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Optical Coherence Tomography in Imaging of Papilledema

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Abstract: OCT can play an important role in monitoring the disease and process ing of papilledema. Following the peripapillary RNFL thickness over different visits provides a quantitative and sensitive measurement of changes in the papilledema. While the Frisén grading scale for clinical papilledema ranges from grade I to V, the peripapillary RNFL thickness can range from 50 µm to over 500 µm giving it a much larger dynamic range to objectively evaluate for change. In addition, there is significant variability among experts in grading papilledema based on the Frisén scale, and therefore the peripapillary RNFL is easier to follow objectively for change, especially when the patient is seen by different care providers. A decrease in peripapillary RNFL thickness in can be either a result of improving papilledema or increase in axonal loss from disease progression. Combining the macular GCIP thickness with the peripapillary RNFL thickness allows one to evaluate for optic neuropathy in the presence of papilledema.

Keywords: *Optical Coherence Tomography, Papilledema*

Introduction.

Optic Disc Drusen (ODD) is refractive, hyaline-like calcified nodules made of mucoproteins and mucopolysaccharides that are located within the optic nerve head. its Prevalence is 3.4-24/1000. . Most patients are subjectively asymptomatic; however, some may complain of transient visual obscuration [1]

The etiology is unknown, but drusen appear to be degenerative axonal byproducts. It has been postulated that small scleral foramina impede normal axoplasmic flow leading to stasis. Abnormal axonal metabolism then leads to deposition of calcium crystals in mitochondria, which are extruded into the extracellular space. Continuous calcifications of these small microbodies coalesce to form groupings of drusen [1]

The early model of time-domain OCT (TD OCT) provided image resolution of 8 to 10 µm. On early OCT devices, drusen appeared as rounded hyporeflectant areas, but diagnostic accuracy was limited by low resolution of the image [1]

Since 2006, spectral-domain (SD) OCT has increased the signal to noise ratio and improved resolution to 5 to 7 µm in tissue Swept-source (SS) technology is a high-penetration technique that uses a laser light source to sweep the retina at a given frequency. It increases the diagnostic capacity of OCT to detect ONHD to detailed

visualization and measurement of drusen TD OCT and SD OCT have both qualitative and quantitative parameters to assist clinicians in differentiating optic disc edema due to papilledema or other optic neuropathies from ONHD. Qualitative parameters are related to subjective interpretation of the image to identify features related to changes in retinal structure due to drusen versus papilledema. Such features indirectly suggest the presence of drusen but do not directly visualize drusen. Early quantitative criteria included the peripapillary retinal nerve fiber layer (RNFL) thickness, peripapillary ring volume, and the subretinal hyporeflective space thickness [1]

Peripapillary RNFL Thickness and Ring Volume

Several investigators have found the peripapillary RNFL thickness to be a useful parameter to differentiate between true disc edema and ONHD. A normal RNFL thickness in all four quadrants favors pseudopapilledema but an increased RNFL thickness in all four quadrants is more suggestive of papilledema. This finding depends in large part on the severity of edema and/or optic disc elevation

Mild increase in thickness of the peripapillary RNFL is not useful as it is found in both early papilledema and pseudopapilledema. Another limiting factor is non-standardization of the definition of abnormal RNFL thickness among various TD and SD OCT devices. Obviously, diagnostic accuracy relies on the selected threshold. In ONHD in initial stages, it is common to find an increase of peripapillary RNFL thickness by OCT, but as drusen continue to develop, the RNFL thickness decreases [1]

It appears that the nasal sector provides the greatest diagnostic information. For example, it has a sensitivity of 80% and a specificity of 70% of diagnosing true disc edema when the nasal RNFL thickness was greater than 86 μm **(Johnson et al., 2009).**

Sub-retinal Hypo-reflective Space

OCT examination revealed a triangular peripapillary subretinal hyporeflective space (SHYPS) is located between the sensory retina and the retinal pigment epithelium (RPE) using Stratus OCT in cases of optic disc edema such as non-arteritic anterior ischemic optic neuropathy, anterior optic neuritis, and papilledema

The SHYPS appearance was thus proposed as a differential OCT feature between optic disc edema and ONHD. In optic disc edema, SHYPS has a smooth internal edge and gradually thins with the apex pointing away from the optic nerve head, giving a recumbent “lazy V” pattern in cases of true disc edema. Drusen shows an undulating, termed “lumpy-bumpy,” internal contour and its thickness decreases abruptly in drusen

The SHYPS thickness is greater in eyes with disc edema compared to those with ONHD but the ability to discriminate both conditions based on these qualitative criteria alone was low (63%) [1]

Optical coherence tomography (OCT) is a non-contact, non-radiation, fast, efficient, safe, and cost-effective ocular imaging technique that provides high resolution. Resolution of OCT is much higher than that of other medical imaging methods such as ultrasound or magnetic resonance imaging (MRI). Additionally, It provides cross-sectional images of the retina and optic nerve head (ONH). It has become one of the most important tools in ophthalmic practice. [1]

OCT was first described in 1993 as a system capable of measuring different reflective properties of the retinal layers of the human eye. The first commercial OCT system was introduced in 1996, allowing for a better understanding of retinal diseases. In 2001, a second-generation OCT system was developed, providing higher resolution images with faster acquisition time [2].

The system currently available is known as spectral-domain OCT. It provides cross-sectional images of the macula and optic disc with high resolution to differentiate all retinal layers and subcellular photoreceptor elements [1].

Fundus examination has been the traditional method to identify the structural effects of optic neuropathies, which include optic disc edema, optic disc pallor, and retinal nerve fiber layer (RNFL) defects. Consequently,

changes in RNFL structure, including wedge defects, represent visible effects of axonal loss caused by retrograde degeneration, typically from an afferent visual pathway lesion involving the optic nerve, chiasm, or tracts [3].

OCT has become the standard tool for imaging in macular diseases, diabetic retinopathy and glaucoma, to name a few examples from a wide range of retinal applications. The ability to segment retinal layers allows for thickness measurement, which improves glaucoma diagnosis, because thinning of the nerve fiber layer marks the onset and progression of the disease. The anterior segment of the eye also benefits from OCT imaging [4].
OCT imaging can capture and quantify axonal loss through measurements of retinal nerve fibre layer (RNFL) thickness, and neuronal damage through measurements of ganglion cell layer (GCL) or combined ganglion cell layer-inner plexiform layer (GCIPL) thickness [4].

In the setting of trans-synaptic "neuroaxonal" degeneration, post-geniculate lesions in the afferent visual pathway can also cause optic nerve pallor, and corresponding RNFL defects, which can all be readily captured by OCT. [5]
Low-coherence interferometry is the principle of spectral domain OCT to acquire high-resolution (within 4–6 microns), images of retinal structural architecture, in vivo [3].
Emerging OCT techniques, such as swept source imaging, provide even better resolution, faster scanning, and repeatability [5].
Recent advances in segmentation techniques allow the thickness of individual layers of the retina to be quantified with OCT. This, in turn, can facilitate indirect quantification of axonal loss (RNFL thinning) and neuronal damage [ganglion cell-inner plexiform layer (GCIP) thinning] referable to various mechanisms of optic nerve, chiasm, and optic tract injury [3].
Notably, OCT measured thinning of the macular GCIP has been found to have a strong relationship with visual loss across a spectrum of optic neuropathies including glaucoma, optic neuritis, ischemic optic neuropathy, hereditary optic neuropathy, toxic optic neuropathy, optic nerve glioma, and idiopathic intracranial hypertension (IIH) [5].
As with any technology, there are limitations, pitfalls and potential errors that must be considered, especially when using derived measurements in clinical decision-making. Foremost, different OCT machines have different measurement protocols and so patients must be reviewed on the same machine using the same scanning protocol for accurate longitudinal comparisons to be made. Secondly, all OCT measurements are compared to a normative database. Often these normative databases are made up of Caucasian middle-aged subjects, and as such this must be considered when evaluating measurements from a patient not in this demographic, for example a child or a patient of different ethnicity [6].
Optical Coherence Tomography in Imaging of Papilledema
OCT can play an important role in monitoring the disease and processing of papilledema [7].

Following the peripapillary RNFL thickness over different visits provides a quantitative and sensitive measurement of changes in the papilledema. While the Frisén grading scale for clinical papilledema ranges from grade I to V, the peripapillary RNFL thickness can range from 50 μm to over 500 μm giving it a much larger dynamic range to objectively evaluate for change. In addition, there is significant variability among experts in grading papilledema based on the Frisén scale, and therefore the peripapillary RNFL is easier to follow objectively for change, especially when the patient is seen by different care providers [8].
A decrease in peripapillary RNFL thickness can be either a result of improving papilledema or an increase in axonal loss from disease progression. Combining the macular GCIP thickness with the peripapillary RNFL thickness allows one to evaluate for optic neuropathy in the presence of papilledema [9, 10].
In monitoring papilledema using OCT, a reduction in the peripapillary RNFL thickness with a preserved macular GCIP thickness indicates successful treatment. However, a concordant reduction in the RNFL thickness

and macular GCIP thickness indicates worsening optic neuropathy and could be an indication of treatment failure [9].

Therefore, combining the peripapillary RNFL analysis with the macular GCIP analysis allows one to differentiate treatment response from worsening disease. This is especially important in patients unable to perform visual fields due to age or mental capacity [9].
OCT provides an objective measurement of the structural integrity of the optic nerve, allowing ready detection of worsening optic neuropathy [7].
However, it is important to note that there can be errors in segmentation of the GCIP in the setting of high degrees of papilledema. Segmentation errors will lead to a falsely thin GCIP thickness and could raise a false alarm of worsening disease if they are not recognized. Fortunately, these artifacts can be easily identified because they result in significant reductions in the GCIP thickness in a non-physiologic pattern [5].
The Bruch's membrane configuration with OCT has been shown to correlate with intracranial pressure and therefore can be followed in papilledema (Fig.1) [11].

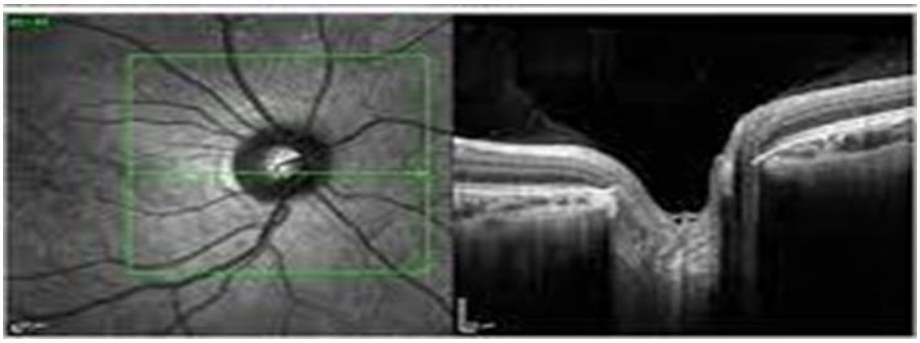

Figure (1): (A) Positive angling of Bruch's membrane in the setting of raised intracranial pressure. At baseline, there is an upward defection of the Bruch's membrane complex toward the vitreous in this patient with grade IV papilledema from idiopathic intracranial hypertension (red arrows). (B) After this patient underwent a ventriculoperitoneal shunt, there is improvement in the papilledema and a downward deflection of the Bruch's membrane complex (blue arrows) [12].

Patients with raised intracranial pressure have an upward deflection of Bruch's membrane toward the vitreous and this can be useful in differentiating papilledema from pseudopapilledema. The treatment of papilledema will lead to normalization of Bruch's membrane complex orientation toward the posterior direction [13].
This observation was confirmed in the IIH Treatment Trial, in which patients had ventriculoperitoneal shunts had a significant posterior displacement of Bruch's membrane [14].
While changes in the fundus appearance of papilledema typically take days to develop, alterations in the Bruch's membrane complex configuration occur more rapidly and can be seen within an hour of cerebrospinal fluid lowering procedures. It has been shown that OCT testing performed immediately after lumbar puncture-induced lowering of the intracranial pressure shows measurable posterior defection of Bruch's membrane, even in the absence of detectable changes in peripapillary RNFL thickness [15].
Therefore, clinically relevant changes in intracranial pressure, caused for example by shunt failure, could possibly be best detected by evaluation of the Bruch's membrane complex morphology. This OCT feature could be particularly useful in assessing patients with pre-existing optic atrophy, among which RNFL values (and fundus examination of the optic nerve) may not be a reliable means of tracking worsening elevations in intracranial pressure [12].
Lastly, OCT has an important clinical role to detect retinal causes of vision loss from papilledema and evaluate the disease severity [7].

Patients with decreased vision from optic neuropathy secondary to severe papilledema require aggressive treatment, while decreased vision due to subretinal fluid or choroidal folds is typically more benign [9].

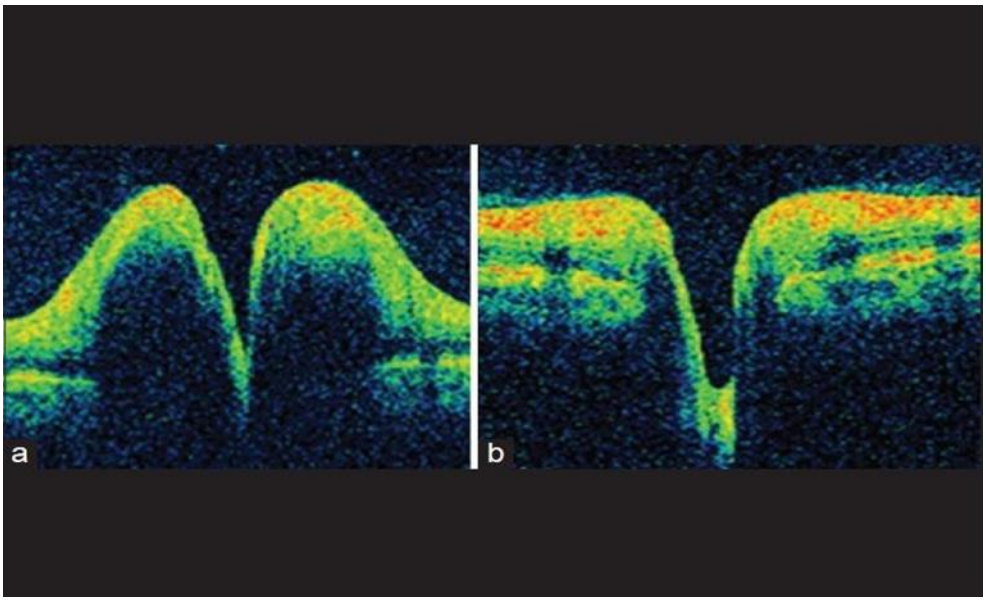

Figure (2): Line optical coherence tomography scan through the optic nerve head demonstrating inward deflection of the retinal pigment epithelium (upper left and lower left) toward the vitreous in a patient with papilledema. Upper right and bottom right are the same patient after treatment with acetazolamide [16].

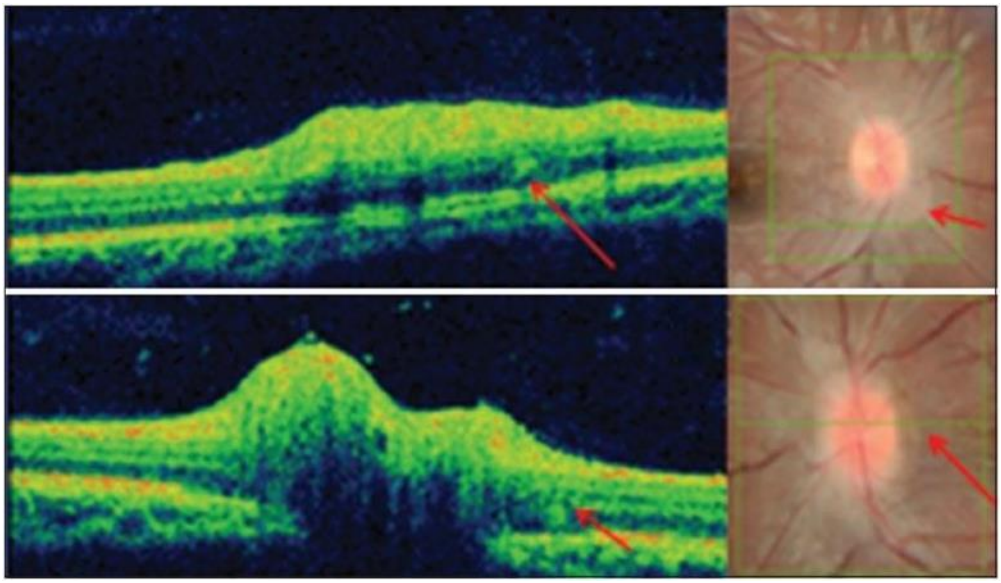

Figure (3): Pre- (a) and post-treatment (b) retinal nerve fiber layer in papilledema [17].

Use of optical coherence tomography in monitoring papilledema

Rebolleda and Muñoz-Negrete have quantitatively correlated RNFL thickness with visual field sensitivity losses. They showed that for every 10 μm of mean RNFL thickness increase at baseline, there was a 0.6-dB decrease in mean deviation at the last follow-up. OCT in conjunction with perimetry is helpful in determining RNFL thickness returns toward normal whether the patient improving or that they are actually losing nerve fibers. Hence, serial OCT imaging and perimetry can be the standard in monitoring papilledema. A noticed

discrete hyperreflective echoes above the RPE present in patients with resolving papilledema seen in regressing disc swellings OCT can definitely be used as a tool to monitor the treatment in papilledema [18].

Use of OCT to Differentiate Papilledema from Pseudopapilledema

An edematous optic nerve appearance is a relatively common clinical finding, the causes of which may be both dangerous and benign. To diagnose a potential cause of optic disc edema, the first step is taking a thorough history. Next, it is important to perform a comprehensive examination of afferent and efferent visual pathway functions and investigations, including OCT.

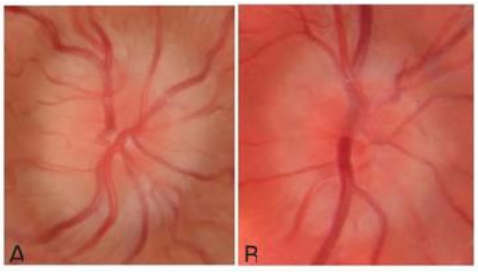

FIGURE 4. Fundus photos showing an elevated appearance of the optic nerve head in a case of papilledema (A) and ODD (B).

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The etiology is unknown, but drusen appear to be degenerative axonal byproducts. It has been postulated that small scleral foramina impede normal axoplasmic flow leading to stasis. Abnormal axonal metabolism then leads to deposition of calcium crystals in mitochondria, which are extruded into the extracellular space. Continuous calcifications of these small microbodies coalesce to form groupings of drusen [20].

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Swept-source (SS) technology is a high-penetration technique that uses a laser light source to sweep the retina at a given frequency. It increases the diagnostic capacity of OCT to detect ONHD to detailed visualization and measurement of drusen [23].

TD OCT and SD OCT have both qualitative and quantitative parameters to assist clinicians in differentiating optic disc edema due to papilledema or other optic neuropathies from ONHD [24].

Qualitative parameters are related to subjective interpretation of the image to identify features related to changes in retinal structure due to drusen versus papilledema. Such features indirectly suggest the presence of drusen but do not directly visualize drusen. Early quantitative criteria included the peripapillary retinal nerve fiber layer (RNFL) thickness, peripapillary ring volume, and the subretinal hyporeflective space thickness [24].

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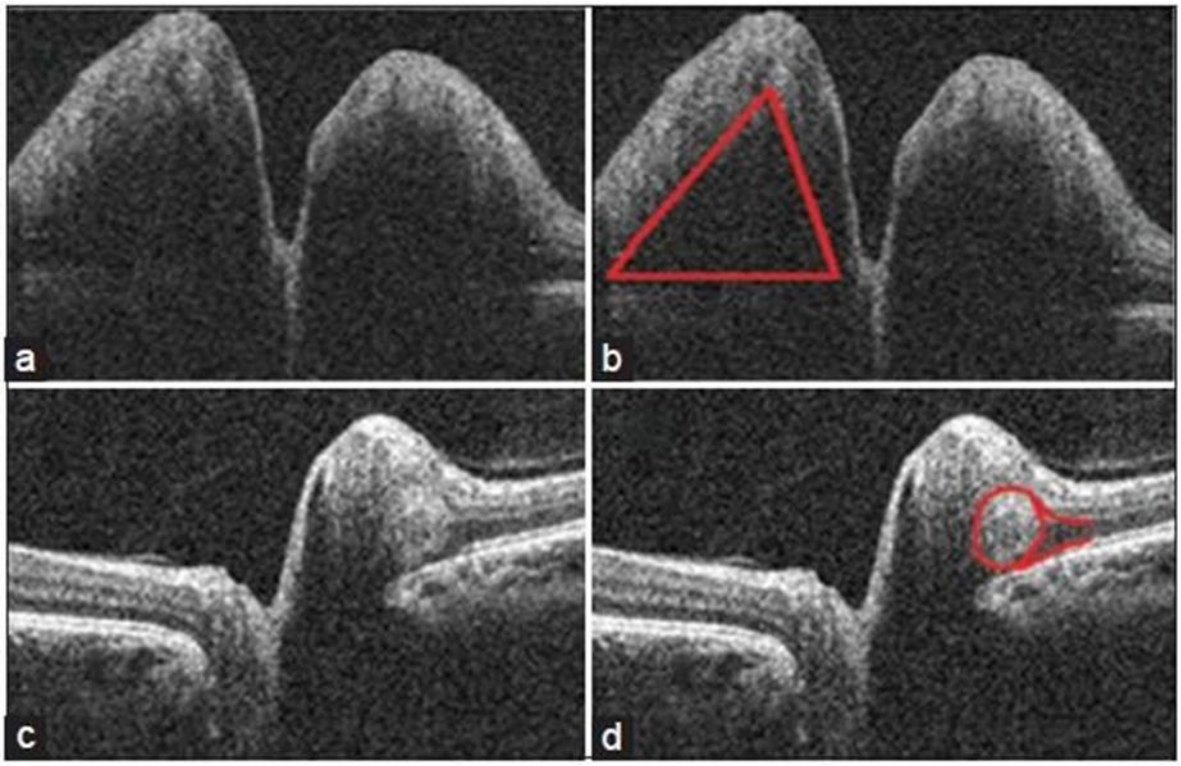

Figure (5): The triangular subretinal hyporeflective space in papilledema (a, b) and the buried optic nerve head drusen in pseudopapilledema (c, d) [17].

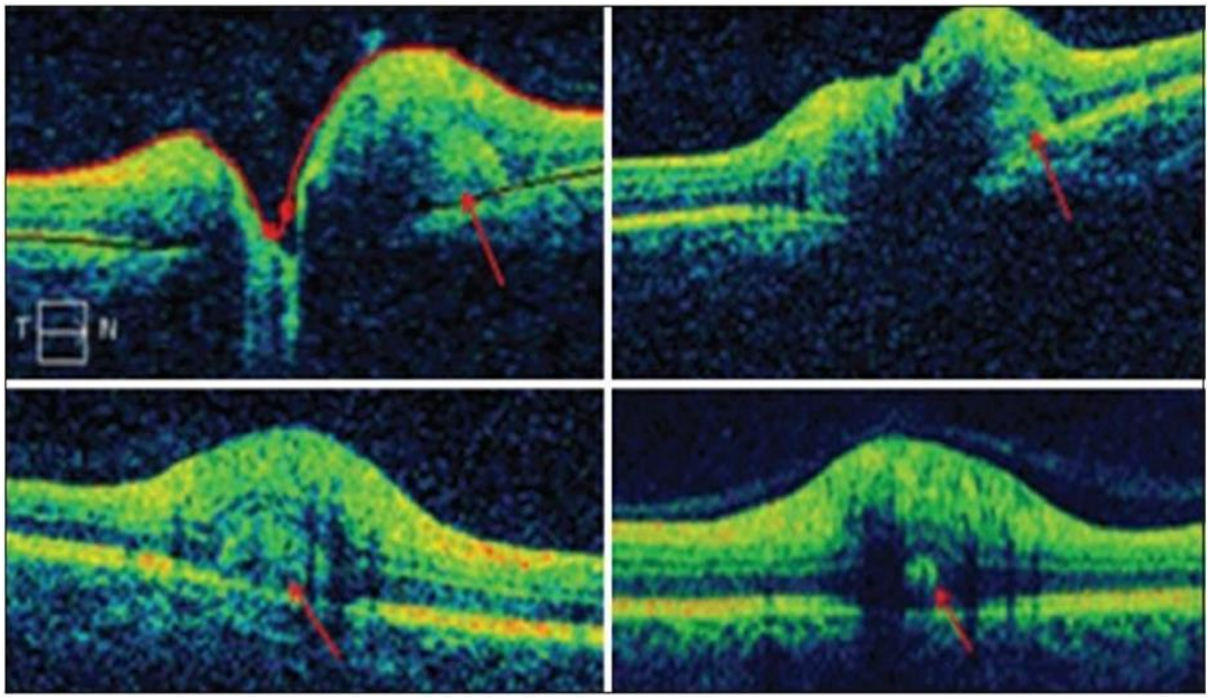

Figure (6): Buried optic nerve head drusen seen as a round hyperreflective echo (red arrow) above the retinal pigment epithelium [17].

Hyperreflective bands

Hyperreflective bands are not seen in eyes with papilledema. Using EDI-OCT, the visualization of lamina cribrosa sometimes mimics hyperreflective bands found in eyes with ODD. However, in this case, they are restricted to a very deep anatomical location in the optic nerve head [22].

The finding of hyperreflective bands in different depths of the prelaminar part of the optic nerve head suggests that the eye or fellow eye has ODD. However, not all eyes with ODD have these bands, and it is therefore not a reliable tool for the differentiation of papilledema and ODD.

scleral canal size

OCT measures of scleral canal size, measured as the termination of the Bruch membrane, have gained recent attention as a means of differentiating ODD from papilledema. Specifically, scleral canals have been shown to be smaller in patients with ODD [28]. A recent study by Thompson et al [29] has also shown that the Bruch membrane opening is enlarged in eyes with mild papilledema and narrows as the papilledema resolves. But the main problem is a huge variation of scleral canal size in the general population [30].

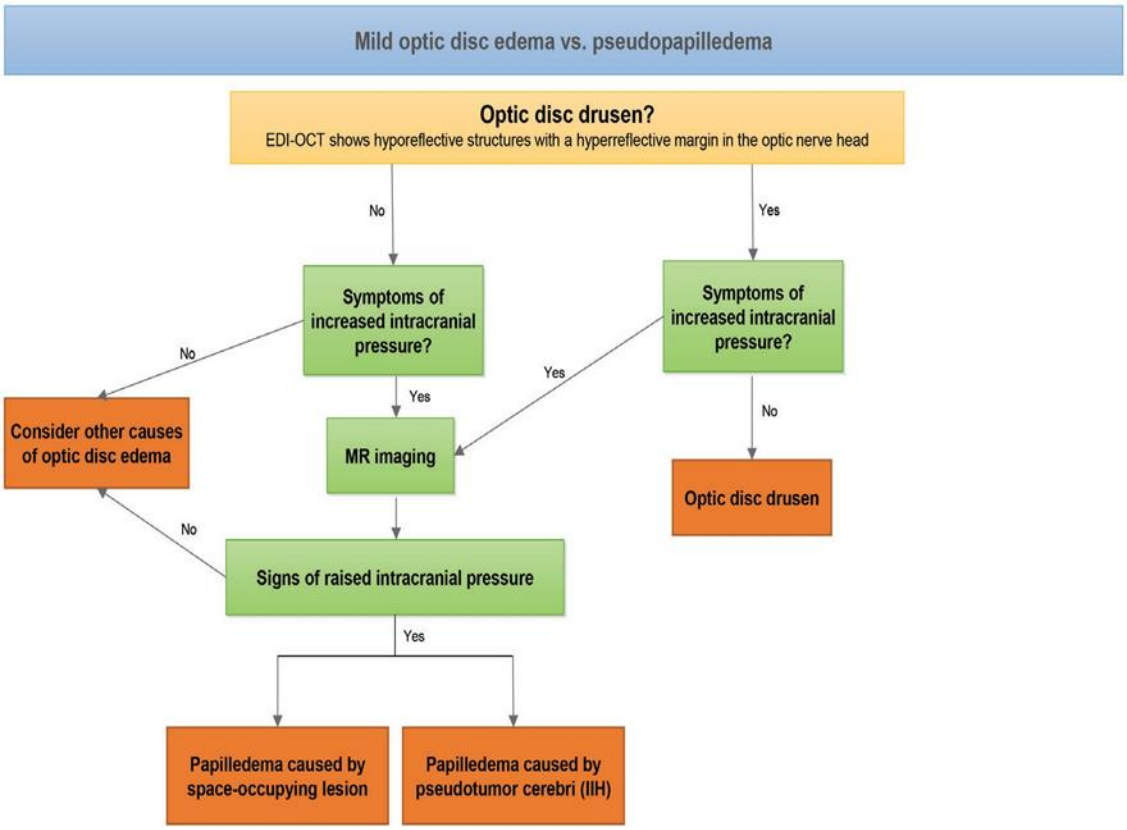

FIGURE 6. Flow chart illustrating the approach to a patient with the appearance of optic disc edema. [3]

Direct Visualization of Optic Nerve Drusen by OCT

Current OCT techniques now provide high-resolution images of drusen, these globular masses of mucopolysaccharide matrix within the optic nerve head, even in the absence of calcium deposition [31].

ONHD appeared as a highly reflective round subretinal structure with a well-defined margin that displaced the adjacent tissues, so that the RPE diverged from the outer nuclear layer covering the drusen, coming out in a hyporeflective, boot-shaped area adjacent to the drusen [22]

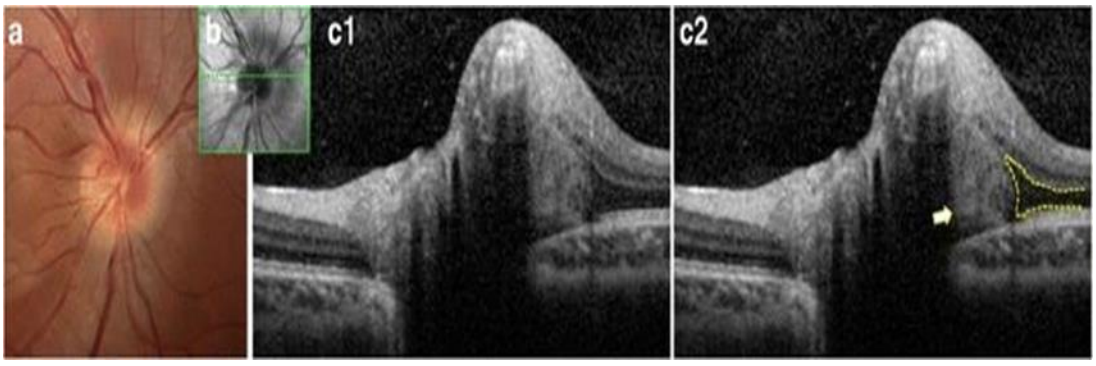

Figure (7): Image representative of optic nerve drusen appearance on SD OCT (right eye). a Fundus photography with no visible drusen. b Infrared image showing the scanned area (green line). c1 Horizontal section of SD OCT. c2 Same image with labels. The reflectance of ONHD (arrow) was similar to that of the outer and inner plexiform layers. The outer plexiform layer and retinal pigment epithelium diverge as they approach the optic nerve head. A boot-shaped area is observed adjacent to the ONHD (yellow dashed line) [32].

EDI OCT was used to detect ONHD, which appeared as ovoid regions of low reflectivity with short hyper-reflective borders, or as cluster hyper-reflective bands without the signal-poor center. These authors also reported ONHD in clinically normal optic discs having a normal B-scan ultrasound [21].

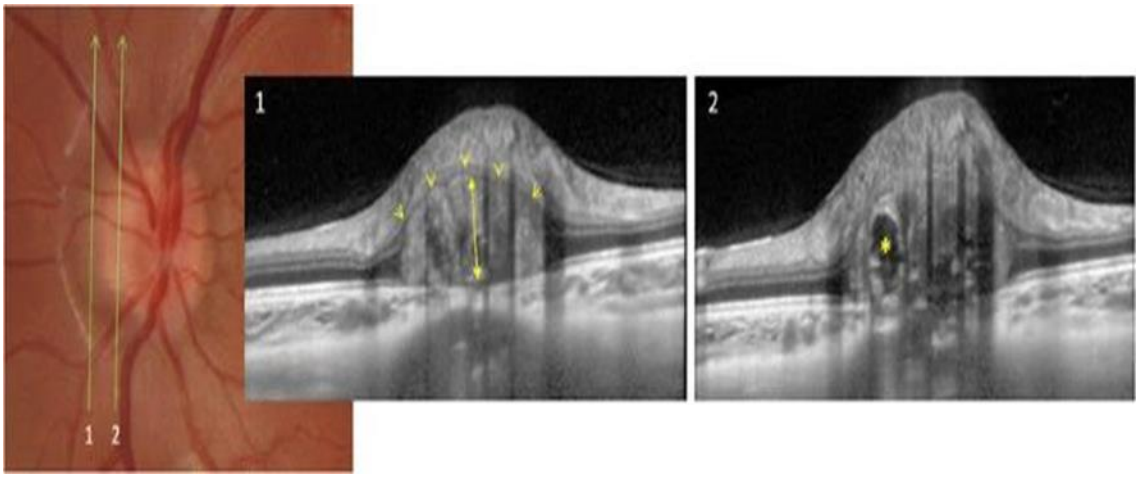

Figure (7): Enhanced depth imaging (EDI) spectral-domain optical coherence tomography showing different types of optic nerve head drusen (ONHD) in the same eye depending on the location of the OCT scan (represented by green vertical lines). 1-The halo seen around the disc on fundus photographs corresponding with retinal nerve fiber elevation resulting from the presence of a peripapillary subretinal hyper-reflective drusen (yellow arrows). The optic nerve head drusen height can be measured perpendicular to retinal pigment epithelium (yellow double arrow). 2-Confluent hyporeflective (asterisk) and multiple granular hyper-reflective drusen are shown [32].

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