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Optic nerve head drusen

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Abstract

Optic disc drusen are congenital and developmental anomalies of the optic nerve head seen commonly in clinical practice, often as an incidental ophthalmologic finding during routine exams. Optic disc drusen are a form of calcific degeneration in some of the axons of the optic nerve. Visual acuity is often not affected but the visual fields of these patients can be abnormal and deteriorate over time. Optic disc drusen are familial and are not uncommon. They are thought to be the result of pathology at the level of the optic nerve head itself. The diagnosis can be made with clinical findings combined with B scan ultrasound and computed tomography. In addition, newer modalities using optic nerve head tomography are proving to be very useful. Since children as well as adults are affected, it is important to consider optic nerve head drusen in the differential diagnosis of papilledema or optic nerve swelling.

Definition

Optic disc drusen are a form of calcific degeneration in some of the axons of the optic nerve. The name comes from a 16th century German word, *druse*, which geologic miners used to refer to rocks with crystal-filled centers.[1] In 1858 Müller used the plural form of the word, drusen, to describe calcific depositions found in histological specimens of optic nerves. Histologically, the colloidal substance was found intra- and extracellularly.[2,3] The clinical findings[4] and associated visual field defects were described years later.[4–7] Hyaline or colloid bodies are synonyms for drusen.

Prevalence and pattern of inheritance

Studies have shown the overall prevalence to be between less than 0.4% and 3.7%.[1,8,9] Lorentzen and later others examined family members of patients with drusen. Lorentzen found that the incidence of optic disc drusen increases up to ten times that of general population in family members. Genetically, optic disc drusen have an autosomal dominant pattern of inheritance.[10,11] Antcliff found that family members had either buried drusen or anomalous vessels and/or no optic cup.[12] Inheritance of small optic disc size is thought to be a risk factor in drusen formation. They appear more often in whites and rarely in blacks. Small inherited optic disc size and mesodermal dysplasia resulting in vascular dysplasia are factors that may influence the development of optic disc drusen.[8,13–15]

Clinical signs and symptoms

Most patients with optic disc drusen are asymptomatic. Up to 8.6% have reported transient visual obscurations.[16] An afferent pupillary defect is present when involvement is asymmetric. Visual field defects appear in nearly 90% of cases.[1,17] If progressive and severe the loss of field can lead to blindness, even in young adults.[16,18,19] The majority of visual field losses are peripheral in nature. Progressive central visual loss is rare. When visible, optic disc drusen look like yellow crystals within the substance of the optic nerve head. The margins are often indistinct (Fig. 1). Papilledema is what optic disc drusen mimic.[20] The difference is that with papilledema the vessels are obscured by nerve fiber layer edema that involves the peripapillary retina. Other signs of true papilledema are cotton wool spots, multiple hemorrhages around the disc, hyperemia, venous congestion, Patton's lines and exudates. It is important to distinguish pseudopapilledema from true papilledema. In true papilledema there is increased intracranial pressure. Pseudopapilledema, as the name suggests, occurs when the optic nerves look swollen because of increased intracranial pressure. Optic disc drusen is a common form of pseudopapilledema. Initially, the optic disc appears swollen and cupless because the optic disc drusen

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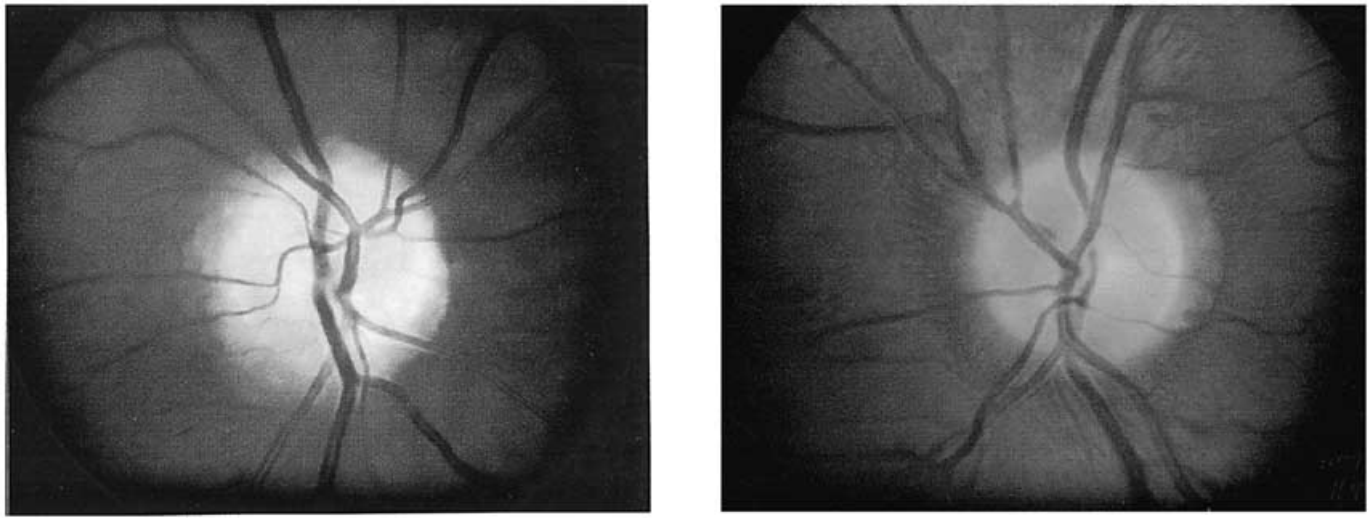

Figure 1A&B. Bilateral optic nerve head drusen. The margins are not sharp and the vessels seem unaffected, differing from papilledema.

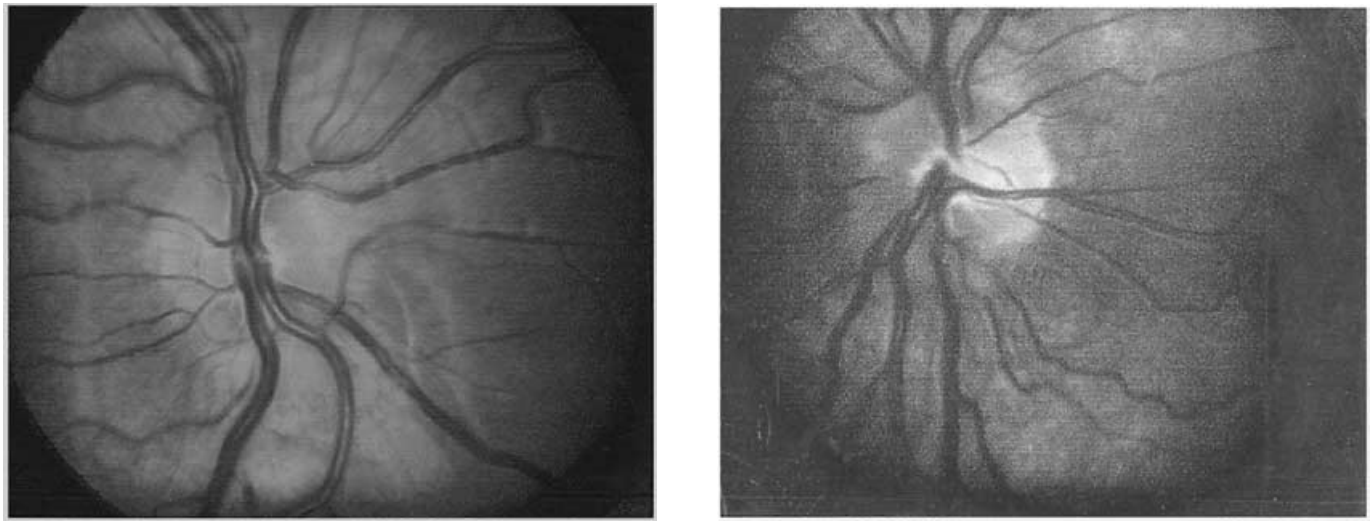

Figure 2A&B. Fundus photographs of the right and left eyes of a 5-year-old boy. The margins of the discs are blurred and the cups are nonexistent. The surfaces are lumpy bumpy. There are no signs of acute or chronic papilledema. The child's MRI and lumbar puncture were within normal limits, including the opening pressure.

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are buried. Relying on clinical appearance alone can lead to missing true papilledema. Diagnostic testing must follow the clinical exam. Children are often first diagnosed with pseudopapilledema after referral to the ophthalmologist (Fig. 2A&B).

Hoover and others have studied the physical changes in optic nerves with disc drusen over time. The appearance of colloid bodies occurs during the teenage years through early adulthood (Fig. 3A–D).[21] Optic disc drusen, over time, appear as elevated, lumpy irregularities on the anteriormost portion of the disc.[22] The nasal optic disc is the usual place exposed drusen are noted. These lesions are bilateral in more than 85% of cases, buried or visible.[1,21,23] The optic disc is anomalous in other ways by being small with abnormal branching of the vessels. Ciloretinal arteries are associated with optic disc drusen.[24,25] Often the scleral canal is small.[26] The optic nerve that contains drusen is anomalous by nature. In addition to structural abnormalities, vascular anomalies are seen such as; bi- and trifurcations of vessels, tortuosity of vessels and opticociliary shunts.[26]

Visual field defects can first appear during childhood; even before drusen appear on the disc.[27] Hoover showed that the mean age for detection was 14 years old (Fig. 4A–D).[21] Over time the visual field defects become more numerous and worsen in degree of severity. The pattern is most commonly an arcuate nerve fiber layer defect.[20,28] The changes in the visual field occur along with appearance and enlargement of optic disc drusen.[28] An afferent pupillary defect accom-

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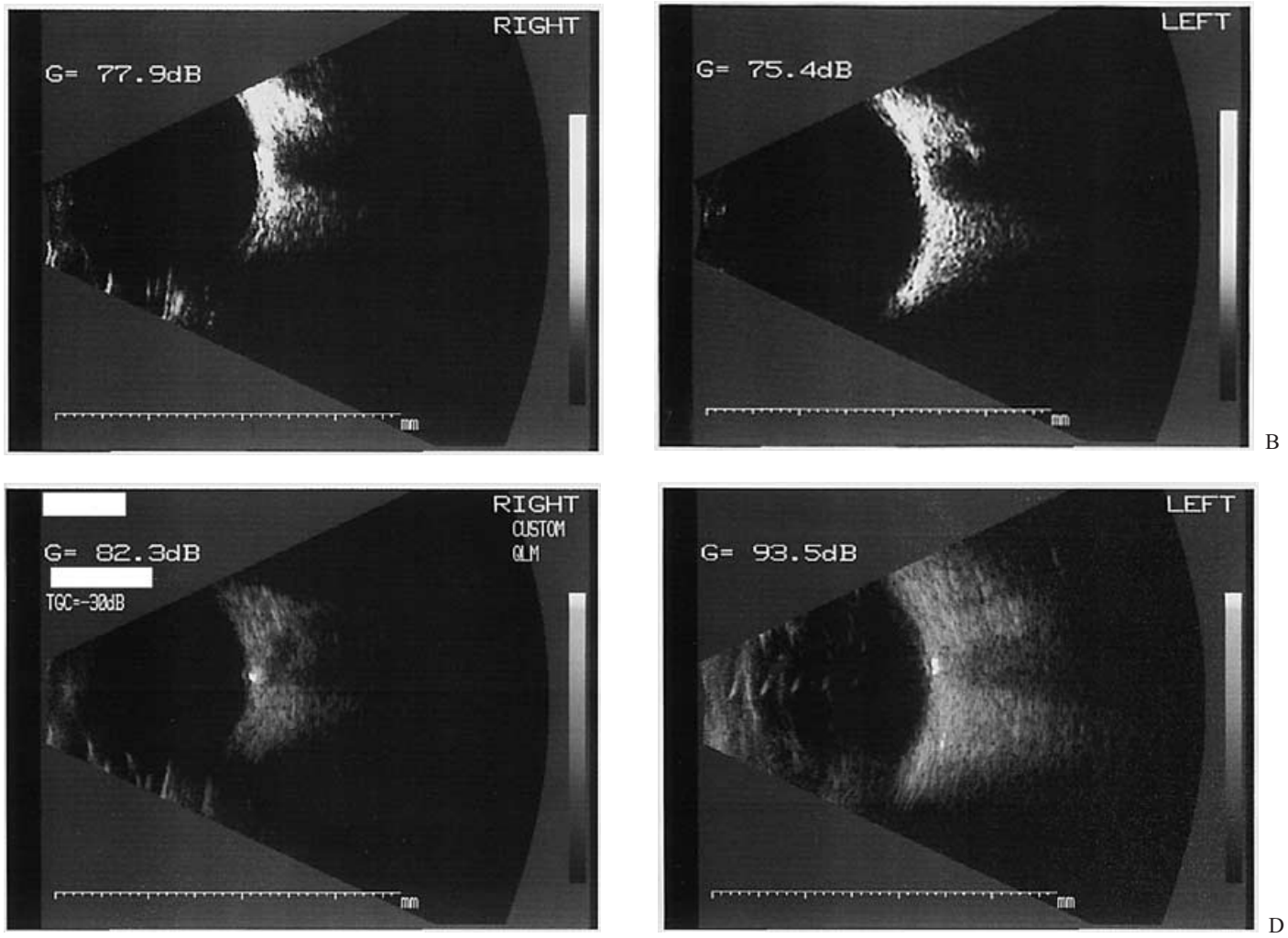

Figure 3A–D. B scan ultrasounds of the right and left eyes of a 15-year-old boy with optic nerve head drusen. The nerve head of each eye has an area of hyperechoic reflections consistent with drusen. The lower set of scans has a higher gain, exposing the drusen more clearly.

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panies asymmetric optic nerve function and is therefore present in the more affected eye. This may be a general sign to tip off the physician of the presence of an optic neuropathy. The afferent pupillary defect can be seen in a patient with asymmetric visual field defects and drusen of the nerve.[29] The incidence of abnormal visual field has been reported by various authors to occur in nearly 90% of adult patients.[11,15,17,28,30] As with glaucoma and other insidious causes of visual field degradation, the defects go unnoticed and progress over time (Fig. 5A&B).[28,30–33]

There are numerous theories about the evolution of visual field defects due to optic disc drusen. The pathogenesis of optic disc drusen is thought to be due to slowed axoplasmic flow, thus forming calcific excrescences.[3,12,34,35] Anatomy of the optic disc may play a role, due to small size and congenital dysplasia.[8,13,14,35,36] The field defects could arise from pressure on the nerve fiber layer resulting from a combination of the presence of the optic disc drusen and vascular compromise.[7,11]

Clinical diagnosis and progression

A number of diagnostic tests are available for the detection of drusen. Fundoscopic evaluation with direct and indirect ophthalmoscopy is useful in detection and re-evaluation of abnormal optic nerves. Disc photographs and drawings have been a mainstay (Figs. 2A, B, 4C&D). Visual field testing over time is useful in detection of malfunction of the optic nerve and progression of visual field defects.[37] B-scan ultrasonography can expose calcium deposits even if they are invisible ophthalmoscopically. B scan ultrasound is easy even for the smallest and most uncooperative patients.[38] This test has been proven to be the most reliable of all techniques available. The use of high gain helps to isolate optic disc drusen (Fig. 3A–D). Deeper lesions can be visualized due to the highly reflective nature of drusen.[23,39–42] Fluorescein angiography is also useful. In the pre-injection phase optic disc optic disc drusen demonstrate autofluorescence.[43] Autofluorescence is a phenomenon in which exposed optic disc

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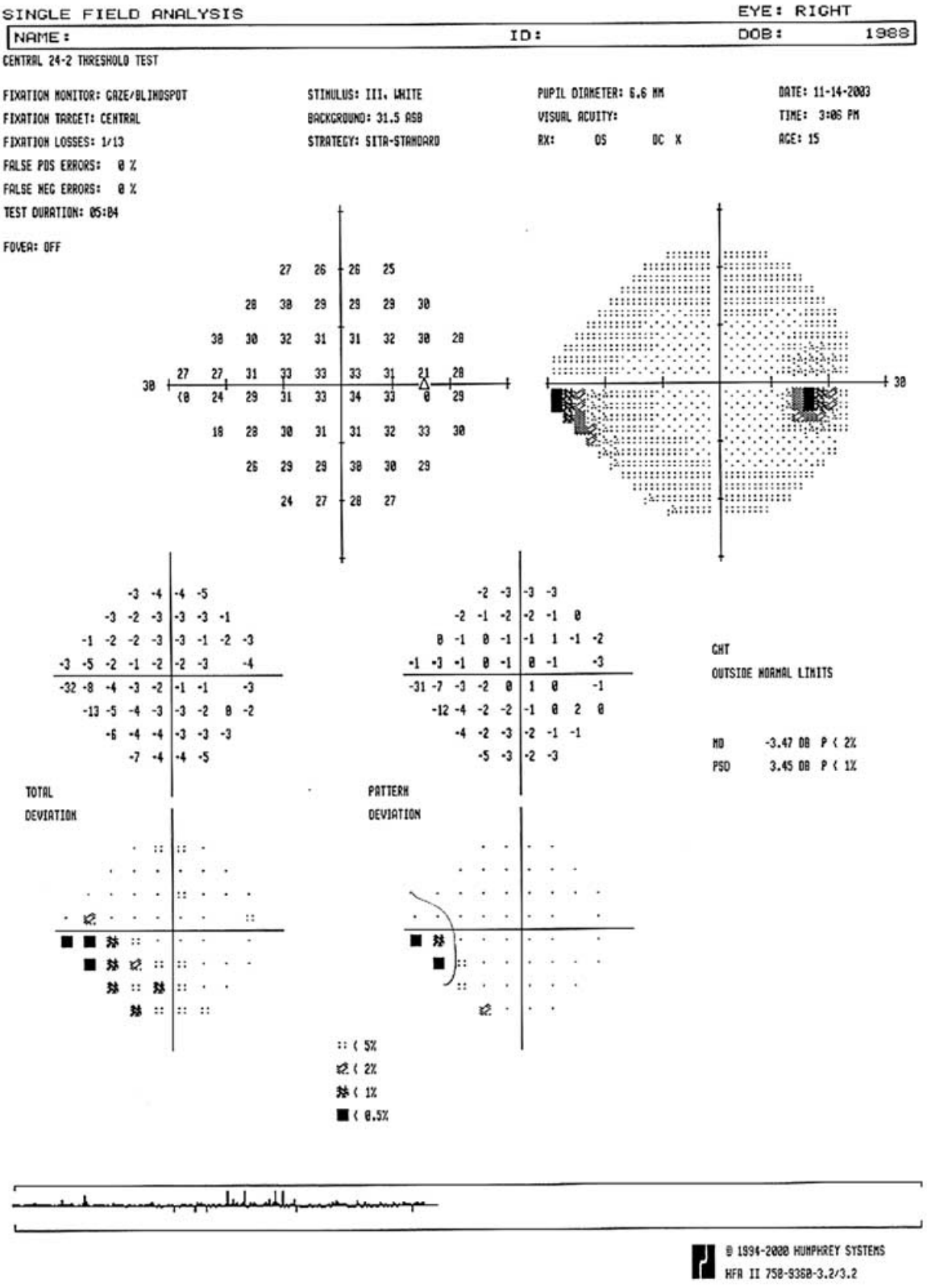

A

Figure 4A–D. The same 15-year-old boy. A&B. Humphrey visual field reveals an inferior nasal step OD. C&D. Disc photos OD and OS. The margins are fuzzy but the vessels remain easily identifiable.

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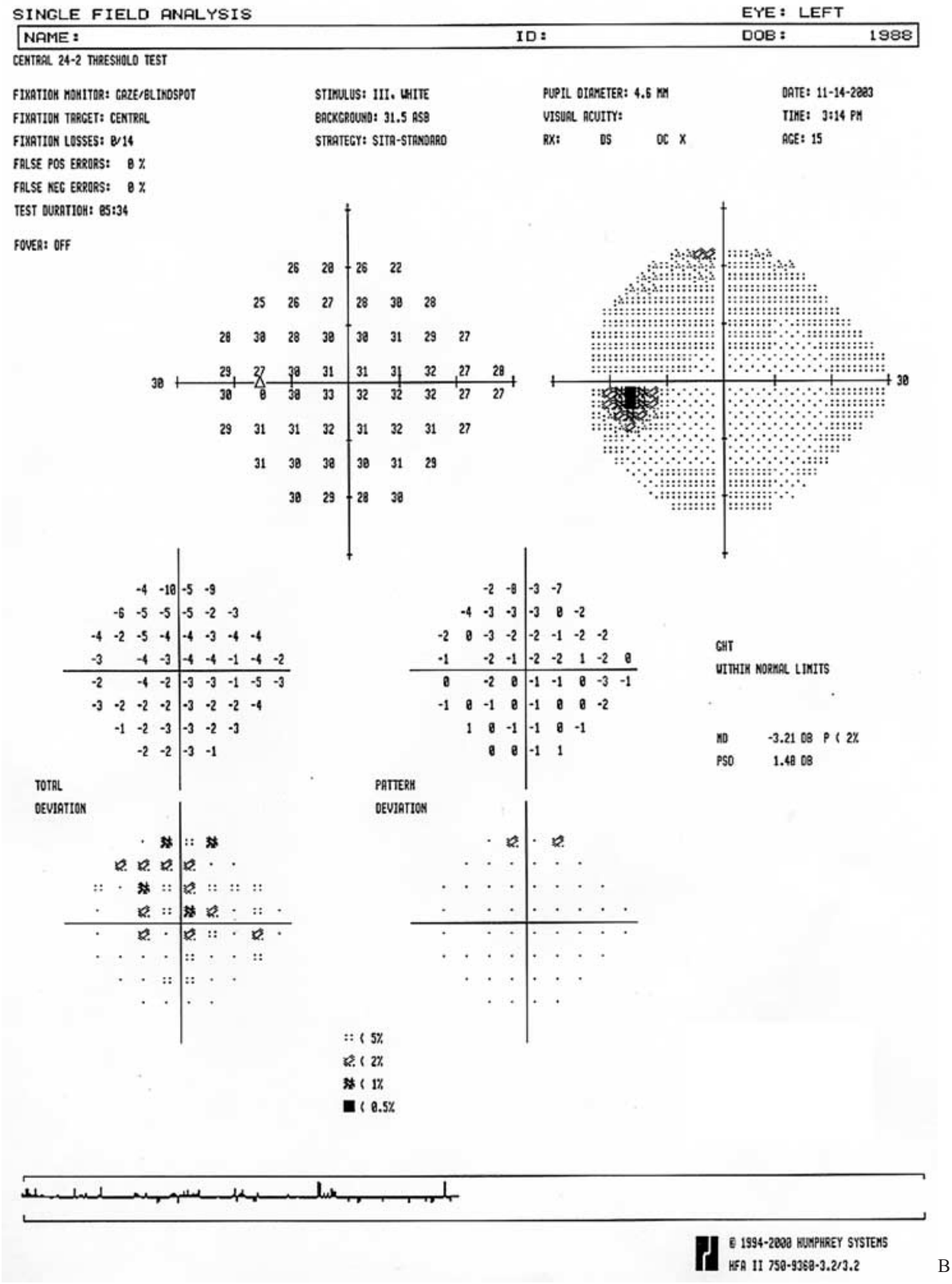

Figure 4A–D. Continued.

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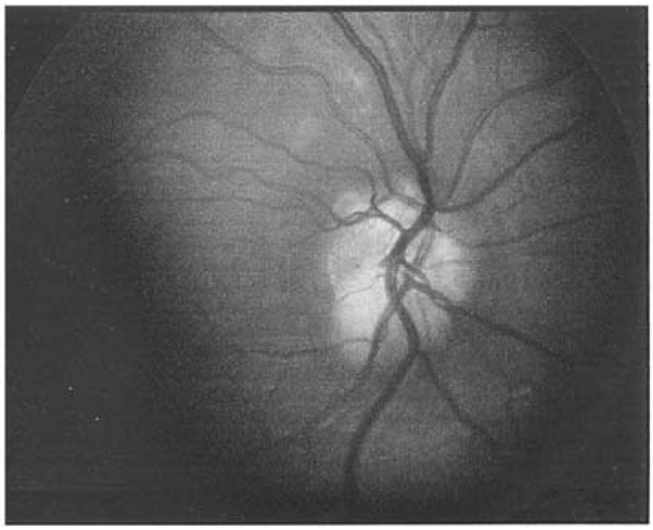

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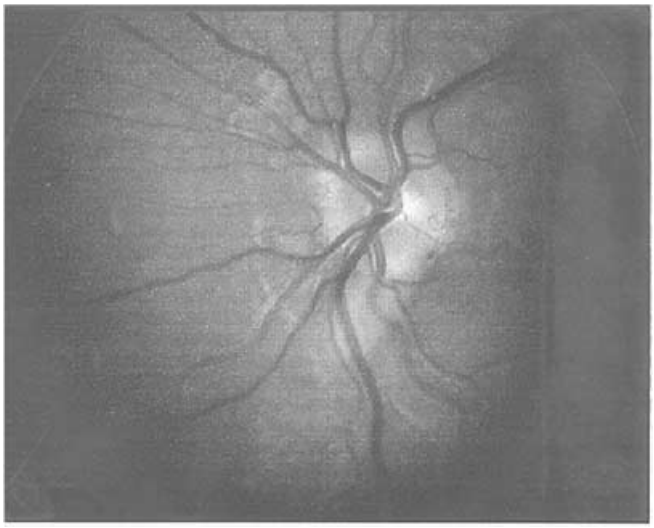

D

Figure 4A–D. Continued.

drusen naturally glow in the dark when viewed through the fundus camera prior to injection of fluorescein. Post fluorescein injection, heterogeneous hyperfluorescence is seen in the early phase. In the late phase staining is observed (Fig. 6). The normal capillary network can be seen coursing over buried drusen.[43] Computed Tomography (CT) and even facial X-rays can show the presence of calcium in the optic Nerve, but small lesions can be missed (Fig. 7A&B).[26,39,43] Electroretinograms are useful when nerve fiber layer (NFL) and visual acuity are subnormal. Scholl *et al*. evaluated 24 eyes with optic disc drusen. Nineteen (79%) showed reduction of the pattern ERG (pERG) or absence of the N95 component. These two findings reflect poor ganglion cell layer function.[44] Visual evoked potentials (VEP) are abnormal in more than 95% of cases due to peripapillary nerve fiber layer malfunction according to Stevens.[45] In fact the p100 latency is prolonged just like those found in optic nerves affected by demyelinating disease. Therefore, the VEP alone should not be used to make a diagnosis of optic neuritis alone due to similar findings in optic disc drusen.[46]

Newer technologies are available. Tomography of the nerve head is proving to be useful. Optical Coherence Tomography (OCT), GDx® (Scanning Laser Polarimetry) and Heidelberg Retinal Tomography (HRT) are commercially available (Figs. 8–14). These tests examine nerve fiber layer thickness. Nerve fiber layer (NFL) loss is a pathologic finding observed with optic disc drusen. The three dimensional views are useful as well. Thinning or loss can be seen with red free photography, with ophthalmoscopy with the red free light and histologically.[47–49] Nerve fiber analysis by way of digital photography and computerized assessment offers a quantifiable methodology. It is reproducible over time by different observers.[50] This application is more reliable than red free photography.[48,51] Often, the appearance of the optic nerve head and visual field do not correlate with the NFL analysis. The NFL analysis may show progressive pathologic changes prior to detection by other methods. Studies have shown these modalities have the ability to show thinning of the peripapillary NFL thinning associated with optic disc drusen.[51,52] This is helpful where glaucoma and drusen exist simultaneously.[51,53] Another simultaneous entity to consider in light of field loss is pseudotumor cerebri.[55] Pseudotumor cerebri, like optic disc drusen, is another diagnosis of exclusion. People who suffer from Pseudotumor cerebri have few symptoms. History of transient visual obscurations, diplopia, visual field loss and headaches, among other nonspecific complaints are noted in these patients. Diagnostic testing reveals normal neuroimaging. Lumbar puncture is notable for an opening pressure greater than 200–250 mmHg. The cerebrospinal fluid analysis is normal. Optic disc drusen, glaucoma and pseudotumor cerebri all have similar visual field defects. It is important to investigate the possibility of a second disease if clinical signs warrant it.

Complications of drusen

Pathologic vascular abnormalities occur in a variety of ways in association withoptic disc drusen. Optociliary shunts are collateral networks that form between the retinal venous system and the choroidal network as a result of increased central retinal venous pressure.[57] As optic disc drusen enlarge with age shunt vessels be come more apparent.

Vascular occlusions can occur due to the structural abnormality of the nerve head. Anterior ischemic optic neuropathy (AION) is the most common cause of visual loss in patients with optic disc drusen.[58] The resulting vascular occlusion is in part due to anatomic predisposition and disc crowding over time.[58] These patients have a form of what has been referred to as the "disc at risk" because their discs and canals are smaller than those of normals.[58,59] Auw-Haedrich asserts that these patients are more likely to have an ischemic event of the optic nerve than those who possess small canals without drusen because the arteries feeding the nerve

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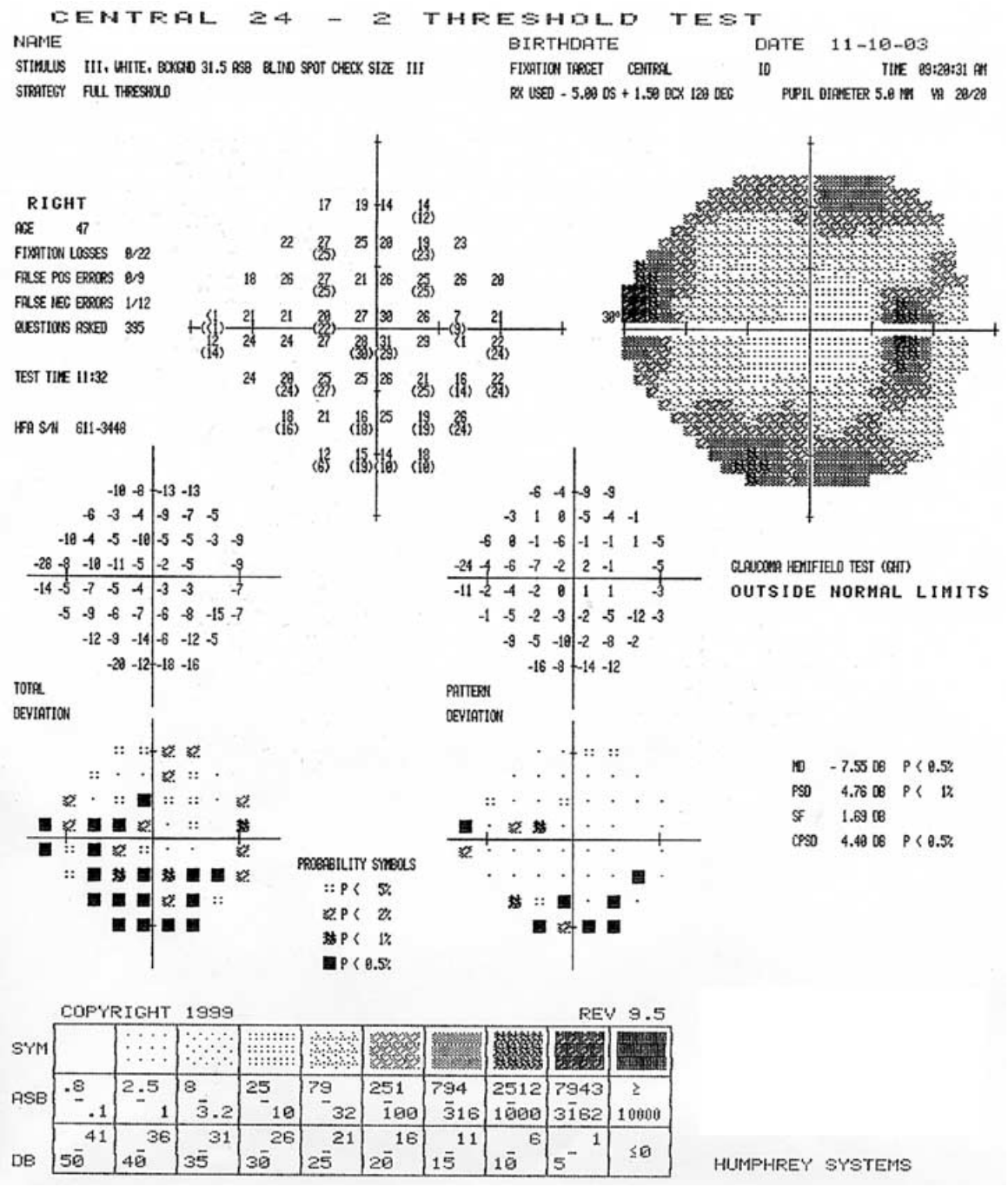

A

Figure 5A&B. Humphrey visual fields of a 47- year-old woman with optic disc drusen. Her intraocular pressures are normal. She has significant field loss bilaterally.

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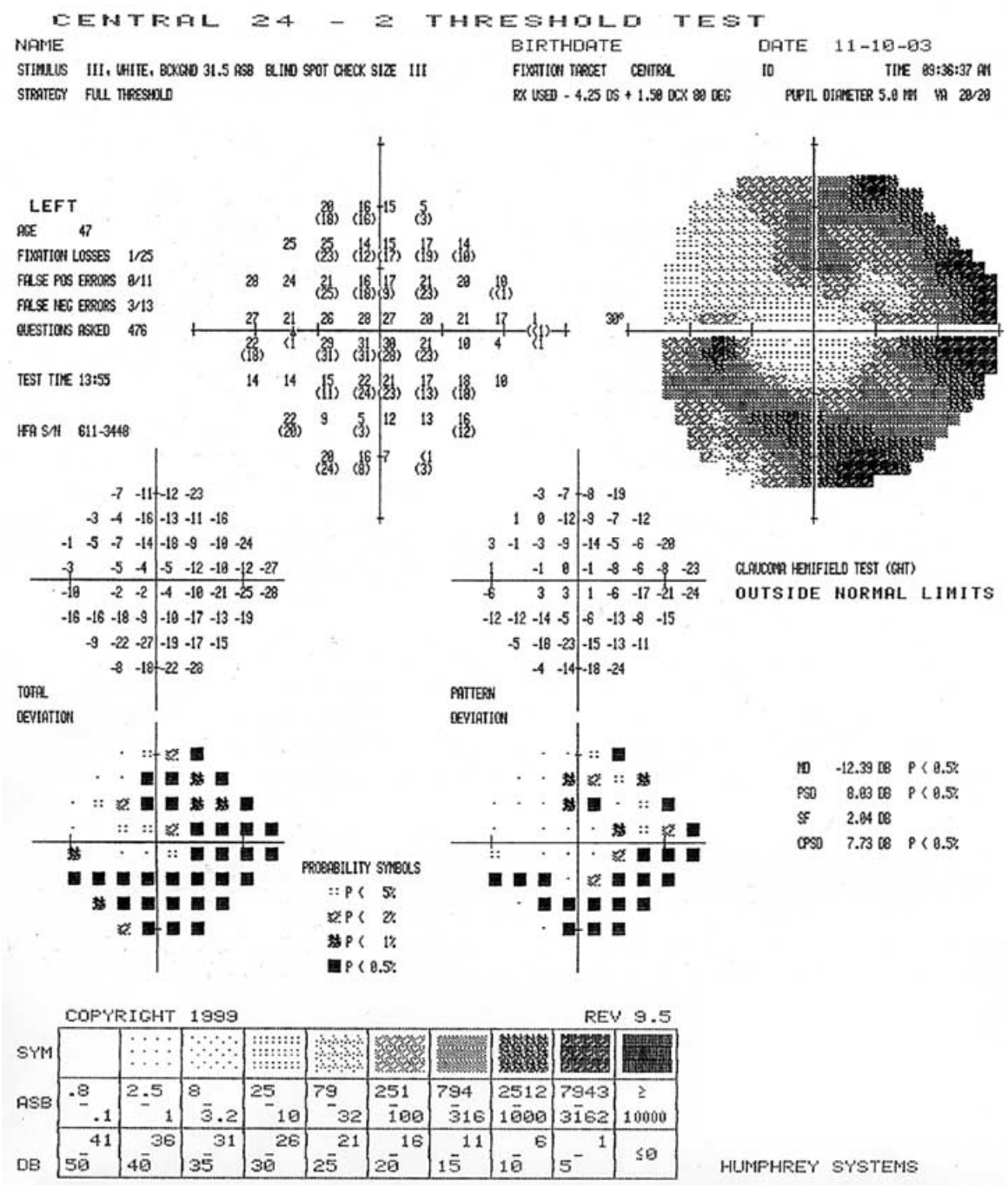

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Figure 5A&B. Continued.

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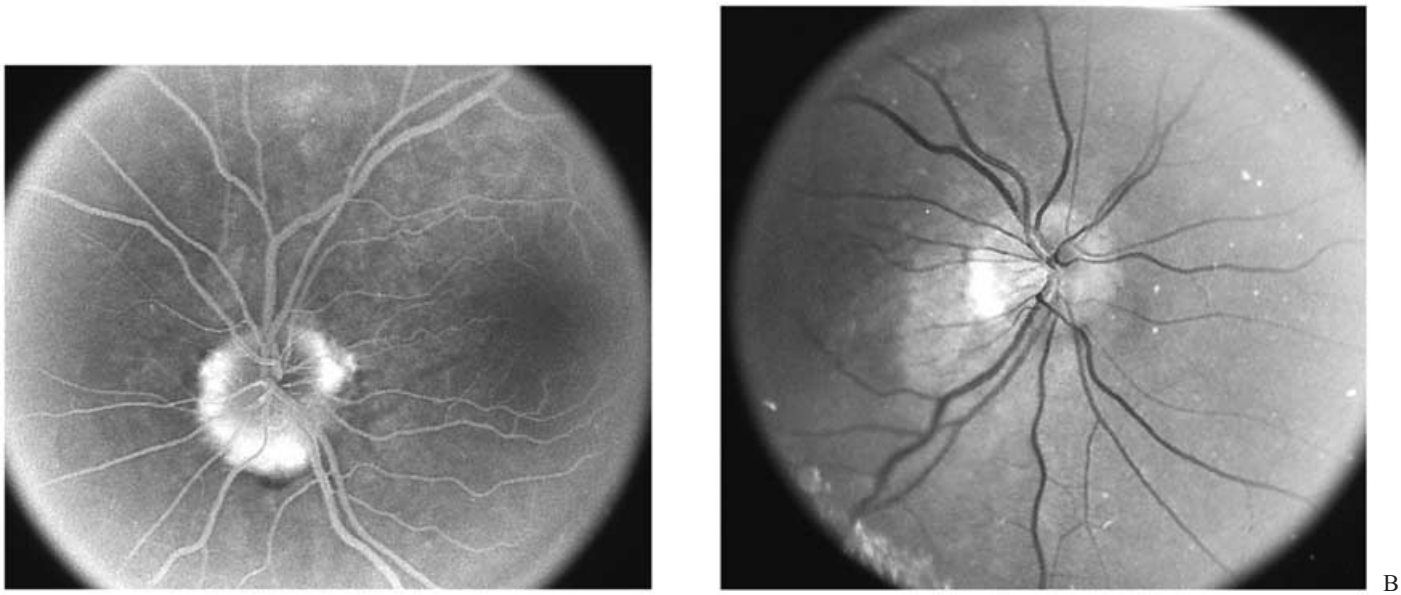

Figure 6A. Red free photo of drusen. Note the blurry margin of the disc, the unobscured vessels and the absent cup.
Figure 6B. Fluorescein Angiogram arteriovenous phase hyperfluorescence demonstrating late staining without leakage.

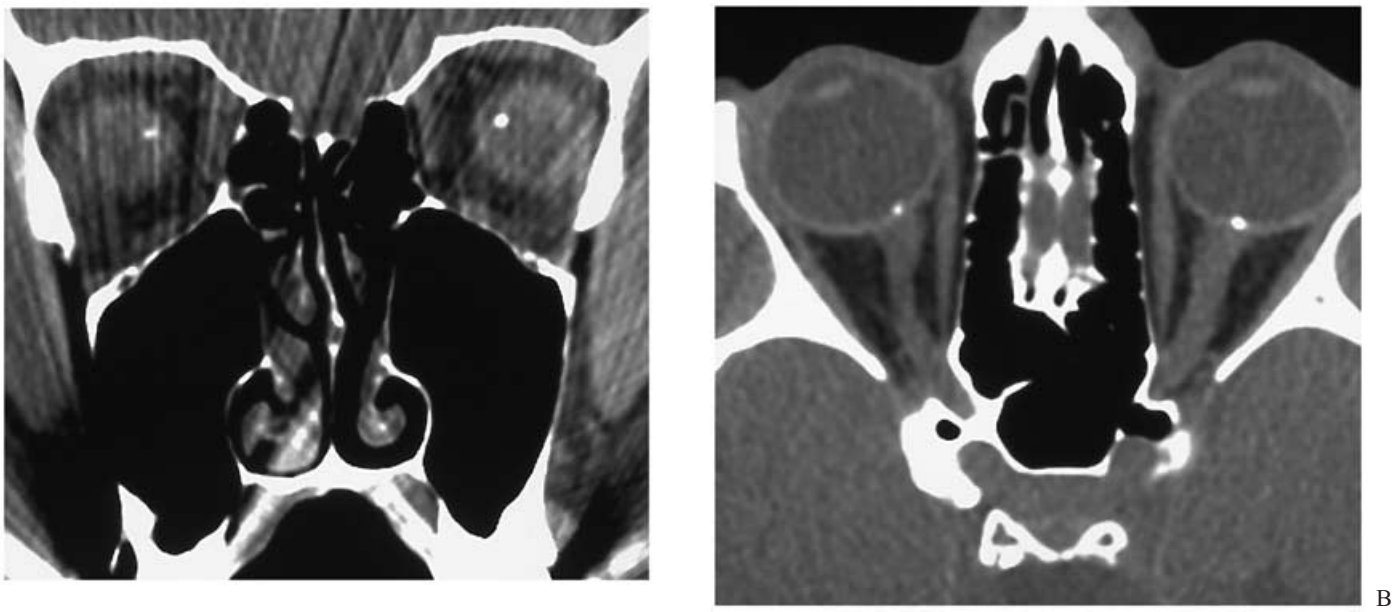

Figure 7A&B. Two views of a CT scan demonstrating the calcific nature of optic nerve head drusen in the nerve heads of a 22-year-old man.

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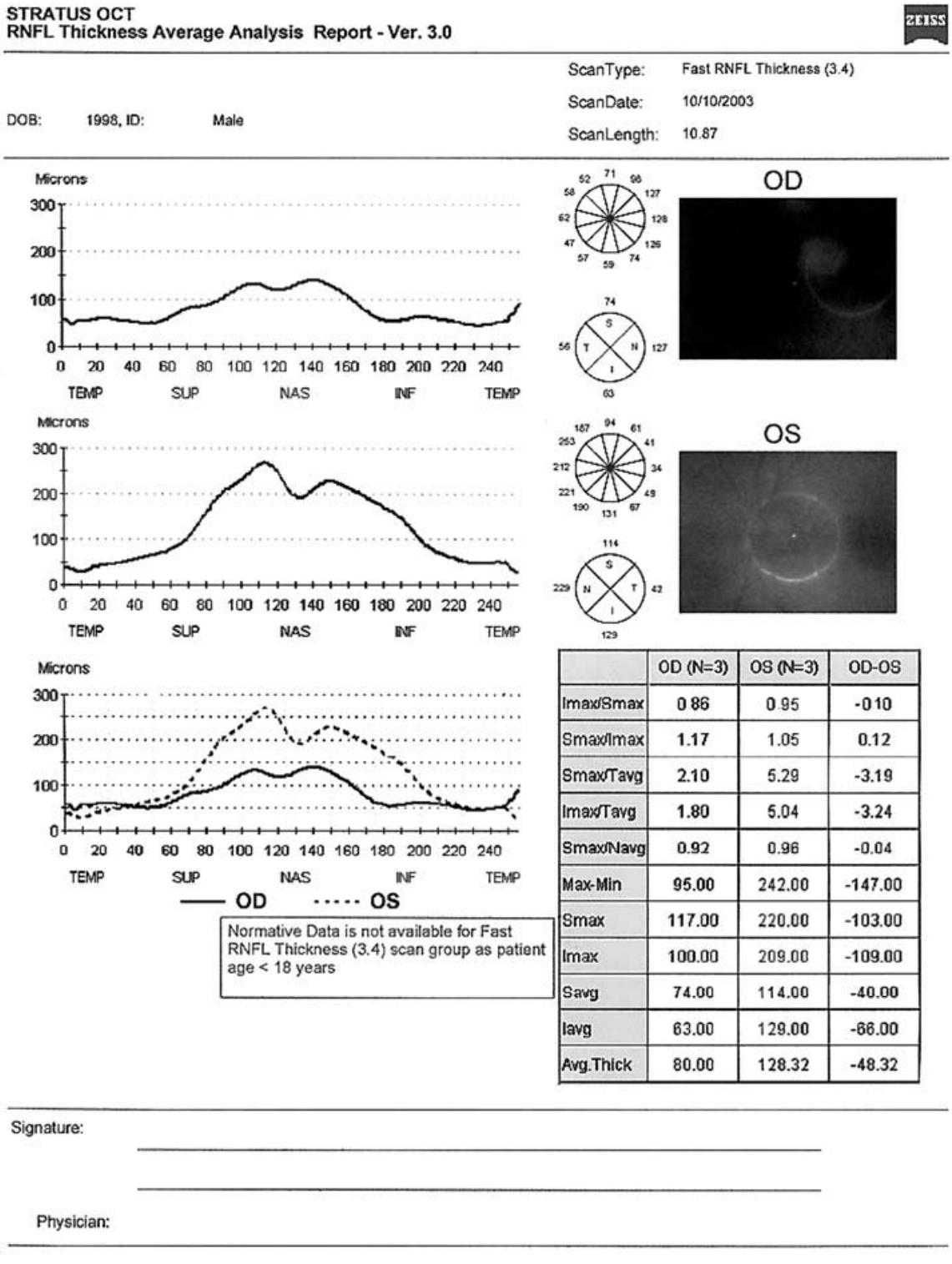

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Smax/Imax	1.17	1.05	0.12
Smax/Tavg	2.10	5.29	-3.19
Imax/Tavg	1.80	5.04	-3.24
Smax/Navg	0.92	0.96	-0.04
Max-Min	95.00	242.00	-147.00
Smax	117.00	220.00	-103.00
Imax	100.00	209.00	-109.00
Savg	74.00	114.00	-40.00
Iavg	63.00	129.00	-66.00
Avg.Thick	80.00	128.32	-48.32

Figure 8. OCT of the same 5-year-old in Fig. 2A&B. Note the increased thickness of the nerve heads.

Figure 9A&B. GDx® nerve fiber analysis of the same 47-year-old woman in figs. 5A&B with optic nerve head drusen. The nerves are elevated or thickened bilaterally. There is little change over a one-year period. The left eye has tortuous vessels. Both have ill-defined margins. Her MRI was negative.

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GDx® Nerve Fiber Analyzer **Symmetry Analysis**

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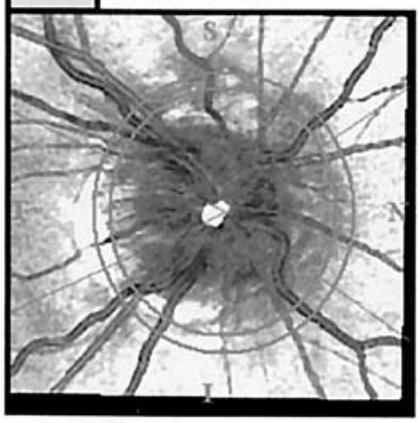

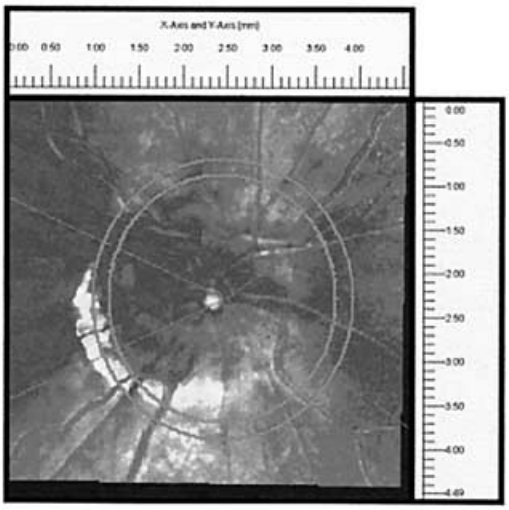

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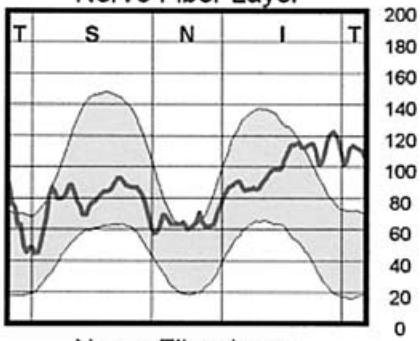

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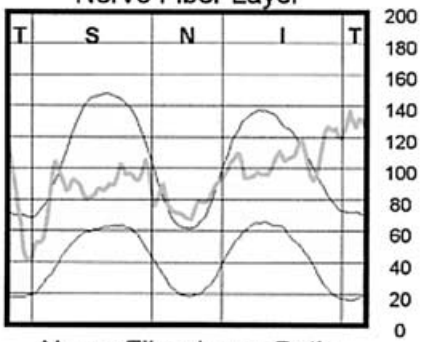

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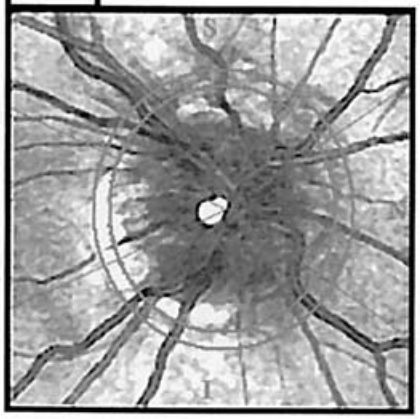
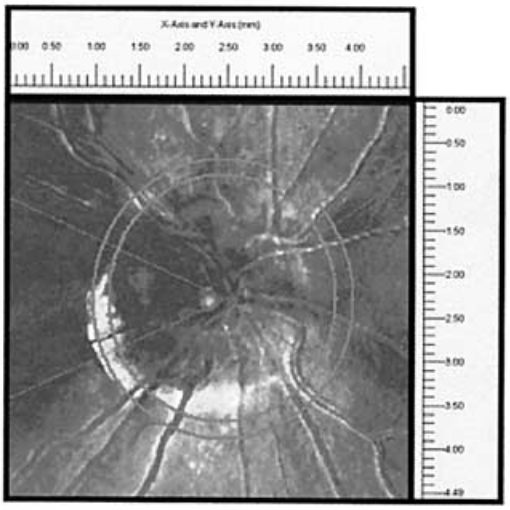
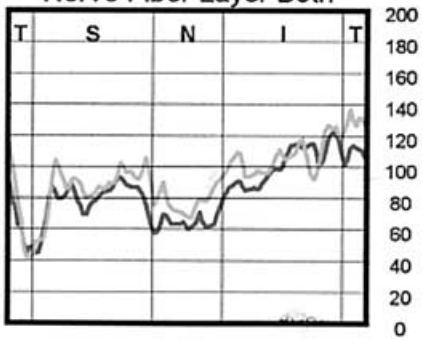




Nerve Fiber Layer Both



NERVE FIBER ANALYSIS

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Superior Ratio	1.33	3.8%	1.64		-0.32	Ellipse Modulation	1.79		2.26		-0.48
Inferior Ratio	1.61		1.87		-0.26	Average Thickness	79		83		-4
Superior/Nasal	1.41	1.2%	1.32	0.6%	0.09	Ellipse Average	83		93		-9
Max. Modulation	0.71	2.7%	0.87	5.6%	-0.17	Superior Average	76		85		-8
Superior Maximum	86		88		-2	Inferior Average	101		106		-5
Inferior Maximum	105		100		5	Superior Integral	0.229		0.251		-0.022

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GDx® Nerve Fiber Analyzer — Symmetry Analysis

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Age: 46, Gender: Female, Race: White

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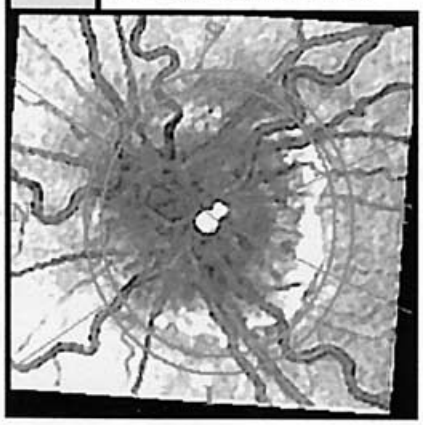

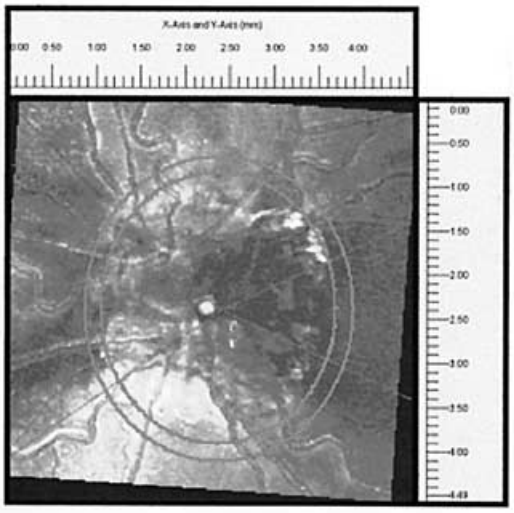

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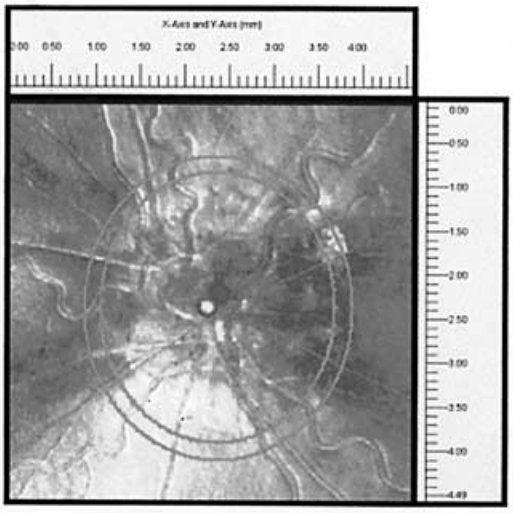

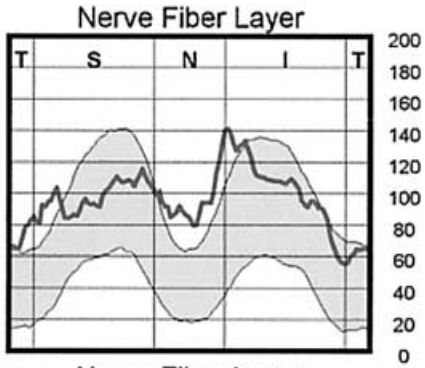

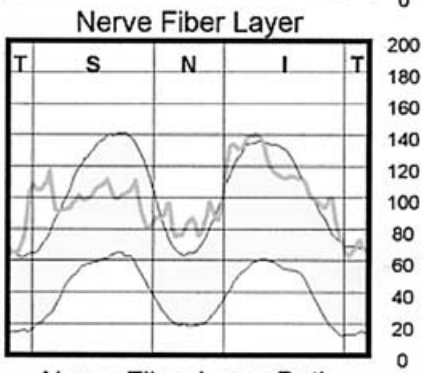

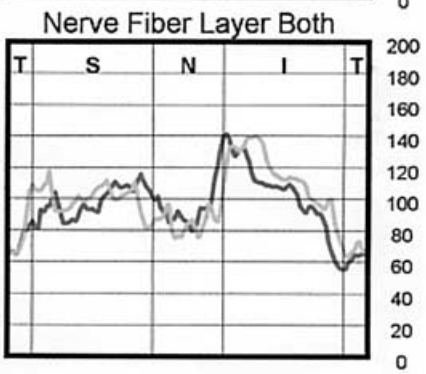

NERVE FIBER ANALYSIS

	Act. Value	Probability	Act. Value	Probability	Difference		Act. Value	Probability	Act. Value	Probability	Difference
Symmetry	0.79	3.1%	0.78	3.1%	0.00	The Number	54		58		
Superior Ratio	1.50	2.6%	1.48	2.4%	0.02	Ellipse Modulation	1.57	7.4%	1.25	3.0%	0.32
Inferior Ratio	1.91		1.89		0.02	Average Thickness	92		95		-3
Superior/Nasal	1.25	1.5%	1.26	1.7%	-0.02	Ellipse Average	94		97		-3
Max. Modulation	0.91	5.3%	0.89	4.8%	0.02	Superior Average	98		100		-2
Superior Maximum	96		98		-2	Inferior Average	101		111		-9
Inferior Maximum	122		124		-3	Superior Integral	0.322		0.327		-0.005

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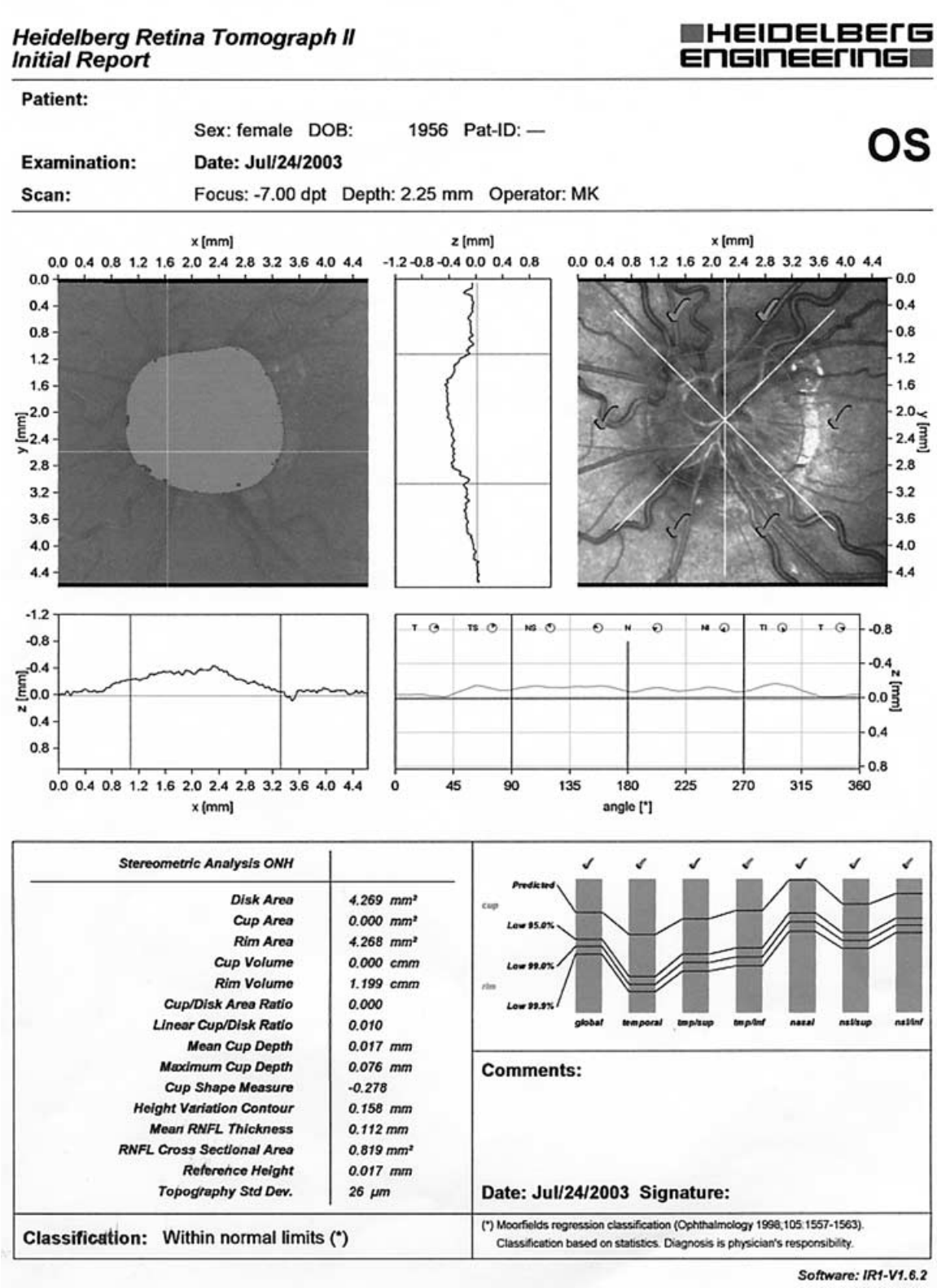

A

Figure 10A&B. HRT nerve fiber layer analysis of the same 47-year-old woman. The NFL is thickened, cup nonexistent and vessels are tortuous. All findings consistent with drusen.

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B

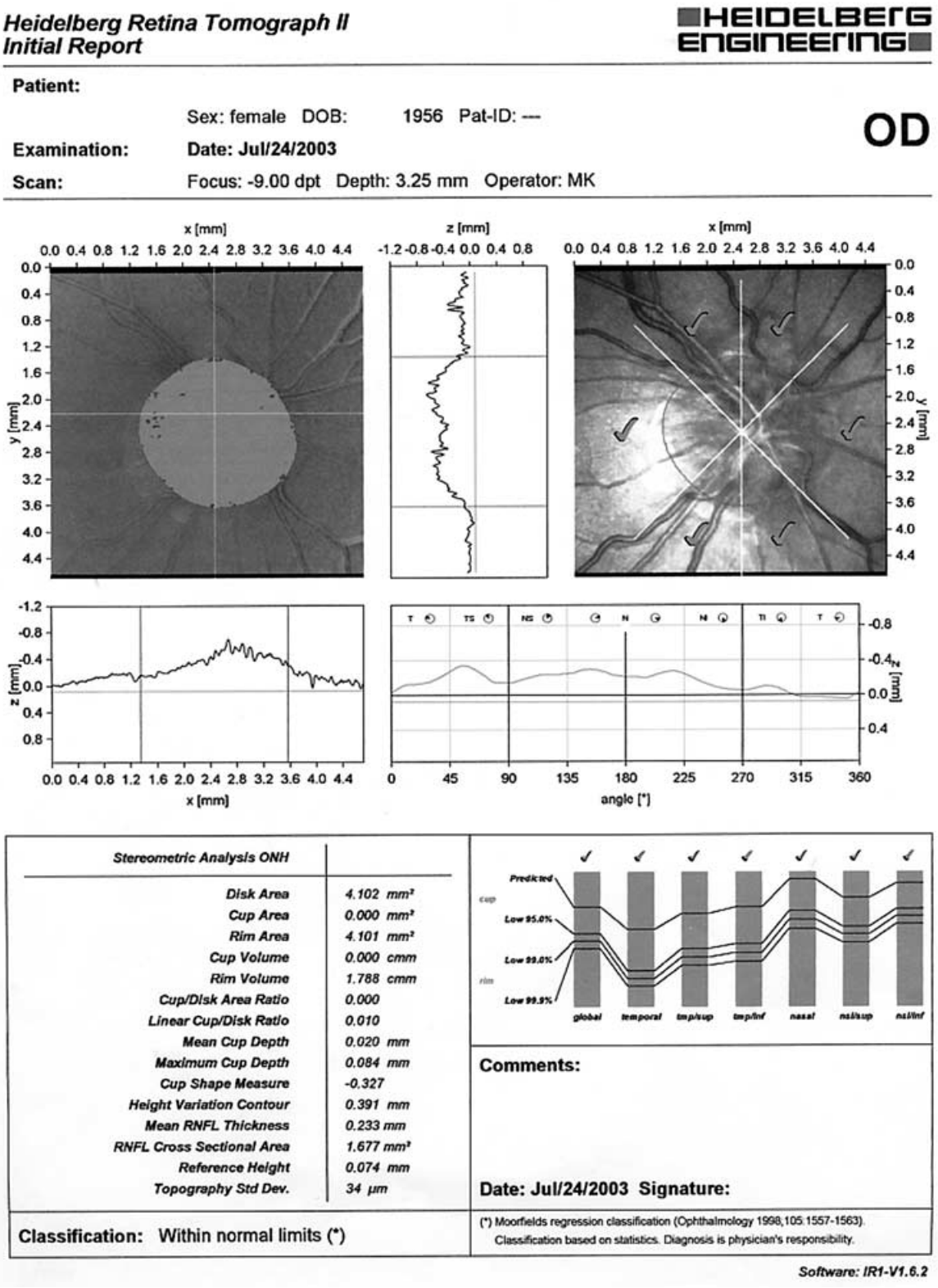

Figure 10A&B. Continued.

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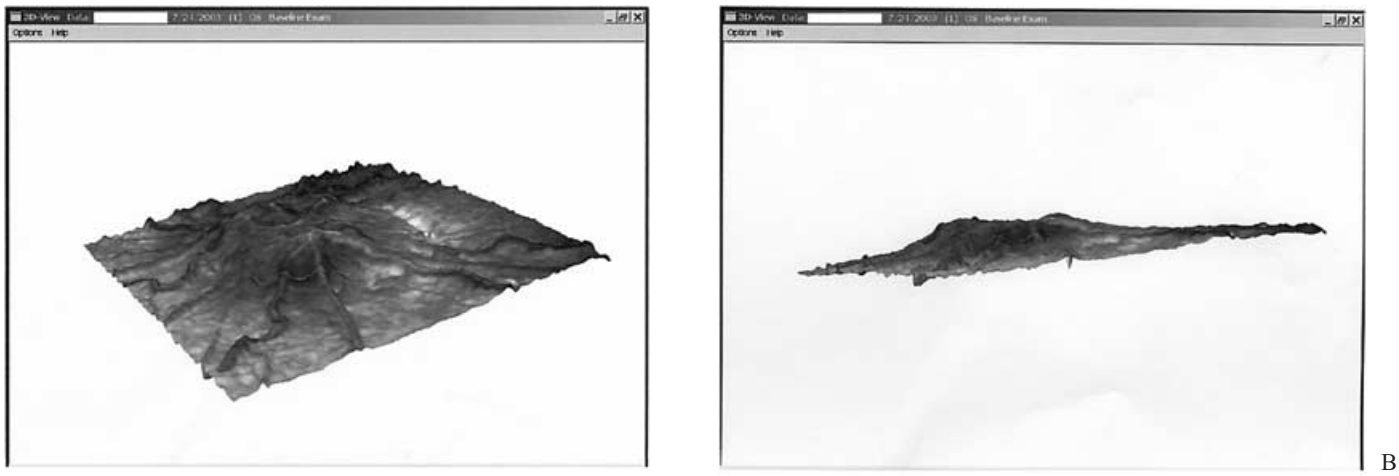

Figure 11A&B. Three dimensional HRT view of the left eye of the same 47-year-old woman. Note the vessels overlying the NFL without being obscured and the scleral crescent.

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become ischemic as the drusen enlarge.[26] Unlike the typical person suffering from the non-arteritic form of AION, patients with optic nerve drusen and AION are younger. They can be in their teens or early adulthood when AION occurs. In addition, these patients do not typically suffer from the usual risk factors seen associated with AION.[8,18,20,23,37,58,60–62]

Other types of vascular occlusions occur with optic nerve drusen. Central retinal artery occlusion (CRAO) has been reported in children and adults.[23,66,67] The pathophysiology in these cases is evidently not just drusen alone. There are other conditions which link with drusen in the production of CRAO. Systemic hypertension,[63] migraine,[28,64,65] oral contraceptives,[64] high altitude[68] and atrioseptal defect[68] have been reported. Central retinal vein occlusion (CRVO), on the other hand, may occur in conjunction with optic disc drusen because veins are more easily compressed than arteries.[69,70] One study linked contraceptive use with drusen resulting in CRVO.[71] Peripapillary subretinal neovascularization secondary to optic disc drusen has been reported in children and young adults.[13,72,73] These neovascular membranes do occasionally hemorrhage. The subsequent visual symptoms usually resolve with mild to moderate visual loss. Harris *et al*. reported that six of seven cases of patients with optic disc drusen and neovascular membranes regained vision of at least 20/40 without treatment.[74] They recommended observation of patients with optic disc drusen and neovascular membranes.[75]

Hemorrhages associated with optic disc drusen, other than those previously mentioned, include superficial flame-shaped hemorrhages and deep peripapillary hemorrhages. The splinter hemorrhages emerge on or adjacent to the disc. This is unlike papilledema, which usually has multiple flame-shaped hemorrhages in the NFL[43] that can obscure vision. Patients with optic disc drusen have hemorrhages appearing singly and are visually insignificant.[28,76,77] Deeper hemorrhages can appear encircling the disc in the subretinal or subretinal pigment epithelial spaces. The hemorrhages may be due to occult neovascularization, direct venous compression or vascular wall erosion by sharp-edged drusen.[61,75]

Systemic diseases associated with drusen

The association between drusen and retinitis pigmentosa (RP) has long been Known.[78] The incidence of the combination has been reported to be between 0% and 10%.[57,79] These disc drusen appear different from idiopathic disc drusen. Drusen associated with RP have normal-sized discs and scleral canals.[80,81] There is no disc elevation.[35]

Another systemic disease associated with drusen is pseudoxanthoma elasticum (PXE). The prevalence of PXE is 1 : 160 000 in the general population.[82] Angioid streaks, also a rare disease, occur in 1 : 80,000.[83] But 85% of patients with PXE have angioid streaks.[84] Disc drusen have been reported in 4.5%[85] to 21%[86] of patients with angioid streaks. The reason for the association may be abnormal mineralization of tissues leading to the formation of angioid streaks and drusen.[87]

Treatment for optic disc drusen

Several treatment modalities can be considered in cases of optic disc drusen with progressive visual loss. In the presence of visual field loss and optic disc drusen enlargement intraocular pressure lowering medications should be considered.[12,31,88–90] In the case of simultaneous glaucoma with optic disc drusen, visual field loss may be due to either entity. These patients must be followed carefully with serial visual fields, nerve fiber analysis, and repeated intraocular pressure testing. Surgical treatment consisting of optic nerve sheath fenestration is controversial and has been reported to be successful by only one author.[91,92] Laser photocoagulation of

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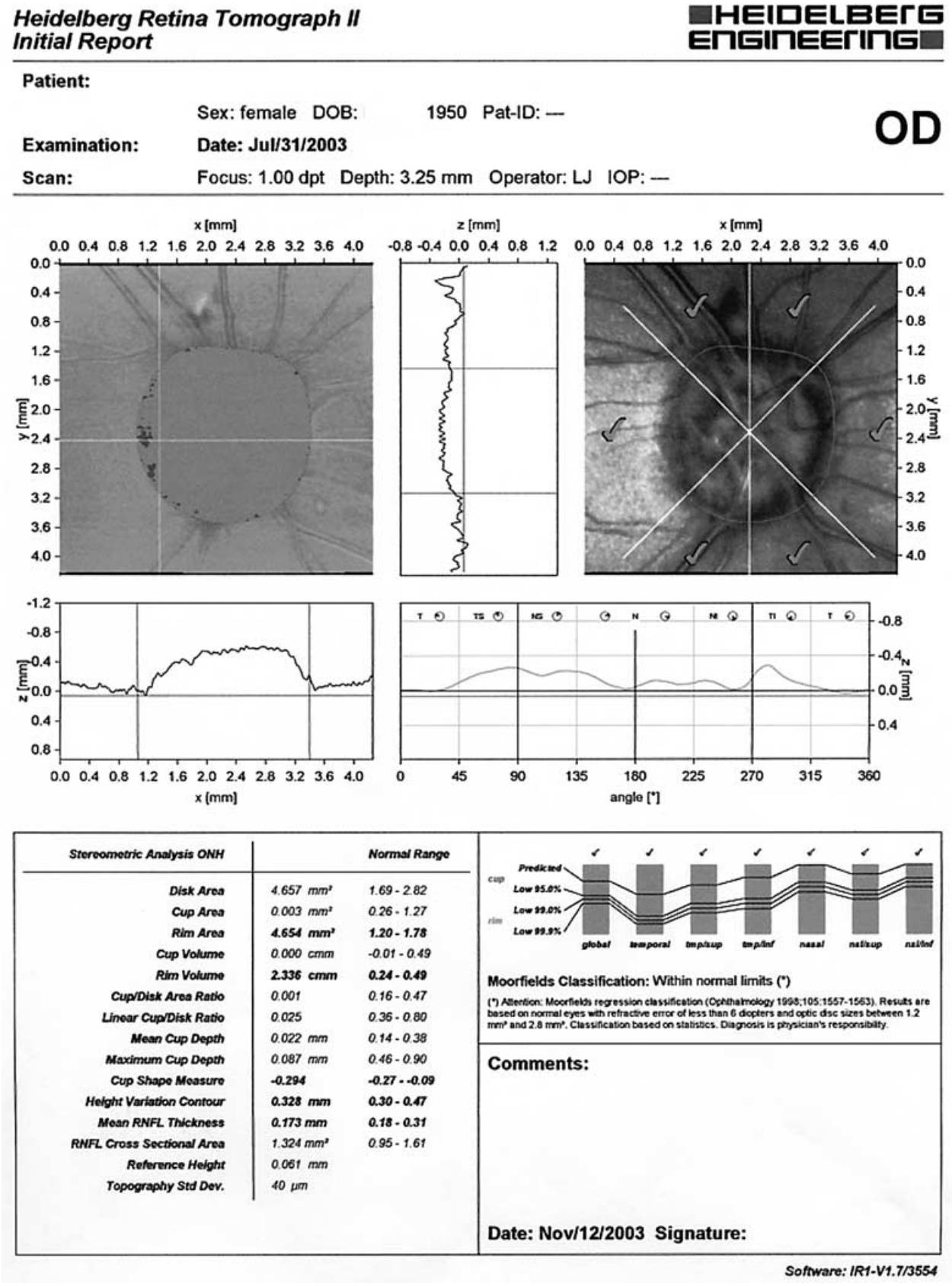

A

Figure 12A&B. HRT of another woman with optic nerve head drusen. Her visual fields have remained normal for two years. Note OD has thinning of the NFL.

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Heidelberg Retina Tomograph II
Initial Report

HEIDELBERG ENGINEERING

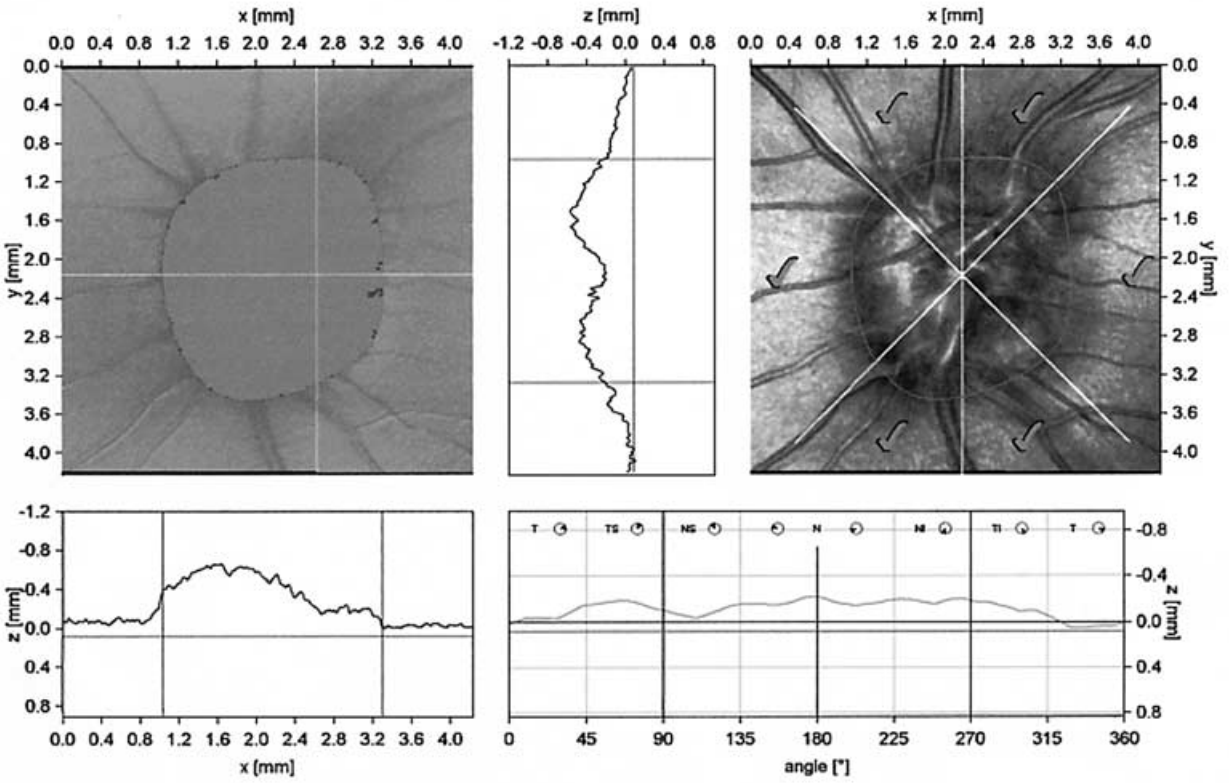
Patient:

Sex: female DOB: 1950 Pat-ID: —

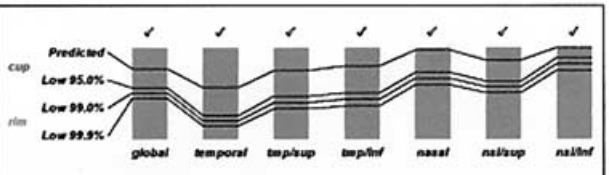
OS

Examination: **Date: Jul/31/2003**

Scan: Focus: 0.00 dpt Depth: 3.00 mm Operator: LJ IOP: —



Stereometric Analysis ONH		Normal Range
Disk Area	4.727 mm²	1.69 - 2.82
Cup Area	0.000 mm²	0.26 - 1.27
Rim Area	**4.727 mm²**	**1.20 - 1.78**
Cup Volume	0.000 cmm	-0.01 - 0.49
Rim Volume	**2.344 cmm**	**0.24 - 0.49**
Cup/Disk Area Ratio	0.000	0.16 - 0.47
Linear Cup/Disk Ratio	0.000	0.36 - 0.80
Mean Cup Depth	0.010 mm	0.14 - 0.38
Maximum Cup Depth	0.034 mm	0.46 - 0.90
Cup Shape Measure	**-0.236**	**-0.27 - -0.09**
Height Variation Contour	**0.278 mm**	**0.30 - 0.47**
Mean RNFL Thickness	**0.203 mm**	**0.18 - 0.31**
RNFL Cross Sectional Area	1.562 mm²	0.95 - 1.61
Reference Height	0.084 mm	
Topography Std Dev.	16 µm	



Moorfields Classification: Within normal limits (*)

(*) Attention: Moorfields regression classification (Ophthalmology 1998;105:1557-1563). Results are based on normal eyes with refractive error of less than 6 diopters and optic disc sizes between 1.2 mm² and 2.8 mm². Classification based on statistics. Diagnosis is physician's responsibility.

Comments:

Date: Nov/12/2003 Signature:

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B

Figure 12A&B. Continued.

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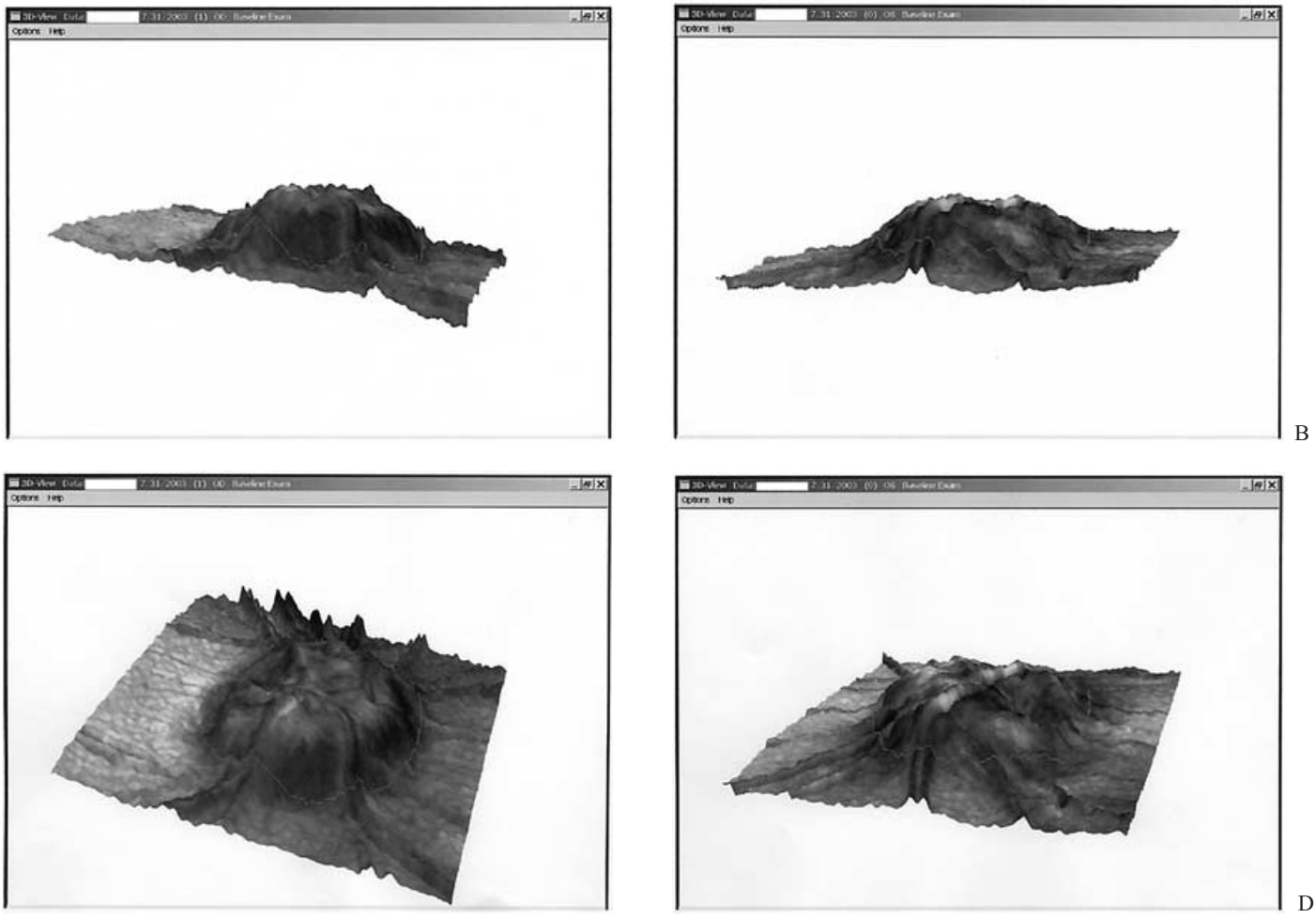

Figure 13A–D. Three dimensional HRT views of the woman in fig. 6A. Note the dramatic heights of the nerves in addition to the indistinct margins.

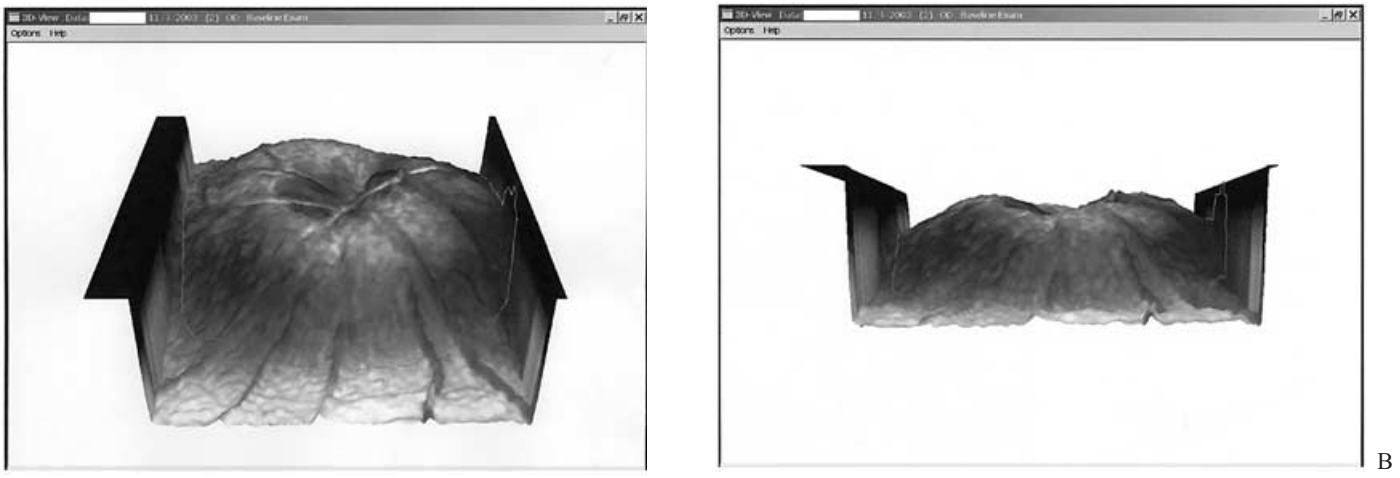

Figure 14A&B. HRT three dimensional views of the right eye of a 7-year-old girl. These buried drusen are remarkable in size. Her vision, MRI and visual fields are normal.

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subretinal neovascular membranes should be considered only if central acuity is threatened. As noted before, most peripapillary membranes regress spontaneously with good visual potential.[74]

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