9. Discussion

The discussion focuses on two issues: Firstly, the presumed advantages of PPPV are tested against the current evidence provided by the published studies and secondly, the results of PPPV obtained at the CCBF are compared to those published by other groups.

9.1. Advantages, disadvantages and unsolved issues of primary vitrectomy: Assessment of the current literature

The proposed advantages of primary vitrectomy are threefold: PPPV enables better intraoperative control, decreases the number of intraoperative and postoperative complications compared to scleral buckling surgery, and, consequently, produces better anatomical and functional results. Testing this hypothesis against the published series of PPPV, the features of PPPV compared to scleral buckling surgery can be divided into three groups: advantages of PPPV supported by the data provided in the scientific literature, the presumed advantages of PPPV, and the disadvantages of PPPV (Table 18). This analysis has been published by the applicant in the "Controversies in Ophthalmology" series of the British Journal of Ophthalmology [91].

9.1.1. Advantages of PPPV

The removal of opacities in the vitreous and of capsular remnants or synechia are clear advantages of PPPV. The better intraoperative control of PPPV is supported by the high rates of intraoperative reattachment achieved by internal drainage and endotamponade, even in very difficult cases. Surgeons nowadays have become more familiar with this technique compared to scleral buckling surgery, as the indications for vitrectomy and the total number of cases outside retinal detachment surgery have increased immensely during the past decade [2]. Further, endo-illumination, indentation, a higher magnification, the removal of opacities, membranes and the unfolding of detached retina with perfluorocarbon liquids enable a better view of the pathological anatomy and an

improvement in the identification of previously unseen breaks, as documented in 77 of 87 cases of previously unseen breaks. The problems associated with external drainage [103], such as choroidal haemorrhage, retinal incarceration and retinal perforation, as well as that of scleral perforation during suturing of the exoplant (if PPPV is not combined with additional scleral buckling surgery) are avoided. The series of PPPV published demonstrate a low rate of intraoperative complications, the most frequently observed being iatrogenic breaks (6% of cases in series reporting this complication) and that of lens damage in phakic eyes in 3%. Other major intraoperative complications have been reported in single cases only, and do not seem to occur on a large scale.
Looking at the advantages of PPPV in the postoperative period, major drawbacks of scleral buckling surgery are avoided: only minor changes of refraction occur compared to those following scleral buckling surgery [83, 88]. Postoperative choroidal detachments, summarised by Ambati and Arroyo to occur in 23% to 44% of eyes following scleral buckling surgery [4], have been reported in only 3 patients following PPPV. Infections, in- and extrusions of episcleral buckling material complicating scleral buckling surgery [82, 100], are precluded completely (if no additional scleral buckling is performed) and have not been reported in the literature reviewed above. Postoperative imbalance of extraocular muscles, leading to long-term diplopia occurring in 5 to 25% following scleral buckling surgery [27], has been documented to occur in one report of PPPV[108] but have not been mentioned in other series.

9.1.2. Presumed advantages of PPPV

One of the major reasons for the increasing use of PPPV is the expectation that better anatomical and functional results are achieved with this method in more complicated forms of RRD. The combined primary success rate of the studies of PPPV reviewed was 85%. Compared to the primary success rates of larger, consecutive studies of scleral buckling surgery (75% to 91%) summarised by Wilkinson [104], this further encourages the use of PPPV, particularly as more complex situations of RRD are operated on with PPPV. PPPV is thought to be particularly successful in pseudophakic / aphakic patients. In these situations, a more thorough removal of the peripheral vitreous is possible.

Further unclear hole situations and small retinal breaks are more common; and postoperative cataract formation is not a concern. Indeed, the primary success rates of 91% in pseudophakic and aphakic patients seem to be significantly superior to those of scleral buckling surgery in most reports summarised by Bartz-Schmidt [8], as well as to those published in recent series with a primary success of 89% [12] or 83%[29]. It is worth emphasising again at this point that complicated cases are included in the PPPV-series that are generally excluded in the scleral buckling series (and treated with vitrectomy). Moreover, the final success rates of 95% with PPPV in more complex cases of RRD seem to be exceptionally good compared to the majority of reports of scleral buckling surgery (range 88 to 97%)[104] and in 98% of pseudophakic and aphakic patients compared to 80% to 96% [104]. One of the presumed advantages of PPPV might be that re-detachments following PPPV are “easier” cases compared to failures after scleral buckling surgery: the former are often caused by a single missed/new break, and a repetition of the internal tamponade with treatment of the new break is frequently sufficient to treat the re-detachment. However, for methodological reasons described above, the data provided to date is inadequate for a sound comparison of anatomical or functional results of PPPV and scleral buckling surgery [105]. The same holds true for postoperative PVR formation and macular pucker. Although various hypotheses why PPPV should result in a lowering of postoperative PVR have been proposed (e.g. removal of the vitreous with its chemotactic and mitogenic stimuli, and the “wash-out” of RPE cells out of the sub-retinal space and vitreous cavity[24, 87]), there still are considerable rates of postoperative PVR in 6% of all patients following PPPV. Furthermore, macular pucker was seen in 9% of patients in studies in which this complication was investigated.

Finally, the supremacy of functional results following PPPV has yet to be proven, although the calculated percentage of 63% of patients with a visual acuity of 0.4 or better in series of PPPV summarised above compares very favourably with the 39% to 56% of successful cases only following scleral buckling surgery [104]. Again, the functional results following PPPV in pseudophakic / aphakic patients seem to be even more superior to scleral buckling surgery when comparing the published results. However, the need for appropriate data is underlined by two recent retrospective studies which compared PPPV to scleral buckling in more complex situations of RRD and another series including patients with flap tears only [68, 75]. Neither study could demonstrate a significant advantage of PPPV over scleral buckling concerning anatomical and functional success.

9.1.3. Disadvantages of PPPV

In addition to the advantages and presumed advantages of PPPV, some definite disadvantages of this procedure have also been documented in the literature. The major intraoperative complication, iatrogenic breaks (although supposedly not significantly influencing the outcome of the surgery) will probably not be completely eliminated even if the greatest intraoperative care is taken. The same holds true for intraoperative damage to the lens and the postoperative increase in nuclear cataract, which was established in more than a third of phakic patients. These complications not only cause a decrease in visual acuity and a myopic shift of postoperative refraction but will cause loss of accommodation in young patients and, sooner or later, lead to the necessity of an additional surgery in most patients. If similar success rates can be achieved with both surgical methods, this has to be seen not only from the patient`s point of view but also against the background of the management of surgical and financial resources [62]. The same reasoning has to be applied regarding the costs of the procedure of PPPV itself, which are significantly higher compared to scleral buckling surgery alone, although some authors argue that, in the long run, PPPV is cheaper than scleral buckling surgery on the basis of a higher anatomical success rate and lower number of reoperations following PPPV [24].

The analysis of the literature further suggests that a higher number of postoperative breaks can be found following PPPV compared to scleral buckling surgery. No definite distinction can be made if a break, which is detected postoperatively, has developed de novo or has just been missed before or during the surgery. However, if one postulates that more breaks are identified during PPPV compared to scleral buckling surgery, there is no other explanation for the high rate of postoperative breaks compared to series of conventional surgery than that these breaks developed after the initial surgery. Possible mechanisms for the development of new breaks following PPPV are accidental touching of the retina during surgery that will later result in a retinal tear; new tangential forces from scar formation, especially in the region of the sclerotomies; contraction forces of the remaining vitreous cortex; formation and contraction of an epiretinal membrane and / or continuing PVD after PPPV [25, 53, 68, 73]. Finally, it is worth mentioning that 4 series of PPPV have identified a total of 27 patients with a long-lasting rise in the intraocular pressure following the procedure.

Advantages of PPPV	Removal of vitreous opacities Removal of capsular opacities Improved visualisation of peripheral retina and identification of breaks Better intraoperative control in difficult situations Internal tamponade of all breaks Internal drainage avoids hazards of external drainage High intraoperative reattachment rate Removal of vitreomacular traction in aphakic / pseudophakic patients with vitreous incarceration Internal photocoagulation or cryotherapy for the treatment of breaks Average surgeon nowadays more experienced with this technique Drainage of suprachoroidal fluid if present Avoidance of the hazards of scleral perforation* Less postoperative changes in refraction* Lower incidence of postop. double vision* Lower incidence of postop. serous choroidal detachment*
Presumed advantages of PPPV	Improved primary success rate in complex situations Improved final success rate in complex cases Improved functional results in complex cases Improvement of cystoid macular edema in pseudophakia
Disadvantages of PPPV	Higher rate of cataract formation in phakic patients Special equipment and training needed Higher cost for single operation Need for qualified assistance Higher rate of iatrogenic breaks Higher rate of missed/new breaks postoperatively Higher rate of persistent postop. pressure rise
Unsolved issues	PVR-rate Macular pucker Need for additional scleral buckling Type of tamponade 360° Laser Costs of complete case

Table 18: Advantages, presumed advantages and disadvantages of PPPV (*= if not combined with SBS).

9.2. Results of primary vitrectomy at the Charité, Campus Benjamin Franklin

In our two studies of PPPV at the CCBF, we focused on the anatomical and functional outcome of PPPV and examined the significance of different risk factors for a bad postoperative outcome [39, 44]. Few studies of PPPV have analysed possible risk factors for postoperative failures. In a prospective study, Kon et al. focused on postoperative PVR [52]. They found that aphakic and pseudophakic patients with a defective posterior capsule, patients with high vitreous protein levels and those with preoperative PVR were associated with postoperative PVR. In addition, postoperative PVR was associated with a decreased anatomical and functional success. Asaria and colleagues used this work to predict the risk of postoperative PVR following PPPV [6]. Factors which were used to grade patients into a high-risk group were the degree of myopia, pseudophakia or aphakia, preceeding cryo or laser, preoperative PVR, vitreous haemorrhage, size of the detachment and macula off detachments. Oshima et al. compared SBS and PPPV in a retrospective study of patients with macula-off detachments [75]. Overall, they found that preoperative visual acuity, preoperative ocular hypotony and the duration of macular detachment were the three best predictors of a good postoperative visual acuity. Other factors that have been associated with decreased success rates after PPPV are: limited surgical experience of the surgeon [68], female gender of the patient [37], extent of the detachment [37], increasing age of the patient [89], longer duration of retinal detachment [89] and worse preoperative visual acuity [89].

The majority of risk factors identified in this series do not differ from the ones established in these series or those for SBS [104] and correlate to the characteristics of the disease that cannot be influenced by the type of operating procedure, amblyopia, high myopia, preoperative PVR, macula-off detachments, hypotony, total retinal detachment, central breaks, large breaks or unseen breaks [35, 86, 104]. There is a trend towards the selection of PPPV over SBS in these cases, especially for large and central breaks or unclear hole situations, but our results underline that PPPV is no “magic cure” for these difficult situations as they are flawed by poorer results following PPPV as well. In contrast to other series of PPPV, we found that the use of endocryo, detachments of the inferior quadrants and the surgeon performing the operation were associated with a worse outcome.

Regarding the association of the use of endocryopexy and anatomical and functional failures, there is no immediate explanation for this finding and we are unaware of similar reports in the literature. Possible rationales for this outcome are 1) the induction of minuscule fractures within the retinal tissue, especially if the cryoprobe is moved to quickly, leading to the induction of future retinal breaks or lesser resistance to traction; 2) focal shrinkage of residual vitreous or residual epiretinal membranes surrounding the probe resulting in traction on the retinal edge of the break; 3) increased scarring with exertion of tangential traction on the neighbouring retina; or 4) incomplete freezing of the entire edge of the retinal break due to the lesser optical control. After SBS, some authors found that cryopexy might lead to higher PVR-rates compared to the use of laser [10]. This has also been postulated following PPPV [1]. It remains to be seen if the negative effects of endocryopexy in our series are a peculiar phenomenon in our hands or if this can be confirmed in other series of PPPV.

The higher rate of redetachments in patients with detachments involving into the lower quadrants is of significant importance if PPPV is employed. As a consequence of our analysis, a modification of our surgical technique is indicated or SBS might be discussed as a primary therapeutic option in some of these cases. With relatively short-acting tamponades, e.g. SF_6-air mixtures as used in this study, breaks in the inferior quadrants are probably not sufficiently supported by the internal tamponade in the usual supine position after 48-72 hours. In addition, inferior detachments on average tend to be of longer duration and display a higher rate of preoperative intravitreal fibrocellular proliferations compared to detachments of the upper quadrants [1]. To improve success-rates of PPPV in patients with breaks including the inferior quadrants, several suggestions have been published, including support of these breaks with an additional encircling band [30, 80, 110], long-acting tamponades, e.g. C_3F_8, C_2F_6, silicone or heavy silicone [1, 84, 94, 106], and strict positioning of the patient [85, 94]. In contrast to our findings, two recent series achieved relatively high success rates with PPPV without additional measures for detachments with inferior breaks [85, 101]. Both groups argue that a complete removal of traction on inferior breaks plus strict postoperative positioning on the back or side according to the location of the breaks are sufficient to achieve good success rates and discard the need for additional scleral buckling.

The controversy regarding the advantages and disadvantages of additional buckling in association with PPPV is not confined to detachments of the inferior retina. While some authors are of the opinion that additional buckling might improve the results of the surgery overall or in selected cases [1, 24, 68, 80], others argue that with modern vitrectomy techniques and a thorough cleaning of the vitreous base, additional buckling might not be necessary but harmful [16, 84, 101]. In a prospective, non-randomised study, Pournaras and Kapetanios compared PPPV with PPPV and additional SBS in pseudophakic patients and did not find statistically significant differences between the two groups [78]. Wickham et al. in a retrospective comparative series for detachment with inferior breaks describe comparable success rates with both methods [101]. Both authors conclude that if comparable success rate are achieved with PPPV alone, additional SBS might cause additional problems without improvement of the outcome and, therefore, seems to be unwarranted. In our series, additional scleral buckling was associated with a lower final success rate and a final visual acuity of <0.1. However, this has to be viewed against the background that additional buckling was chosen by most surgeons only in very complicated situation, e.g. preoperative PVR and inferior retinal detachments. As there is no convincing data on this issue as yet [67], it is to be hoped that the results of the “Scleral Buckling versus Primary Vitrectomy in Rhegmatogenous Retinal Detachment Study (SPR-study)” will shed light also on this controversial topic in the future [41].

Surgeon-related aspects have long been identified as significant prognostic factors related to the outcome of all types of surgery, e.g. survival following surgery for colorectal cancer [45]. Increased sub-specialisation in ophthalmic surgery has increased the anatomical success rates of surgery for RRD [50]. Focusing on PPPV, Miki et al. found that more experienced surgeons achieved better postoperative results than less qualified ones [68]. Oshima et al. explain their excellent results of PPPV by the fact that only experienced surgeons contributed to their series [75]. Our analysis showed that beginning surgeons achieved better results than those classified as “specialists”. Several explanations can be put forward to give reason for this finding: The more senior surgeons contributed cases still from the relatively “early days” of PPPV with a higher rate of retinotomies for internal drainage and less frequent use of PFCL; beginning surgeons profited from this learning curve as they usually assisted the operations for several years before performing the surgery; and very complicated cases, e.g. PVR, younger patients or bad visualisation of the fundus, were usually not included in the first 30 operations of a beginning surgeon. Another possible reason might be that beginning surgeons used wide-angle viewing systems in almost all of the cases compared to the more senior surgeons, who performed most of their vitrectomies with their routine set-up of conventional contact lenses. Unfortunately, the type of viewing system used was not recorded in the operating notes; our data, therefore, does not allow an analysis of the influence of wide-angle viewing system on the postoperative outcome. However, the quintessence of our findings is that beginning surgeons at least achieve results comparable to more experienced surgeons. In the group of training surgeons, this is one of the strong arguments for the choice of PPPV over SBS which is associated with a “galaxy“ of possible problems in challenging situations [67].

One of the major results of our studies and a primary target for improvement is the substantiation of the finding from an earlier series on PPPV of our group that new retinal breaks, and not PVR, were the most common reason for retinal redetachment following PPPV [39]. These postoperative breaks seem to occur mostly in previously normal appearing retina without apparent signs of retinal degenerations. This supports the opinion of Miki et al. that a “progression of PVD into apparently “normal” areas but with strong vitreoretinal adhesions” seems to be the major cause of postoperative breaks [68] and do not assume that these breaks are missed breaks in previously attached retina [80] as discussed before [39]. Because the search for breaks in attached retina nowadays is greatly facilitated with wide angle viewing systems, internal illumination and indentation, we are even more convinced that the majority of these breaks leading to redetachment occurred after the initial operation. This theory is further supported by the encounter of new retinal breaks developing during accomplishment of PVD in macular hole surgery in up to 3% and postoperative retinal detachments in 3 to 11% of patients [9, 56]. These mostly non-myopic eyes without spontaneous development of PVD in a large proportion usually do not display typical retinal degenerations predisposing to retinal breaks and carry a very low risk for developing RRD without a preceding intraocular intervention. As a consequence, a thorough vitrectomy not only around the breaks, visible degenerations and the sclerotomies but all the way to the periphery in the whole circumference [68], prophylactic treatment of degenerative areas in attached retina [14], the use of trocar microcannular systems to reduce traction on the vitreous base during change of instruments [15] or 360° peripheral photocoagulation [5] might be possible ways to further improve the anatomical results of PPPV for RRD.

Comparing our overall results to the current literature, the primary and final success rates for retinal redetachment following PPPV published to date vary between 64-100% and 79-100%, respectively [91]. A visual acuity of ≥0.4 could be achieved in none to 79% of patients in different series with differing inclusion criteria. Our anatomical and functional results display only slight improvements compared to our initial series of PPPV [39] and lower success rates than most published series. A possible explanation for these findings could be that in the current study population included patients with preoperative PVR who were excluded from the majority of the previous studies. If preoperative PVR is included, lower success rates are to be expected; e.g. our results are comparable to another study of Schmidt et al. with similar inclusion criteria. In their series, analogous results were achieved with 71.2% primary success compared to our 70.7%, a final success rate of 95.2% compared to our 97.5% and a visual acuity of 0.4 or better in 50.7% compared to our 48.2% [84]. Comparing the results to SBS, we cannot answer the question if PPPV achieves better results than SBS in these more complicated types of RRD. Only few studies have been published evaluating SBS and PPPV in a comparable cohort of patients. Oshima et al. did not find significant differences in the major outcome variables comparing SBS and PPPV in a retrospective study of macula-off detachments [75]. Miki et al. found similar reattachment rates following PPPV for RRD caused by superior flap tears compared to SBS in a retrospective study [68]. Roider et al. retrospectively analysed situations with difficult hole situations [81]. They found 83% primary success in the PPPV and 93% in the SBS group. Tewari et al. compared SBS and PPPV in cases with undetected retinal breaks in a prospective, randomized fashion [95]. The authors found a higher reattachment rate following PPPV but a better postoperative visual acuity following SBS; both differences did not reach statistical significance. Afrashi et al. conducted a retrospective study on patients with multiple breaks [1][. They found a statistically significant improved reattachment rate using a combination of encircling band and PPPV with silicone oil compared to SBS. Interpreting these results, the studies comparing the two techniques that have been published to date at least underline that in questionable cases, both methods can be employed with similar success rates; no study has shown a strong disadvantage regarding postoperative anatomical and functional success of either method. It is, therefore, justified to use one of the two methods depending on the preferences of the surgeon until the results of the SPR-Study will be available [41].

The results underline that PPPV is still associated with a relatively high complication rate. The decision for PPPV should be reserved to more complicated cases of RRD and not expand without concern into the group of less complex situations. Due to the broad spectrum of different anatomical situations in RRD, a tailored approach with different methods for diverse situations seems to be more reasonable than a “one method for all” concept. Thererfore, it is likely that PPPV as well as SBS will remain important techniques for the treatment of RRD.