identified in the PVD clinic were documented in eye casualty may further support this notion. The eye casualty at University Hospital Coventry and Warwickshire is not routinely staffed with consultant ophthalmologists and therefore this may inadvertently result in an under-detection of pathology. The additional findings in the PVD clinic for

categories 3.4.2 and 3.4.3 is highly relevant as certainly for the retinal degenerations, one could hypothesise that if these had been retinal breaks they may have been overlooked. The study by Qureshi & Goble (2009) adds further credence to this impression, the detection of tobacco dust was proportional to the level of experience. Although Richardson *et al.* (1999) did not speculate whether breaks were missed in their study when patients attended eye casualty, this is a distinct possibility as all patients may not have had as thorough examination as when they were reassessed the PVD clinic

Sensitivity of 3-mirror fundoscopy

In category 3.4.2, the sensitivity of fundus examination with a slit-lamp and a non-contact condensing lens gave a sensitivity of 84% and examination with a 3-mirror contact lens resulted in a marginal improvement of 86%. For patients in category 3.4.4.1 a sensitivity of 86% and 89% was achieved for examination with a condensing lens and a 3-mirror lens respectively. When combining the findings of both categories this study found a sensitivity of 85% for slit-lamp examination with a condensing lens and 87% for the 3-mirror lens. Although this figure is greater than that found by Richardson *et al.* (1999) but marginally less than the figure reported by Natkunarajah *et al.* (2003), it must be borne in mind the number of patients assessed for this particular element was almost five and three times respectively larger than the former studies. Furthermore the findings in this study for category 3.4.4.1 were verified by two individuals, although the vitreo-retinal consultant was not masked to the findings of the optometrist and this intrinsically could bias the findings of the subsequent observer.

Sensitivity of pigment in the anterior vitreous

An additional focus of this chapter was to determine the sensitivity of pigment in the anterior vitreous for the presence of retinal breaks. A summary of previous studies assessing this characteristic for retinal breaks without detachment is contained in table 3.7.1

Study	Size	Sensitivity
Hamilton and Taylor (1972)	16 eyes with flat holes	63%
Brod *et al.* (1991)	16 eyes with retinal breaks	94%
Sharma *et al.* (1999)	8 eyes with retinal breaks	88%
Tanner *et al.* (2000)	25 eyes with retinal breaks	92%

Table 3.7.1 Summary of previous studies evaluating the sensitivity of pigment in the anterior vitreous for the presence of retinal breaks

The current study was of 56 retinal breaks, of which 26 required intervention, from these 26 only 13 were found to have pigment in the anterior vitreous, thus a sensitivity of 50%. When

limiting this to horseshoe and operculated breaks requiring treatment this finding was present in 13 of 19 eyes resulting in a sensitivity of 68%.

Interestingly of the six breaks requiring treatment but not exhibiting pigment in the anterior vitreous three were in the inferior hemisphere, with one break in each of the superior, nasal and temporal quadrants. Certainly for these inferior breaks this may be of significance as the effects of gravity and the cortical vitreous may have been prevented the release of pigment into the vitreous. If the total number of eyes with retinal breaks is considered, in the first instance it appears tobacco dust as a sign has a very poor sensitivity, however when limited to those breaks that are most likely resultant of PVD the sensitivity increases dramatically. Coffee *et al.* (2007) noted this finding to be positive in only one of the two eyes with delayed breaks in their study. Therefore a negative finding does not negate the presence of a retinal break and simply cannot substitute detailed examination of the retina as was demonstrated by Coffee *et al.* (2007) and this current study. When considering the thirty eyes with retinal breaks not treated, there is an obvious contrast for the presence of tobacco dust. The first attributable explanation is that none of these breaks were found to have subretinal fluid. In cases of a retinal break there is the possibility is that little or no pigment is shed particularly if the defect does not migrate to the retinal pigment epithelium. Similar defects can be seen in cases of lamellar hole and also in inner leaf breaks in acquired retinoschisis, although these can often mimic full-thickness defects they do not penetrate to the RPE and as such do not disrupt in the same manner as a full thickness defect. Another plausible justification could be that the vitreous detachment around the retinal break may be limited and with the vitreous cortex still adherent to the retinal surface in nearby surrounding location (Pederson *et al.* 1982; Machemer 1984; Foulds 1987). This is a recognised entity as described by Kuhn & Aylward (2014) from direct surgical observation. Thus even if pigment were to be shed from the RPE then it could remain contained in this space and not continue on to its expected voyage to the anterior vitreous.

Finally none of the round holes in this study were found to be associated with tobacco dust. This in itself suggests these breaks may not necessarily have been a result of PVD and attributable to another pathological process which may not involve the RPE in the same manner (Foos & Allen 1967)

Naturally one could question examiner experience, Qureshi & Goble (2009) demonstrated the sensitivity of an optometrist was significantly less than a vitreo-retinal consultant. Although it was an optometrist that undertook the examinations in the PVD clinic, all patients

with retinal breaks were re-examined by a vitreo-retinal consultant. There was one-hundred percent agreement for this feature between the optometrist and vitreo-retinal consultant.

Smiddy *et al.* (1989) and Snead *et al.* (2008b) have demonstrated with histology pigment cells associated with retinal breaks may settle on the retinal surface with time, therefore this may further lead to a reduction in the visibility of pigment cells in the anterior vitreous in chronic retinal breaks. Finally as postulated by Boldrey (1983), vitreous pigment cells may become less pigmented with time and therefore if the breaks had been chronic in nature they may not have been recognised. It is certainly feasible to accept the breaks that were not treated could have been chronic in nature, although only two breaks were associated with surrounding pigmentary changes. Therefore in this scenario tobacco dust may have initially been present, but over time may have become less pigmented and/or become associated with an epiretinal membrane and hence not detected on clinical examination.

Despite the design and findings of this study there were limitations. The first of these limitations is the lack of imaging to confirm the presence of PVD or other findings, however due to the lack of resources this was not feasible. The determination of refractive error was not accurate, however as indicated axial length measurements may have been more insightful as refraction can be affected by numerous factors. One such factor would be nuclear sclerosis of the crystalline lens inducing myopia and therefore the patient would be classified as myopic when this would not necessarily be the case. Preferably all patients should have been examined with 3-mirror fundoscopy in conjunction with the other two techniques and ideally by more than one examiner, however due to time constraints this was only possible in selected cases. Furthermore the value of this study could have been further improved if all patients had been examined at the initial examination in the same manner as they were in the PVD clinic. Unfortunately, again due to various constraints this was not a realistic prospect.

3.8 Conclusion

The primary aim of this study was to determine whether patients examined in eye casualty for symptoms of photopsia and/or floaters and diagnosed with uncomplicated posterior vitreous detachment required further review in a dedicated clinic. With regard to retinal breaks a higher incidence has been reported in this study compared to previous studies, nevertheless one could contest that only half of the retinal breaks identified required treatment and this was a similar figure as reported previously, therefore consequently has not been of supplementary value. However, in total 9.5% of the total population studied required further assessment/intervention. Additionally of the 151 eyes in category 3.2, less than one-quarter were identified at the initial visit in eye casualty. When combining these figures 16.1% of patients were found to have pathology in the PVD clinic that had not been identified previously. This is a frank dissimilarity to previous findings.

Additionally, this current study did not find duration of symptoms/any specific characteristics such as duration of symptoms/refractive error or other factors to be a reliable indicator of pathology. In view of these findings it is recommended for patients with symptoms of acute PVD to be examined with dilated fundoscopy in conjunction with scleral indentation by an examiner competent in the technique at the onset of symptoms and again after a period of 4-6 weeks unless the patient develops new symptoms in which case earlier examination should be prompted. The value of this is not only monetary but also has the potential to negate a negative impact on the quality of life of an individual who may develop a retinal break.

Chapter Four: The Treatment of Retinal Breaks by an Optometrist

4.1 Introduction

As described in the first chapter, one of the most serious complications of PVD is the development of a retinal break (Novak & Welch 1984; Dayan *et al.* 1996; Coffee *et al.* 2007; Hollands *et al.* 2009; Mitry *et al.* 2010b; American Academy of Ophthalmology 2014; Kuhn & Aylward 2014). If a retinal break is detected in a patient with symptoms then current clinical guidelines recommend treatment due to the high risk of developing retinal detachment (Carvounis & Holz 2006; Mitry *et al.* 2010b; International Council of Ophthalmology 2011; American Academy of Ophthalmology 2014; Kuhn & Aylward 2014; Makhzoum *et al.* 2014). The treatment of retinal breaks can be undertaken in a variety of methods, the aim is to create adhesion between the retina and the underlying structures to prevent further migration of fluid under the retina resulting in detachment of the retina. One of the most frequently employed techniques for this is Argon laser retinopexy (Carvounis & Holz 2006; Mitry *et al.* 2010b; Lock & Fong 2011; Khan *et al.* 2013; American Academy of Ophthalmology 2014; Kuhn & Aylward 2014). In this procedure an Argon laser is focussed on to the retina to create numerous visible burns to surround the retinal break, this process induces adhesion of the retina to the underlying structures. The procedure can either be performed with the patient in a seated position with a slit-lamp delivery system, or alternatively an indirect ophthalmoscope laser delivery system can be used with the patient in a supine position. Successful treatment dramatically reduces the risk of retinal detachment by 5-10 fold (Carvounis & Holz 2006).

One of the first studies to report on the success rates of Argon laser retinopexy for the treatment of retinal breaks was by Zweng in 1972 in which 61 were breaks treated with Argon laser. Although there were limited details regarding characteristics of the breaks, all breaks were successfully treated with none requiring surgical intervention. Pollak and Oliver (1981) reported on their outcomes of argon laser retinopexy of 74 horseshoe retinal breaks treated during a 5½ year period, each reviewed for at least 6 months after treatment. In total there were 28 breaks measuring one-third to one disc diameter in size and a further 46 measuring greater than one but up to three disc diameters in size. Only one eye with a solitary break measuring less than one disc diameter went on to develop a retinal break, thus resulting in an impressive success rate of 98.6% in preventing retinal detachment. Unfortunately the authors do not disclose whether any retreatments were necessary. Smiddy *et al.* (1991) conducted their study in Miami, USA which consisted of 171 eyes treated by non-trainee clinicians during a period of 53 months in the mid- to late- 1980s. The average age of patients included in this study was 59 years, with a predominant male population

(63%). Almost three-quarters of patients exhibited symptoms; 14% had symptoms of photopsia; 39% floaters; and 20% loss of vision. Of significance is 95% of breaks were anterior to the equator, and 60% of breaks were in the superior quadrant, 29% of breaks were in the horizontal meridian, with the remainder inferiorly. Morphologically, three-quarters of breaks were of the horseshoe configuration, with operculated and round holes representing 11% and 14% respectively. With respect to treatment modality, laser retinopexy alone was applied in over half of breaks (54%), cryotherapy in one-third (34%) and a combination of both in 12%. All eyes were reviewed for a minimum of three months. The outcome of this study found 22% of eyes ultimately required further intervention, with the majority of retreatments (55%) arising within the first month and a further 22% after six months. Notably phakic eyes were deemed to be at less risk statistically of treatment failure compared to pseudophakic or aphakic eyes.

A more recent study by Ghosh and associates (2005) assessed the effectiveness of Argon laser retinopexy in an emergency clinic environment by trainee ophthalmic doctors. In this study of 100 patients treated with retinopexy alone at Birmingham, UK, 90% of patients were symptomatic. Almost three-fifths (59%) were female, and the mean age of patients in this study was 58 years of age, with 75% of breaks were located in the superior hemisphere. Ultimately this study found 24% required further treatment, a very similar figure to the Smiddy *et al.* (1991) study. A sequel to the study by Ghosh *et al.* (2005) was undertaken by Petrou & Lett (2014) after a 10 year period in the same unit. Identical to the original study, 100 consecutive eyes, of which almost all (93%) exhibited symptoms, were evaluated after having an emergency argon laser procedure by a trainee ophthalmic doctor. The mean age of patients in this study was 54 years of age, with a gender bias skewed towards females (58%), with 72% of breaks were located superiorly. Although these characteristics were almost identical to the study ten years prior, alarmingly this study found 40% of patients required further intervention compared to the previous figure of 24%, a significant increase, both statistically and clinically compared to the findings 10 years earlier. The author cites the change in the training curriculum of trainee ophthalmologists as the primary factor resulting in deterioration of outcomes. A similar study by Khan *et al.* (2013) of 45 patients in Edinburgh, UK, assessed outcomes of these patients treated between July 2010 and January 2011. The overwhelming majority of breaks were horseshoe in configuration (84%) with the remainder being operculated. Primary treatment was successful in 54% of cases, over one-third (35%) required up to a total of three treatments. The authors do however acknowledge the relatively small sample size of their study and that it also assessed outcomes from an emergency care environment, where the experience level of clinicians is recognised to be highly variable. Despite these limitations a noteworthy finding of this study

was that if a blood vessel was bridging the retinal break this was associated with a poorer outcome and correlated with a need for further intervention. Moreover, the presence of a vitreous haemorrhage was identified as a risk factor for the further development of retinal detachment.

In contrast to these studies, a retrospective review of by Levin *et al.* (2009) at their institution in San Francisco, USA of 166 eyes treated with laser retinopexy between a period spanning 10 years from January 1997 and December 2006 found only 15% of eyes required additional intervention. Interestingly there was a significantly greater male preponderance (72%), with a mean age of 60 years and less than half (43%) of all treated eyes were symptomatic. The variance in the results of this study may be due to the fact that less than half the patients were symptomatic and almost one-quarter of breaks treated had no predisposing risk factors. Furthermore, the patients in this study were treated as outpatients rather than in an emergency environment. In contrast to the study by Ghosh *et al.* (2005) that suggested slit-lamp delivery of laser may be inadequate for the treatment of peripheral retinal breaks, Levin *et al.* (2009) do not attribute the method of laser delivery as a factor for envisaging further treatment, despite over 80% of procedures being performed using the indirect laser. In conjunction, it was recognised the decision for additional treatment can be subjective and in the absence of risk factors further treatment may not be deemed necessary and hence the lower rate of retreatment and variance between the studies.

Ultimately the literature emphasises the need to review patients following laser retinopexy with meticulous examination to ensure satisfactory treatment has been performed, and in fact a significant proportion may need further specialist intervention (Goldberg & Boyer 1980; Smiddy *et al.* 1991; Sharma *et al.* 2004). Furthermore, to ensure these potentially sight threatening conditions are managed safely and effectively, it may be appropriate to improve access to such specialist services to reduce undesirable outcomes for both patients and clinicians.

4.1.1 Findings of a retrospective audit

To compare the outcomes of the optometrist, a retrospective audit of retinal breaks treated in the eye department as an outpatient procedure at University Hospital Coventry and Warwickshire between 1st January 2012 and 31st December 2012 was undertaken. This audit was registered with the research and development department at University Hospital Coventry and Warwickshire and as such they confirmed ethics approval was not required for this audit. To identify the patients treated, a manual search of the vitreo-retinal outpatient clinic lists from this time period was undertaken. The clinical records of each patient were then reviewed and the following details were collected:

1) Gender
2) Age
3) Configuration of retinal break (horseshoe, round or operculated)
4) Date of first treatment
5) Clinic in which patient attended (eye casualty, outpatients)
6) Date of first and subsequent follow-ups
7) Details of any further intervention (laser, surgery)

During this twelve month period 113 breaks from 104 eyes were treated with laser retinopexy as the primary intervention. Of these 113 breaks, 55 breaks from 51 eyes required further intervention (49%); 44 eyes required a second laser retinopexy procedure (42%), 4 eyes required a total of three laser retinopexy procedures (4%) and 3 eyes necessitated surgical intervention (3%). The mean time until patients were seen after the initial treatment was 17 days (SD 14.1, range 1-77), one patient went on holiday and did not return for 73 days and two did not attend their appointments until 74 and 77 days later. When excluding these three the mean time until the first review was 15 days (SD 10.4, range 1-45). The mean age of these 104 eyes was 59 years (SD 12.3, range 14-83), 58% of breaks were in males and the left eye was affected in 56% of cases. The superior hemisphere was affected in 68%, with the supero-temporal quadrant being involved most frequently (41%). The findings of this audit are in table 4.1.1.1

	Trainee	Non-trainee	Consultant
Number of breaks	29 (26%)	60 (53%)	24 (21%)
Slit-lamp	22 (76%)	40 (67%)	0
Head-mounted	7 (24%)	20 (33%)	24 (100%)
Primary success	13 (45%)	29 (48%)	20 (83%)
Slit-lamp	9 (41%)	18 (45%)	0
Head-mounted	4 (57%)	11 (55%)	20 (83%)
Right	10	28	11
Left	19	31	13
Age	61.2	59.1	56
SD	11.2	12.1	13.9
Range	(30-77)	(14-83)	(23-77)
Male	20	27	17
Female	9	33	7
Quadrant			
S	2 (7%)	9 (15%)	6 (25%)
ST	14 (48%)	26 (43%)	6 (25%)
T	6 (21%)	5 (8%)	1 (4%)
IT	2 (7%)	4 (7%)	3 (13%)
I	0	3 (5%)	3 (13%)
IN	1 (3%)	2 (3%)	2 (8%)
N	0	3 (5%)	1(4%)
SN	4 (14%)	8 (13%)	2 (9%)
Configuration			
Horseshoe	18 (62%)	43 (72%)	9 (38%)
Operculated	10 (34%)	13 (22%)	7 (29%)
Round	1 (3%)	4 (6%)	8 (33%)

Table 4.1.1.1 A summary of the findings of a retrospective audit for retinal breaks treated in the ophthalmology department at University Hospital Coventry and Warwickshire in 2012

Of the 113 breaks 70 were horseshoe (62%), 30 operculated (27%) with 13 round (11%) in configuration. Of the round holes only 3 required further retinopexy (25%) and none progressed to retinal detachment or required surgical intervention. The mean age of eyes with round hole breaks was 42.5 years (SD 14.0, range 23-66), with 77% affecting the right eye. Over two-thirds of these breaks were in males (69%), with over three-quarters (77%) in the superior hemisphere. Ten of the operculated breaks (33%) required further retinopexy and again none progressed to retinal detachment or required surgical intervention. The mean age of eyes with operculated breaks was 62.8 years (SD 12.9, range 14-77), with 70% of breaks in the superior hemisphere. Males and females were affected equally, however the left eye was more likely to be affected (60%). Horseshoe tears were the largest proportion of retinal breaks treated comprising nearly two-thirds of all treated breaks. A total of 5 eyes required surgical intervention, one for the development of a new retinal break resulting in retinal detachment, in one eye a subsequent vitreous haemorrhage developed, in the remaining three there was progression of subretinal fluid. Of the 70 horseshoe breaks 39 (56%) required further retinopexy.

The mean age of eyes with horseshoe breaks was 60.4 years (SD 9.0, range 30-83). There was a greater predilection for males to be affected (59%), the left eye (60%) was more frequently involved also, with superior hemisphere being involved in 70% of cases.

Analysis of these 113 breaks revealed 69 breaks (64 eyes) of these were treated in the eye casualty (61%) with the remaining 44 (39%) treated in the vitreo-retinal outpatient clinic. A subgroup analysis was undertaken for the two different clinical settings (tables 4.1.1.2 and 4.1.1.3). For all 64 eyes in the eye casualty the laser retinopexy was performed by either a training grade ophthalmologist or a non-training grade ophthalmologist. The non-training grade ophthalmologists performed retinopexy in 43 eyes consisting of 47 breaks. The procedure was performed at the slit-lamp for 35 breaks of which 20 required further laser retinopexy and one required surgical intervention, a total of 21 requiring further intervention (60%). For 12 breaks retinopexy was performed using the head-mounted indirect ophthalmoscope, of these 6 required further laser retinopexy and one required surgical intervention, a total of 7 requiring intervention (58%). Overall 28 of 47 breaks (60%) treated by non-training grade ophthalmologists in eye casualty required further intervention. The remaining 22 breaks in 21 eyes in eye casualty were treated by training grade ophthalmologists. The slit-lamp was used for 19 breaks of which eleven required further retinopexy, but 2 of these went on to requires surgical intervention, thus only 42% had successful primary retinopexy. Three breaks were treated with the head-mounted indirect ophthalmoscope of which two were deemed to require further retinopexy, however no eyes went on to require surgery. Overall 13 of 22 breaks (59%) treated by training grade ophthalmologists required further intervention. There was no statistically significant difference between training grade and non-training grade ophthalmologists for treatment outcomes when assessed with Chi-Square analysis (p=1).

	Trainee	Non-trainee
Number of breaks	22 (32%)	47 (68%)
Slit-lamp	19 (86%)	35 (74%)
Head-mounted	3 (14%)	12 (26%)
Primary success	9 (41%)	19 (40%)
Slit-lamp	8 (42%)	14 (40%)
Head-mounted	1 (33%)	5 (42%)
Right	8	21
Left	14	25
Age	61.7	61.4
SD	10.6	8.2
Range	(30-76)	(45-83)
Male	15 (68%)	21 (45%)
Female	7 (32%)	26 (55%)
Quadrant		
S	2 (9%)	8 (17%)
ST	10 (45%)	20 (43%)
T	4 (18%)	3 (6%)
IT	1 (5%)	4 (9%)
I	0	2 (4%)
IN	1 (5%)	2 (4%)
N	0	3 (6%)
SN	4 (18%)	5 (11%)
Configuration		
Horseshoe	14 (64%)	36 (77%)
Operculated	8 (36%)	11 (23%)
Round	0	0

Table 4.1.1.2 A summary table comparing the outcomes of trainee and non-trainee ophthalmologists for the treatment of retinal breaks in eye casualty

In the outpatient clinic a total of 44 breaks were treated from 40 eyes. A consultant vitreo-retinal ophthalmologist performed treatment using the head-mounted indirect ophthalmoscope in 23 breaks in 19 eyes of which only four required further retinopexy (17%) with no eyes progressing to require surgical intervention. Training grade ophthalmologists performed retinopexy in 8 breaks of 8 eyes of which 5 were performed with the head-mounted indirect ophthalmoscope and 2 required further retinopexy (40%). There were 3 breaks treated using the slit-lamp method, one eye went on to develop a new break and required surgery and one further required additional retinopexy. Therefore treatment was only successful in 33% by a trainee ophthalmologist using the slit-lamp method, and 50% overall required further intervention. Non-training grade ophthalmologists treated 13 breaks of 13 eyes; 5 with the slit-lamp method and 8 with the head-mounted indirect ophthalmoscope. None of the eyes treated by the non-training grades went on to require surgery, however 1 (20%) treated with the slit-lamp and 2 (25%) treated with the head-mounted indirect ophthalmoscope required further retinopexy. The retreatment by the non-trainee ophthalmologists therefore was 23%. A Chi-Square analysis between the three groups found no statistically significant difference for treatment outcomes (p=1 for non-

training grade vs consultant; p= 0.15 for training grade vs consultant; p= 0.35 for non-training grade vs training grade).

	Trainee	**Non-trainee**	**Consultant**
Number of breaks	7 (18%)	13 (30%)	24 (52%)
Slit-lamp	3 (43%)	5 (38%)	0
Head-mounted	4 (57%)	8 (62%)	24 (100%)
Primary success	4 (50%)	10 (77%)	20 (83%)
Slit-lamp	1 (33%)	4 (80%)	0
Head-mounted	3 (60%)	6 (75%)	20 (83%)
Right	2	7	11
Left	5	6	13
Age	59.7	51.1	56
SD	13.9	19.2	13.9
Range	(38-77)	(14-71)	(23-77)
Male	5	6	17
Female	2	7	7
Quadrant			
S	0	1 (8%)	6 (25%)
ST	4 (57%)	6 (46%)	6 (25%)
T	2 (29%)	2 (15%)	1 (4%)
IT	1 (14%)	0	3 (13%)
I	0	1 (8%)	3 (13%)
IN	0	0	2 (8%)
N	0	0	1(4%)
SN	0	3 (23%)	2 (9%)
Configuration			
Horseshoe	4 (57%)	7 (54%)	9 (38%)
Operculated	2 (29%)	2 (15%)	7 (29%)
Round	1 (14%)	4 (31%)	8 (33%)

Table 4.1.1.3 A summary table comparing the outcomes of trainee, non-trainee and a consultant ophthalmologist for the treatment of retinal breaks in the outpatient clinic

The primary success rate was notably higher in the outpatient clinic setting compared to eye casualty for both the training grade and non-training grade ophthalmologists. This was an intriguing finding as it was not an expected one, there were however notable differences between the two clinical settings. The first difference is that in eye casualty the slit-lamp method of delivery was predominantly used, whereas in the outpatient clinic the head mounted indirect ophthalmoscope was more frequently employed. This in itself may lead to a higher success rate as has been suggested (Ghosh *et al.* 2004). Secondly the number of retinal breaks treated in eye casualty was significantly greater than those treated in the outpatient clinic, as there is significant disparity between the two groups it is not possible to directly compare the outcomes. However there may have been other intrinsic factors such as the nature of retinal breaks and the environment itself that may have been contributory. Firstly, although the configuration of break was noted, other morphological feature such as the amount of subretinal fluid, presence of haemorrhage, size of the break or co-existing

vitreo-retinal traction were not and these may have influenced the outcome. One factor that was not considered was the nature of the environment. Eye casualty is subjected to a variety of pressures, one of which is time, which is often less of an issue in an outpatient clinic setting. Furthermore in the outpatient clinic supporting staff i.e. a consultant is often available to impart guidance and other clinicians to continue the clinic whilst procedures are being performed. Additionally when patients attend eye casualty they may be anxious and this may have a negative impact on their co-operation and tolerability when undergoing retinopexy. Whereas attendance to an outpatient clinic may be associated with lower levels of anxiety and improved co-operation as often patients have a greater understanding of their condition which has been imparted to them from a previous examination. The level of the trainees and/or previous experience was not taken into consideration and these are likely to have been underlying factors. Staff in the vitreo-retinal clinic, whether trainee or non-trainee, are typically more experienced in vitreo-retinal matters than those in eye casualty and this may have been significant to the outcomes. Furthermore the outcomes of the trainees and non-training ophthalmologists are combined figures for each respective group and are not representative of a single clinician in each. The need for retreatment can subjective (Levin *et al.* 2009) and this again could have been influential in this analysis, however in all cases the need for retreatment was documented and justified; progression of subretinal fluid in 5 cases, 14 cases of poor laser uptake with a further 21 cases with insufficient treatment applied to the anterior margin.

One of the most influential factors is that the breaks presenting in eye casualty are more likely to be acute presentations which may possess the potential to progress rapidly despite treatment. This is due to the fact that retinal adhesion following retinopexy is still in a weakened state within the first 24 hours and during this time there is a risk of progression however (Yoon & Marmor 1988; Folk *et al.* 1989; Kita *et al.* 1991). Whereas those identified in the outpatient clinic may have a longer duration, possess less threatening features with less susceptibility to progress and therefore the retinopexy adheres better resulting in an improved outcome.

With the results of this insightful audit and concurrent evidence in the literature, there was a need to improve the competency of those undertaking laser treatment and this was to be addressed through the pre-existing training and development programme. Secondly, from the competency and skill demonstrated by the optometrist, it was suggested by the vitreo-retinal consultant that the optometrist develop further and undertake laser retinopexy procedures for retinal breaks. One of the reasons for this was as part of the programme of trainee ophthalmologists, they work in each hospital for a six month period and then move to

another unit. Furthermore the number of trainee and non-trainee ophthalmologists with adequate experience in retinopexy procedures has declined due to a change in the curriculum (Petrou & Lett 2014), findings which to some extent are reverberated in this study. Therefore a lack adequately trained personnel to perform laser retinopexy for retinal breaks exists. The rationale for training the optometrist was firstly the optometrist possessed the skills required for vitreo-retinal examination, and secondly was previously skilled in undertaking laser procedures.

For ophthalmic doctors in the United Kingdom, there is a formal training programme in place which is directed by the Royal College of Ophthalmologists. Practical experience is gained by the trainee performing the procedure whilst under direct supervision by a senior experienced doctor working under the auspices of a consultant ophthalmologist. To develop the role of the optometrist, the consultant vitreo-retinal ophthalmologist discussed the proposed development with peers and also the Royal College of Ophthalmologists to devise an appropriate training programme. As a result of these discussions it was decided that the optometrist should undergo a training programme equivalent to that of an ophthalmic trainee doctor.

For the first part of this process the optometrist was required to acquire further theoretical knowledge, and this was accomplished by a directed lecture from the laser protection advisor for the hospital. This one-to one lecture consisted primarily of laser applications and safety precautions to be undertaken whilst operating the laser equipment. The theoretical base was further supplemented by successful completion of an online laser course provided by Health Education for England on their e-learning for Healthcare website which is endorsed and written by the Royal College of Ophthalmologists (http://www.e-lfh.org.uk/home/). There were 23 separate lectures covering various aspects of ophthalmic laser treatment and procedures. With regard to developing the practical skills of retinopexy, the optometrist attended and successfully completed a formal practical laser training course at Hull Royal Infirmary. This course had been approved by the Royal College of Ophthalmologists and was chiefly designed for ophthalmic subspecialty doctors embarking on laser procedures. Following completion of the theoretical and practical elements a written proposal was approved by the consultant, clinical director and medical director authorising the optometrist to undertake the procedure whilst under supervision by the consultant vitreo-retinal ophthalmologist. It was envisaged to audit the outcomes of the patients treated by the optometrist and compare these against local and national outcomes.

4.1 Methods

Similar to the methods described in previous chapters, patients were examined by the optometrist in the posterior vitreous detachment clinic. When retinal breaks were identified, a clinical judgement was made as to whether intervention was required based upon the current vitreo-retinal guidelines for treatment (American Academy of Ophthalmology 2014; Makhzoum *et al.* 2014). In addition all patients identified with retinal breaks were examined by the vitreo-retinal consultant to verify the proposed management plan. The patient was then informed of the risks and benefits of treatment and no treatment. If the patient agreed to treatment, informed consent was obtained from the patient both verbally and written.

The decision as to which laser delivery method was employed, whether slit-lamp based or head mounted binocular indirect, was determined primarily (but not exclusively) by the following factors:

1- Location of break(s)
    a. If the break was anterior to the equator, then the head-mounted indirect ophthalmoscope delivery system was favoured
    b. For equatorial, or breaks posterior to the equator, the slit-lamp delivery system was favoured

2- Patient co-operation and comfort
    a. Where patients were unable to tolerate adequate positioning for indirect ophthalmoscopy, such as physical restriction due to arthritis, and/or scleral indentation then the slit-lamp delivery system was employed
    b. If the patient was unable to maintain adequate positioning on the slit-lamp, such as those with a large mid-section preventing a stable position on the slit-lamp, then preference was to use the binocular indirect delivery system

For all procedures the vitreo-retinal consultant was continually present in the laser room, when the optometrist judged the treatment had been completed, the consultant examined the patient to ensure treatment had been completed satisfactorily. If the consultant judged the treatment was inadequate then the procedure would be completed by the consultant. Furthermore, if the optometrist was unable to complete the procedure, for reasons such as inadequate laser uptake or difficult in maintaining satisfactory visualisation of the area(s) to be treated, the consultant intervened to complete the procedure. Once the procedure had been completed, details of the procedure were documented in the medical notes, noting the location of the break; area treated; and laser settings used.

Each patient was then scheduled a planned review for 7 and 28 days later for re-examination, primarily to evaluate the treatment and also to exclude the development of addition breaks. At each review the patient underwent full ophthalmic examination as previous by the optometrist followed by the vitreo-retinal consultant. Planned reviews were scheduled for 3, 6 and 12 months to assess the outcomes of the optometrist to ensure there was no compromise to patient safety. This was to be followed by continual 6-monthly reviews thereafter.

4.3 Results

During the period 1st January 2014 to 31st October 2015 the optometrist treated 43 breaks in 40 eyes of patients who attended the PVD clinic. The optometrist was not able to complete the treatment of five retinal breaks; 3 were deemed to have insufficient treatment applied to the anterior margin; in one patient the optometrist had difficulty with visualisation due to the presence of a cortical lens opacity; and in one patient there were co-operation difficulties. In these five cases the consultant successfully completed the procedures. Of the remaining 37 breaks, 4 required further treatment. In total therefore 9 of 43 breaks required further intervention (21%). The characteristics of the breaks treated are in table 4.3.1

Number of breaks	43
Slit-lamp	7 (16%)
Head-mounted	36 (84%)
Primary success	9 (79%)
Slit-lamp	5 (71%)
Head-mounted	29 (81%)
Right	24
Left	19
Age	62.1
SD	14.4
Range	24-84
Male	17
Female	27
Quadrant	
S	3 (7%)
ST	15 (35%)
T	9 (21%)
IT	4 (9%)
I	1(2%)
IN	3 (7%)
N	2 (5%)
SN	6 (14%)
Configuration	
Horseshoe	27 (62%)
Operculated	12 (29%)
Round	4 (9%)

Table 4.3.1 A summary of the retinal breaks treated by the optometrist

With regard to the 3, 6 and 12 month planned reviews, the consultant was satisfied with the progression of the skill of the optometrist in performing laser retinopexy procedures; at the 3 month review the consultant completed the treatment 2 out of 4 cases (50%); at the 6 month review the optometrist had completed a further 7 procedures of which the consultant needed to complete 2 (29%). By the 12 month review a total of 25 breaks had been treated by the optometrist of which the consultant was required to complete the treatment in 5 cases, and a further 3 cases required further laser treatment at the 7-day review (32%). The consultant

was satisfied the optometrist had demonstrated satisfactory competency with the laser equipment at the 12 month review and that it was no longer necessary for the consultant to be present in the laser room with the optometrist during each laser procedure. However, the consultant continued to review each patient immediately after the procedure and at the 7- and 28- day reviews. The next scheduled review was for 18 months and by this point the optometrist had completed a total of 35 procedures, an additional 10 procedures since the 12 month review with none requiring intervention or further treatment. Following the 18 month review, the consultant was satisfied it was no longer necessary to review each patient immediately after procedure, but would continue to examine at the 7- and 28-day reviews. Until 31st October 2015 the optometrist had performed a further 8 procedures with only one requiring further laser treatment at the planned 7-day review.

During the period 1st January 2014 to 31st October 2015, a total of 43 procedures had been performed by the optometrist of which the consultant had to complete the procedure in 5 cases, all within the first 8 months, beyond this point the consultant did not need to intervene. After the 8 month period until 31st October 2015, the optometrist completed 25 procedures with only 4 cases necessitating further treatment, a primary success rate of 84% in this period. Importantly, no patient treated by the optometrist between 1st January 2014 and 31st October 2015 went on to develop retinal detachment.

Similar to the previous chapter the sensitivity of 3-mirror fundus examination and a +90D condensing lens for the detection of retinal breaks was assessed. The sensitivity of 3-mirror and +90D lens was identical and found to be 88%, there were 5 horseshoe breaks were missed with these two methods of examination however were detected upon examination with indentation. Expectedly, it was found in patients with lens opacities or poor dilation assessment of the peripheral fundus was more problematic with slit-lamp fundoscopy compared to examination with scleral indentation. In addition the sensitivity of pigment in the anterior vitreous was also re-evaluated. In these 40 eyes this feature was absent in 5 eyes, thus a sensitivity of 85%. Interestingly it was found eyes without posterior vitreous detachment did not exhibit pigment in the anterior vitreous in conjunction with a retinal break

4.4 Discussion

Previous studies have reported on the primary success rate of laser retinopexy for the treatment of retinal breaks (Smiddy *et al.* 1991; Levin *et al.* 1999; Ghosh *et al.* 2005; Khan *et al.* 2013; Petrou & Lett 2014). This figure has varied depending upon the treating clinician, the setting in which the patient was treated and the method employed for treatment. The primary success rate of the optometrist for the treatment of retinal breaks with laser retinopexy was 79%. This was a comparable figure to the primary success rates of non-trainee ophthalmologists (77%) and a vitreo-retinal consultant (83%) for patients treated in the outpatient clinic. Interestingly the optometrist had a greater primary success rate compared to the collective outcomes of trainee ophthalmologists in a similar setting. However this could be attributable to the fact the optometrist had been subjected to an extensive training programme for this competency and previously (chapters 2 and 3). It is not typical for trainee ophthalmologists to receive as extensive supervision as the optometrist had, typically trainees undertake the first few procedures under direct supervision and then are permitted to perform without direct supervision. Whereas in contrast the optometrist was under direct supervision for 12 months, however this was primarily to ensure there was no detriment to patient safety due to the pioneering nature of this work. The improvement in the competence of performing the procedure was evident and after the first 6 months the consultant no longer needed to complete any of the procedures. Although treatment was performed with either a slit-lamp or a head-mounted binocular indirect, both of which the optometrist was competent in using. Nevertheless compared to when examination alone is undertaken, modification to alignment and positioning are required when performing retinopexy to ensure the necessary effect achieved and is visualised. This essentially is why the consultant completed some of the initial procedures and with guidance the need for the consultant to intervene was negated.

With regard to the characteristics of eyes treated, naturally as expected there were minor differences. Firstly, the mean age of patients treated by the optometrist was marginally older than those treated by trainee, non-trainee and consultant ophthalmologists however this was not statistically significant (p=0.82, 0.28 and 0.10 respectively). The difference in age between the groups is likely to be attributable to the number of patients treated in each group and also due to the lesion types treated; approximately one-tenth of the lesions treated by the optometrist were round holes whereas round hoes comprised approximately one-third of the total treated by the non-trainees and consultant in the outpatient clinic. Commonly round holes that require treatment and found in younger patients, whereas horseshoe and operculated breaks are principally the result of posterior vitreous

detachment. The mean age of patients treated in eye casualty was almost identical to the mean age found by optometrist, again attributable to the nature and distribution of breaks treated which were similar in proportion. Compared to previous studies the mean age of patients treated was relatively comparable, although those treated by the optometrist were marginally older. A result likely to be due to the relatively small number of patients that would not be reflective of the overall population and also the composition of lesions treated within each study.

Interestingly the majority of patients treated by the optometrist were females, with the right eye being most frequently involved. This in contrast to the other clinicians, the trainees and consultant treated more males and the left eye was most frequently involved. Whereas for those treated by non-trainees there was almost equal distribution of laterality and gender involvement. When the findings for the ophthalmologists were combined there was a slight bias towards the left eye being affected (56%) and this correlated to the findings of Ghosh *et al.* (2004) and Petrou & Lett (2014). However there were a greater proportion of males affected (58%) when the results were combined for the ophthalmologists which was in contrast to the former studies. The differences again are likely to be attributable to the small number of patients, the variances in environment and also the comparatively short duration of each study.

Across all clinician groups horseshoe breaks were the predominant type of break treated. This was an anticipated observation as treatment is advised for these breaks when associated with PVD whereas this is not always necessary with other breaks (Byer 1998; International Council of Ophthalmology 2011; American Academy of Ophthalmology 2014; Makhzoum *et al.* 2014; Wilkinson 2014). Similarly the supero-temporal quadrant was most often affected with the superior hemisphere harbouring most breaks, this was a consistent with previous studies in the literature and previous chapters. Overall the lesions treated by optometrist were comparable in nature to those treated by the ophthalmologists at the same institution and those reported previously.

The issue of sensitivity of pigment in the anterior vitreous for the presence of a retinal break was dealt with in the previous chapter. Overall the sensitivity of this particular feature was found to be greater in this chapter than the former. An observation made in this chapter was that eyes without PVD were less likely to exhibit pigment in the anterior vitreous in the presence of a retinal break. Interestingly there were 3 eyes of the 5 without this feature that did have a PVD, however in these 3 eyes the break was in the inferior hemisphere. Despite this the sensitivity was comparable to previous studies (Brod *et al.* 1991; Sharma 1999;

Tanner *et al.* 2000). Furthermore with regard to the sensitivity of +90D and 3-mirror slit-lamp fundoscopy compared to scleral indentation, this was found to be similar to the previous chapter and comparable to previous findings reported (Natkunarajah 2003). On reflection, patients with PVD are in the age category in which lens opacities occur and pupil dilation is not always optimal. These two factors are predominantly the reason why it was found scleral indentation was superior. Additionally in cases of poor dilation and/or lens opacity, with indentation the area of interest can be physically moved to improve visibility and hence was superior. Furthermore, although breaks may have been visible with the 3-mirror or +90D lens treatment may have been inadequate as often the anterior margin was more difficult to visualise, and this was the prevailing reason for using the head mounted indirect laser. One significant limitation in determining the sensitivity of these examinations was that only the optometrist documented findings with respect to these features and these were not validated by the consultant vitreo-retinal surgeon or other ophthalmologists. This pressures of a busy outpatients clinic were not practical for validating these observations, however they had been validated in previous chapters (see chapter 2 and 3).

4.5 Conclusion

This study demonstrates how optometrists can, with optimal circumstances, undertake advanced roles that have been traditional undertaken by ophthalmologists. A finding that is in agreement with previous studies (Azuara-Blanco 2007; Hau *et al.* 2007; Marks *et al.* 2012; Parkins 2014). However a significant limitation was that although the optometrist had demonstrated sufficient competency in the technique of laser retinopexy for retinal breaks this was restricted to patients treated in the outpatient department. Extrapolating the outcomes of non-trainee ophthalmologists to the optometrist, may however result in a lower primary success rate. Expanding the role of the optometrist to treat retinal breaks in eye casualty would be the next natural stage of progression in this pioneering development, and it is envisaged this will become a reality once the 24 month review has been completed. Nevertheless these outcomes have been positive and highly favourable for the optometrist to continue, together with being encouraging progress for optometry. Furthermore this revolutionary development will hopefully be a recognised as a breakthrough and inspire other optometrists to evolve in a similar manner.

Chapter Five: Vitreous opacities in Posterior Vitreous Detachment

5.1 Introduction

The focus of this final chapter was derived from observations noted during the clinical examination of patients in the posterior vitreous detachment clinic. Changes in the vitreous attributable to posterior vitreous detachment have been well documented previously (Pischel 1952; Johnson 2005; Snead *et al.* 2008b; Kakehashi *et al.* 2014; Kuhn & Aylward 2014). A brief description of reddish brown dots in the vitreous of older eyes is mentioned Pischel (1952), however there does not appear to be any specific detail in the literature regarding the presence of vitreous opacities in the mid- to posterior vitreous that may also be visible in posterior vitreous detachment (Coupland 2008). These opacities are estimated to be approximately 20-50µm in diameter and most numerous anterior to the Weiss ring or opening in the posterior hyaloid membrane (fig. 5.1.1, 5.1.2 and 5.1.3). The opacities can often be detected in the anterior vitreous also, but fewer in quantity (fig. 5.1.4).

The normal vitreous contains a limited variety of cells with the majority residing in the cortical vitreous (Balazs *et al.* 1964, Sebag 1992, Coupland 2008). Hyaloctes are most numerous in number with each being approximately 10-15µm in size, functionally they are involved in metabolic and phagocytic processes. Fibroblasts account for less than one-tenth of the vitreous cell population but may be confused with hyalocytes. Both fibroblasts and hyalocytes are numerous at the vitreous base however fibroblasts have a significant concentration around the optic disc also, whereas hyalocytes are found in posterior pole and equator with in reducing density (Balazs *et al.* 1964; Sebag 1992). The histological work by Sebag and Balazs (1985) demonstrated the presence of hyalocytes in the vitreous cortex but also larger ‘debris’ was noted with no further reference to this. Laminocytes have been documented by Snead *et al.* (2008b) on the posterior hyaloid membrane by histology and direct clinical observation. These laminocytes were found to be particularly concentrated around the Weiss ring. Upon clinical examination, laminocytes and the opacities described in this chapter appear to be identical in nature. In fact the ‘debris’ identified by Sebag and Balazs (1985) may indeed be laminocytes and the opacities referred to.

Although there is no description of these opacities being visible elsewhere in the vitreous other than the posterior hyaloid membrane, Snead *et al*. (2008b) have identified laminocytes in the histology of epiretinal membranes, is likely these are the glial cells documented by Foos (1974) as the major constituent of epiretinal membranes.

It is hypothesised once vitreo-papillary adhesion is released, these cells are liberated and enter into the vitreous body, with some degree of migration anteriorly. It is important to

differentiate the cells from similar entities such as erythrocytes or RPE cells as these have a strong correlation for the presence of a retinal break (Brod *et al.* 1991; Sharma *et al.* 1999; Tanner *et al.* 2000; Williamson 2013). On the contrary, this finding described, as yet has not been associated with any such pathological process merely a representative observation that PVD has occurred.

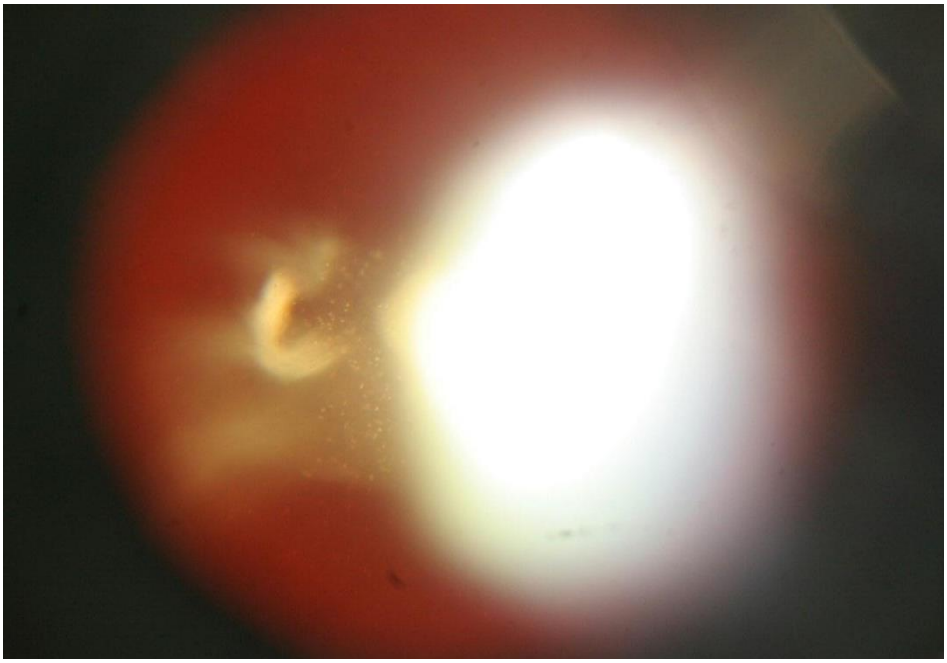

Fig 5.1.1 A colour photograph taken of the mid-vitreous using a slit-lamp camera, with 25x magnification. To the left of the illuminated slit beam multiple small opacities are visible anterior to the thickened posterior hyaloid membrane

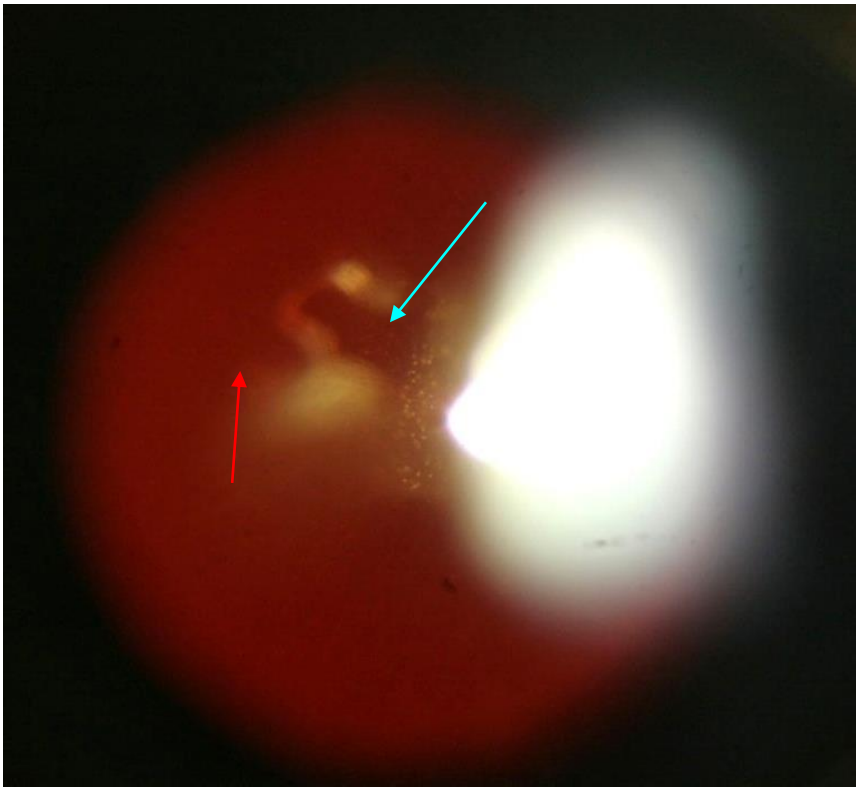

Fig 5.1.2 A colour slit lamp photograph of a Weiss ring at 16x magnification. The vitreous opacities (blue arrow) are seen anterior to the Weiss ring (red arrow)

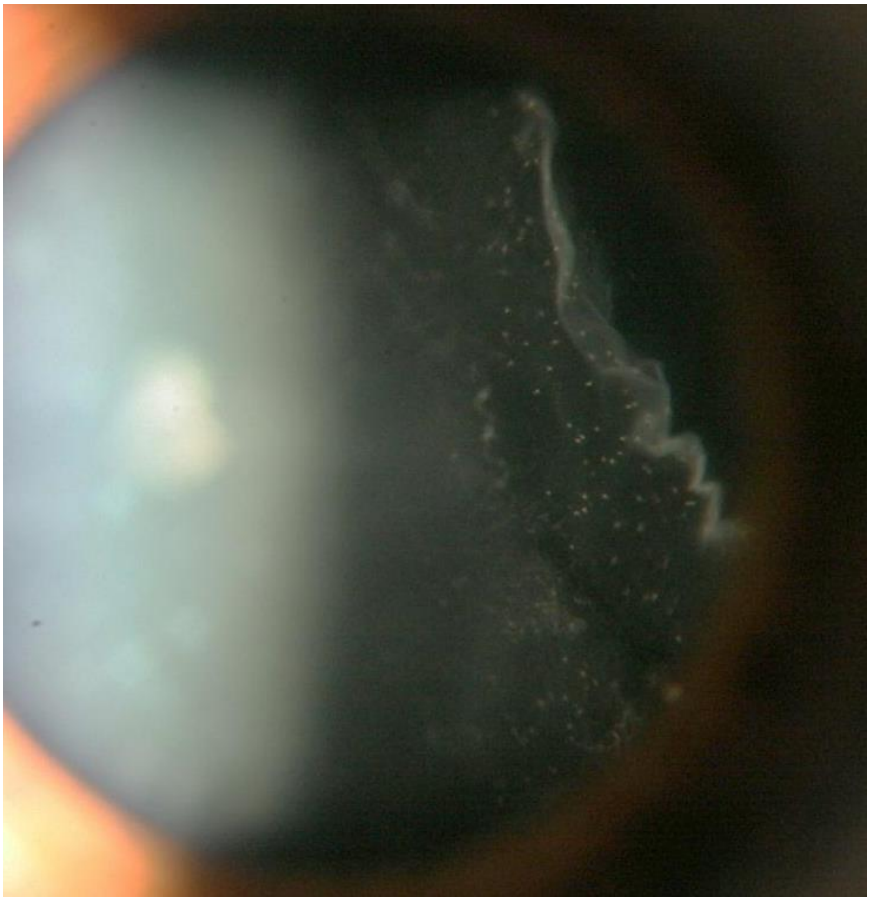

Fig 5.1.3 A colour slit lamp photograph of the crinkled posterior hyaloid membrane with the vitreous opacities visible to the left of this

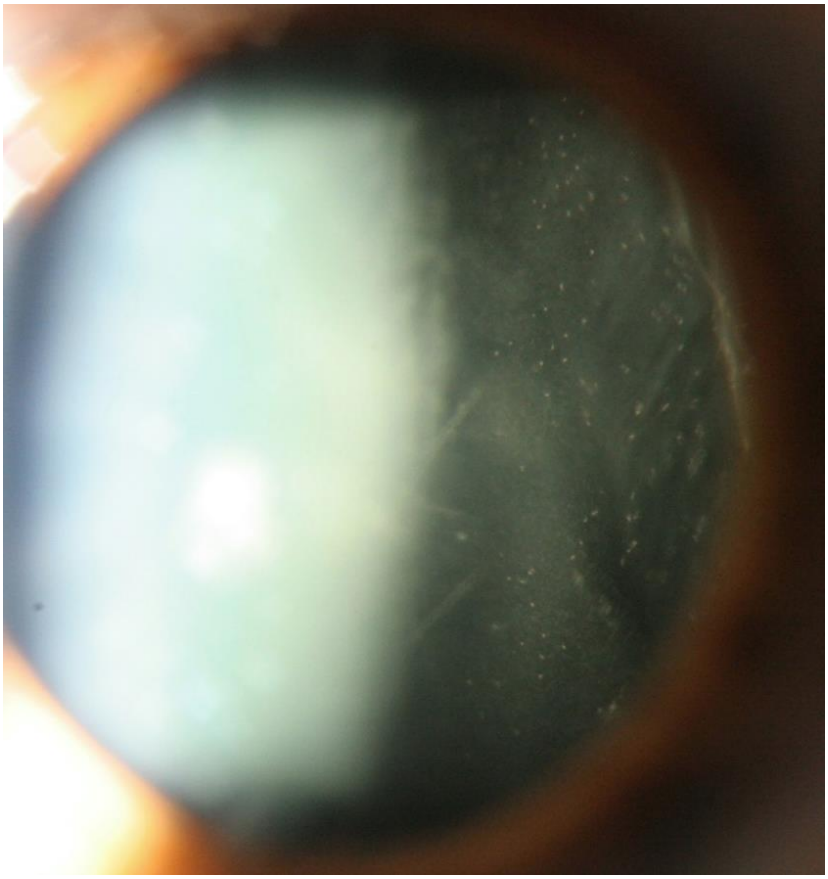

Fig 5.1.4 A colour slit lamp photograph of the same eye in fig. 5.1.3 depicting the vitreous opacities visible as red-brown dots within the anterior vitreous

As described in the introductory chapter, Shafer's sign is the presence of pigment granules in the anterior vitreous secondary to a retinal break (Brod *et al.* 1991; Sharma *et al.* 1999; Tanner *et al.* 2000; Williamson 2013). Clinical examination with the slit-lamp is the only described method for observation of this sign.

Pischel (1952) and Snead *et al.* (1994 and 2008a) describe a similar technique of examining the vitreous with oblique- slit-lamp illumination, this however is compromised by factors such as presence of media opacity, extent of pupillary dilation and patient co-operation. As such clinical examination alone may not be the most appropriate technique to study these opacities. Histological examination would be the preferred method of analysis, as such studies have provided the most accurate descriptions of vitreous anatomy (Worst 1976; Jongebloed & Worst 1987; Sebag & Balazs 1989; Kishi & Shimizu 1990; Sebag 2002 and 2008a), however from a practical sense this would be undesirable. Firstly for a histological examination a sample of the vitreous would be required, which could be accomplished by means of a vitreous biopsy. A recent study by Mudhar & Sheard (2013) confirmed cells are

more likely to be present in the cortical vitreous rather than in the core vitreous in a vitreous biopsy, however to obtain such a sample lead to the formation of retinal breaks in 40% in their study of five patients. The very nature of vitreous biopsy is invasive and in rare cases can result in devastating complications, the most severe of which would be loss of sight (Lobo & Lightman 2003; Ramkissoon *et al.* 2010). As the presence of these opacities has not been found to have an untoward complications, it would not be justifiable to undertake vitreous biopsy for this purpose and it is envisaged ethical approval would not be granted due to the potential risks. Secondly the sample of vitreous obtained is likely to be disturbed and may actually alter the observation.

The presence of a Weiss ring and a detached vitreous cortex are visible morphological changes to the vitreous structure attributable to posterior vitreous detachment (Johnson 2005; Snead *et al.* 2008b). These changes are visible upon clinical examination, and have also been documented with imaging techniques such as B-scan ultrasonography and optical coherence tomography. A reasonable approach therefore would be to utilise diagnostic imaging to permit further study of the described opacities. Ultrasonography has proved to be the technique of choice for imaging the vitreous as a whole (Arzabe *et al.* 1991; Mojana *et al.* 2010; Kičová 2014), and was the technique of choice to objectively demonstrate the vitreous status in investigative licensing studies of a recently approved pharmacologic vitreolysis agent (de Smet *et al.* 2009). Furthermore it is unparalleled in the presence of media opacity for assessment of the posterior segment (DiBernardo 1992; Nischal 1995; Rabinowitz 2004; Lorenzo-Carrero 2009).

Arzabe *et al.* (1991) found ultrasound to be a comparable technique to slit-lamp biomicroscopy for examination of the vitreous in their study of 29 eyes with proliferative diabetic retinopathy for determining the presence of PVD. All eyes had sufficiently clear ocular media to permit adequate visualisation of the fundus by microscopy. A Cohen's kappa of 0.93, indicating almost perfect agreement between the two methods was found for the two techniques. A significant limitation of this study was the relatively small number of eyes studied, and also only eyes with proliferative retinopathy were studied. As such these findings may not necessarily be a repeatable in eyes without proliferative diabetic retinopathy.

A recent study by Kičová *et al.* (2012) compared the accuracy of B-scan ultrasonography, time-domain optical coherence tomography (TD-OCT) and examination with slit-lamp and condensing lens for the detection of posterior vitreous detachment against intra-operative observation. In this study thirty patients scheduled for vitrectomy for vitreo-macular

pathology underwent pre-operative evaluation of the posterior vitreous using the three techniques by independent examiners. This study found 10 MHz B-scan ultrasonography had the highest degree of correlation with intraoperative findings, with 83% of cases being diagnosed correctly. Examination with slit-lamp microscopy was correct also in 76% of cases, with OCT being the least accurate with only 12.5% of cases diagnosed correctly. Interestingly, in this study the presence of a Weiss ring alone was not considered to be representative of PVD, only when the posterior hyaloid was concomitantly posterior was visible also then PVD was diagnosed. It would have been a useful adjunct in this study to determine the reliability of Weiss ring alone as an indicator of PVD. For OCT evaluation, two separate instruments were employed; Zeiss Stratus and Optovue RTVue-100. Although both have a high degree of axial resolution, approximately 10μm and 5μm respectively, both are restricted by the depth of field that can be assessed which is around 1,000μm. Therefore if PVD has occurred and the posterior cortex lies outside of the 1,000μm field, then it will not have been detected by OCT which impedes the application of OCT for this purpose. It is important to note in this study each examination was performed by an independent expert examiner for each aspect. This is highly relevant to clinical practice as the result, and interpretation of the examination, will rely upon the competency of the examiner as acknowledged by the authors. It would be interesting to see if and how the results were affected if less experienced examiners had also been included in this evaluation. Furthermore as the inclusion criterion for this study was quite stringent with a relatively small sample, this may have in fact influenced the outcome. It would be valuable to repeat this study and include eyes without vitreo-macular complications to ascertain the most reliable non-invasive technique for the detection of PVD.

Despite the findings of Kičová and colleagues (2012), TD-OCT has without a doubt been insightful in understanding vitreoretinal relationships. A prospective study of 209 eyes by Uchino *et al.* (2001) classified various stages of PVD based upon observations with OCT. This informative study demonstrated that PVD was not an acute phenomenon, rather an insidious one which may in fact take years to complete. Additionally in this study OCT showed the process of PVD to commence in the perifoveal region, often commencing in the supero-temporal quadrant. An anomalous aspect of this study was almost 80% of study eyes were from males, needless to say this is not representative of the population and one must be careful when extrapolating these results. The largest group studied was a cohort aged between 50-59, in which less than 10% of eyes had complete PVD, with approximately 30% of eyes with no PVD and around 50% of eyes with incomplete PVD. The findings of this study are in agreement to the landmark autopsy study by Foos & Wheeler (1982) in which they found the prevalence of PVD to be less than 10% in those aged 50 or less, and over

60% in eyes aged 70 or above. Although OCT was able to reliably detect PVD in the evolutionary stages, once PVD had occurred the reliability of OCT diminished.

Time domain-OCT has empowered our knowledge and understanding of the vitreoretinal relationships, notably the natural history and evolution of posterior vitreous detachment, it has however been limited by the acquisition speed and resolution achievable (Reichel *et al.* 2009). With recent developments in OCT imaging, notably the introduction of spectral-domain OCT (SD-OCT), there has been a greater improvement in the details and understanding of the vitreous. Mojana *et al.* (2010) have utilised SD-OCT to successfully image the vitreous in 113 subjects with symptoms of posterior vitreous detachment. All subjects were also examined clinically with a slit-lamp biomicroscope to compare the findings of the two techniques. Additionally a subgroup of patients were also examined using traditional ultrasound to evaluate the correlation of this technique with SD-OCT. This study found OCT and clinical findings were highly comparable with a kappa coefficient of 0.82 for the detection of complete PVD. However SD-OCT had a significantly greater degree of sensitivity for the detection of incomplete PVD. In the 30 eyes that also underwent ultrasound examination, there was almost perfect agreement between SD-OCT for all stages of PVD. Although it appears all three techniques were relatively comparable, particularly for macroscopic changes, SD-OCT was far superior for the visualisation of finer details of the posterior vitreous such as the vitreous anatomy and morphological changes of the retina and vitreous as a result of degenerative processes. This is in contrast to the findings of Kičová *et al.* (2014) and clearly demonstrates the vast improvement of SD-OCT

Swept-Source OCT (SS-OCT) has also been implemented for imaging the vitreous. SS-OCT has advantages over SD-OCT; greater scanning speeds with improved sensitivity and imaging depths are possible (Liu *et al.* 2014; Stanga *et al.* 2014) Stanga and co-workers (2014) also used a SS-OCT to image the vitreous and quantify anatomical features of the vitreous. Widefield OCT is a further enhancement and permits greater visualisation of peripheral retina and vitreous (Kolb *et al.* 2015). Liu *et al.* (2014) employed a wide-field three dimensional OCT to obtain in vivo images of the vitreous of 22 healthy eyes. However in this study the instrument employed was a prototype and not commercially available. Nevertheless, perceptive images of the vitreous and cellular opacities were obtained which may provide direction for the future.

Reviews by Sebag (2002 and 2008a) appraising the various imaging modalities for the vitreous including ultrasonography and optical coherence tomography have revealed at present there is no sole satisfactory imaging technique to examine the vitreous body as a

whole; a notion which has been confirmed by others (Mojana *et al.* 2010; Duker *et al.* 2013). Essentially ultrasonography is limited by the degree of resolution it can offer. Conventional 10MHz B-scan ultrasonography is unable to detect structures less than 150-200 μm (Sebag 2002 and 2008a; Mojana *et al.* 2010) and is therefore not the most appropriate imaging modality to study these opacities, which are beyond the resolution capability of this technique. Although TD-OCT has greater resolution, it is limited by the depth of field of approximately 1000 microns (Kičová *et al.* 2012). Comparatively SS-OCT has overcome these limitations with enhanced resolution and depth of field. Unfortunately, there is limited access to this imaging modality in the hospital sector and thus it cannot be utilised in this study. However there has been a very recent refinement to spectral domain OCT in the form of enhanced vitreous imaging (EVI) technique, which as its name suggests, improves visualisation of the vitreous and vitreoretinal interface. Pang *et al.* (2014) have utilised this advent to document in detail the various stages of vitreous detachment and associated morphological alterations. Hence this study employed this new technique applied to TD-OCT as it is a more readily available imaging modality.

5.2 Methods

5.2.1 Sample size

To study the vitreous opacities in the posterior vitreous, a sample size calculation was undertaken using the formula and information below:

$$(Z^2 \times P(1 - P))/e^2$$

Z= 1.96 (normal standard deviation with 95% confidence interval)
P= Prevalence
e= Margin of error

1) *Population size*. The population of adults aged 40 and above in Coventry and Warwickshire has been determined to be 432,765 (Office for National Statistics 2014)
2) *Prevalence*. As detailed above the great majority of patients with clinical PVD have been found to harbour these opacities, in the order of 95%
3) *Confidence level*. This was selected to be 95%
4) *Margin Of error*. This was selected to be 5%

Based on this the minimum sample size was determined to be 73.

5.2.2 Ethics approval

This study was registered with the research and development department at University Hospital Coventry and Warwickshire as a retrospective study. Due to the nature of this study it was deemed ethics approval was not necessary by the research and development department. All patients underwent clinical examination as described in chapter 2 as per standard examination. In addition to clinical examination, optical coherence tomography was undertaken when a vitreoretinal abnormality was present or if symptoms were suggestive of posterior vitreous detachment but without definitive signs on clinical examination. This included eyes such as those exhibiting cells within the vitreous, epiretinal membrane and vitreomacular traction. Images of the contralateral eye would also be taken routinely, the purpose of this was twofold; firstly to provide a comparison against the eye with abnormality and; secondly to determine if the contralateral eye exhibited any similar changes that may contribute prognostic information for either eye.

5.2.3 Inclusion and exclusion criteria

To enhance understanding of these opacities, patients were categorised into the following groups:

1) Patients with bilateral PVD. From previous studies it is accepted that PVD does not occur simultaneously in both eyes of an individual (Byer 1994; Hikichi & Yoshida 2004), rather it is a sequential event affecting one eye first. The purpose of studying such eyes was to determine whether the opacities appear altered with the passage of time i.e. are the opacities more numerous in eyes with recent onset PVD compared to eyes with longstanding PVD?
2) Patients with unilateral PVD. Studying this group of patients would help to ascertain whether these opacities arise in eyes without PVD, or only those with PVD. The eye without PVD would effectively act as an age-matched control against which comparisons can be made
3) Eyes without PVD. This group will be similar to the eyes without PVD in group 2. Similarly the purpose of studying these eyes would provide a control group for comparative observations

The patients for this study were identified from reviewing the medical records of all patients who attended the vitreoretinal clinic and had been examined by the author between 20th May and 31st October 2015. Specific exclusion criteria for this chapter was:

- previous history of intraocular intervention, e.g. crystalline lens extraction, intravitreal injection or vitrectomy
- previous intraocular inflammation e.g. uveitis
- previous history of significant blunt ocular trauma
- where full examination or imaging was not possible

5.2.4 Examination

All patients had previously undergone detailed examination of both eyes as described in chapter 2, with specific attention to the presence or absence of the following details:

- Vitreous opacities as described
- Weiss ring
- Visualisation of the posterior hyaloid membrane on slit-lamp microscopy
- Stage of PVD according clinical examination
    - No PVD
    - Partial PVD
    - Complete PVD without collapse
    - Complete PVD with collapse
- OCT in enhanced vitreous image mode of the vitreous centred on the fovea and optic disc
- Categorisation of the stage of PVD according to OCT, adapted from Uchino *et al.* (2001) and Johnson (2005)
    - Stage 0: No vitreo-retinal separation
    - Stage 1: less than 50% perifoveal vitreous detachment with vitreofoveal and vitreopapillary adhesion
    - Stage 2: 50% or greater perifoveal detachment with vitreofoveal and vitreopapillary adhesion
    - Stage 3: Complete vitreofoveal detachment with vitreopapillary adhesion
    - Stage 4; Peripapillary and foveal detachment, with vitreopapillary adhesion
    - Stage 5: Complete vitreopapillary detachment

5.2.5 Protocol for OCT image acquisition

Following clinical examination, each patient had had OCT images taken of the posterior vitreous of both eyes centred on the fovea and then on the optic nerve using a Heidelberg Spectralis Spectral Domain Optical Coherence Tomographer (Heidelberg, Germany). The procedure for image acquisition had been undertaken according to the literature as provided by the manufacturer (Heidelberg Engineering) and as described by Pang *et al.* (2014), a brief description of the procedure was as follows:

For each patient a new entry had been created on the patient database if the patient had not been imaged previously. For those who had a record on the database, the details of the patient had been updated if necessary. Once the record had been created/updated the

image acquisition commenced. All patients were instructed to remove the spectacles and/or contact lenses and position on to the chinrest and forehead rest. The acquisition mode had been set to reflectance mode and 30º image near infrared (IR) image was centred on the fovea of the right eye. This had then been optimised by altering the illumination and focussing to provide a well-focussed and evenly illuminated image. To acquire the OCT image, the infrared with OCT (IR+OCT) mode had been selected and the OCT image focussed to just below the markers in conjunction with a +2.00 dioptre change in the focus of the instrument. Once the image had been suitably focussed and aligned, the 6-line star pattern had been selected (each line scan length of 6mm) and image acquisition began using the automatic real-time software function. The 6-line star pattern had then been centred on the optic disc and another image was acquired in the same manner. This sequence had then repeated to capture images of the left eye in the same manner.

5. 3 Results

For this retrospective analysis, patients that attended the PVD clinic from the 20th May 2015 until the 29th October 2015 were included. In contrast to previous chapters, the inclusion of patients was not restricted to those whom had been seen in the eye casualty recently for symptoms of PVD. Essentially patients had been referred from four main sources; eye casualty, GPs, community optometrists and other ophthalmology clinics. Primarily this was in order to determine the stage of PVD or otherwise in which the aforementioned opacities were apparent. In total 145 patients were included, of which 35 patients had no evidence of PVD in either eye, 34 patients with bilateral PVD and the remaining 66 patients with PVD in one eye only. The characteristics of these three groups are in table 5.3.1.

	No PVD	Unilateral PVD	Bilateral PVD
N	35	66	34
Mean age	43.4	64.1	67.8
SD	15.7	9.0	5.5
Range	16-79	32-84	51-79
Males	6 (17%)	21 (32%)	8 (24%)
Females	29 (83%)	45 (68%)	26 (76%)
Myope	18 (51%)	16 (24%)	10 (29%)
Emmetrope	11 (31%)	31 (47%)	14 (42%)
Hyperope	6 (17%)	19 (29%)	10 (29%)

Table 5.3.1 Characteristics of the three groups of patients evaluated

As expected the mean age of eyes without PVD were almost two decades younger than the other two groups ($p<0.0001$), and eyes with bilateral PVD were older than eyes with unilateral PVD ($p=0.01$). Unsurprisingly the standard deviations and age ranges were greatest in eyes with no PVD and least in eyes with bilateral PVD. Overall, almost one-quarter (24%) were males, with a greater female presence in all three groups. Interestingly the majority of patients without PVD were myopic, these were usually patients with symptoms suggestive of PVD or lesions suspicious of retinal breaks referred for assessment. In the other two groups there was an almost equal distribution of myopes and hyperopes in each group with emmetropes in majority. The three groups were then combined to form two groups, one for eyes with complete PVD which contained 134 eyes and the other without PVD with 133 eyes. Eyes were deemed to have complete PVD if the vitreous cortex was visibly detached from the retina and mobile on eye movements when viewed through a slit-lamp with a +90D condensing lens as described by Kakehashi *et al.* (2014), additionally on OCT the vitreous was confirmed to be detached from the retinal surface. The features of the two groups are summarised in table 5.3.2.

	PVD	No PVD
N	134	133
Mean age	66.0	53.2
SD	7.6	16.1
Range	32-84	16-80
Right	74 (55%)	61 (46%)
Left	60 (45%)	72 (54%)
Males	37 (28%)	32 (24%)
Females	97 (72%)	101 (76%)
Myope	36 (27%)	46 (34%)
Emmetrope	59 (44%)	56 (42%)
Hyperope	39 (29%)	31 (24%)

Table 5.3.2 Characteristics of eyes with and without PVD

The eyes without PVD were used as a control group against the eyes with PVD. The control group were over a decade younger than the PVD group, as expected this was statistically significant ($p<0.0001$). An interesting observation was in the PVD group there was a bias for right eyes to be affected, whereas this was the contrary in eyes without PVD. With regard to gender, the male to female ratio was approximately 1:3 in both groups. One-third of the control group were myopic, whereas in the PVD group the myopes were least in majority.

The primary focus of this chapter was to determine in which eyes the aforementioned opacities were visible. On clinical examination eyes with complete PVD were found to harbour these opacities, albeit in varying degrees. Most frequently the opacities were found either on or adjacent to the posterior cortex as viewed through the slit-lamp. The optimal technique to visualise the opacities was to centre the observation system in the centre of the pupil with 10-16x magnification and to place the illumination system approximately 20-30° to either nasal or temporal. The slit-lamp beam width was adjusted to approximately 0.3-0.5mm horizontally and 2-3mm vertically. The slit-lamp was then focussed forwards into the vitreous cavity (reducing the angle of illumination if necessary) to bring the posterior vitreous into view. Once the plane of the opacities was located, the angle of illumination could be altered to produce retro-illumination thus permitting an enhanced view. The observation of these opacities was hampered in the presence of significant media opacities, particularly lens opacities which are a frequent finding in this age group. When pupil dilation was sub-optimal (less than approximately 6mm) this further impeded the view. Overall compared to viewing a Weiss ring on a slit-lamp with a condensing lens, locating these was initially more problematic due to the aforementioned factors such as pupil dilation and media opacity, but also due to the size of these opacities and possibly the slit-lamp technique used.

Patients were examined after a mean of 43 days (SD 18.4, range 5-100 days) in the PVD clinic from their initial examination. The opacities were noted in all eyes with PVD when

examined in the PVD clinic and not in any eyes without PVD, thus resulting in a sensitivity of 100% (95% CI 97.3-100%) with a specificity of 100% (95% CI 97.3-100%) for this feature. In one eye it was difficult to be certain of the presence of the conventional features of PVD, thus the sensitivity for the presence of a Weiss ring and/or visualisation of the posterior hyaloid membrane was 99.3% (95% CI 95.9-100%) with a specificity of 100% (95% CI 97.3-100%). The patients with unilateral PVD provided invaluable insight as all eyes with PVD exhibited the opacities whereas in the contralateral eyes there was an absence of opacities. As mentioned earlier the opacities were variable in presence, this was the case even in eyes with bilateral PVD and there was no quantifiable difference between the two eyes for this feature. Furthermore the number or density of opacities did not appear to correlate with the duration of PVD. There were a total of 34 patients with bilateral PVD, of which 4 (12%) had been unaware of any symptoms in the contralateral eye, in 20 eyes the exact duration was uncertain but thought to be greater than at least two years according to patient recollection, and only in 10 was it possible to ascertain the duration of PVD in the contralateral eyes. In eight of these ten patients PVD had occurred 2-10 years prior to the current eye being affected. In two of the ten patients, by the time they were seen in the PVD clinic they had developed symptoms in the contralateral eye, the first with a duration of 5 days and the second 7 days. The opacities were detected in both of the eyes the patient in whom the second eye had become affected seven days after the first. Clinically there was no appreciable difference in the presence of the opacities between the two eyes, they were noted to be more numerous in the eye with recent symptoms. With OCT these opacities were visible as hyper-reflective foci anterior to the retinal surface. Figure 5.3.1 is an EVI-OCT image of the right eye which developed symptoms seven days prior to examination and figure 5.3.2 is an image of the contralateral eye taken at the time of attendance in the PVD clinic 55 days after the initial examination. Regrettably these opacities could only be imaged with OCT in this patient and no other eyes with PVD were found to harbour the opacities on OCT. Nevertheless, the size of opacities was measured to be in the order of 20-80 microns in these 2 eyes

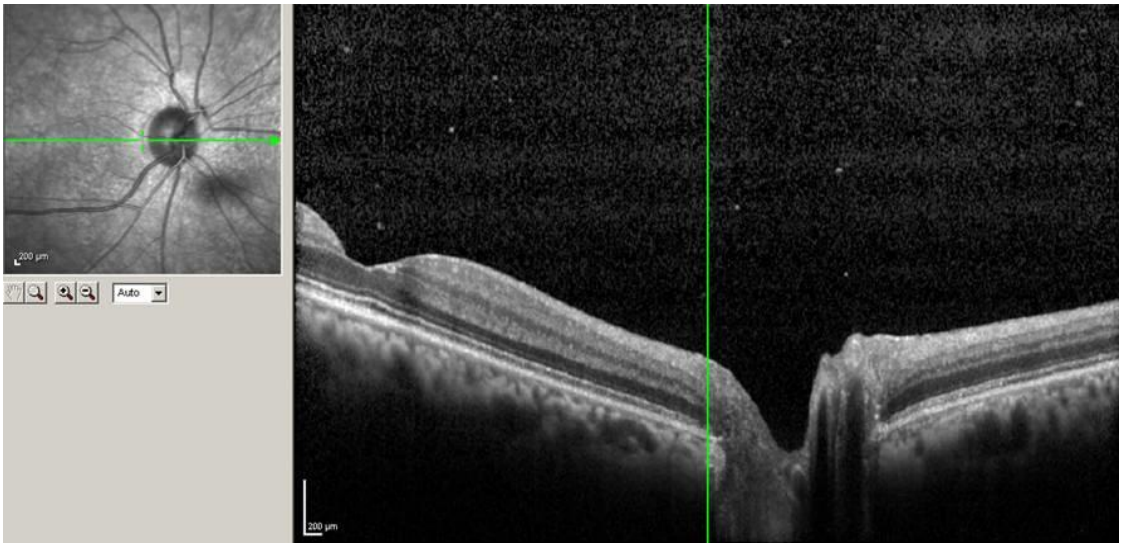

Fig 5.3.1 An infrared image (left) and EVI-OCT image (right) of the right eye of a patient harbouring the aforementioned opacities, note the vitreous body and posterior hyaloid membrane are absent. The vertical green line in the OCT image corresponds to the location in infrared image. A dark opacity is visible inferonasal to the optic disc in the infrared image which is a Weiss ring.

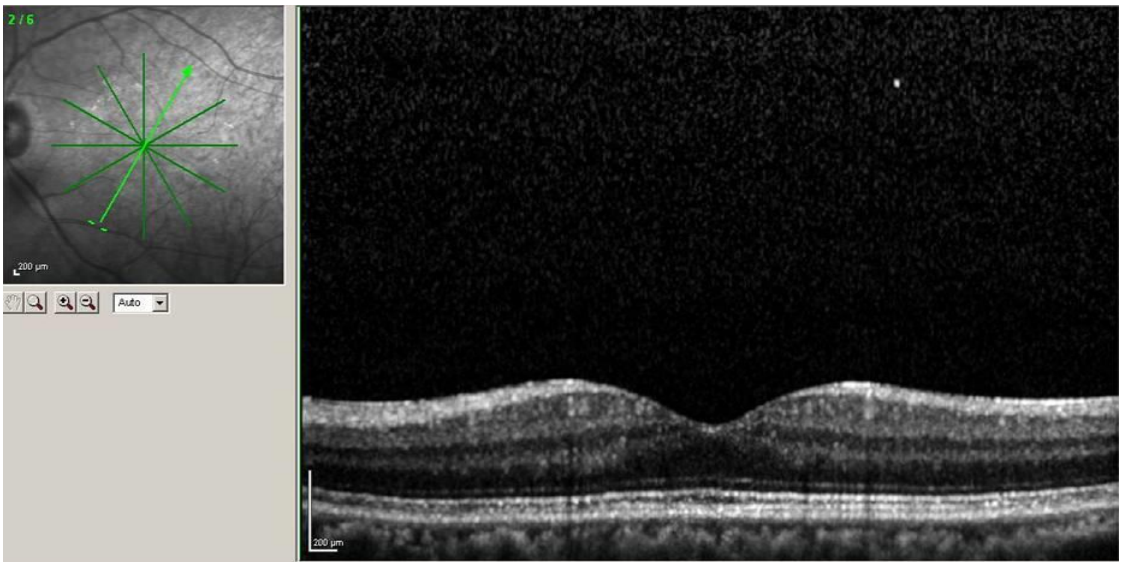

Fig 5.3.2 An infrared image (left) and EVI-OCT image (right) of the left eye centred on the fovea of the same patient in figure 5.3.1, demonstrating one solitary opacity visible in the pre-retinal field corresponding to one of the many opacities seen on examination.

Essentially in all other eyes the opacities were outside of the imaging field of OCT even when the enhanced vitreous imaging mode was enabled. Although OCT was unable to detect these opacities in eyes with complete PVD, they were absent in eyes in earlier stages of PVD both on OCT or clinical examination. Therefore it appears these opacities only become evident in the presence of vitreopapillary separation and not prior to this. Although OCT was a less than satisfactory imaging modality for these opacities in the overall majority, it was however superior to clinical examination for documenting the stage of vitreoretinal

separation prior to complete PVD. Unsurprisingly the vitreous cortex was visualised with OCT in all eyes without complete PVD (stages 0 to 4), a subgroup analysis was undertaken according to the stage of PVD, the findings of which are in table 5.3.3.

	Stage of PVD					
	0	**1**	**2**	**3**	**4**	**5**
N (patients)	34	33	22	31	13	134
Mean age	36.1	49.5	60	67.7	62.4	66.0
SD	12.3	12.2	9.9	7.3	11.7	7.6
Range	16-66	29-70	41-72	53-80	40-75	32-84
Males	9 (26%)	8 (24%)	7 (32%)	6 (20%)	2 (15%)	37 (28%)
Females	25 (74%)	25 (76%)	15 (68%)	25 (80%)	11 (85%)	97 (72%)
Right	18(53%)	16 (48%)	12 (55%)	8 (35%)	7 (54%)	74 (55%)
Left	16(47%)	17 (52%)	10 (45%)	23 (65%)	6 (46%)	60 (45%)
Myope	21(62%)	12 (38%)	6 (27%)	7 (23%)	4 (31%)	36 (27%)
Emmetrope	11 (32%)	12 (38%)	9 (41%)	14 (46%)	5 (38%)	59 (44%)
Hyperope	2 (6%)	8 (24%)	7 (32%)	10 (30%)	4 (31%)	39 (29%)

Table 5.3.3 Categorisation of the stages of PVD with corresponding characteristics

Naturally for each progressive stage of PVD there was an associated increase in mean age. The mean age of eyes without vitreoretinal separation was almost 15 years younger than eyes in the first stage of vitreoretinal separation and this was statistically significant ($p < 0.0001$). There was a further 15 years difference in mean age between the first and second stages of vitreoretinal separation and again this was statistically significant ($p = 0.0009$). For the next stage three stages there were some erroneous findings in that eyes in stage 3 were older than eyes in stage 4 and 5, although the difference in mean ages between stages 2, 3, 4 and 5 were statistically significant (between stage 2 to 3 $p = 0.004$, stage 3-4 $p < 0.0001$, stage 4-5 $p < 0.0001$), the mean age difference between stage 3 and 5 was less than two years and this was not statistically ($p = 0.27$). This suggests the early stages of PVD progress gradually in an insidious manner, whereas once vitreofoveal separation occurs (stage 3) progresses significantly more rapidly.

To further evaluate the correlation between age and stage of PVD, an additional analysis for the proportion of patients for each stage of PVD was plotted for each decade of life (figure 5.3.3). Excluding the second and ninth decades which contained only two and three cases respectively, there evolution of PVD was eloquently visible; a gradual decline of early stages coupled with a progressive increase of eyes in the later stages. It is important to note however there were a disparate number of patients in the final stage of PVD compared to all other stages.

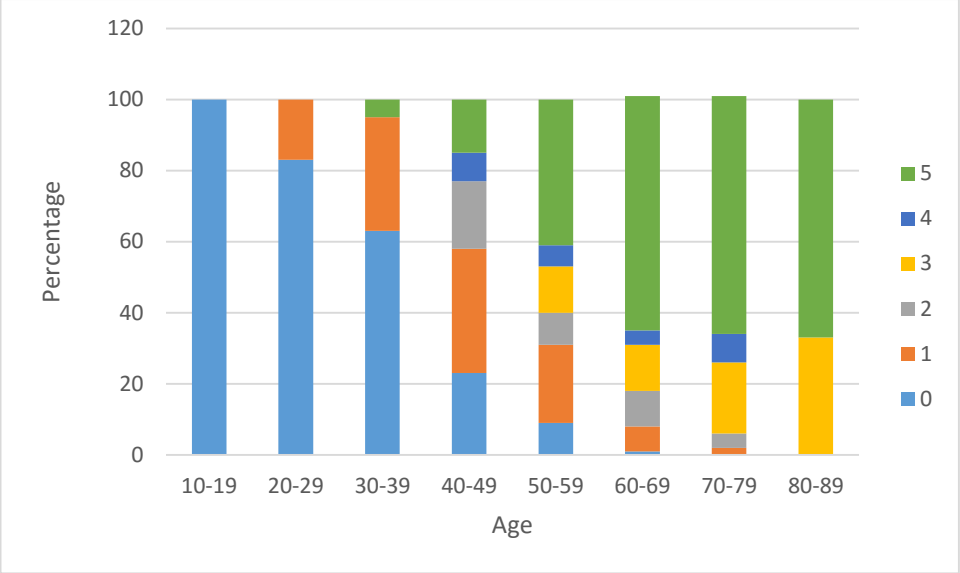

Fig 5.3.3 A graph to represent the stages of PVD per decade of life

Figure 5.3.3 demonstrates the early stage of PVD commences in the third decade affecting almost 20% in this age group. Over the next decade there was an almost doubling of eyes with the first stage of PVD and less than 5% of eyes had developed complete PVD by this point. The fifth decade of life demonstrated the evolving nature of PVD with less than one quarter of eyes having no vitreoretinal separation and almost 20% having complete vitreo retinal separation with remaining 60% in the intermediary stages. By the sixth decade the preponderance of eyes with complete PVD was evident with over 40% of eyes exhibiting this, additionally the proportion of eyes without vitreoretinal separation was less than 10% at this stage. From the seventh decade and above complete PVD was present in almost two-thirds of eyes with further diminishing of earlier stages.

5.4 Discussion

The implementation of OCT in conjunction with clinical examination proved to be highly beneficial despite the limitations in the detection of vitreous opacities. One of the most poignant findings was the progression of the various stages of PVD with OCT. Although the current study was designed to evaluate opacities within the vitreous associated with PVD, there were remarkably similar parallels to the study by Uchino *et al.* (1991). Nevertheless there were significant dissimilarities also, the first obvious difference was the current study used SD-OCT whereas the former employed TD-OCT. A second most influential difference was the disparity in the grading of the stages of PVD according to OCT. The first 4 stages (0-3) were identical as was the final stage, however there was an additional stage in the current study in which stage 4 was defined as residual peri-papillary adhesion, a stage not included in the former but recognised by Johnson (2005). For this study this was an important stage as whilst there was peri-papillary adhesion there were no opacities within the vitreous, whereas once vitreo-papillary adhesion had been released the opacities were recognised in the vitreous. If the former grading system had been used there may have been some discrepancy as to which stage the opacities become apparent in the vitreous. A potentially less influential discrepancy between the two studies was that in the current study there was a greater proportion of females with a male to female ratio of 1:3, whereas in the former study males were the largest in proportion with a ratio of 3:1 to females. Previous studies of PVD, including previous chapters here, have found the female gender to present more frequently with PVD (Byer 1994; Hayreh & Jonas 2004; Chuo *et al.* 2006), therefore although the landmark study by Uchino *et al.* (1991) provided valuable insight it is not necessarily representative of the actual population. Secondly in the current study there was a significantly greater number of eyes with complete PVD (134 vs 18 eyes), however there was a different objective for each study and therefore this was disparity was anticipated. Notwithstanding, overall the progression of the stages of PVD per decade of life in both studies correlated reasonably well. A previous chapter has examined in detail the characteristics of eyes with PVD (see chapter 3), with regard to the eyes evaluated in this chapter the characteristics were similar to the previous chapter and were consistent with findings in the literature.

A significant limitation in this study was the inability to consistently document the presence of the opacities with OCT. This is primarily due to the limitation in the depth of imaging field of OCT even with the enhanced vitreous imaging modality. The plane of focus can be altered with OCT permitting visualisation of the posterior hyaloid, however this is at the detriment of image quality such that small opacities are not recognised due to the resultant noise as the

reference plane of the retina is no longer in the field resulting in erratic signals. As an alternative, the opacities could have been documented with slit-lamp photography, however this would not be without limitations also. One such limitation would be the variability of the plane in which images would be taken. With OCT the retina is used as the reference, whereas with photography the image plane is not consistent and directly dependant upon the plane of focus. Therefore localisation of structures and measurements would be erroneous and inaccurate. Nevertheless standardisation of the procedure by using predetermined settings for illumination and magnification for imaging together with the use of a grading scale could have been a potential improvement for the depiction of the opacities. Grading scales for evaluating the vitreous exist such as the Nussenblatt scale (Nussenblatt *et al.* 1985) and a modification of this (Davis *et al*. 2010) however these are employed in uveitis and where fundus view is obscured. As the opacities found in the study do not obscure the fundus view to any appreciable degree, application of these scales would be ineffective. Recently techniques to analyse the degree of vitreous inflammation using SD-OCT have been demonstrated (Keane *et al.* 2014 and 2015) however due to the location of these opacities these techniques may prove to be equally ineffective. The opacities in this study are not as large and numerous as the opacities found in vitreous inflammation, and furthermore the depth of imaging field remains restricted. It would have been desirable to employ swept-source OCT as potentially the limitations of EVI-OCT may have been overcome, however this was not possible due to the aforementioned factors as described in the introduction.

In retrospect it would have been helpful to document the vitreous status with OCT and to search search for these opacities at the initial examination as this could have also to provide additional insight regarding the onset and duration. This was demonstrated in the one patient in whom it was possible to document the opacities with OCT. The opacities were more apparent and closer in apposition to the retinal surface in the eye with recent onset symptoms and therefore studying eyes with recent onset PVD may provide valuable insight into the nature and origin of these opacities. This study did not further the knowledge in determining the origin of these opacities, however one could speculate they may originate from the internal limiting membrane in the form of glial cells or laminocytes as these have been implicated in the formation of epiretinal membrane as a result of PVD (Foos 1974; Snead *et al*. 2008a). Another possibility is that these opacities may be remnants of the vitreous cortex. Regardless of the origin, once vitreopapillary adhesion is released the opacities appear to migrate anteriorly through the opening in the posterior hyaloid membrane (the Weiss ring) and intermingle within the vitreous body, but remain in close apposition to the posterior hyaloid membrane where they are seen to be most abundant.

Although there were significant inadequacies in imaging, certain refinements to the methodology could have been highly beneficial. The first of these refinements would have been to utilise more than one assessor, this would permit an evaluation of the interobserver repeatability together with an enhanced calculation of the sensitivity and specificity of these opacities. Furthermore if a masking process had been implemented such as that employed Tanner *et al.* (2000), in that one examiner assessed for the presence of the opacities and another independent examiner assessed for the presence of PVD conventionally i.e. presence of Weiss ring and/or visualisation of a detached posterior hyaloid membrane, this would have dramatically reduced the inherent confounding bias in this study. Despite these limitations, a high degree of sensitivity and specificity of these opacities for the presence of PVD was found. Nevertheless it is possible this may be significantly more variable than found in this study based on the acknowledged limitations of the study and also the findings of previous studies on the sensitivity of Shafer's sign (Hamilton & Taylor 1972; Brod *et al.* 1991; Sharma *et al.* 1999; Tanner *et al.* 2000), from these studies the sensitivity of Shafer's sign for the presence of a retinal break is between 63-94%. Additionally the level of experience of the examiner will influence the detection of this sign as found by Qureshi & Goble (2009).

In light of these studies and the limitations of the current study further work needs to be undertaken to validate and enhance the findings of this study. With respect to this longitudinal studies in eyes with evolving and recent onset PVD may provide valuable information as to which eyes may be at risk of developing pathology. It may be that eyes with a greater number of opacities have an increased predisposition to the development of epiretinal membrane. Nevertheless it appears that these opacities are innocuous and that eyes with these opacities do not appear to be exposed to a risk of developing pathological changes, however this requires substantiation.

In cases where a Weiss ring is not easily distinguishable as is the case in around 12.5% of eyes with PVD (Akiba *et al.* 2001; Kakehashi *et al.* 1998; Tanner *et al.* 2000) the emergence of these opacities in an eye may assist in the diagnosis of such cases. The long-term implications are as of yet uncertain to some degree due to the cross-sectional nature of this study, and it was not possible to determine how these opacities evolve with time. However, from the 34 patients with bilateral PVD it appears the opacities persist in the vitreous once they appear as they were noted in eyes in which PVD had occurred up to 10 years prior and these eyes did not appear to have any other abnormality. The presence of this finding will aid clinicians in confirming the diagnosis of PVD, additionally the absence of this finding suggests there is still attachment of the vitreous to the posterior pole and there may still be a

risk of subsequent retinal breaks. The hypothesis suggests these opacities exist in complete PVD, however due to the indeterminate origin of the opacities and differing aetiology they do not exclude the concomitant presence of a retinal break. Most importantly, one must be able to differentiate these opacities from Shafer's sign. Pigment cells in Shafer's sign are quoted to measure 30-50 microns in size (Williamson 2013), similarly the opacities in this study have been found to be more variable in size at 20 - 80 microns. With regard to colour both can be variable, but are often brown in colour as also noted by Pischel (1952), therefore neither size nor colour can be used to accurately distinguish between the two. In contrast location and density are the most reliable differentiators, in Shafer's sign the pigment cells are often found to be more numerous in the anterior vitreous, whereas the opacities described here are most evident in the mid to posterior vitreous adjacent to the posterior hyaloid membrane. Regardless of whether pigment cells or the aforementioned opacities are seen, a retinal break must be excluded. Where there is any uncertainty further referral is recommended to exclude the presence of potentially sight-threatening pathology.

5.5 Conclusion

The recognition of these opacities is a stimulating prospect as it may influence the clinical management of patients exhibiting this feature. Nevertheless the findings are limited and further work needs to be undertaken to validate, consolidate and expand upon the knowledge that has been gained from this preliminary study. In the current study OCT even with the enhanced vitreous imaging procedure was extremely poor in the detection of the opacities. Nevertheless it was possible in one patient and it was therefore possible to obtain an accurate size of these opacities. Future studies with OCT should be directed towards the assessment of eyes during the acute stage of PVD. Furthermore employing other OCT modalities which are capable of imaging larger areas of the vitreous such as swept-source OCT in a longitudinal study may provide insight into the evolution of these opacities.

Chapter Six: Final Conclusion

Ageing induces changes throughout the body and the vitreous is no exception. The onset of age and the impact of a number of variables on PVD and retinal breaks were discussed in the first chapter. Although initially PVD may seem to be trivial, devastating complications can arise as a result of this seemingly innocuous process. Both optometrists and ophthalmologists are involved in the management of PVD, although there is some degree of variance as to the examinations undertaken. Primarily optometrists in the UK are not required to undertake scleral indentation, however this is a recommended examination by Ophthalmologists in the UK and elsewhere (Royal College of Ophthalmologists 2010; American Academy of Ophthalmologists 2014; College of Optometrists 2014). Typically optometrists do not receive the same degree of exposure to retinal breaks as their ophthalmologist colleagues, and therefore may potentially overlook sight-threatening features (Qureshi & Goble 2009). Furthermore if a retinal break is undetected by the optometrist and later progresses, they are likely to present to an ophthalmologist (which may be by virtue of the counselling they have received by the optometrist), with the optometrist being unaware of the development unless they receive communication either from the patient, treating clinician or in the most unfortunate circumstances litigation.

The second chapter demonstrates with appropriate training optometrists do have the ability to perform equally comparable examinations as ophthalmologists, a finding that consolidates the notion of previous studies (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Marks *et al.* 2012). One of the features of this study was the number of retinal breaks detected in patients with an uneventful PVD at the initial visit. This essentially prompted an evaluation of the PVD clinic to ascertain whether it was necessary to review patients if the initial examination has been uneventful, a topic that has been contested with contrasting views in the literature (Jaffe 1968; Tasman 1968; Kanski 1975; Novak & Welch 1984; Byer 1994; Dayan *et al.* 1996; Richardson *et al.* 1999; van Overdam *et al.* 2001 and 2005; Coffee *et al.* 2007; Hollands *et al.* 2009; Schweitzer *et al.* 2011; Williams *et al.* 2011). The primary objective of the third chapter was to provide a decisive outcome for this ambiguity. The outcome for this specific entity was 4.3% of patients were noted to have retinal breaks when assessed in the PVD clinic, with 50% of these requiring treatment. One patient was found to have developed retinal detachment without progression of symptoms. Importantly a further

16.1% had conditions that were undetected at the initial examination, almost a third (31.1%) of these warranted further intervention. In total one-fifth of patients were found to have additional findings in the PVD clinic, with a total of 7.2% requiring intervention. Furthermore symptoms were not a reliable indicator for the presence of pathology and were not specific for PVD or retinal breaks alone (Novak & Welch 1984; Dayan *et al.* 1996; Hollands *et al.* 2009; Goodfellow *et al.* 2010; Schweitzer *et al.* 2011; Hurst *et al.* 2015). Ultimately therefore patients with symptoms should be examined at the onset of PVD and at least once again 4-6 weeks later, not least to detect retinal breaks but also to ensure the initial diagnosis and management is correct.

A number of findings from previous studies were also confirmed. Firstly the demographics of patients with PVD and retinal breaks were in agreement with previous studies with the greatest incidence in the sixth and seventh decade (Jaffe 1968; Tasman 1968; Combs & Welch 1982; Novak & Welch 1984). Refractive error differences exhibited an influence on the age of onset (Akiba 1993; Byer 1994; Yonemoto *et al.* 1994 and 1996), with myopes developing PVD 5-10 years earlier than non-myopes. With respect to fundus examination there was no significant difference in the sensitivity of slit-lamp biomicroscopy with a +90D lens or a 3-mirror contact lens, both were inferior to indirect ophthalmoscopy with indentation, with approximately 10-15% of lesions undetected in comparison which concurred with the findings of Natkunarajah *et al.* 2003. This further consolidated the notion of indirect ophthalmoscopy with indentation is the gold standard of assessment for this purpose. Interestingly the sensitivity of Shafer's sign was variable; in the order of 7-14% in eyes that did not require treatment, increasing up to 68% in chapter three to 85% in chapter four. One could speculate whether the improvement in sensitivity was proportional to the experience of the optometrist which developed by the time treatment procedures were undertaken. However the findings were verified by a consultant vitreo-retinal ophthalmologist with adequate experience to evaluate this feature.

In chapter three a total of 1107 patients were examined of which 1027 (93%) were discharged from the PVD clinic. Applying a number needed to treat calculation (in this case a number needed to review), this would equate to reviewing 13 uneventful patients with PVD to find one requiring intervention of some nature. The cost-effectiveness and burden on the health economy of reviewing such patients is therefore warranted. The cost of retinal detachment repair in a hospital setting has been evaluated by Chang & Smiddy (2014) and is in the order of circa £5000, with laser retinopexy alone equating to approximately one-fifth of the cost. The national NHS tariff payment for an ophthalmology outpatient appointment is approximately £100 (NHS England 2013), therefore the cost of reviewing the 1027 patients

who were discharged at the first visit is £102,700. Additionally the cost of retinopexy for the twenty-five patients amounts to a further £25,000, and £2,500 for the cost of reviewing patients with retinal breaks and did not require treatment. The cumulative cost of reviewing these patients is therefore approximately £130,200. In contrast presuming all patients in category 3.4.3 would have required further examination, amounting to £5500, and assuming all twenty-five patients treated for retinal breaks would have progressed to retinal detachment, the total for these two groups would be in the order of £130,500. Overall there would be a marginal (£300) cost benefit, and on the basis of this it could be suggested there is no significant benefit to the health economy in reviewing this group of patients following an initial uneventful examination. This impression does however assume if these patients were not reviewed and retinal detachment were to ensue, then the delay in seeking attention would not alter the complexity of the detachment or subsequent surgical repair or outcome. It is recognised delays in treatment can result in more complex detachments which may arise due to the stimulation of membrane proliferation on the retina and vitreous, termed proliferative vitreoretinopathy, as a result of the presence of liberated RPE cells from retinal breaks and other factors implicated in the response of an eye to a retinal break (Hilton *et al.* 1983; Nagasaki *et al.* 1998, Tseng *et al.* 2004; Pastor *et al.* 2005). Patel and colleagues (2004) have demonstrated the cost of resources is approximately doubled in eyes with more complicated detachments, therefore the cost of treating the twenty-five patients with retinal breaks could potentially be in the region of £250,000. With this in mind, reviewing patients following an acute episode of PVD even if the initial examination is uneventful does appear to be cost-effective.

In addition to cost effectiveness the quality of life of and impact of retinal detachment even if successfully repaired needs to be considered. Okamato *et al.* (2008) and Smretschnig *et al.* (2015) have found quality of life and visual function to be reduced in those treated for retinal detachment compared to age-matched controls. This may present an additional burden on the economy as rehabilitation for the patient or modifications to the environment may be required to overcome the negative impact of retinal detachment even if successfully repaired. These factors also need to be taken into consideration, and as such it would be prudent to prevent retinal detachment, but also be pragmatic in that the majority of retinal breaks associated with posterior vitreous detachment develop within the first four weeks of the onset of symptoms (Sharma *et al.* 2004). Therefore when no retinal breaks have been detected at the initial visit and again at a subsequent visit a few weeks later, further subsequent reviews beyond this are highly unlikely to be cost-effective.

Although indirect ophthalmoscopy is the gold standard to detect retinal breaks (Ruiz 1969; Sharma *et al.* 1999; Natkunarajah *et al.* 2003), it is worth understanding the cost-effectiveness of this undertaking. A potential cost-improvement could be to delegate the follow-up examination to community optometrists as part of a shared care scheme if the initial examination is uneventful. Locally optometrists are paid approximately £60 for each patient seen for minor eye conditions that can be managed by optometrists. If the PVD review was scheduled in such a clinic this could potentially equate to approximately £41,080 cost reduction. Extrapolating the results of chapter 3 for the sensitivity of +90D examination for the detection of retinal breaks, found to be approximately 85%, then of the 25 cases necessitating treatment 4 cases would potentially be overlooked. Once again assuming these 4 cases progress to retinal detachment, the cost of repair would sum to £20,000. Additionally, assuming all 21 remaining cases of retinal breaks are detected then overall the intervention costs equate to approximately £41,000. In this scenario there would be negligible cost-improvement. Furthermore one does need to be mindful of the potential litigation that may arise in the 4 cases in which breaks may be missed. The costs and impact of this may further dilute any benefit of delegating the follow-up examination to be undertaken without scleral indentation as described.

The pioneering work of chapter four will be of immense interest to both optometrists and ophthalmologists. The findings of this study are in parallel with the second chapter and previous studies in that optometrists are capable of undertaking extended roles traditionally performed by ophthalmologists in a safe and appropriate manner (Azuara-Blanco *et al.* 2007; Hau *et al.* 2007; Marks *et al.* 2012). In essence the optometrist was able to undertake treatment of retinal breaks with a comparable primary success rate to that of other ophthalmologists. Needless to say the results of this require further validation, however hopefully this will be seen in a positive manner by both professions and encourage other optometrists to progress in a similar manner to further extend the role of optometry as a healthcare profession.

Naturally one could question the consequence of optometrists undertaking this procedure and one such effect could be that this potentially has a negative impact upon trainee ophthalmologists by reducing the number of retinal breaks they are exposed to treating. In the UK currently there are approximately 14,000 registered optometrists, with only 6% working in hospitals of which the majority undertake traditional optometry roles (Creer *et al.* 2014; College of Optometrists 2015). Furthermore in the institution where this study has been performed there has been no appreciable impact upon the exposure of trainees to retinal breaks as the majority present in eye casualty which is staffed by trainee ophthalmologists. Also evident from the study was the optometrist treated 43 breaks in

almost 2 years equating to approximately one break per month, of which all breaks were identified and treated in the outpatient PVD clinic. Traditionally these would have all been treated by the consultant, and therefore by the optometrist undertaking these treatments there is no disadvantage to trainee ophthalmologists.

Chapter five has demonstrated the importance of imaging in the diagnosis and management of patients with PVD. The opacities were noted only once complete vitreo-retinal separation occurred and not in other eyes, thus this feature being diagnostic for the presence of PVD. The prognostic value of this feature does need further study and validation, but it appears this may be a more useful sign that either a Weiss ring or visualisation of the posterior cortex alone. Further education of eye professionals will be useful in the recognition of this sign and may stimulate further interest into the aetiology of their nature. Although the benefit of OCT was limited, it permitted measurement of the opacities which in future may be critical for differentiation from other similar opacities which may be more sinister. Early examination and assessment with OCT may prove to be more informative in this regard.

List of References

Akiba J (1993) Prevalence of posterior vitreous detachment in high myopia. *Ophthalmology* **100**: 1386-1388

Akiba J, Ishiko S and Yoshida A (2001). Variation of Weiss's ring. *Retina* **21**: 243-246

Al-Asadi S Z (2013) Vitreous floaters and photopsia as predictors of vitreoretinal pathology. *Bas J Surg* **(19th March)** 50-55

American Academy of Ophthalmologists (2014) Preferred Practice Pattern. Posterior vitreous detachment, retinal breaks and lattice degeneration

Anderson J R (1932) Anterior dialysis of the retina: Disinsertion or avulsion at the ora serrata *Br J Ophthalmol* **16**: 641-670

Arzabe C W, Akiba J, Jalkh A E, Quiroz M A, Trempe C L, McMeel J W and Celerio J M (1991) Comparative study of vitreoretinal relationships using biomicroscopy and ultrasound. *Graefes Arch Clin Exp Ophthalmol* 229: 66-68

Azuara-Blanco A, Burr J, Thomas R, Maclennan G and McPherson S (2007) The accuracy of accredited glaucoma optometrists in the diagnosis and treatment recommendation for glaucoma. *Br J Ophthalmol* **91**: 1639-1643

Balazs E A and Denlinger J L (1982). Ageing changes in the vitreous. In: Dismukes K and Sekular R (eds). *Ageing and human visual function*. Alan R Liss, Inc: New York: 45-57

Berens C, Cholst M, Emmerich R and McGrath H (1954) Moore's lightning streaks: a discussion of their innocuousness. *Trans Am Acad Ophthalmol Soc* **52**: 35-58

Bermab E R (1969) Mucopolysaccharides (glycosaminoglycans) of the retina: identification, distribution and possible biological role. *Mod Probl Ophthal* **8**; 5-31

Bishop P N, Crossman M V, McLoed D and Ayad S (1994) Extraction and characterisation of the tissue forms of collagen types II and IX from bovine vitreous. *Biochem J* **299**: 497-505

Bishop P N (2000) Structural macromolecules and supramolecular organisation of the vitreous gel. *Prog Retin Eye Res* **19**: 323–344.

Blach R K (1967) Peripheral retinal degeneration. *Br J Ophthalmol* **51**: 714-715

Blindbæk S and Grausland J (2014) Prophylactic treatment of retinal breaks – a systematic review. *Acta Ophthalmologica* **93**: 3-8

Boldrey E E (1983) Risk of retinal tears in patients with vitreous floaters. *Am J Ophthalmol* **96**: 783-787

Bos, K J, Holmes D F, Kadler K E, McLeod D, Morris N P and Bishop P N (2001) Axial structure of the heterotypic collagen fibrils of vitreous humour and cartilage. *J Mol Biol* **306**: 1011-1022

Bovino J A and Burton T C (1980) Measurement of the relative afferent pupillary defect in retinal detachment. *Am J Ophthalmol* **90**: 19-21

Brod R D, Lightman D A, Packer A J and Saras H P (1991) Correlation between vitreous pigment granules and retinal break in eyes with acute posterior vitreous detachment. *Ophthalmology* **98**: 1366-1369

Byer N E (1974) Changes in and prognosis of lattice degeneration of the retina. *Trans Am Acad Ophthalmol Otolaryngol* **78**: 114-125

Byer N E (1982) The peripheral retina in profile: a stereoscopic atlas. Criterion Press, California: 105

Byer N (1994) Natural history of posterior vitreous detachment with early management as the premier line of defense against retinal detachment. *Ophthalmology* **101**: 1503-1514

Byer N E (1998) What happens to untreated asymptomatic retinal breaks, and are they affected by posterior vitreous detachment? *Ophthalmology* **105**:1045-1050

Carrero J L (2012) Incomplete posterior vitreous detachment: prevalence and clinical relevance. *Am J Ophthalmol* **153**: 497-503

Carvounis P E and Holz E R (2006) Management of retinal breaks and conditions predisposing to retinal detachment. *Comp Ophthalmol Update* **7**:13-22

Chapman-Davies A and Lazarevic A (1996) Prevalence of retinal tears in an optometric population. *Clin Exp Optom* **1**: 12-18

Chen T Y, Yang C M and Liu K R (2006) Intravitreal triamcinolone staining observation of residual undetached cortical vitreous after posterior vitreous detachment. *Eye* **20**: 423-427

Cheng S C K, Lam C S Y and Yap M K H (2010) Retinal thickness in myopic and non-myopic eyes. *Ophthal Physiol Opt* **30**: 776-784

Chuo J Y, Lee T Y Y, Hollands H, Morris A H, Reyes R C, Rossiter J D, Meredith S P and Maberley D A L (2006) Risk factors for posterior vitreous detachment: a case-control study. *Am J Ophthalmol* **142**: 931-937

Coffee R E, Westfall A C, Davis G H, Mieler W F and Holz E R (2007) Symptomatic posterior vitreous detachment and the incidence of delayed retinal breaks: case series and meta-analysis. *Am J Ophthalmol* **144**: 409-413

College of Optometrists (2014) Guidance for professional practice

College of Optometrists (2015) The optical workforce survey 2015.

Colyear B H Jr and Pischel D K (1956) Clinical tears in the retina without detachment. *Am J Ophthalmol* **41**: 773-792

Combs J L and Welch R B (1982) Retinal breaks without detachment: natural history, management and long-term follow-up. *Trans Am Ophthalmol Soc* **80**; 64-97

Cooling R J (1986) Traumatic retinal detachment-Mechanisms and management. *Trans Ophthalmol Soc UK* **105**: 575-579

Coupland S E (2008) The pathologist's perspective on vitreous opacities. *Eye* **22**: 1318-1329

Creer R, Jackson A J and Harper R (2014) Optometry at the interface: the evolving role of the hospital optometrist. *Optometry in Practice* **15**: 185-191

David T T, Smye S, Dabbs T and James T (1998) A model for the fluid motion of vitreous humour of the human eye during saccadic movement. *Phys Med Biol* **43:** 1385-1399

Davis M D (1974) Natural history of retinal breaks without detachment. *Arch Ophthalmol* **92**: 183-194

Davis J, Madow B, Cornett J I, Stratton R, Hess D, Porciatti V and Feuer W J (2010) Scale for photographic grading vitreous haze. *Am J Ophthalmol* **150**: 637–641

Dayan M R, Jayamanne D G R, Andrews R M and Griffiths P G (1996) Flashes and floaters as predictors of vitreoretinal pathology: is follow-up necessary for posterior vitreous detachment. *Eye* **10**: 456-458

Delori F, Pomerantzeff O and Cox M S (1969) Deformation of the globe under high-speed impact: Its relation to contusion injuries. *Invest Ophthalmol* **8**: 290-301

de Smet M D, Gamdorfer A, Stalmans P, Veckeneer M, Feron E, Pakola S and Kampik A (2009) Micropalsmin intravitreal administration in patients with vitreomacular traction scheduled for vitrectomy: the MIVI I trial. *Ophthalmology* **116**: 1349-1355

Diamond J (1992) When are simple flashes and floaters ocular emergencies? *Eye* **6**: 102-104

DiBernando C, Blodi B and Frazier Byrne S (1992) Echographic evaluation of retinal tears in patients with spontaneous vitreous haemorrhage. *Arch Ophthalmol* **110**: 511–514

Dobbie J G (1963) A study of the intraocular fluid dynamics in retinal detachment. *Arch Ophthalmol* **69**: 159-164

Dolgin E (2015) The myopia boom. *Nature* **519**: 276-278

Duker J S, Kaiser P K, Binder S, de Smet M D, Gaudric A, Reichel E, Sadda S R, Sebag J, Spaide R F and Stalmans P (2013) The International Vitreomacular Traction Study Group Classification of Vitreomacular, Adhesion, Traction and Macular Hole. *Ophthalmology* **120**: 2611-2619

Dunker S, Glinz J and Faulborn J (1997) Morphologic studies of the peripheral vitreoretinal interface in humans reveal structures implicated in the pathogenesis of retinal tears**.** *Retina* **17**:124-130

Eye Disease Case-Control Study Group (1993). Risk factors for idiopathic rhegmatogenous retinal detachment. *Am J Epidemiol* **137**: 749–757

Finneman S C and Chang Y (2008) Photoreceptor-RPE interactions. Chapter 4 in Visual Transduction and Non-Visual Light Perception. Humana Press, New Jersey: 67-86

Folk J C, Thompson H S, Farmer S G, O'Gorman T W and Dreyer R F (1987) Relative afferent pupillary defect in eyes with retinal detachment. *Ophthalmic Surg* **18**: 757-759

Folk J C, Sneed S R, Folberg R, Coonan P and Pulido J S (1989) Early retinal adhesion from laser photocoagulation. *Ophthalmology* **96**: 1523-1525

Foos R Y and Allen R A (1967) Retinal tears and lesser lesions of the peripheral retina in autopsy eyes. *Am J Ophthalmol* **64**: 643-655

Foos R Y, Spencer L M, Straatsma B R (1969) Trophic degenerations of the peripheral retina. In: Transactions of the New Orleans Academy of Ophthalmology: Symposium on Retina and Retinal Surgery. St Louis: C V Mosby: 90–102

Foos R (1974) Vitreoretinal juncture-simple epiretinal membranes. *Albrecht Von Graefes Arch Klin Exp Ophthalmol* **189**: 231-50

Foos R Y and Wheeler N C (1982) Vitreoretinal juncture. Synchysis senilis and posterior vitreous detachment. *Ophthalmology* **89**: 1502–1512

Foulds W S (1985) Do we need a retinal pigment epithelium (or choroid) for the maintenance of retinal apposition? *Br J Ophthalmol* **69**: 237-239

Foulds W S (1987) Is your vitreous really necessary? The role of the vitreous in the eye with particular reference to retinal attachment, detachment and the mode of action of vitreous substitutes. *Eye* **1**: 641-664

Friedman S M and Margo C E (2000) Choroidal neovascular membranes: reproducibility of angiographic interpretation. *Am J Ophthalmol* **130**: 839-841

Fujiwara T, Imamura Y, Margolis R, Slakter J S and Spaide R F (2009) Enhanced depth imaging optical coherence tomography of the choroid in highly myopic eyes. *Am J Ophthalmol* **148**: 445-450

Ghazi N G and Green W R (2002) Pathology and pathogenesis of retinal detachment. *Eye* **16**: 411-421

Ghosh Y K, Banerjee S and Tyagi A K (2005) Effectiveness of emergency argon laser retinopexy performed by trainee doctors. *Eye* **19**: 52-54

Goff M J, McDonald H R, Johnson R N, Ai E, Jumper J M and Fu A D (2006) Causes and Treatment of Vitreous Hemorrhage. *Comp Ophthalmol Update* **7**: 97-111

Goldberg R E and Boyer D S (1980) Sequential retinal breaks following a spontaneous initial retinal break. *Ophthalmology* **88**: 10-12

Goodfellow J F B, Mokete B and Williamson T H (2010) Discriminate characteristics of photopsia in posterior vitreous detachment, retinal tears and retinal detachment. *Ophthal Physiol Opt* **30**: 20-23

Gutteridge I F (1993) The prevalence of posterior vitreous detachment – a prospective study in an optometric patient population. *Clin Exp Optom* **76**: 8-16

Hamilton A M and Taylor W (1972) Significance of pigment granules in the vitreous. *Br J Ophthalmol* **56**: 700-702

Hawley C, Albrow H, Sturt J and Mason L (2010) UK Eye Care Services Project. Phase One: Systematic Review of UK Eye Care Services. *The College of Optometrists*, London.

Hau S, Ehrlich D, Binstead K and Verma S (2007) An evaluation of optometrists' ability to correctly identify and manage patients with ocular disease in the accident and emergency department of an eye hospital. *Br J Ophthalmol* **91**: 437-440

Hayreh S and Jonas J B (2004) Posterior vitreous detachment: Clinical correlations. *Ophthalmologica* **218**: 333-343

Heidelberg Engineering. How to acquire the perfect image
http://www.heidelbergengineering.co.uk/wp-content/uploads/2012/03/SPECTRALIS_HRA+OCT_How_to_acquire_the_perfect_image_english_web.pdf
Accessed 5th May 2015

Heidelberg Engineering. Spectralis enhanced vitreous imaging
http://www.heidelbergengineering.com/international/wp-content/uploads/2014/08/93864-001_SPECTRALIS_Presentation_Enhanced_Vitreous_Imaging.pdf
Accessed 5th May 2015

Hikichi T and Trempe C L (1994) Relationship between floaters, light flashes, or both, and complications of posterior vitreous detachment. *Am J Ophthalmol* **177**: 593-598

Hikichi T, Hirokawa H, Kado M, Akiba J, Kakehashi A, Yoshida A and Trempe C L (1995) Comparison of the prevalence of posterior vitreous detachment in whites and japanese. *Ophthalmic Surg* **26**: 39-43

Hikichi T and Yoshida A (2004) Time course of development of posterior vitreous detachment in the fellow eye after development in the first eye. *Ophthalmology* **111**:1705-1707

Hilton G, Machemer R, Michels R, Okun E, Schepens C and Schwartz A (1983) The classification of retinal detachment with proliferative vitreoretinopathy. *Ophthalmology* **90**: 121-125

Hollands H, Johnson D, Brox A C, Almeida D, Simel D L and Sharma S (2009) Acute-onset floaters and flashes. Is this patient at risk for retinal detachment? *JAMA* **302**: 2243-2249

Hollyfield, J G, Varner H, Rayborn ME and Osterfield A M (1989) Retinal attachment to the pigment epithelium. Linkage through an extracellular sheath surrounding cone photoreceptors. *Retina* **9**: 59-68

Hollyfield J G, Varner H and Rayborn M E (1990) Regional variation within the interphotoreceptor matrix from fovea to the retinal periphery. *Eye* **4**: 333-339

Holz F G, Jorzik J, Schutt F, Flach U and Unnebrink K (2003) Agreement among ophthalmologists in evaluating fluorescein angiograms in patients with neovascular age-related macular degeneration for photodynamic therapy eligibility (FLAP-study). *Ophthalmology* 110: 400-405

Hurst J, Johnson D, Law C, Schweitzer K and Sharma S (2015) Value of subjective visual reduction in patients with acute-onset floaters and/or flashes. *Can J Ophthalmol* **50**: 265-268

Ikuno Y and Tano Y (2009) Retinal and choroidal biometry in highly myopic eyes with spectral-domain optical coherence tomography. *Invest Ophthalmol Vis Sci* **50**: 3876-3880

Ikuno Y, Fujimoto S, Jo Y, Asai T and Nishida K (2013) Choroidal thinning in high myopia measured by optical coherence tomography. *Clin Ophthalmol* **7**: 889-893

International Council for Ophthalmology (2011) International Clinical Guideline, Posterior Vitreous Detachment, Retinal Breaks and Lattice Degeneration (Initial and follow-up evaluation)

Ip M, Garza-Karren C, Duker J S, Reichel E, Swartz J C, Amirikia A and Puliafito C A (1999) Differentiation of degenerative retinoschisis from retinal detachment using optical coherence tomography. *Ophthalmology* **106**: 600-605

Jaffe N S (1968) Complications of acute posterior vitreous detachment. *Arch Ophthalmol* **79**: 568-571

Johnson M W (2005) Perifoveal vitreous detachment and its macular complications. *Trans Am Ophthalmol Soc* **103**: 537-567

Johnson M W (2010) Perspective: Posterior vitreous detachment: evolution and complications of its early stages. *Am J Ophthalmol* **49**: 371-382

Jongebloed W L and Worst J F (1987) The cisternal anatomy of the vitreous body. *Doc Ophthalmol* **67**: 183-196

Kakehashi A, Kado M, Akiba J and Hirokawa H (1997) Variations of posterior vitreous detachment. *Br J Ophthalmol* **81**: 527- 532

Kakehashi A, Inoda S, Shimizu Y, Makino S and Shimizu M (1998) Predictive value of floaters in the diagnosis of posterior vitreous detachment. *Am J Ophthalmol* **125**: 113-115

Kakehashi A, Takezawa M and Akiba J (2014) Classification of posterior vitreous detachment. *Clin Ophthalmol* **8**: 1-10

Kampik A (2012) Brief overview of the molecular structure of normal and aging human vitreous. *Retina* **32**: S179-180

Kanski J J (1975) Complications of acute posterior vitreous detachment. *Am J Ophthalmol* **80**: 44-46

Keane P A, Karampelas M, Sim D A, Sadda S R, Tufail A, Sen H N, Nussenblatt R B, Dick A D, Lee R W, Murray P I, Pavesio C E and Denniston A K (2014) Objective measurement of vitreous inflammation using optical coherence tomography. *Ophthalmology* **121**: 1706-14

Keane P A, Balaskas K, Sim D A, Aman K, Denniston A K, Aslam T, And For The Equator Study Group (2015) Automated analysis of vitreous inflammation using spectral-domain optical coherence tomography. *Transl Vis Sci Technol.* **4**: 1-10

Khan A A, Gupta A and Bennett H (2013) Risk stratifying retinal breaks. *Can J Ophthalmol* **48**: 546-548

Khan A A, Mitry D, Goudie C, Singh J and Bennett H (2015) Retinal detachment following laser retinopexy. *Acta Ophthalmol* April 2015. Advance online publication. doi: 10.1111/aos.12709

Khandhadia S, Madhusudhana K C, Kostakou A, Forrester J V and Newsom R S B (2009). Use of optomap for retinal screening within an eye casualty setting. *Br J Ophthalmol* **93**: 52-55

Kičová N, Bertelmann T, Irle S, Sekundo W and Mennel S (2012) Evaluation of a posterior vitreous detachment: a comparison of biomicroscopy, B-scan ultrasonography and optical coherence tomography to surgical findings with chromodissection. *Acta Ophthalmol* **90:** e264-268

Kim R and Yao X Y (1993) Oxygen dependency of retinal adhesion. *Invest Ophthalmol Vis Sci* **34**: 2074-2078

Kishi S, Demaria C and Shimizu K (1986) Vitreous cortex remnants at the fovea after spontaneous vitreous detachment. *Int Ophthalmol* **9**: 253-260

Kishi S and Shimizu K (1990) Posterior precortical vitreous pocket. *Arch Ophthalmol* **108**: 979-982

Kita M, Negi A, Kawano S and Honda Y (1991) Photothermal, cryogenic, and diathermic effects on retinal adhesive force *in vivo*. *Retina* **11**: 441-444

Kolb J P, Klein T, Kufner C L, Wieser W, Neubauer A S and Huber R (2015) Ultra-widefield retinal MHz-OCT imaging with up to 100 degrees viewing angle. *Biomedical Optics Express* **9**: 1534-1552

Kuhn F and Aylward B (2014) Rhegmatogenous Retinal detachment: a reappraisal of its pathophysiology and treatment. *Ophthalmic Res* **51**: 15-31

Langham M E and Regan C D J (1969) Circulatory changes associated with onset of primary retinal detachment. *Arch Ophthalmol* **81**: 820-829

Law J C and Sternberg P (2007) Not Just a PVD: Differential diagnosis of flashing lights. *Retinal Physician* [ONLINE] Available at: http://www.retinalphysician.com/articleviewer.aspx?articleID=101095 [Accessed 16th February 2014]

Le Goff MM and Bishop PN (2008) Adult vitreous structure and postnatal changes. *Eye* **22**: 1214-1222

Levin M, Naseri A and Stewart J M (2009) Resident-performed prophylactic retinopexy and the risk of retinal detachment. *Ophthalmic Surg Lasers Imaging* **40**: 120-126

Lincoff H and Gieser R (1971) Finding the retinal hole. *Arch Ophthalmol* **85**: 565-569

Linder B (1966) Acute posterior vitreous detachment and its retinal complications. *Acta Ophthalmol* **87** (suppl): 1

Liu J J, Witkin A J, Adhi M, Grulkowski I, Kraus M F, Dhalla A H and Fujimoto J G (2014) Enhanced vitreous imaging in healthy eyes using swept source optical coherence tomography. *PloS one* **9:** e102950

Lobo A and Lightman S (2003). Vitreous aspiration needle tap in the diagnosis of intraocular inflammation. *Ophthalmology* **110:** 595-599

Lock J H-J and Fong K C S (2011) Review: An update on retinal laser therapy. *Clin Exp Optom* **94**: 43-51

Logan N S, Gilmartin B, Wildsoet C F and Dunne M C (2004) Posterior retinal contour in human adult anisomyopia. *Invest Ophthalmol Vis Sci* **45**: 2152-2162

Lois N and Wong D (2003) Pseudophakic retinal detachment. *Surv Ophthalmol* **48**: 467-487

Lorenzo-Carrero J, Perez-Flores I, Cid-Galano M, Fernandez-Fernandez M, Heras-Raposo F, Vaquez-Nunez R and Lopez-Fuentes M (2009) B-scan ultrasonography to screen for retinal tears in acute symptomatic age-related posterior vitreous detachment. *Ophthalmology* **116**: 94-99

Los L I, van der Worp R J, van Luyn M J A and Hooymans J M (2003) Age-related liquefaction of the human vitreous body: lm and tem evaluation of the role of proteoglycans and collagen. *Invest Ophthalmol Vis Sci* **44**: 2828–2833

Machemer R (1984) The importance of fluid absorption, traction, intraocular currents, and chorioretinal scars in the therapy of rhegmatogenous retinal detachments. XLI Edward Jackson Memorial Lecture. *Am J Ophthalmol* **98:** 681-693

Makhzoum O, Hero M and Chaggar A S (2014) University Hospital Coventry and Warwickshire (UHCW) NHS Trust Vitreoretinal Guideline: Retinal Holes, Tears and Lattice Degeneration.

Margo C E, Harman L E and Mulla Z D (2002) The reliability of clinical methods in ophthalmology. *Surv Ophthalmol* **47**: 375-386

Marks J R, Harding A K, Harper R A, Williams E, Haque S, Spencer A and Fenerty C (2012) Agreement between specially trained and accredited optometrists and glaucoma specialist consultant ophthalmologists in their management of glaucoma patients. *Eye* **26**: 853-861

Michaelson I C (1948) The mode of development of the vascular system of the retina. With some observations on its significance for certain retinal diseases. *Trans Ophthalmol Soc UK* **68**: 137-180

Mitry D, Charteris D G, Fleck B W, Campbell H, Singh J (2010a) The epidemiology of rhegmatogenous retinal detachment: geographical variation and clinical associations. *Br J Ophthalmol* **94**: 678-684

Mitry D, Fleck B W, Wright A F, Campbell H and Charteris D G (2010b) Pathogenesis of rhegmatogenous retinal detachment. Predisposing anatomy and cell biology. *Retina* **30**: 1561-1572

Mojana F, Kozak I, Oster S F, Cheng L, Bartsch D-U G, Brar M, Yuson R M and Freeman W R (2010) Observations by spectral-domain optical coherence tomography combined with simultaneous scanning laser ophthalmoscopy: imaging of the vitreous. *Am J Ophthalmol* **149**: 641-650

Moore R F (1935) Subjective "Lightning Streaks". *Br J Ophthalmol* **19**: 545–547

Moore R F (1947) Subjective "Lightning Streaks". *Br J Ophthalmol* **31**: 46-50

Morgan I G, Ohno-Matsui K and Saw S-M (2012) Myopia. *Lancet* **379**: 1739-1748

Morita H, Funata M and Tokoro T (1995) A clinical study of the development of posterior vitreous detachment in high myopia. *Retina* **15**: 117-124

Morse P H and Eagle Jr R C (1975) Pigmentation and retinal breaks. *Am J Ophthalmol* **79**: 190-193

Mudhar H S and Sheard R (2013) Diagnostic cellular yield is superior with full pars plana vitrectomy compared with core vitreous biopsy. *Eye* **27:** 50-55

Nagasaki H, Shinagawa K and Mochizuki M (1998) Risk factors for proliferative vitreoretinopathy. *Prog Retin Eye Res* **17:**77-98

Natkunarajah M, Goldsmith C and Goble R (2003) Diagnostic effectiveness of noncontact slitlamp examination in the diagnosis of retinal tears. *Eye* **17**: 607-609

Netland P A, Mukai S and Covington H I (1994) Elevated intraocular pressure secondary to rhegmatogenous retinal detachment. *Surv Ophthalmol* **39**: 234-240

NHS England (2013) National tariff payment system 2014/15 Annex 5A

Nischal K K, James J N and McAllister J (1995) The use of dynamic ultrasound B-scan to detect retinal tears in spontaneous vitreous haemorrhage. *Eye* **9:** 502-506

Novak M A and Welch R B (1984) Complications of acute posterior vitreous detachment. *Am J Ophthalmol* **97**: 308-314

Nussenblatt R B, Palestine A G, Chan C C and Roberge F (1985) Standardization of vitreal inflammatory activity in intermediate and posterior uveitis. *Ophthalmology* **92**:467–471

Office for National Statistics (2014) UK population estimates: 2013 mid-year estimates from the Office for National Statistics

Okamoto F, Okamoto Y, Hiraoka T and Oshika T (2008) Vision-related quality of life and visual function after retinal detachment surgery. *Am J Ophthalmol* **146**: 85-90

O'Malley P F and Allen R A (1967) Peripheral cystoid degeneration of the retina. Incidence and distribution in 1,000 autopsy eyes. *Arch Ophthalmol* **77**: 769-776

Pang C E, Freund K B and Englebert M (2014) Enhanced vitreous imaging technique with spectral-domian optical coherence tomography for evaluation of posterior vitreous detachment. *JAMA* **132:** 1147-1150

Parkins D J, Curran R, Pooley J E and Ryan B (2014) The developing role of optometrists as part of the NHS primary care team. *Optometry in Practice* **15**: 177-184

Pastor J C, Rodríguez de la Rúa E, Aragón J, Mayo-Iscar A, Martínez V, García-Arumí J, Giraldo A, Sanabria-Ruiz Colmenares M R and Miranda I (2005) Interaction between surgical procedure for repairing retinal detachment and clinical risk factors for proliferative vitreoretinopathy. *Curr Eye Res* **30**: 147-153

Patel, N, Bunce, Asaria, R Z H and Charteris, D G (2004) Resources involved in managing retinal detachment complicated by proliferative vitreoretinopathy. *Retina* **24**: 883-887

Pederson J E, Cantrill H L and Cameron J D (1982) Experimental retinal detachment II. Role of the vitreous. *Arch Ophthalmol* **100**: 1155-1159

Petrou P and Lett K S (2014) Effectiveness of emergency argon laser retinopexy performed by trainee physicians: 10 years later. *Ophthalmic Surg Lasers Imaging Retina* **45**: 194-196

Pierro L, Camesasca F I, Mischi M and Brancato R (1992) Peripheral retinal changes and axial myopia. *Retina* **12**: 12-17

Pischel D K (1952) Detachment of the vitreous as seen with the slit-lamp. *Trans Am Ophthalmol Soc* **50**: 329-346

Qureshi F and Goble R (2009) The inter-observer repeatability of Shafer's sign. *Eye* **23**: 661-662

Rabinowitz R, Yagev R, Shoham A and Lifshitz T (2004) Comparison between clinical and ultrasound findings in patients with vitreous haemorrhage. *Eye* **18:** 253-256

Ramkissoon Y D, Aslam S A, Shah S P, Wong S C and Sullivan P M (2010). Risk of iatrogenic peripheral retinal breaks in 20-G pars plana vitrectomy. *Ophthalmology* **117**: 1825-1830

Reichel E, Ho J and Duker J S (2009) OCT units: Which one is right for me? *Rev Ophthalmol* **16**: 62-68

Repetto R, Stocchino A and Cafferata C (2005) Experimental investigation of vitreous humour motion within a human eye model. *Phys Med. Biol.* **50**: 4729-4743

Richardson P S R, Benson M T and Kirkby G R (1999). The posterior vitreous detachment clinic: do new retinal breaks develop in the six weeks following an isolated symptomatic posterior vitreous detachment? *Eye* **13**: 237-240

Romem M and Singer L (1978) Long-term follow-up of photocoagulated retinal breaks. *Br J Ophthalmol* **62**: 240-242

Roufail E D and Polkinghorne P (2006) Vitreous floaters. *Compr Ophthalmol Update* **7**: 171-177

Royal College of Ophthalmologists (2010) Management of acute retinal detachment.

Ruiz R S (1969) Traumatic retinal detachments. *Br J Ophthalmol* **53**: 59-61

Salicone A, Smiddy W E, Venkatraman A and Feuer W (2006) Management of retinal detachment when no break is found. *Am J Ophthalmol* **113**: 398-403

Schaal K B, Pang C E, Pozzoni C and Englebert M (2014) The premacular bursa's shape revealed in vivo by swept-source optical coherence tomography. *Ophthalmology* **121**: 1020-1028

Schweitzer K D, Eneh A A, Hurst J, Bona M D, Rahim K J and Sharma S (2011) Predicting retinal tears in posterior vitreous detachment. *Can J Ophthalmol* **46**: 481-485

Sebag J and Balazs E A (1985) Human vitreous fibres and vitreoretinal disease. *Trans Ophthalmol Soc UK* **104**: 123 -127

Sebag J (1987a) Ageing of the vitreous. *Eye* **1:** 254-262

Sebag J (1987b) Age-related changes in the human vitreous structure. *Graefe's Arch Clin Exp Ophthalmol* **225**: 89-93

Sebag J and Balazs E A (1989) Morphology and ultrastructure of human vitreous fibers. *Invest Ophthalmol Vis Sci* **30**: 1867–1871

Sebag J (1992) Anatomy and pathology of the vitreo-retinal interface. *Eye* **6**: 541-552

Sebag J (2002) Imaging vitreous. *Eye* **16**: 429-439

Sebag J (2004) Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease. *Graefe's Arch Clin Exp Ophthalmol* **242**: 690-698

Sebag J (2008a) To see the invisible: The quest of imaging vitreous. *Dev Ophthalmol* **42**: 5-28

Sebag J (2008b) Vitreoschisis. *Graefe's Arch Clin Exp Ophthalmol* **246**: 329-332

Sebag J (2011) Floaters and the Quality of Life. *Am J Ophthalmol* **152**: 3-4

Shafer D M (1965). Comment. In: Schepens CL, Regan CDJ, eds. Controversial aspects of the management of retinal detachment. London: J & A Churchill: 51.

Sharma S, Walker R, Brown G C and Cruess A F (1999) The importance of qualitative vitreous examination in patients with acute posterior vitreous detachment. *Arch Ophthalmol* **117**: 343-346

Sharma M C, Regillo C D, Shuler M F, Borrillo J L and Benson W E (2004) Determination of the incidence and clinical characteristics of subsequent retinal tears following treatment of the acute posterior vitreous detachment-related initial retinal tears. *Am J Ophthalmol* **138** 280-284

Shechtman D L and Calderon D E (2008) Posterior Vitreous Detachment: A Common Process with Potential for Ocular Morbidity. *Review of Optometry* [ONLINE] Available at: http://www.revoptom.com/continuing_education/tabviewtest/lessonid/105928 [Accessed 16th February 2014]

Shuey N H, Anderson A J and Siderov J (1995) Scleral indentation: a review of the procedure and indications for use. *Clin Exp Optom* **78**: 106-109

Shunmugam M, Shah A N, Hysi P G and Williamson T H (2014) The pattern and distribution of retinal breaks in eyes with rhegmatogenous retinal detachment. *Am J Ophthalmol.* **157**: 221-226

Sigelman J (1980) Vitreous base classification of retinal tears: Clinical application. *Surv Ophthalmol* **25**: 59-74

Smiddy W E, Maguire A M, Green R, Michels R G, De La Cruz Z, Enger C, Jaeger M and Rice T A (1989) Idiopathic epiretinal membranes: ultrastructural characteristics and clinicopathologic correlation. *Ophthalmology* **96**: 811-821

Smiddy W E, Flynn H W Jr, Nicholson D H, Clarkson J G, Gass J D, Olsen K R and Feuer W (1991) Results and complications in treated retinal breaks. *Am J Ophthalmol* **112:** 623-631

Smretschnig E, Falkner-Radler C I, Binder S, Spörl J, Ristl R, Glittenberg C and Krepler K (2015) Vision-Related Quality of Life and Visual Function after Retinal Detachment Surgery. *Retina* 2015 Oct 27. [Epub ahead of print]

Snead M P, Snead D R J, Mahmood A S and Scott J D (1994) Vitreous detachment and the posterior hyaloid membrane: A clinicopathological study. *Eye* **8**: 204-209

Snead M P, Snead D R, James S and Richards A J (2008a) Clinicopathological changes at the vitreoretinal junction: posterior vitreous detachment. *Eye* **22**: 1257-1262

Snead D R J, James S and Snead M P (2008b) Pathological changes in the vitreoretinal junction 1; epiretinal membrane formation. *Eye* **22**: 1310-1317

Song S J and Smiddy W E (2014) Ocriplasmin for symptomatic vitreomacular adhesion: an evidence-based review. *Core Evid* **9**: 51-59

Spraul C W and Grossniklaus H E (1997) Vitreous haemorrhage. *Surv Ophthalmol* **42**: 3-39

Stalmans P, Benz M S, Gandorfer A, Kampik A, Girach A, Pakola S, Haller J A for the MIVI-TRUST Study Group (2012) Enzymatic vitreolysis with ocriplasmin for vitreomacular traction and macular holes. *N Eng J Med* **36**: 606-615

Stanga P E, Sala-Puigdollers A, Caputo S, Jaberansari H, Cien M, Gray J, D'Souza Y, Charles S J, Biswas S, Henson D B and Mcleod D (2014) In vivo imaging of cortical vitreous using 1050-nm swept-source deep range imaging optical coherence tomography. *Am J Ophthalmol* **157**: 397-404

Stefani F R, Maia M, Falabella P, Pfister M, Niemeyer M, Kashani A H, Humayun M S and Koss M J (2014) Profile of ocriplasmin and its potential in the treatment of vitreomacular adhesion. *Clin Ophthalmol* **8**: 847-856

Straatsma B R, Landers M B and Kreiger A E (1968) The ora serrata in the adult human eye. *Arch Ophthalmol* **80**: 3-20

Straatsma B R, Foos R Y and Spencer L M (1969) The retina: Topography and clinical correlations. In: Transactions of the New Orleans Academy of Ophthalmology: Symposium on Retina and Retinal Surgery. St Louis: C V Mosby: 1–26

Tan H S, Mura M, Oberstein S Y L and Bijl H M (2011) Safety of vitrectomy for floaters. *Am J Ophthalmol* **151**: 995-998

Tanner V, Harle D, Tan J, Foote B, Williamson T H and Chignell A H (2000) Acute posterior vitreous detachment; the predictive value of vitreous pigment and symptomatology. *Br J Ophthalmol* **84**: 1264-1268

Tasman W S (1968) Posterior vitreous detachment and peripheral retinal breaks. *Trans Am Acad Ophthalmol Otolaryngol* **72:** 217-224

Tasman W (1972) Peripheral retinal changes following blunt trauma. *Trans Am Ophthalmol Soc* **70**: 190-198

Thomson H S, Montague P, Cox T A and Corbett J J (1982) The relationship between visual acuity, pupillary defect and visual field loss. *Am J Ophthalmol* **93**: 681-688

Townsend W (1992) Scleral depression. *Optom Clin* **2**: 127-144

Tseng W, Cortez R T, Ramirez G, Stinnett S and Jaffe G J (2004) Prevalence and risk factors for proliferative vitreoretinopathy in eyes with rhegmatogenous retinal detachment but no previous vitreoretinal surgery. *Am J Ophthalmol* **137**:1105-15

Tsui I, Pan C K, Rahimy E and Schwart S D (2012) Ocriplasmin for vitreoretinal diseases. *J Biomed Biotechnol* 2012; Epub Oct 14: 354979

Uchino E, Uemura A and Ohba N (2001) Initial stages of posterior vitreous detachment in healthy eyes of older persons evaluated by optical coherence tomography. *Arch Ophthalmol* 119: 1475-1479

van Overdam K A, Bettink-Remeijer M W, Mulder P G and van Meurs J C (2001) Symptoms predictive for the later development of retinal breaks. *Arch Ophthalmol* **119**: 1483-1486

van Overdam K A, Bettink-Remeijer M W, Klaver C C, Mulder P G, Moll A C and van Meurs J C (2005) Symptoms and findings predictive for the development of new retinal breaks. *Arch Ophthalmol* 123: 479-484

Verhoeff F H (1941) Moore's subjective "Lightning Streaks". *Trans Am Ophthalmol Soc* **39**: 220-226

Viera A J and Garrett J M (2005) Understanding Interobserver Agreement: The Kappa Statistic. *Fam* Med, **37**: 360-363

Weidenthal D T and Schepens C L (1966) Peripheral fundus changes associated with ocular contusion. *Am J Ophthalmol* 62: 465-477

Wenner Y, Wismann S, Preising M N, Jäger M, Pons-Kühnemann J and Lorenz B (2014) Normative values of peripheral retinal thickness measured with Spectralis OCT in healthy young adults. *Graefes Arch Clin Exp Ophthalmol* **252**:1195-2005

Wilkinson C P (2014) Interventions for asymptomatic retinal breaks and lattice degeneration for preventing retinal detachment. *Cochrane Database of Systematic Reviews* Issue 9

Williams K M, Watt L and Williamson T H (2011) Acute symptomatic posterior vitreous detachment and delayed retinal breaks. *Acta Ophthalmologica* **89**: e100-101

Williamson T H (2013) Vitreoretinal surgery, 2nd ed. Springer: London

Worst J G (1976) The bursa intravitrealis premacularis: new developments in ophthalmology. *Doc Ophthalmol Proc Ser* 7: 275-279

Yonemoto J, Ideta H, Sasaki K, Tanaka S, Hirose A and Oka C (1994) The age of onset of posterior vitreous detachment. *Graefes Arch Clin Exp Ophthalmol* **232**: 67-70

Yonemoto J, Noda Y, Masuhara N and Ohno S (1996) Age of onset of posterior vitreous detachment. *Curr Opin Ophthalmol* **7**: 73-76

Yoon Y H and Marmor M F (1998) Rapid enhancement of retinal adhesion by laser photocoagulation. *Ophthalmology* **95**: 1385-1388

Youssri A I and Young L H Y (2002) Closed-globe contusion injuries of the posterior segment. *Int Ophthalmol Clin* **42**: 79-86

Zayit-Soudry S, Alfasi M, Goldstein M, Moisseiey, J, Axel-Seiger R, Pollack A, Yassur Y and Loewenstein A (2007) Variability among retina specialists in evaluating fluorescein angiograms of patients with neovascular age-related macular degeneration. *Retina* **27**: 798-803

Zweng H C (1972) Laser photocoagulation in rhegmatogenous retinal separation. In: Pruett R C, Regan C D J, eds *Retina Congress.* New York. Appleton-Century-Crofts: 551-554