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Update on Vitreomacular Traction and Macular Holes: Current and Emerging Management Options

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Diseases of the vitreomacular interface (VMI) are commonly encountered in clinical practice and include epiretinal membrane, anomalous posterior vitreous detachment, vitreomacular traction, and macular hole. New, less invasive treatment options and an updated classification system make a review of the topic particularly timely. This edition of *Ophthalmology Rounds* will review the anatomy, epidemiology, natural history, classification, diagnosis, and treatment of disorders at the VMI.

Vitreomacular interface (VMI) pathology is common and encountered on a daily basis in most ophthalmology practices. The widespread use of spectral-domain optical coherence tomography (SD-OCT) has allowed us to sensitively and accurately visualize the VMI, which was previously difficult if not impossible by standard biomicroscopy alone. Recently, the International Vitreomacular Traction Study Group (IVTSG)[1] has released an international, anatomically based classification scheme that purports to allow us to all speak the same language when discussing diseases of the VMI, aid in predicting clinical outcomes, and be utilizable in clinical studies.

Diseases of the VMI – which include epiretinal membrane (ERM), anomalous posterior vitreous detachment (PVD), vitreomacular traction (VMT), and macular hole – are particularly of interest at the moment because of the advent of chemical vitreolysis. Until recently, these disorders were either carefully observed or treated surgically by vitrectomy with mechanical posterior hyaloid separation and ERM peeling with or without peeling of the internal limiting membrane. The introduction of ocriplasmin, a vitreolytic agent that is administered as an in-office intravitreal injection, may or may not drastically change the way we treat these disorders. Nevertheless, there is much going on in the world of VMI, which makes a review of the subject particularly timely. The purpose of this article is to review the anatomy, epidemiology, natural history, classification, diagnosis, and treatment of VMI pathology so that the clinician has the background and current information to be up to date on the subject.

Anatomy

The vitreous body is a gel-like structure composed mostly (>99%) of water with interspersed macromolecules (mostly type 2 collagen). The main function of the vitreous is to resist tractional and compressive forces, maintaining the structural integrity of the eye. The vitreous is most firmly attached to the retina anteriorly at the vitreous base, at the optic disc margin, along major blood vessels, and at the fovea.[2] In pathological states, it may often also be attached firmly at areas of lattice degeneration and retinal neovascularization. Ultrastructural examination using scanning electron microscopy discloses collagen fibrils running through the vitreous in an anterior-to-posterior direction.[2-4] The spaces between collagen fibrils are maintained by opticin and chondroitin sulphate.[2] No membranes have been identified within the vitreous, although its posterior fibrils insert at various angles into the basement membrane of Muller and glial cells of the retina, giving the false appearance of a membrane.[2-4] The collagen fibrils blend into the vitreous base and insert into the posterior vitreous cortex. These fibrils attach to the inner limiting membrane (ILM) through adhesion molecules including laminin, fibronectin, and heparin sulphate proteoglycans, which are important because they are the targets of chemical vitreolysis. The ILM is made

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up of the basal lamina of Muller cells which course across the retina. The Muller cells provide architectural and nutritional support to the retina as well as waste removal functions.[5]

Natural History

With progressing age, the vitreous body gradually liquefies. This occurs most commonly in the sixth and seventh decades of life, although vitreous liquefaction may begin at a much younger age in certain conditions (high myopia, vitreous inflammation, or syndromes such as Stickler). As the vitreous body liquefies it begins to form fluid-filled cavities that gradually enlarge and lead to a collapse of the collagen-hyaluronate network, a process called "vitreous syneresis". Over time, liquefied vitreous collects between the posterior hyaloid and the perifoveal retina, eventually leading to a complete separation of the posterior vitreous from the retina (PVD).[2-6] Complete detachment of the posterior vitreous is detected clinically by the appearance of a Weiss ring, a circle of condensed vitreous representing the area where the now detached vitreous was once adherent to the optic disc. A Weiss ring is seen on examination by focusing in front of the optic nerve in the vitreous cavity. Once thought to occur suddenly, it is now understood through OCT and ultrasonography studies that a normal PVD begins early in life and progresses gradually.[7] Pathology occurs when there is a persistent focal adhesion between the vitreous and retina. In the periphery, this can lead to a retinal tear or operculated hole due to traction. In the posterior pole, focal or broad adhesions can lead to VMT and its sequelae. This can be as a benign asymptomatic loss of the foveal contour on OCT to as serious as a full-thickness macular hole (FTMH) and associated loss of central vision. PVD can also lead to epiretinal membrane formation, macular pucker, and macular pseudoholes, although it is important to remember that other etiologies make up a broad differential diagnosis, including trauma, infectious, inflammatory, and vascular causes.[7] Additionally, recent evidence suggests that VMT may also play more of a role in diabetic macular edema (DME) and exudative age-related macular degeneration (AMD) than we previously thought.[8]

Epidemiology

It is difficult to accurately estimate the incidence and prevalence of VMI pathology because it is frequently asymptomatic. In addition, VMI pathology is often associated with, and a confounder in, other conditions such as DME and AMD. Jackson et al[9] estimated that approximately 1.5% of the population have eye disease caused by or associated with abnormal vitreomacular adhesions (VMAs).

The mean age of patients diagnosed with VMT is 65-75 years with a higher prevalence in females. Primary FTMHs tend to occur in individuals over age 65.[2] The prevalence of FTMH varies between studies from as low as 0.2 per 1000 in the Blue Mountains Eye Study[10] to 3.3 per 1000 in the Baltimore Eye Survey.[11] The condition is unilateral in approximately 80% of cases.[2]

Diagnosis

As with any ocular disorder, the patient history must be reviewed in detail. Specifically, it is important to elucidate symptoms such as a monocular decrease in vision, central scotoma, and/or metamorphopsia. Flashes of light, a potential symptom of vitreoretinal traction, should also be noted if present. A thorough past ocular history including presence of other ocular conditions, previous surgeries, ocular medications, and refraction should be taken. A past medical history and complete list of medications are important. A full, dilated ophthalmological examination including fundus examination with slit-lamp biomicroscopy is essential to diagnosis. In terms of imaging, B-scan ultrasonography can prove helpful in examining the vitreous body as a whole. Fundus photography and fluorescein angiography can also be useful in ruling out other differential diagnoses and/or coexisting pathology. The current gold standard diagnostic test is SD-OCT. The SD-OCT findings of VMI pathology will be classified in the next sections.

Classification

Gass classification

The Gass classification of macular holes[12] was – and to many still is – the definitive classification scheme of VMI pathology. His observations were based on careful clinical examination. Although the newer OCT-based classifications may overtake this classic schema, it is still important to know both because it serves as a foundation for the OCT-based systems and because patients are always examined at the slit lamp first. The authors find that the clinical description can be predictive of, though not a substitute for, SD-OCT.

Gass described macular holes in 4 stages (Table 1).[12]

- Stage 1A (impending macular hole) is seen as a central yellow spot with loss of foveolar depression but no vitreofoveal separation. Gass interpreted this yellow spot to be an early serous detachment of the foveolar retina. Stage 1B was similar though seen as a yellow ring rather than just a spot. This ring was thought to represent lateral displacement of xanthophyll pigment or a central occult foveolar hole with bridging contracted prefoveolar cortex.
- Stage 2 FTMHs consist of an eccentric oval, crescent, or horseshoe-shaped defect inside the edge of the yellow ring. These findings were thought to represent a tear in the vitreous tissue bridging a <400-µm round full-thickness retinal hole or a pseudo-operculum.
- Stage 3 FTMHs were defined as an FTMH >400 µm that is seen as a central round defect with a ring of elevated retina with no evidence of a Weiss ring, suggesting that complete PVD had not yet occurred.
- Stage 4 FTMHs were defined as >400 µm, similar to that of stage 3, with the addition of a complete PVD (Weiss ring visible).[12]

New IVTSG Classification

The advent of OCT has allowed us to examine *in vivo* pseudohistological cross-sections of the retina. This has expanded our knowledge and understanding

Table 1: Macular hole classification comparison[1,12]

Gass stage[13]	Clinical description[13]	IVTSG classification[1]
1A	Yellow spot	VMT
1B	Yellow ring	VMT
2	FTMH <400 µm	Small FTMH (<250 µm) ± VMT Medium FTMH (250-400 µm) ± VMT
3	FTMH >400 µm	Large FTMH >400 µm ± VMT
4	FTMH >400 µm + PVD	

IVTSG = International Vitreomacular Traction Study Group; VMT = vitreomacular traction; FTMH = full-thickness macular hole; PVD = posterior vitreous detachment

of VMI pathology and allowed for more precise clinical diagnoses. Numerous OCT-based classification systems have been proposed to classify VMI abnormalities, but none have been as widely adopted as the Gass classification.[12] The IVTSG[1] recently published an OCT-centred consensus-based classification system that they hope will become widely adopted and allow us to speak a common language in the clinic and in research regarding the VMI.[1] The expert panel based their classification on evidenced-based articles, questionnaires, and round-table discussion. This classification divides pathology into VMA, VMT, and FTMH. It then further subdivides these categories based on size and characteristics (Table 2).[1]

VMA (Figure 1A) is defined as PVD with elevation of cortical vitreous above the retinal surface as well as vitreous remaining attached within a 3-mm radius of the fovea. Importantly, there is no change in retinal contour. The adhesion is further subclassified into focal (<1500 µm) or broad (>1500 µm) types. Eyes with associated macular abnormalities from other disease processes are termed "concurrent" VMA while those with none are called "isolated". VMA is not necessarily pathological and is not classified based on patient symptoms. It is thought to be a normal state within the natural history of the PVD.[1]

VMT (Figure 1B) is defined as perifoveal PVD with concurrent retinal anatomic changes on OCT. At least one B-mode OCT scan must have evidence of perifoveal vitreous cortex detachment from the retinal surface but still have macular attachment of the vitreous cortex within 3 mm of the fovea. This scan must also show distortion of the foveal surface, intratretinal structural changes, or elevation of the fovea above the retinal pigment epithelium (RPE). There must be no evidence of FTMH. Again, this traction can be termed focal or broad based on the same 1500-µm cut-off. The authors note that both anterior-posterior vitreous traction and tangential traction from an ERM can contribute to this state, and differentiating a true ERM from a thickened, broadly attached posterior hyaloid can be difficult with OCT.[1]

FTMH (Figures 1C,D) is defined as an interruption of all neural retinal layers from ILM up to, but not including, the RPE. This defect needs only be present on one OCT B-scan to be considered an FTMH. Again, the defect is further subclassified based on size, more specifically the minimum hole width which is measured at the narrowest point of the defect in the mid-retina with a line drawn parallel to the RPE using the OCT caliper function. Small FTMHs are <250 µm in diameter, have a small rate of spontaneous closure and a high rate of closure with vitrectomy. Medium FTMHs are 250–400 µm, while large FTMHs are >400 µm. The presence or absence of VMT is also included. Finally, the hole can be classified as primary if its etiology is related to VMT and secondary if there is/was no pre-existing or concurrent VMT.[1]

The group also defines a number of other circumstances. Impending macular hole describes a patient with an FTMH in one eye and VMT in the other. Lamellar macular holes have a defect in the fovea but with intact photoreceptors at the base. Macular pseudohole is used to describe a lesion that resembles a small- to medium-sized FTMH on slit-lamp biomicroscopy but that shows no loss of tissue on OCT. It is usually due to an opening in an ERM.[1]

Treatment

The management options of VMI pathology have traditionally included observation and vitrectomy with the creation of a PVD, and ERM peeling with or without ILM peeling. The introduction of ocriplasmin to the Canadian market adds a pharmacological option.

Observation

Asymptomatic patients with ERMs, pseudo- and lamellar macular holes, and VMAs on OCT should be

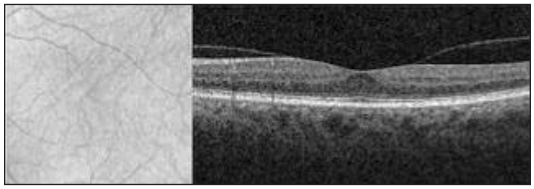
Table 2: IVTSG classification[1]

	Description	Size	Notes
VMA	Perifoveal PVD elevation of cortical vitreous above retinal surface with vitreous remaining attached within a 3-mm radius of the fovea; no change in retinal contour	Focal <1500 µm Broad >1500 µm	Isolated Concurrent
VMT	Perifoveal PVD macular attachment of the vitreous cortex within 3 mm of the fovea distortion of the foveal surface, intratretinal structural changes, elevation of the fovea above the RPE	Focal <1500 µm Broad >1500 µm	
FTMH	Interruption of all neural retinal layers from ILM up to but not including the RPE	Small <250 µm Medium 250-400 µm Large >400 µm	Primary versus secondary ± VMT

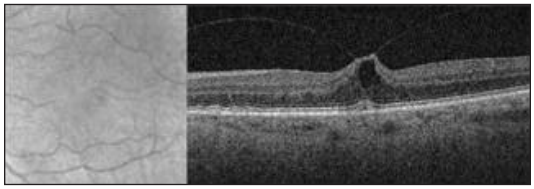
RPE = retinal pigment epithelium; ILM = internal limiting membrane

Figures 1A-D: Vitreomacular interface pathology seen through spectral-domain optical coherence tomography classified by the IVTSG criteria.

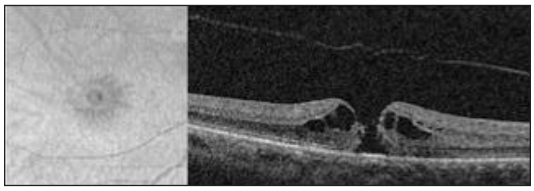
A: Broad vitreomacular adhesions



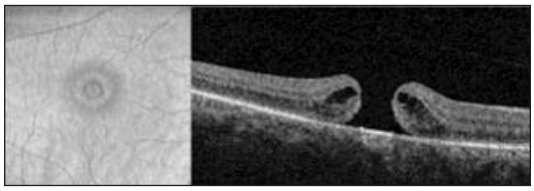
B: Focal VMT



C: Small full-thickness macular hole (FTMH)



D: Large FTMH



observed. Approximately 10% of patients with vitreomacular traction will resolve spontaneously without intervention.[2] A small number of FTMH will also resolve on their own; however, many will enlarge with associated progressive central vision loss.[13] Observation time is subject to a variety of factors, such as symptoms, best-corrected visual acuity (BCVA), likelihood of progressive pathology/vision loss, and coexisting pathology.

Surgery

Pars plana vitrectomy was first described by Machemer,[14] and has long been the treatment of choice for most VMI pathology.

The vitreous body is manipulated, cut, and aspirated so as to remove its adherence (abnormal or not) from the retinal surface using small-gauge instruments introduced through the pars plana via a transcleral/transconjunctival approach. Surgical detachment of the posterior hyaloid is paramount. Next, fine forceps are used to peel away any epiretinal membranes present on the surface of the macula in an attempt to restore normal contour to the retinal surface and release any abnormal areas of traction. The timing of surgery is controversial, with some experts advocating early surgery while others recommend waiting until visual acuity is further deteriorated. A recent prospective study looking at visual acuity outcomes after epiretinal membrane removal over a 10-year period showed that patients with better initial vision achieved a higher level of vision postoperatively, but those with poorer vision had a greater overall change in visual acuity.[15] Although pars plana vitrectomy with membrane peeling is a relatively safe surgical procedure, the risks and benefits of treatment need to be considered as possible perioperative complications include peripheral retinal breaks in 10%–20% of cases which could lead to retinal detachment, RPE damage, nerve fibre layer defects, and retinal and vitreous hemorrhage.[7] The decision of when to operate is surgeon specific and should be made in cooperation with the patient based on his/her overall functional status.

Finally, depending on the pathology (eg, ERM versus FTMH), some surgeons elect to peel the ILM as well. This is often aided with triamcinolone or dyes such as indocyanine green and brilliant blue,[16] which are also controversial and beyond the scope of this article. The rationale behind peeling the ILM is that it removes residual adherent vitreous cortex remnants on the ILM surface and associated fibrocellular collections. Furthermore, the ILM is believed to be more rigid than the retina, so its removal allows the more compliant retina to regain its previous contour more easily. It is also postulated that peeling the ILM causes retinal gliosis, which can help to close a macular hole.[2] Peeling the ILM is controversial and surgeon dependent. A recent meta-analysis[5] and Cochrane review[17] on ILM peeling in FTMH repair revealed no difference in the primary outcome (BCVA at 6 months); however, the ILM-peeled group had better vision at 3 months, suggesting a faster recovery. This group also had a higher proportion of primary closure and fewer required reoperations. There was no difference in rates of intraoperative or postoperative complications. In the case of an FTMH, a gas or air bubble will be left in the eye postoperatively as a tamponade. The type of gas, duration, and positioning of the patient are beyond the scope of this article. Vitrectomy for FTMH has a high closure rate and remains the gold standard for treatment of symptomatic pathology.[7]

Pharmacology

A number of pharmacological agents have been studied in an attempt to bring a safe and

effective vitreolytic agent to market.[18] These include collagenase, chondroitinase, dispase, hyaluronidase, nattokinase, plasmin, tissue plasminogen activator, arginine-glycine-aspartate peptides, and ocriplasmin

Ocriplasmin is a truncated form of the human serine protease plasmin and cleaves fibronectin and laminin (discussed previously), which are key components of the vitreoretinal interface. It was approved by Health Canada for symptomatic VMA in August 2013.[19] Ocriplasmin has been studied in several clinical trials, the most recent of which were 2 multicentre, randomized, double-blind, placebo-controlled, phase 3 studies.[20-23]

The phase 3 trials[20] included 652 patients who had a vitreous adhesion within the 6-mm retinal subfield surrounded by elevation of the posterior vitreous cortex and an Early Treatment Diabetic Retinopathy Study BCVA worse than 20/25. Patients with macular holes >400 µm in size were excluded from this study so as to only look at small- and medium-sized macular holes. Patients were randomized to receive either intravitreal ocriplasmin (n=464) or placebo (n=188) and were followed up to 180 days after injection. Vitrectomy could be offered any time if the BCVA in the study eye worsened by >2 lines or if the underlying condition had not improved within 4 weeks of injection. The primary endpoint was percentage of eyes with OCT-determined nonsurgical resolution of VMA at day 28. Secondary endpoints included the percentage of eyes with total posterior vitreous detachment as determined by B-scan ultrasound, need for vitrectomy, closure of hole, gain of ≥3 lines of vision, change from baseline visual acuity, and 25-item National Eye Institute Visual Function Questionnaire score at 6 months. The primary endpoint was achieved by 26.5% of patients in the ocriplasmin group versus 10.1% of controls. This difference became significant at day 7 and stayed that way throughout the study follow-up. There was a higher magnitude effect in phakic patients reaching the primary endpoint after ocriplasmin (34.2%) than pseudophakic patients (13.4%). More treated women (30.3%) reached the primary endpoint than men (18.7%). At 28 days, 40.6% of eyes treated with ocriplasmin had closure of their macular hole compared to 10.6% of the placebo group. Subgroup analysis showed that holes <250 µm with focal vitreomacular traction and no ERM in phakic females had the best outcomes; ie, close to 60% macular hole closure.

At 6-month follow-up, 17.7% of the ocriplasmin group and 26.6% of the placebo group had undergone vitrectomy during the study for persistent VMA. Regarding safety, serious ocular adverse events were recorded in 7.7% of the ocriplasmin group and 10.7% of the placebo group. Two retinal tears with detachment occurred in the ocriplasmin group before any surgical intervention. Overall, 6 of the ocriplasmin-injected eyes and 5 of the placebo-injected eyes developed tears but it was stated that most were during vitrectomy. Nonserious ocular events were common and related to PVD (floaters).[20]

Phakic patients with small FTMHs and associated focal VMT would appear to be ideally suited for chemical vitreolysis. However, even in these "optimal" cases, the rate of macular hole closure with ocriplasmin was 60%, well below that of surgical closure which remains the goal standard in macular hole therapy. Medium, large FTMHs and those without associated VMT have a lower success rate with ocriplasmin, and surgical repair remains the primary treatment modality.

Pneumatic displacement

There has been some renewed interest in using perfluoropropane gas to pneumatically release VMT. A small retrospective study has recently been published that showed release of vitreomacular traction in 9 of 15 eyes 6 months after bubble injection.[24] The idea of mechanically releasing VMAs with a gas bubble is interesting, especially since 10% of the participants from the placebo group in the ocriplasmin studies achieved this outcome, presumably from mechanical disruption from the placebo injection or simply natural history. Perfluoropropane is a safe, inexpensive gas that we are accustomed to using as a first step in a treatment algorithm for VMT.

Future treatment options

With small-gauge vitrectomy instrumentation, advances in illumination allowing bimanual intraocular techniques, ocriplasmin, and SD-OCT, the future would appear to be now for the management of VMAs, VMTs, and FTMHs. One surgical innovation that will be potentially helpful is the introduction of intraoperative OCT. Currently, handheld and new operating microscope OCT integrated systems allow real-time intraoperative *in vivo* histology.[25-27] Other surgical innovations, such as robot-assisted surgery, are also in the experimental phase.[28]

Conclusion

This is an exciting time for the treatment of diseases of the VMI. The addition of medical therapy for VMI pathology is a paradigm shift in how we approach these problems. Only time and further study will tell whether new less-invasive treatments such as ocriplasmin will change the way we treat our patients. Further advances in vitrectomy surgery may allow us to achieve better, more consistent outcomes. Certainly, these advances cannot come soon enough, as we should expect to see more pathology as our population ages.

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References:

1. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology.* 2013;120(12):2611-2619.
2. Steel DHW, Lotery AJ. Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment. *Eye.* 2013;27(Suppl 1):S1-21.
3. Vitreous. In: Hogan MJ, Alvarado JA, Weddell JE (editors). *Histology of the Human Eye: An Atlas and Textbook.* Philadelphia (PA): WB Saunders Company; 1971: 607-637.
4. Sebag J, Balazs EA. Morphology and ultrastructure of human vitreous fibers. *Invest Ophthalmol Vis Sci.* 1989;30(8):1867-1871.
5. Spiteri Cornish K, Lois N, Scott NW, et al. Vitrectomy with internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole. *Ophthalmology.* 2014;121(3):649-655.
6. Johnson MW. Posterior vitreous detachment: evolution and complications of its early stages. *Am J Ophthalmol.* 2010;149(3):371-382.
7. Macular hole and vitreomacular traction. In: Ryan SJ, Schachat A, Wilkinson C, et al (editors). *Retina,* 5th edition. Philadelphia (PA): Elsevier Saunders; 2013:1963-1987.
8. Jackson TL, Nicod E, Angelis A, et al. Vitreous attachment in age-related macular degeneration, diabetic macular edema, and retinal vein occlusion: a systematic review and metaanalysis. *Retina.* 2013;33(6):1099-1108.
9. Jackson TL, Nicod E, Simpson A, Angelis A, Grimaccia F, Kanavos P. Symptomatic vitreomacular adhesion. *Retina.* 2013;33(8):1503-1511.
10. Mitchell P, Smith W, Chey T, Wang JJ, Chang A. Prevalence and associations of epiretinal membranes. The Blue Mountains Eye Study, Australia. *Ophthalmology.* 1997;104(6):1033-1040.
11. Rahmani B, Tielsch JM, Katz J, et al. The cause-specific prevalence of visual impairment in an urban population. The Baltimore Eye Survey. *Ophthalmology.* 1996;103(11):1721-1726.
12. Gass JDM. Reappraisal of biomicroscopic classification of stages of development of a macular hole. *Am J Ophthalmol.* 1995;119(6):752-759.
13. Chew EY, Sperduto RD, Hiller R, et al. Clinical course of macular holes. The Eye Disease Case-Control Study. *Arch Ophthalmol.* 1999;117(2):242-246.
14. Machemer R, Buettner H, Norton EW, Parel JM. Vitrectomy: a pars plana approach. *Trans Am Acad Ophthalmol Otolaryngol.* 1971;75(4):813-820.
15. Dawson SR, Shunmugam M, Williamson TH. Visual acuity outcomes following surgery for idiopathic epiretinal membrane: an analysis of data from 2001 to 2011. *Eye (Lond).* 2014;28(2):219-224.
16. Williamson TH, Lee E. Idiopathic macular hole: analysis of visual outcomes and the use of indocyanine green or brilliant blue for internal limiting membrane peel. *Graefes Arch Clin Exp Ophthalmol.* 2014;252(3):395-400.
17. Spiteri Cornish K, Lois N, Scott N, et al. Vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with no peeling for idiopathic full-thickness macular holes (FTMH). *Cochrane Database Syst Rev.* 2013;6:CD009306.
18. Johnson M. How should we release vitreomacular traction: surgically, pharmacologically, or pneumatically? *Am J Ophthalmol.* 2013;155(2):203-205.
19. Alcon Canada Inc. Jetrea® (ocriplasmin) product monograph. Date of preparation: August 7, 2013.
20. Stalmans P, Benz MS, Gandorfer A, et al; MIVI-TRUST Study Group. Enzymatic vitreolysis with Ocriplasmin for vitreomacular traction and macular holes. *N Engl J Med.* 2012;367(7):606-615.
21. de Smet MD, Gandorfer A, Stalmans P, et al. Microplasmin intravitreal administration in patients with vitreomacular traction scheduled for vitrectomy: the MIVI 1 trial. *Ophthalmology.* 2009;116(7):1349-1355.
22. de Smet MD, Valmaggia C, Zarranz-Ventura J, Willekens B. Microplasmin: ex vivo characterization of its activity in porcine vitreous. *Invest Ophthalmol Vis Sci.* 2009;50(2):814-819.
23. Gandorfer A, Rohleder M, Sethi C et al. Posterior vitreous detachment induced by microplasmin. *Invest Ophthalmol Vis Sci.* 2004;45(2):641-647.
24. Rodrigues IA, Stangos A, McHugh DA, Jackson TL. Intravitreal injection of expansile perfluoropropane (C3F8) for the treatment of vitreomacular traction. *Am J Ophthalmol.* 2013;155(2):270-276.
25. Ehlers JP, Tao YK, Farisiu S, Maldonado R, Izatt JA, Toth CA. Integration of a spectral domain optical coherence tomography system into a surgical microscope for intraoperative imaging. *Invest Ophthalmol Vis Sci.* 2011;52(6):3153-3159.
26. Pichi F, Alkabes M, Nucci P, Ciardella AP. Intraoperative SD-OCT in macular surgery. *Ophthalmic Surg Lasers Imaging.* 2012;43(6 Suppl):S54-S60.
27. Ray R, Baranano DE, Fortun JA. Intraoperative microscope-mounted spectral domain optical coherence tomography for evaluation of retinal anatomy during macular surgery. *Ophthalmology.* 2011;118(11):2212-2217.
28. Rahimy E, Wilson J, Tsao TC, et al. Robot-assisted intraocular surgery: development of the IRISS and feasibility studies in an animal model. *Eye.* 2013;27(8):972-978.

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