Title Page

Title: Widefield spectral-domain optical coherence tomography imaging of peripheral round retinal holes with or without retinal detachment

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Short Title: SD-OCT imaging of retinal hole retinal detachments

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Key Words:
Round Hole; optical coherence tomography; retinal detachment

Summary Statement:
Peripheral round holes, both with and without retinal detachment, were often associated with vitreous attachment on optical coherence tomography imaging. A U-shape configuration was more commonly seen when associated with retinal detachment or subretinal fluid.

Abstract

Purpose

To describe the widefield spectral-domain optical coherence tomography (SD-OCT) features of peripheral round retinal holes, with or without associated retinal detachment (RD).

Methods

Retrospective, observational study of 28 eyes with peripheral round retinal holes, with and without RD. Patients underwent imaging with a widefield 50-degree SD-OCT (Heidelberg Engineering, Germany) and Optos ultra-widefield imaging systems (Optos, UK).

Results

Vitreous attachment at site of retinal hole was detected in 27/28 (96.4%) cases. Cases were split into 3 groups: RHs with RD (n=12); RHs with subretinal fluid (SRF) (n=5) & flat RHs (n=11), with minimal or no SRF.

91.6% retinal holes associated with SRF or RD had vitreous attachment at the site of the hole. 80% had vitreous attachment at both edges of the retinal hole, in a U shape configuration, which appeared to exert traction. In contrast, flat retinal holes had visible vitreous attachment only at one edge of the retinal hole in 45.4%.

Conclusions

Vitreous attachment was commonly seen at the site of round retinal holes. Vitreous attachment at both edges of the retinal hole in a U shape configuration, was more commonly seen at holes associated with SRF or RD.

Main Manuscript

INTRODUCTION

Since the advent of optical coherence tomography (OCT) imaging over twenty years ago,[1] it has developed an ever increasing role in both diagnosis and clinical decision making. Although OCT is predominantly used in the diagnosis and management of macular pathology, it is now possible to acquire widefield spectral domain optical coherence tomography (SD-OCT) imaging of peripheral retinal pathology, including peripheral round retinal holes.[2]

Peripheral round retinal holes can be a precursor to retinal detachment (RD), and characteristics of round hole RDs have previously been described.[3-5] It was previously thought that there is no direct vitreoretinal traction on peripheral round retinal holes,[6] but Choudhry et al's peripheral OCT imaging series suggested that there was adhesion and possible traction at these sites.[2] Similarly, Manjunath et al previously reported a 'subclinical' RD associated with a round hole with evidence of vitreous attachment on OCT scanning.[7] We planned to review SD-OCT imaging of peripheral round retinal holes, including those complicated by RD, to assess the vitreoretinal interaction. We hoped to characterise OCT features of the retinal holes which may be associated with RD, with a view to guiding prophylactic treatment. This would be of particular use with the advent of possible ultra-widefield OCT systems in the future,[8] which will allow more routine peripheral OCT imaging. Vitreoretinal adhesions at round holes would also be of interest, given the recent increase in the use of vitreolytic agents[9] and the observation that they can induce a complete posterior vitreous detachment (PVD).[10] We are unaware of any previous OCT imaging series of round retinal holes associated with RD.

METHODS

We performed a retrospective institutional image-based and case notes review. Patients with peripheral round retinal holes with or without associated RD, who had undergone OCT imaging were identified in the Vitreoretinal Emergency and Outpatient clinics at Moorfields Eye Hospital between August 2016 and March 2017. Ethics committee approval from Moorfields Eye Hospital was sought prior to gathering any patient data. Imaging was performed by an experienced operator (TC, ophthalmic photographer) using an SD-OCT (Heidelberg Engineering Co, Heidelberg, Germany) and Optos California ultra-widefield retinal imaging system (Optos, Dunfermline, UK). Patients received dilating drops (phenylephrine 2.5% and tropicamide 1%) up to 20 minutes before imaging. Widefield SD OCT was carried out using an HRA+OCT Spectralis Scanning Laser Ophthalmoscope (Heidelberg Engineering Co, Heidelberg, Germany) with a 50°

imaging lens. The scan site was surveyed with a single line scan before a raster scan with the automatic real-time (ART) set to 5 and scan line separation of 6µm was placed over the site. The scan line was oriented tangentially to the fovea and the raster area was adjusted to the approximate size of the hole. Orientation was particularly important to avoid tilted imaging when scanning peripheral pathology. Depending on the nature of the pathology; single line scans with a higher ART were also performed to provide greater detail. Images of insufficient quality were excluded. Single scans through the centre of the hole were analysed. Statistical analysis was performed using Graphpad Prism software, version 7 (GraphPad Software Inc., CA, USA). One-way ANOVA and Fisher exact test was used to compare between the three groups.

RESULTS

A total of 28 eyes of 26 patients with peripheral round retinal holes, with or without RD underwent peripheral SD-OCT and Optos imaging. An additional 6 eyes were excluded due to poor SD-OCT image quality. This was due to combination of inadequate pupillary dilatation, media opacity, poor patient fixation or inability to locate the round hole. Average age of patients included was 34.4 years (range: 18 – 73 years), with an average refraction of -5.07 dioptres (range: 0 – -10D). All eyes were phakic and had no sign of posterior vitreous detachment (PVD) either clinically (assessed with slit lamp biomicroscopy) or on OCT imaging.
The retinal holes were divided into 3 groups: 12/28 (42.8%) retinal holes were judged clinically to have an associated RD, defined as >3-disc diameters of subretinal fluid. 5/28 (17.8%) holes had no RD clinically but associated subretinal fluid on SD-OCT imaging. The remaining 11/28 (39.2%) holes were flat, with minimal (<100 microns) or no associated subretinal fluid. Difference between the three groups are summarised in Table 1.

Retinal Holes with Associated RD

12/12 (100%) had vitreous attachment visualised at the site of the hole on SD-OCT imaging (Figure 1A-F & 2A-E). These attachments mainly comprised of bands of vitreous at the edge of the hole (Figure 1). 10/12 (83.3%) of these eyes had vitreous attachment on both edges of the retinal hole (Figure 1C & 2E). The posterior hyaloid often seemed to form a 'U shape' at its attachment with the inner retina (Figure 1D & 2E), and this U shape was present in 8/10 (80%) of these holes in which this imaging feature was gradable. 9/12 (75%) retinal holes had adjacent areas of cystoid retinal degeneration (figure 1 & 2). The average hole size and adjacent retinal thickness are shown in Table 1.
6/12 (50%) patients presented with reduced vision due to foveal involvement. 3/12 (25%) had noticed floaters and photopsia and the remaining 3/12 (25%) patients were asymptomatic. 6 of

the 12 (50%) holes were associated with lattice degeneration on ultra-widefield imaging. An OCT image of lattice degeneration is shown in Figure 3.

Retinal Holes with Associated Subretinal Fluid

4/5 (80%) had vitreous attachment visualised at the site of the hole on SD-OCT imaging (Figure 4A-E), all of which had vitreous attachment in a U shape configuration (figure 4E). 3/5 (60%) of eyes had associated areas of cystoid retinal degeneration (figure 4D). The average hole diameter and adjacent retinal thickness are shown in Table 1. On Optos imaging, 2/5 holes were associated with snailtrack and 1/5 associated with lattice degeneration.

Flat Retinal Holes

10/11 (90.9%) of flat retinal holes had visible vitreous attachment. 4/11 (36.3%) had a vitreous attachment in a U shape configuration (figure 5B), whilst 5/11 (45.4%) retinal holes had vitreous attachment only at one edge of the hole on the central OCT scan (figure 5A). 5/11 (45.4%) retinal holes were associated with cystoid retinal degenerative changes. The average hole diameter and adjacent retinal thickness are shown in Table 1. 2 operculated holes were imaged alongside this imaging series, shown in Figure 5C, for comparison.

There was no statistical difference in the maximal measured hole diameter or width of vitreous attachment between the 3 groups.

DISCUSSION

This report describes the SD-OCT features of peripheral round retinal holes associated with clinical RD and found a high rate of vitreous attachment at the site of retinal holes (96.4%). This is of particular interest as it has recently become possible to perform OCT imaging of peripheral retinal pathology,[2,11] thus aiding our understanding of possible pathological mechanisms.[11] OCT technology is advancing rapidly[12] and it is likely that peripheral OCT imaging will become a routine part of clinical care in the future. Indeed in a research setting, a 100-degree ultra-widefield OCT imaging field of view is already possible,[8] so it is therefore important to characterise the imaging features of peripheral vitreoretinal pathology. Vitreoretinal adhesions at round holes would also be of interest, given the recent increase in the use of vitreolytic agents[9] and the finding in a recent widefield OCT study that Ocriplasmin seemed to induce a near complete PVD in 20% of patients.[10]

Previous work has shown that round hole detachments progress at a much slower rate when compared to tractional tear detachments,[13] occur in a younger age group and normally without an associated PVD.[3,4] In Norman Byer's observational series, he reported that only 3/150 (2%) round holes developed a retinal detachment that warranted treatment,[6] far lower than the proportion of tractional tears that require intervention.[14] In support of this are histological series that have shown that there is no vitreous attachment associated with the edges of atrophic round holes.[15] Similarly, a previous SD-OCT imaging series of peripheral degeneration found no vitreous attachment at the site of the two of the three retinal holes that were imaged.[7] In contrast, our OCT imaging detected vitreous attachment at the site of the retinal hole in 96.4% cases. This supports the recent SD-OCT imaging series of peripheral retina by Choudhry et al of that also found evidence of vitreoretinal attachment over retinal holes, and they postulated that the vitreous exerted traction on the inner retina at these sites.[2] Although these findings seem to contradict the previous histological reports, there are differences in patient demographics between the two series. Foos' series was in a more elderly population who were more likely to have undergone a PVD.[15] In contrast, no PVD was detectable in any of the patients in our series, making the high frequency of vitreous adherence to the hole edges less unexpected. Foos also excluded any eyes with lattice degeneration.[15] In our series, we found lattice in a number of eyes whose retinal holes had associated RD or SRF and we know from histological and OCT work that vitreous is attached at the edge of lattice with an overlying vitreous bursa.[7,16] If a higher proportion of round holes imaged in our series were secondary to lattice degeneration, this may explain the higher rate of vitreous attachment.

When the hole was associated with SRF or detachment, we observed a higher proportion (80%) formed a distinctive U shape at the vitreo-retinal interface on the central OCT scan, when compared to flat retinal holes. It is possible that this U shaped attachment around the hole indicates the presence of an overlying vitreous bursa. Over 30 years ago, Foos hypothesised that areas of lattice subsequently developed atrophic holes, and liquefied vitreous from an overlying bursa was then able to track subretinally and cause a detachment.[16] This theory may explain why this U shape configuration was more commonly seen in association with RD or SRF in our series. The other possibility is that this U shaped attachment exerts a degree of vitreous traction on the inner retina, similar to the mechanism underlying vitreomacular traction (VMT),[17] which then pre-disposes to SRF accumulation. Indeed, Mori et al found evidence of peripheral retinoschisis in patients with early macula holes, which they presumed to be secondary to vitreous traction.[11] We feel that given the static nature of SD-OCT imaging that it is difficult to know whether the vitreous is causing direct traction, or is simply adherent. Regardless of the mechanism, it would be interesting to assess in future studies if this pattern of vitreous attachment at the retinal hole was a predictor for progressive SRF accumulation.

In contrast, there was a trend for flat retinal holes to have visible vitreous attachment only at one edge of the retinal hole (45.4%). It's possible that the vitreous is still attached adjacent to these holes but not visible as causing traction on the SD-OCT scan due to diffuse vitreous attachment or lack of an overlying bursa. The U shape configuration described above could therefore serve as a potential imaging marker for subsequent SRF accumulation associated with round holes and could potentially guide prophylactic treatment in the future.

Cystoid retinal degeneration has previously been noted in association with peripheral round retinal holes.[2] Mori et al found areas of peripheral retinoschisis associated with early macula holes, which they also postulated were related to abnormal retinal adhesion.[11] We found evidence of cystoid degeneration or perhaps peripheral retinoschisis associated with peripheral round holes. We found this was more common, and the adjacent retina thicker, in retinal holes where there was RD or SRF, when compared to flat retinal holes. One could argue that these changes may have resulted from vitreo-retinal traction, although equally they may simply be due to longstanding separation from the underlying retinal pigment epithelium (RPE), so it is difficult to draw conclusions.

This study has obvious limitations, given its retrospective nature and relative small sample size. It is a cross sectional imaging series, which also makes it difficult to make inferences about the relationship between vitreous attachment and associated SRF or RD. We would instead require a prospective observational series to assess if any SD-OCT features were predictors for SRF accumulation. In this series, SD-OCT imaging of peripheral detached retina was often challenging which did affect image quality. Retinal holes were imaged in only one circumferential plane as imaging in additional planes was not normally possible due to the curvature of the globe. There was an inevitable selection bias given that patients presented or were referred to a tertiary referral centre. In particular, all patients were relatively young and none had a PVR, which may have affected the subset of retinal holes included when compared to previous observational series.

CONCLUSION

In summary, this imaging series of peripheral round hole RDs illustrates that such imaging is not only feasible but shows evidence of vitreous attachment at a high proportion of retinal holes. Vitreous attachment in a U shape configuration was more commonly seen in holes associated with

SRF or RD. Further prospective longitudinal series would be of value to assess the relationship between these SD-OCT features and the progression of round hole RDs.

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Figure Legends

Figure 1: Peripheral retinal hole with associated retinal detachment.

A, Ultra-widefield colour fundus image with a retinal hole outlined in detached retina (black arrowheads). D,E,F, Peripheral spectral-domain optical coherence tomography (SD-OCT) cross sections of the retinal hole (marked with an asterisk), which correspond to (B) colour and (C) near-infrared scanning laser ophthalmoscopy images with overlying raster scans (green lines). Vitreous attachment forms a U shape as it attaches to each edge of the round hole (black & white arrowheads) and cystoid retinal degeneration is noted.

Figure 2: Peripheral retinal hole with associated retinal detachment.

A, Ultra-widefield colour fundus image with 2 retinal holes outlined in detached retina (black arrowheads). B,E, Peripheral spectral-domain optical coherence tomography (SD-OCT) cross sections of the retinal hole, which correspond to (C) colour and (D) near-infrared scanning laser ophthalmoscopy images with overlying raster scans (green and yellow lines). Vitreous attachment in a U shape (marked with white arrows) is noted adjacent to the retinal hole (B) and at both edges of the hole (hole marked with asterisk) (E). The retina adjacent to the hole contains areas of cystoid retinal degeneration. Arrowheads in D represent corresponding locations in B & E.

Figure 3: Lattice Degeneration with subretinal fluid.

A, Ultra-widefield colour fundus image with area of lattice and retinal holes outlined. D, E, Peripheral spectral-domain optical coherence tomography (SD-OCT) cross sections of the area, which correspond to (B) colour and (C) near-infrared scanning laser ophthalmoscopy images with overlying raster scans (green and yellow lines). Vitreous attachment is noted at the area of lattice (D) and overlying the hole (E). Arrowheads in C represent corresponding locations in D & E.

Figure 4: Peripheral round hole with subretinal fluid.

A, Ultra-widefield colour fundus image with retinal hole outlined. D, E, Peripheral spectral-domain optical coherence tomography (SD-OCT) cross sections of the hole, which correspond to (B) colour and (C) near-infrared scanning laser ophthalmoscopy images with overlying raster scans (green and yellow lines). Vitreous attachment is noted at the edges of the retinal hole in a U shape configuration (marked with white arrows) (D, E). Arrowheads in C represent corresponding locations in D & E.

Figure 5: Flat peripheral retinal holes.

Peripheral spectral-domain optical coherence tomography (SD-OCT) of retinal holes with near-infrared scanning laser ophthalmoscopy images shown. A, Vitreous attachment is seen at one edge of the retinal hole (arrowhead), with minimal subretinal fluid. B, Vitreous attachment is noted at both edges of the retinal hole (arrowheads). C, Flat retinal hole with operculum. No vitreous attachment is seen at the hole.