Pseudo-Retinitis pigmentosa

70-jähriger männlicher Patient

- Im Jahr 2009: Diagnose eines Mantelzell-Lymphom des Nasopharynx
- = Non-Hogkin-Lymphom ausgehend von Mantelzellen = B-Lymphozyten in der Rinde von Lymphknoten
- Therapie im Rahmen der Europäischen Mantelzell-Lymphomstudie mit:
  - 8 Zyklen Polychemotherapie (Juni bis Nov. 2009)
  - gefolgt von Interferontherapie und
  - Erhaltungstherapie mit monoklonalen AK

Medikamente

- Zyklophosphamid
- Vincristin
- Doxorubicin
- Prednisolon

Primäre Chemotherapie

- Interferon
- Rituximab (Erhaltungstherapie)

Verlauf 1

- „Sehr gute partielle Remission“
- Ab Januar 2010: Randomisierung im Interferon-Arm (schlecht vertragen)
- Ab April 2010: Erhaltungstherapie mit Rituximab (B-Zell Antikörper)
- Für ein Jahr kein Rezidiv unter zweimonatlicher Gabe von Rituximab

Verlauf 2

- März 2011: Blutung aus dem Nasenrachenraum
- Lokales Rezidiv histologisch gesichert
- Protonenbestrahlung (aus Versehen Stammhirn bestrahlt ?)
- Seither kein Rezidiv
- Polyneuropathie der Füße (Vincristin)

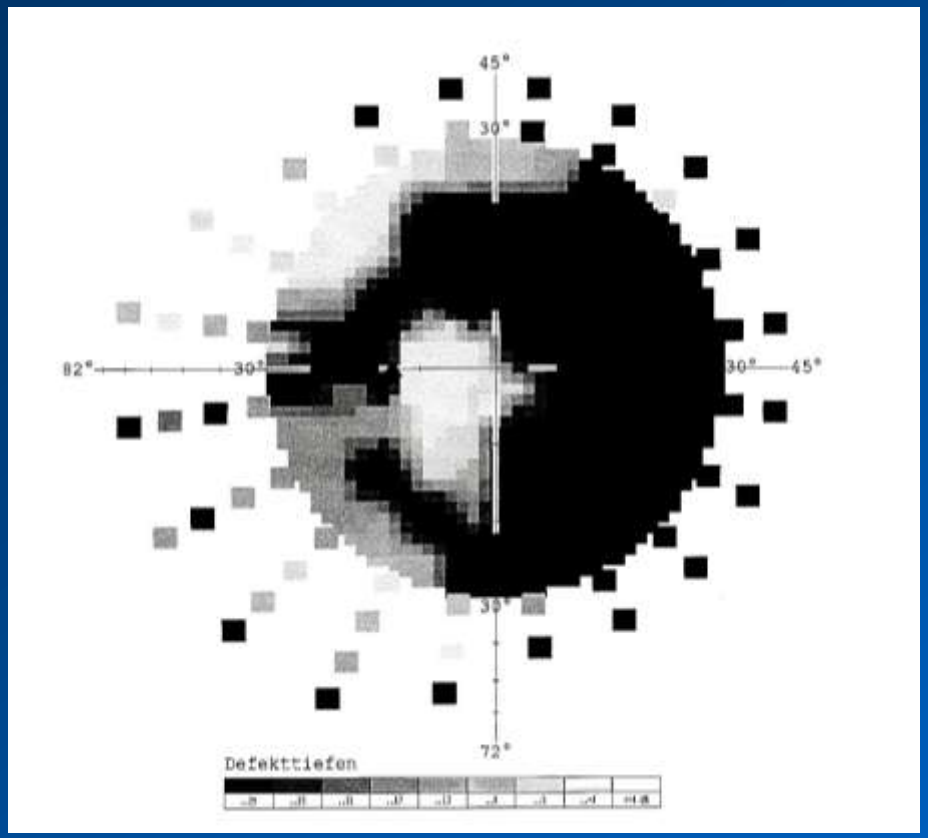
Augenanamnese

- Nach dem sechsten Zyklus der Chemotherapie vorübergehende Sehprobleme
- aber selbst „auf Grauen Star“ geschoben
- 13. Oktober 2011: Katarakt-OP links, seither „außenrum alles unscharf“ und Photopsien
- Vorstellung durch AA bei uns
- Auf Befragen: definitiv **keine** Nachtblindheit

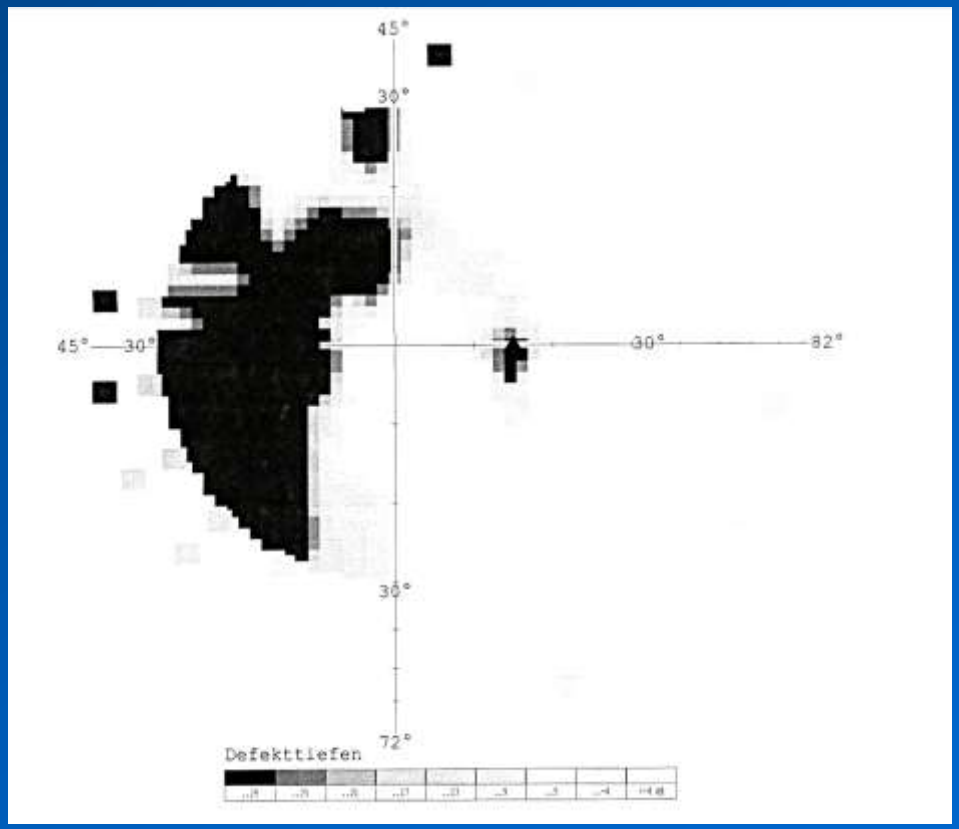
Augenärztlicher Befund

- Visus rechts: 0,5 links: 0,8 partim
- Kat präprovecta rechts, PP links
- mäßige Glaskörpertrübungen li > re
- Fundus rechts: flächige PE-störung außerhalb der Gefäßbögen, Pigment-Retinopathie
- Fundus links: sträker ausgeprägt und zusätzlich makuläre Membran

Gesichtsfelder

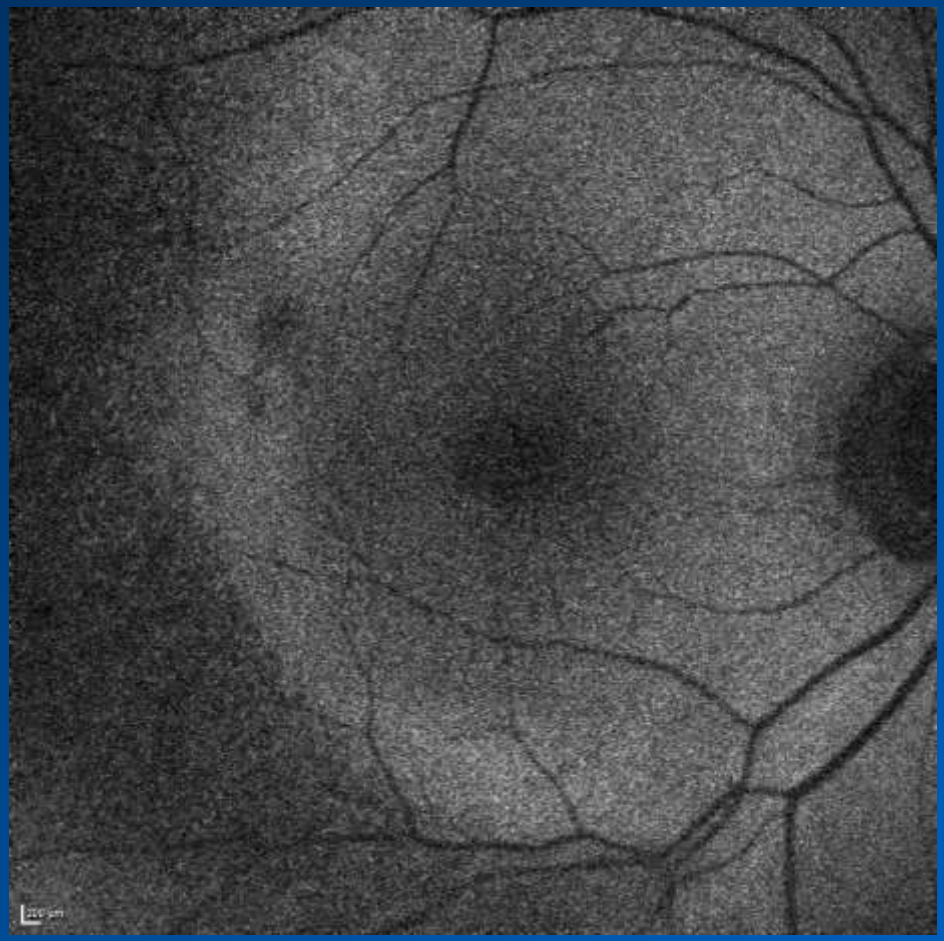


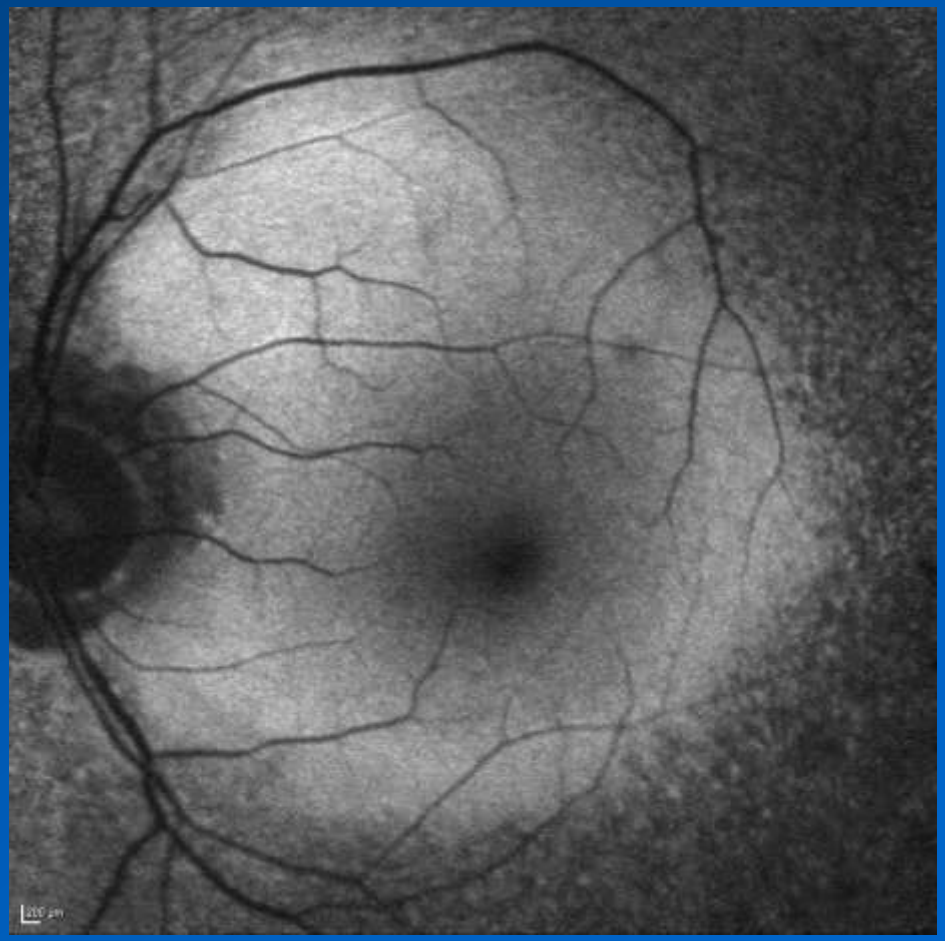
Links



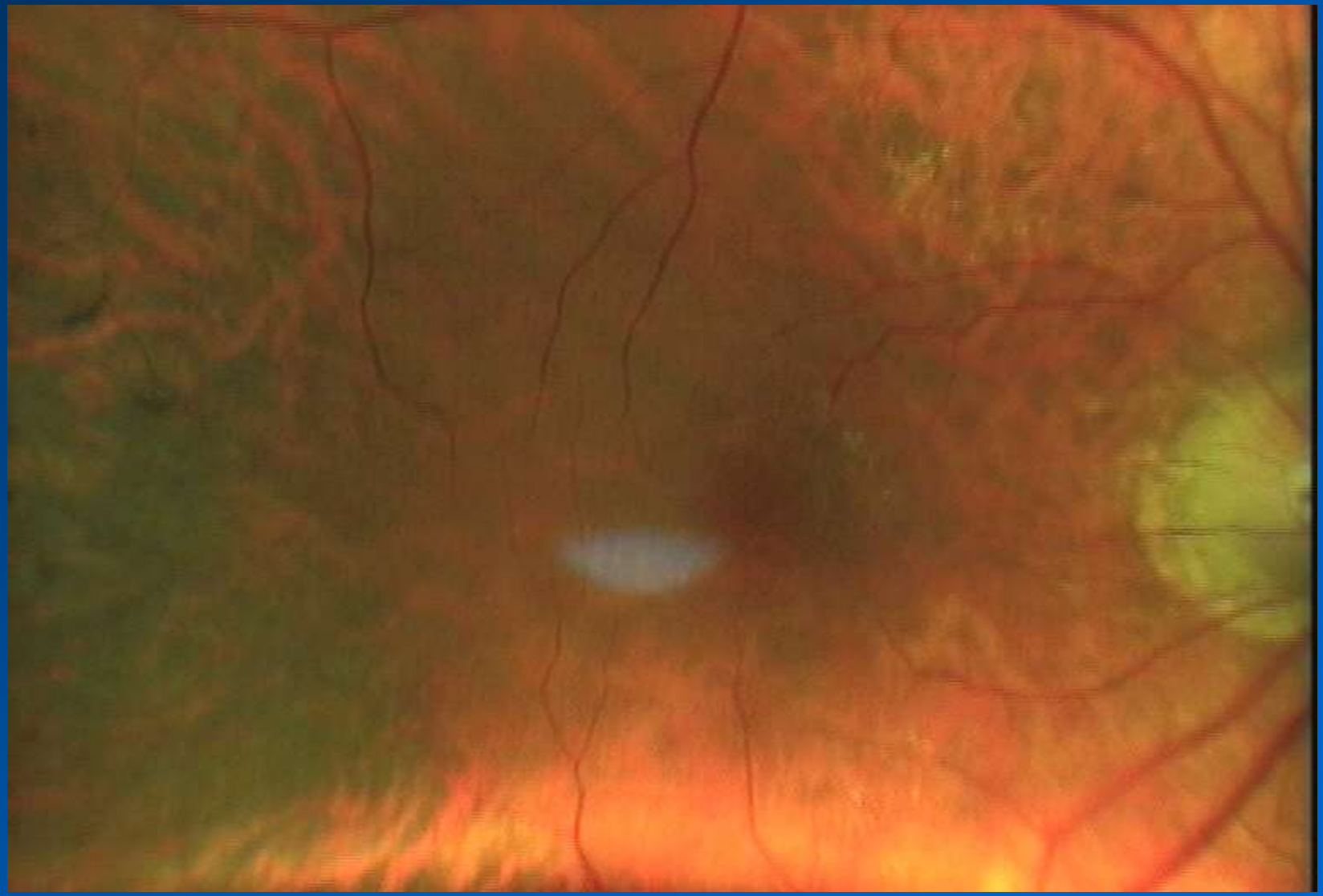
Rechts

Autofluoreszenz



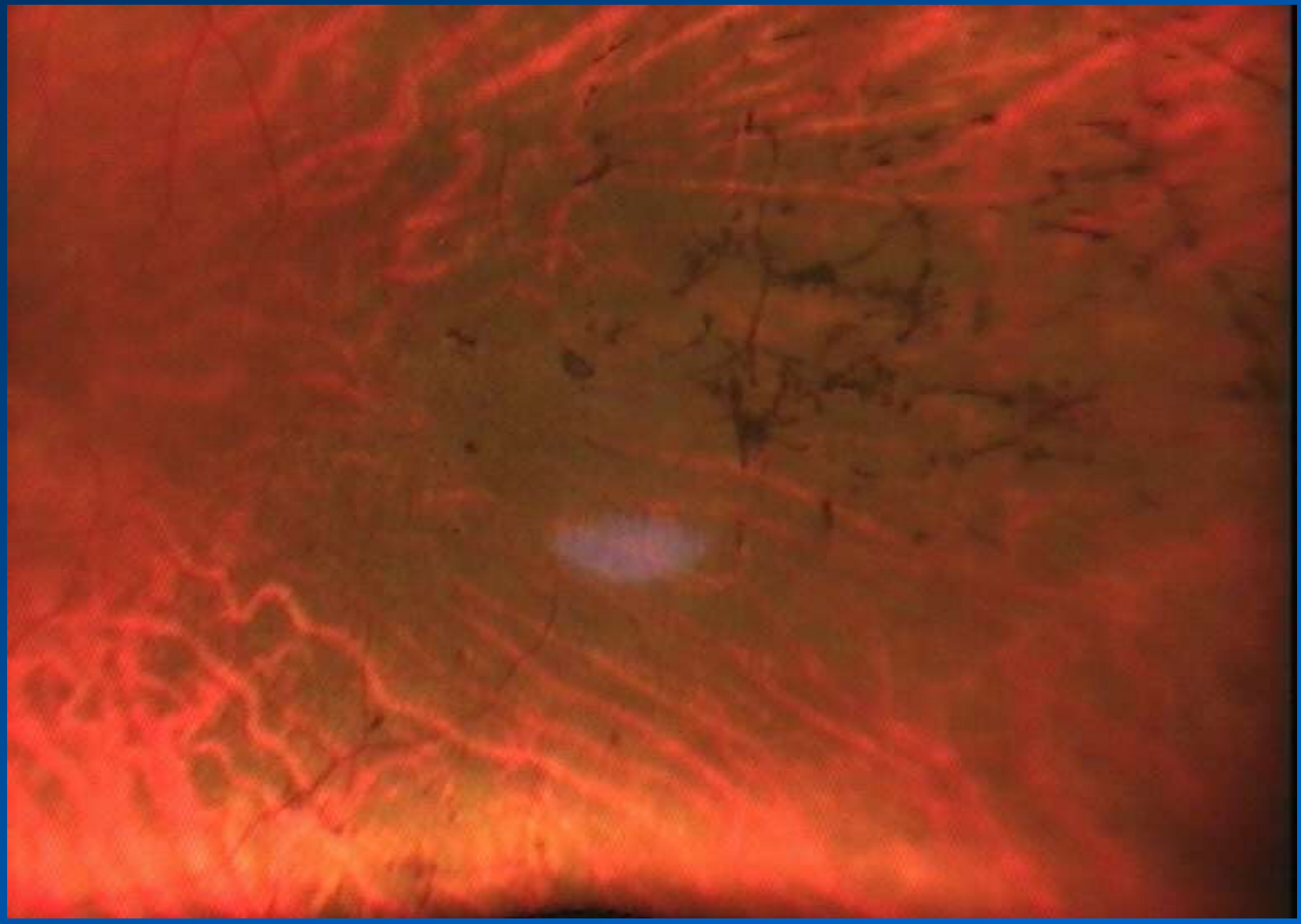


Hinterer Pol rechts

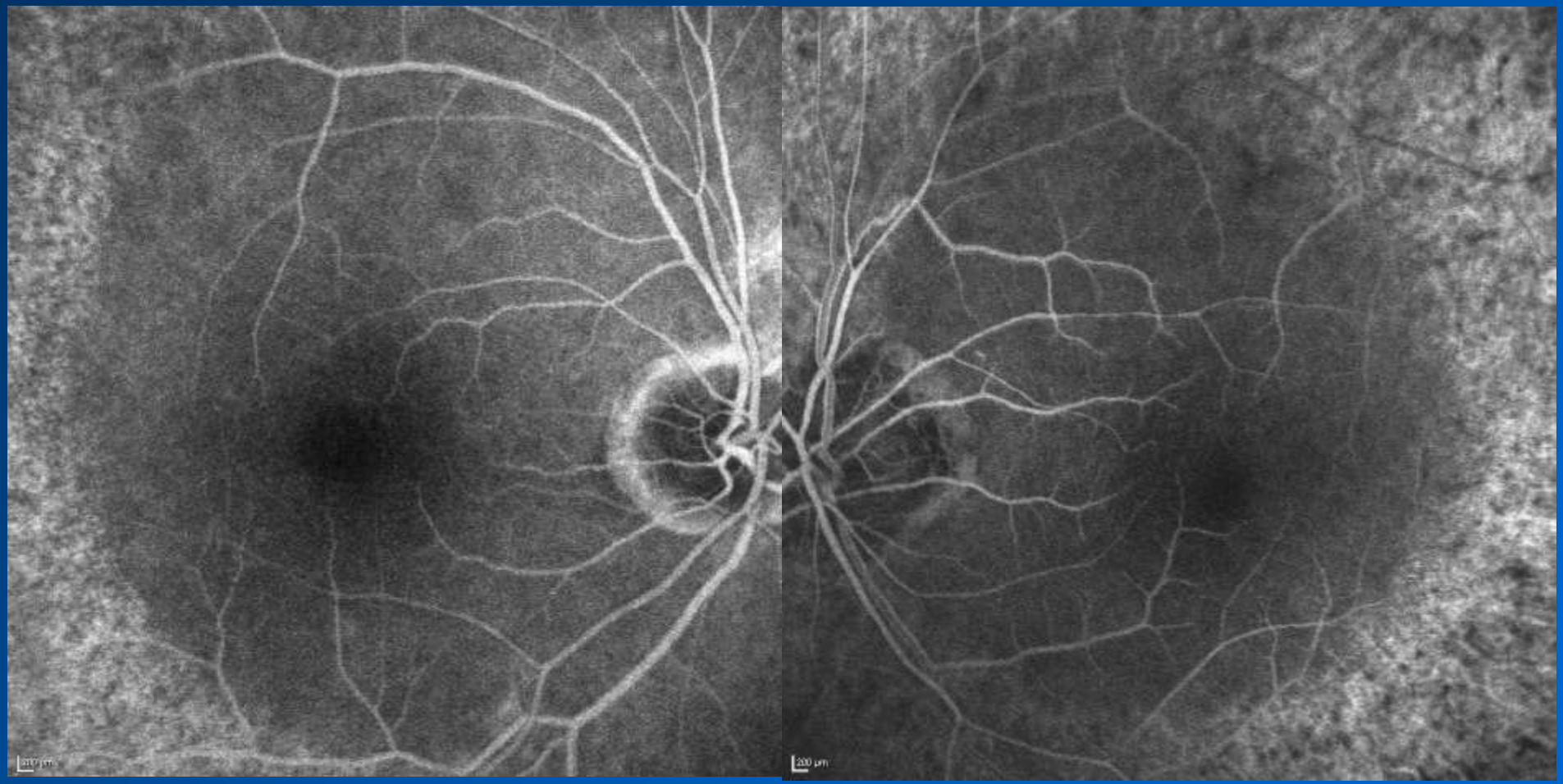


Hinterer Pol links

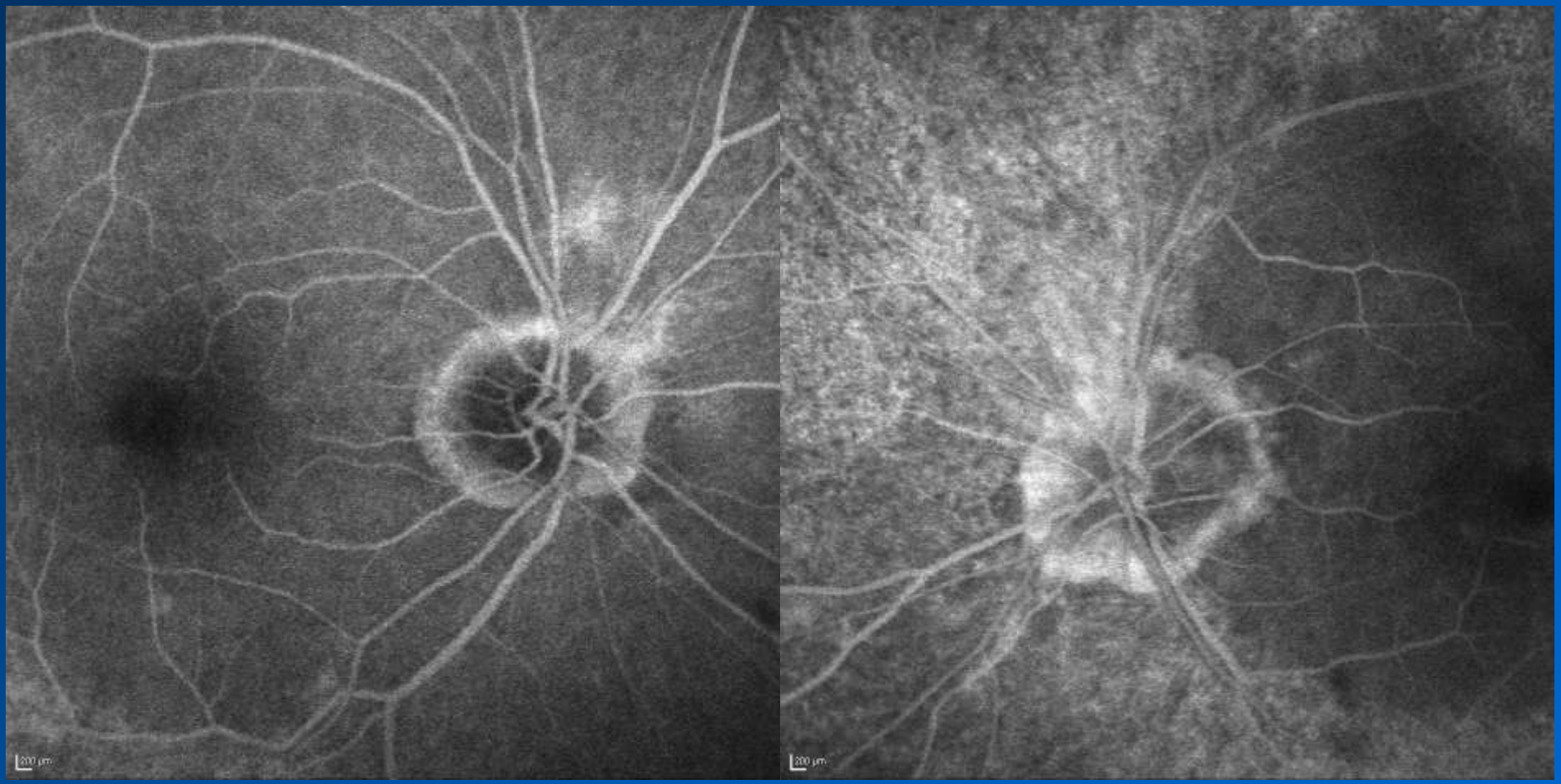
Pigment-Retinopathie links



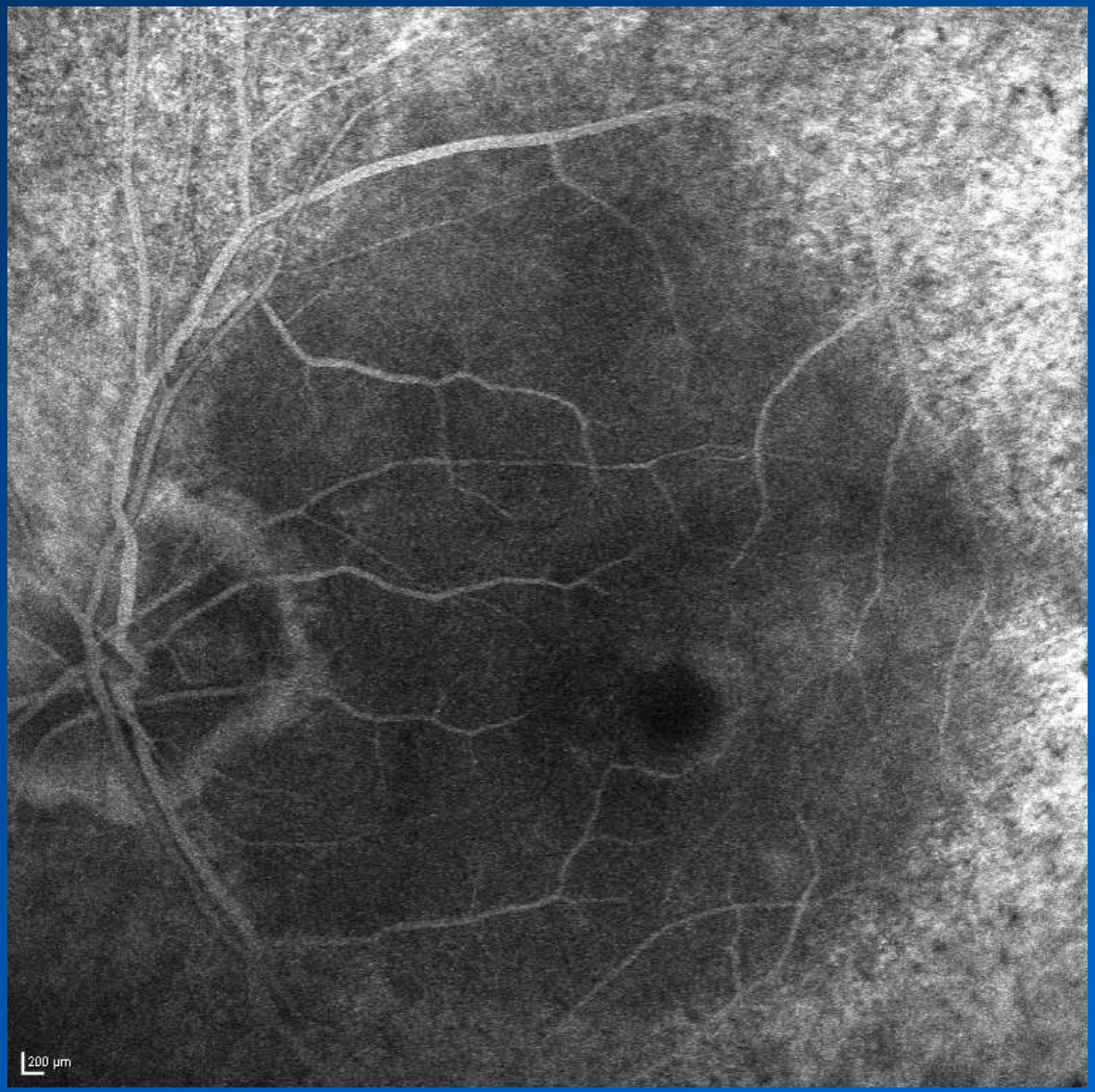
FLA zentral früh



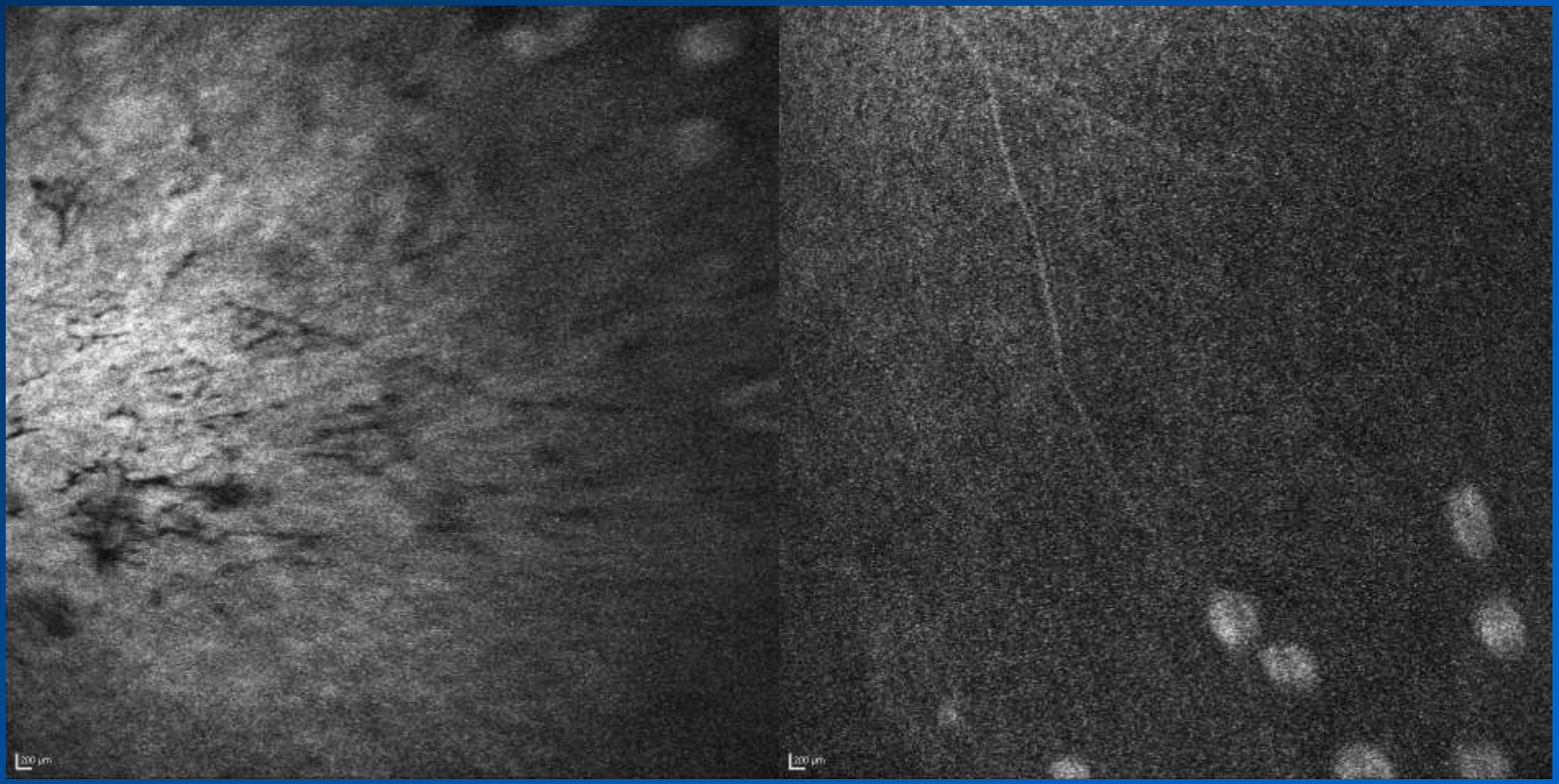
FLA Papille spät



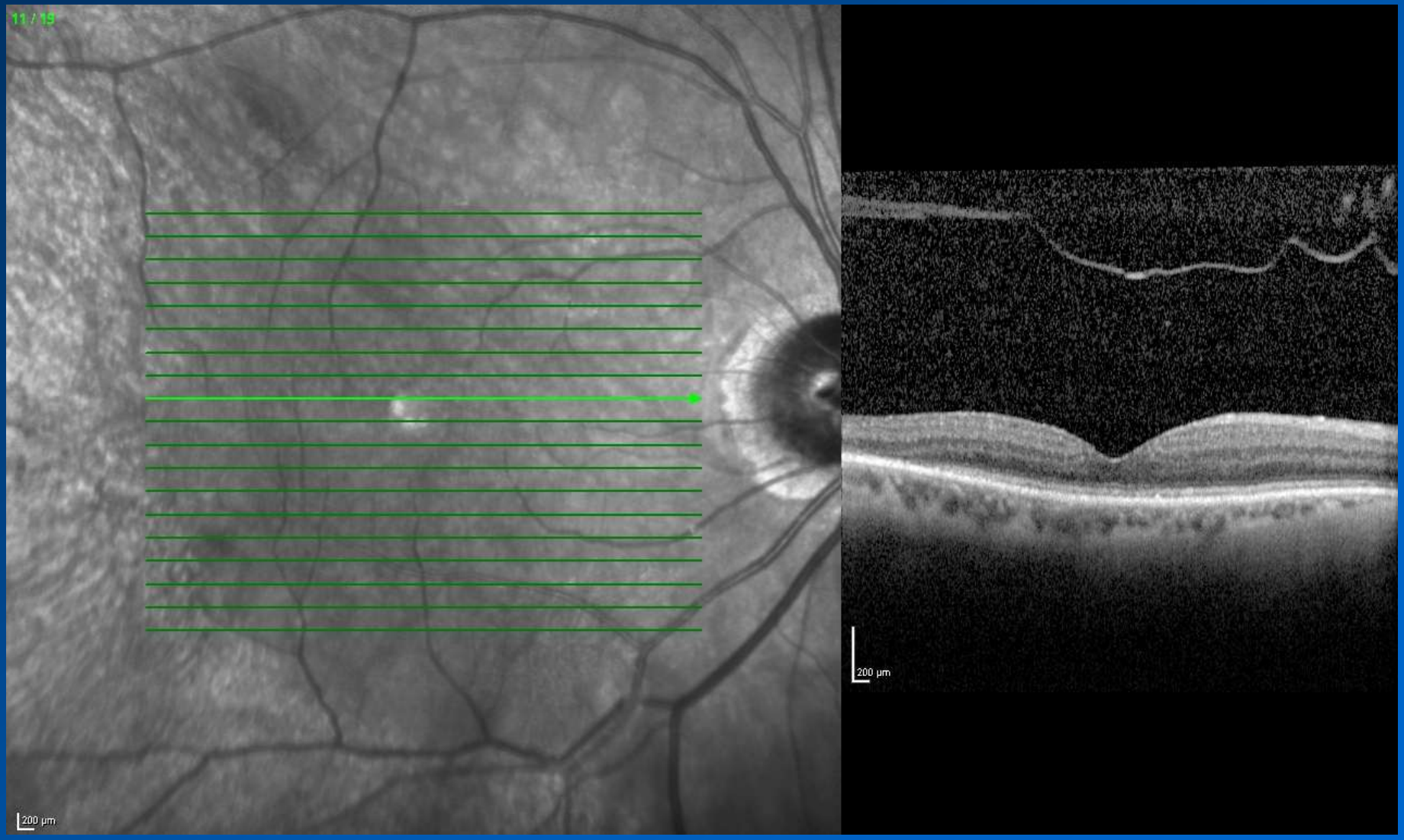
Makula-Leckage links in Spätphase



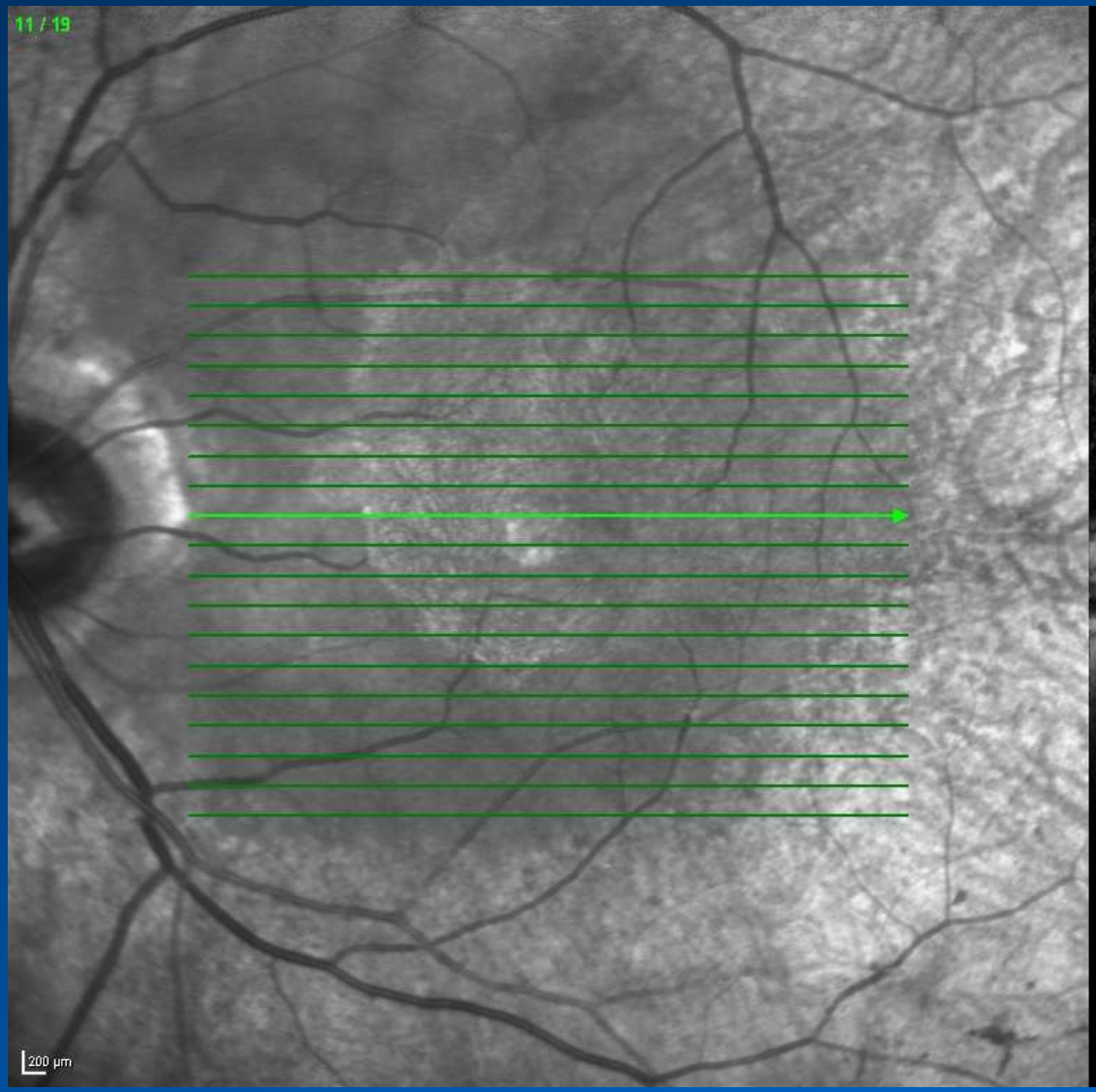
FLA Peripherie

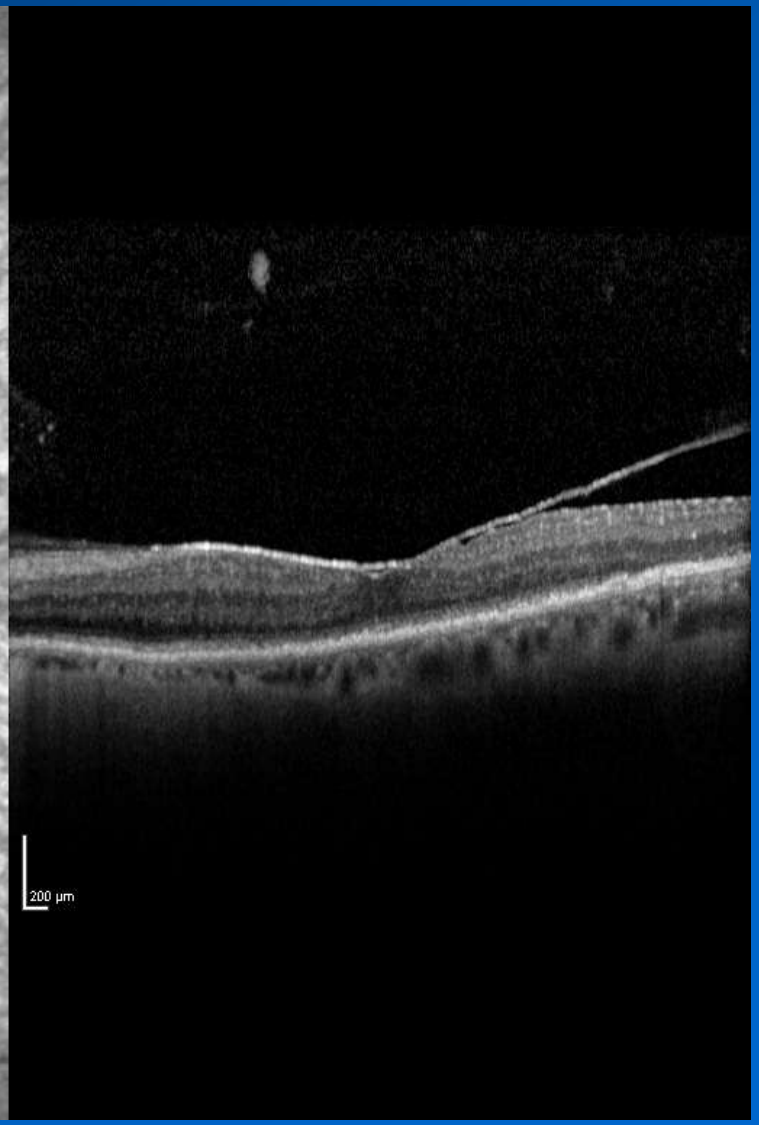


OCT rechts



OCT links

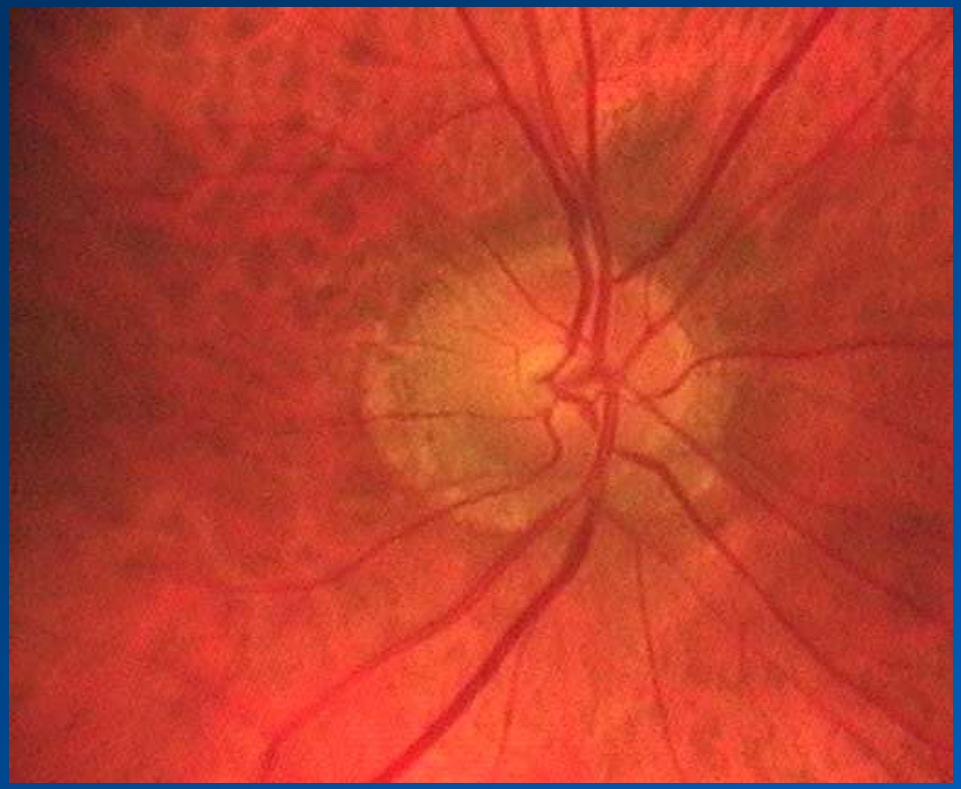




Differentialdiagnose

- Klassische „Retinitis pigmentosa“ ???
- Pseudo-Retinitis pigmentosa
  - toxisch durch Vincristin
  - Strahlen-Retinopathie
  - Carcinoma Associated Retinopathy (CAR)
  - Entzündliche Ursache

Papillenfarbe und Gefäßweite



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  - Entzündliche Ursache

Carcinoma Associated Retinopathy (CAR)

- Schwere panretinale Degeneration als Folge eines Neoplasmas
  - Typischerweise: kleinzelliges Bronchial-Ca, Melanom oder undifferenziertes Cervix-Carcinom
  - Lymphomassoziation nicht gefunden !!
- Autoimmunerkrankung, progressiv, oft vor der Tumordiagnose diagnostiziert
- Fundus unauffällig aber schwerer Funktionsverlust im ERG, Nachtblindheit

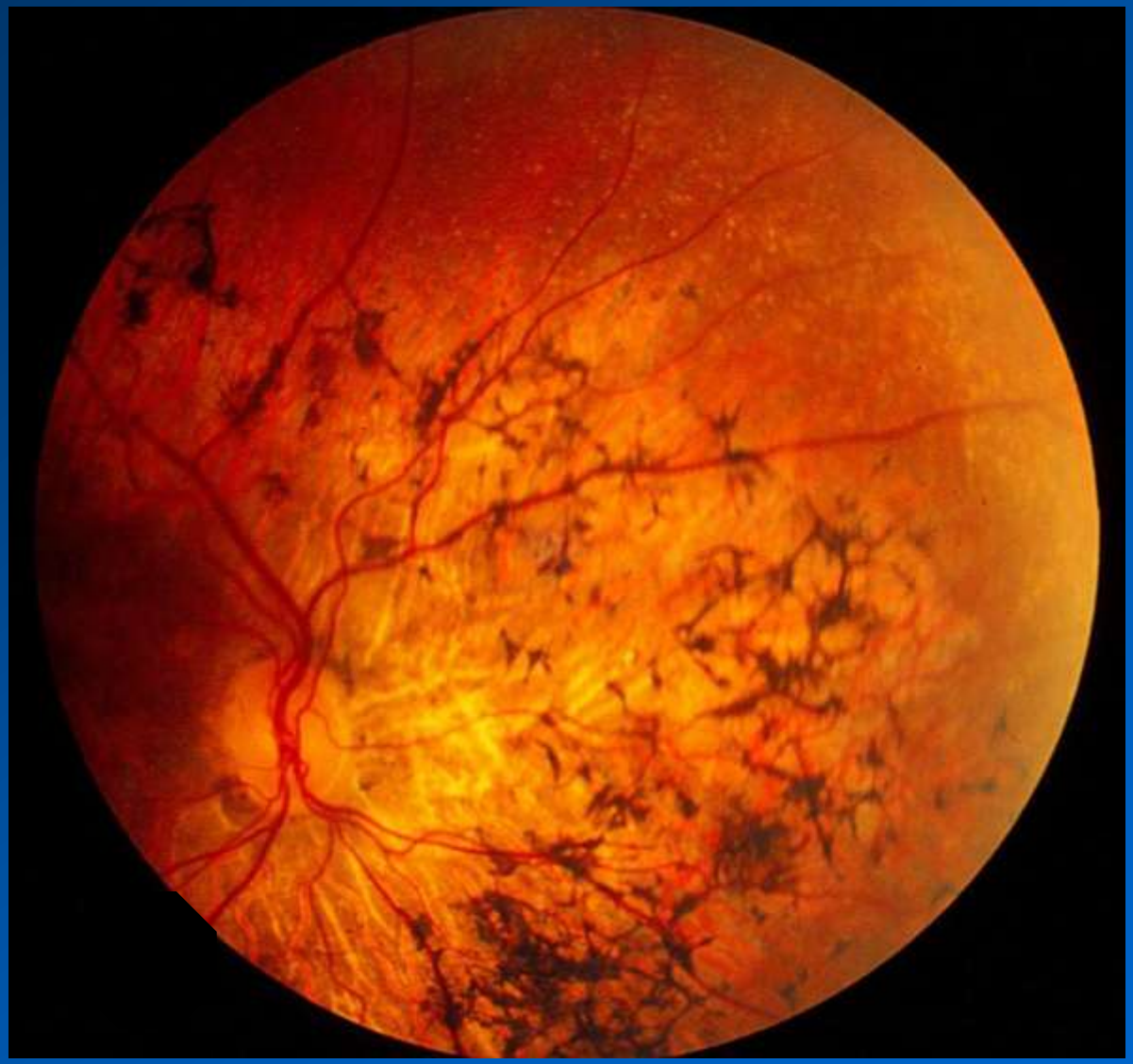
Differentialdiagnose

- Klassische „Retinitis pigmentosa“ ???
- Pseudo-Retinitis pigmentosa
  - toxisch durch Vincristin
  - Strahlen-Retinopathie
  - Carcinoma Associated Retinopathy (CAR)
  - **Entzündliche Ursache**

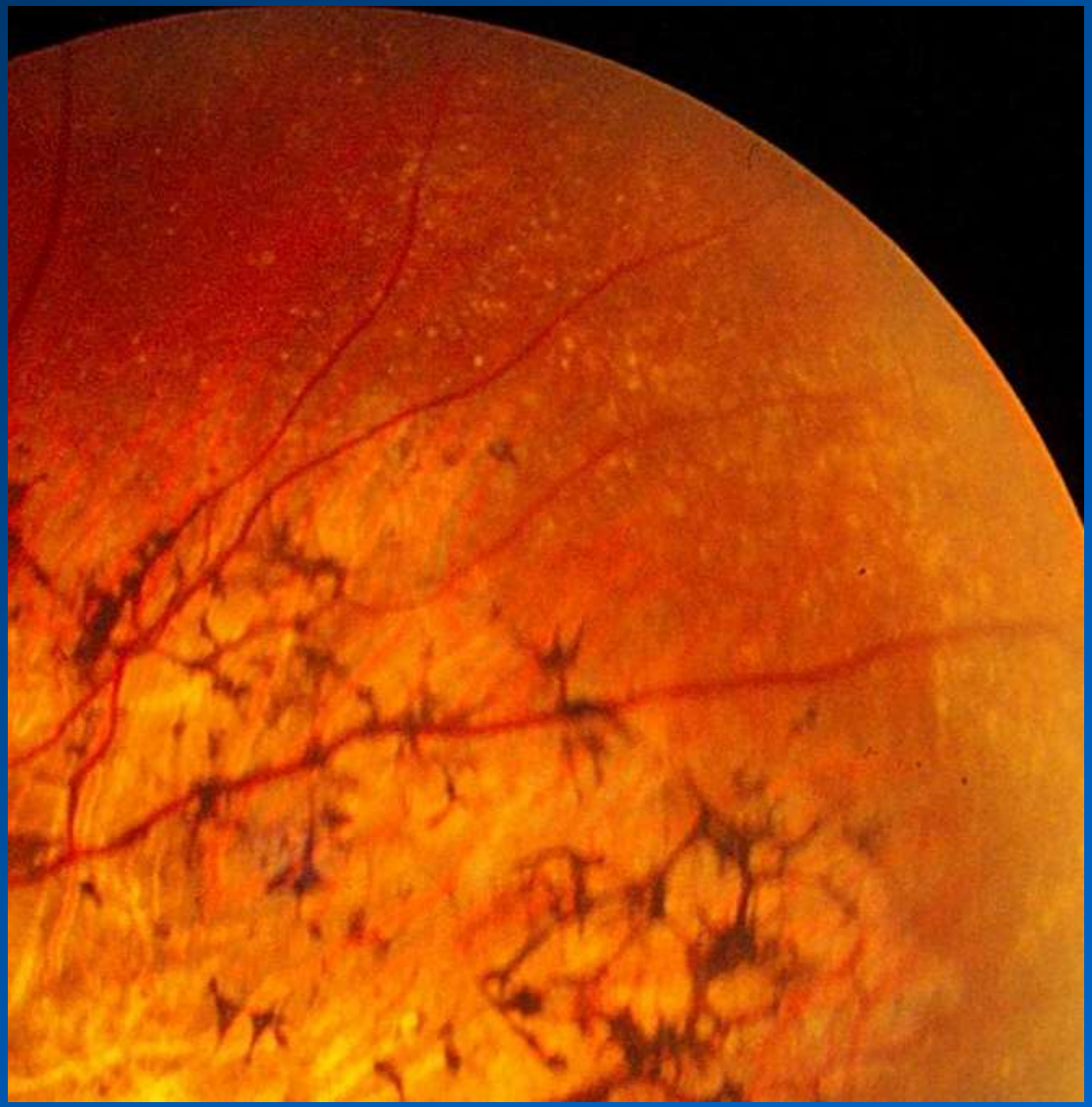
Patientin aus dem Jahr 1987

- 1977 Pigment-Retinopathie als Zufallsbefund fetsgestellt
- Im Verlauf von 10 Jahren leichte Zunahme der Pigmentierung
- Subjektiv keinerlei Beschwerden
- Visus 0,5/0,6
- 1987: Verlaufskontrolle

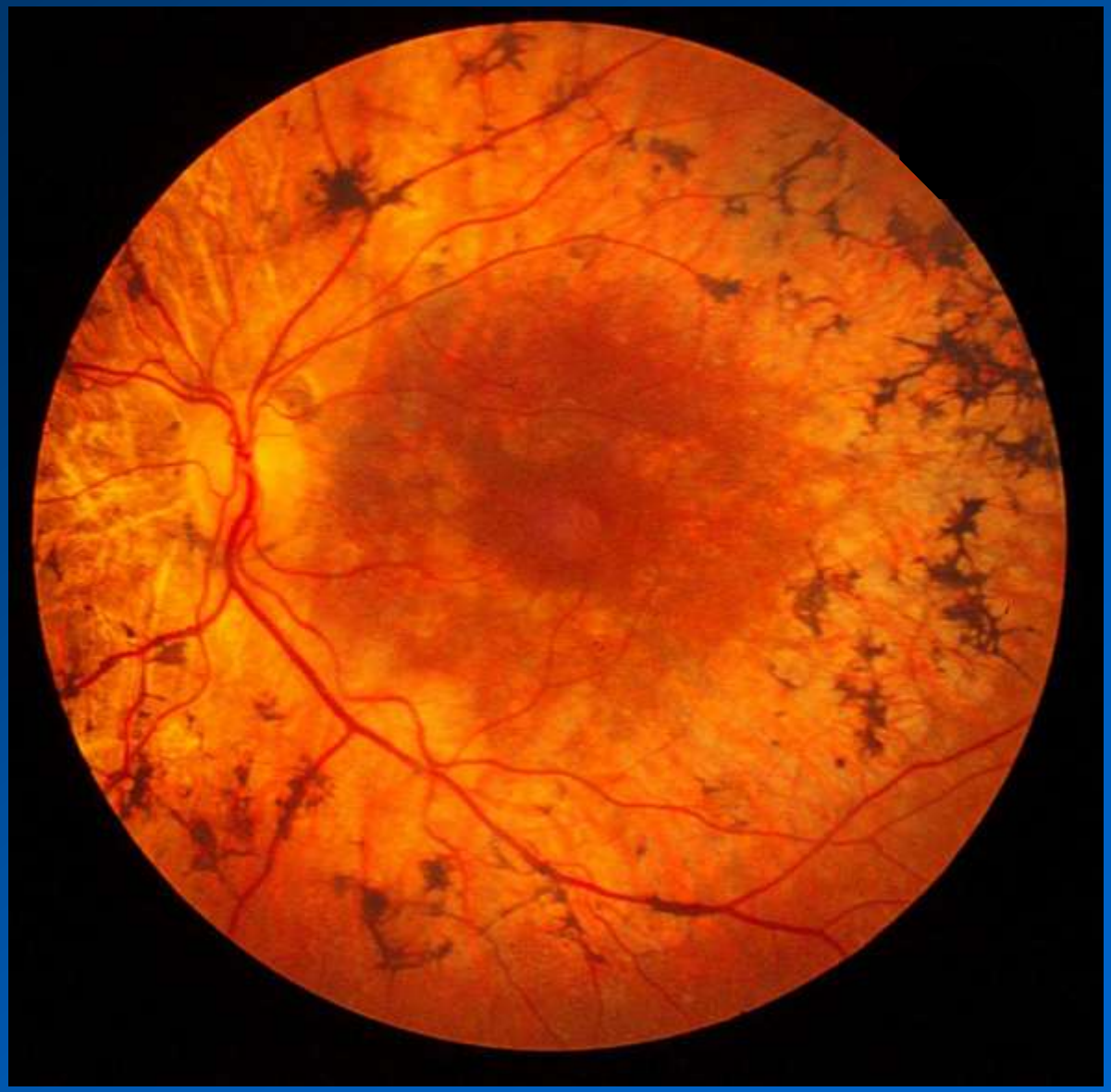
Rechtes Auge



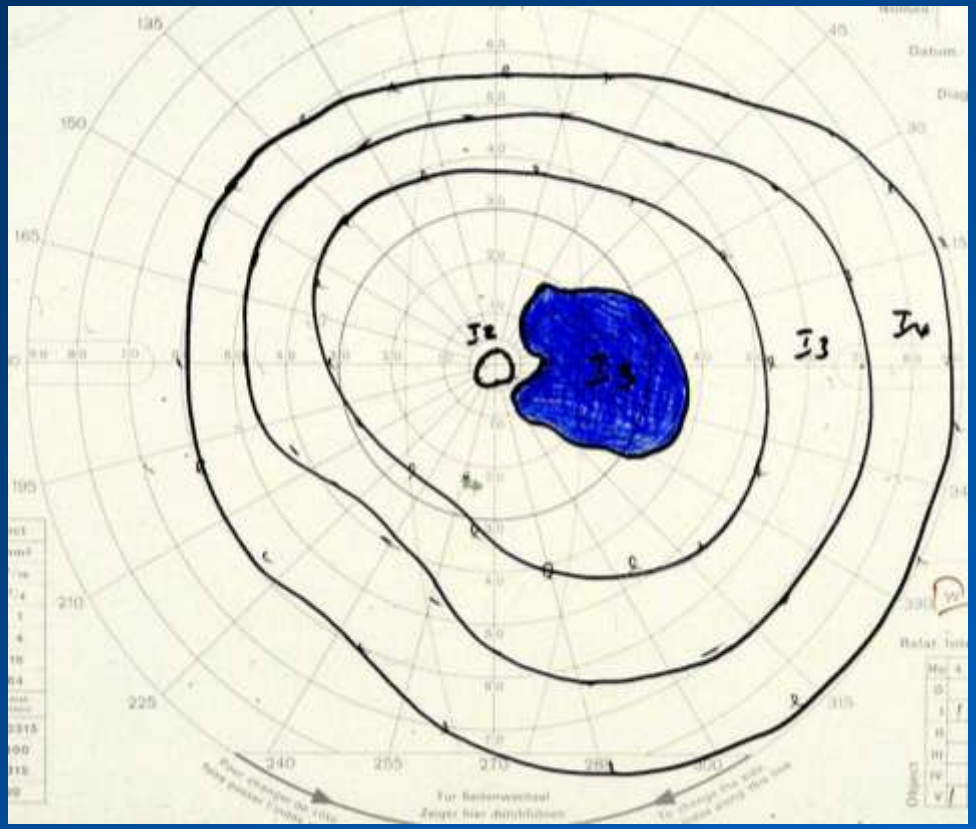
Rechtes Auge, vergößert



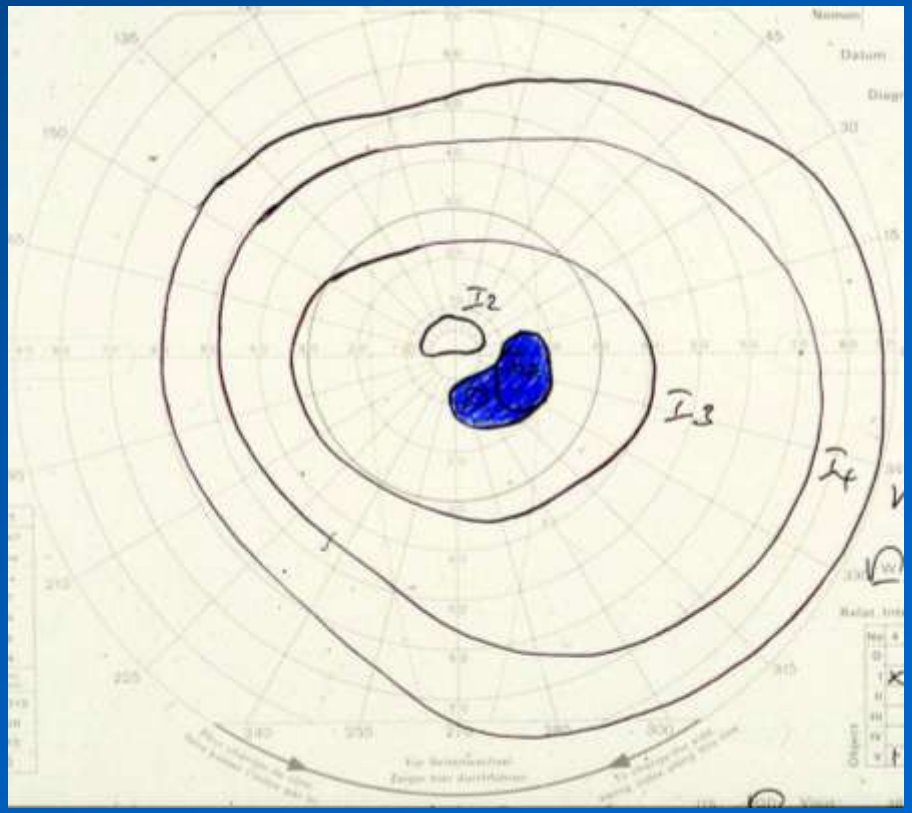
Linkes Auge



Gesichtsfeld rechts im Verlauf

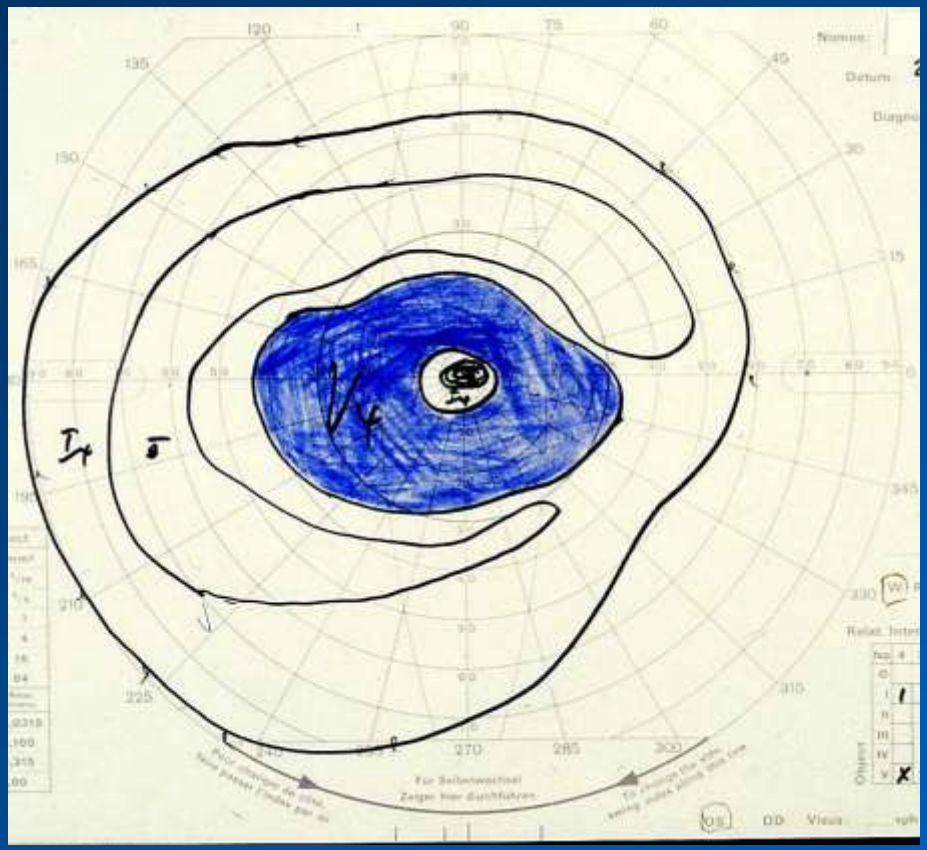


1977

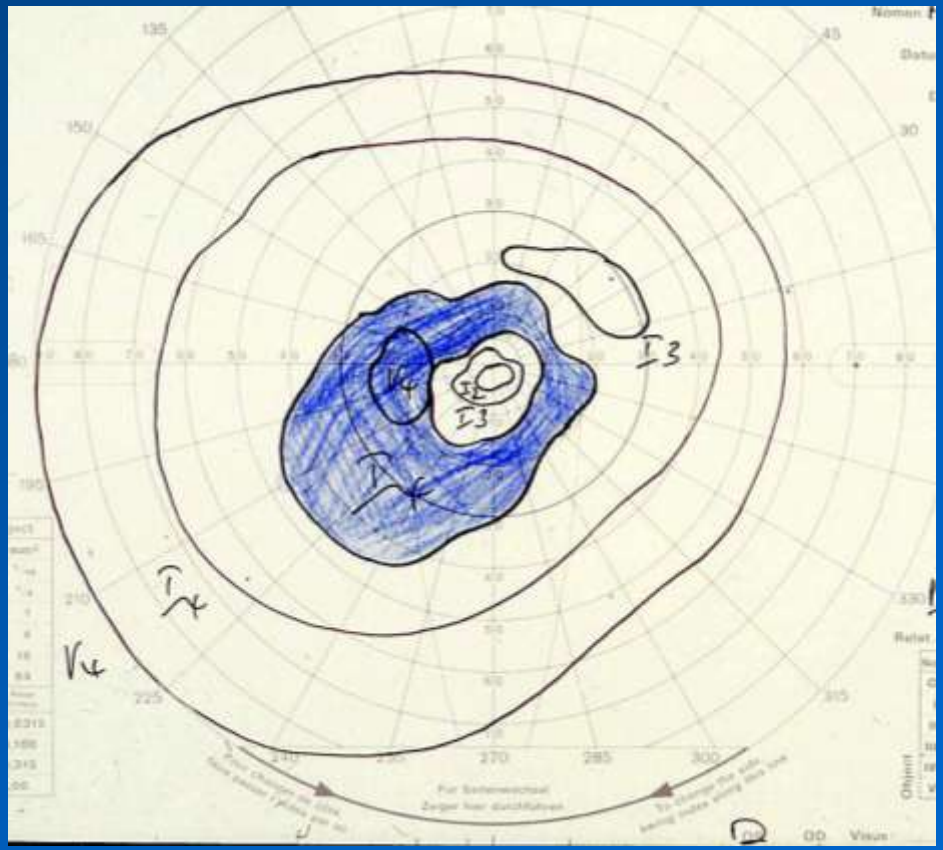


1987

Gesichtsfeld links im Verlauf



1977



1987

Anamnese-Ergänzung

- 1949/50 Syphilis, mit Salvarsan behandelt
- Während der Erkrankung vorübergehende Augenprobleme, aber nicht beim Augenarzt gewesen
- ERG: photopisch und skotopisch reduziert, aber vorhanden
- **Keine Nachtblindheit**

Makula
Netzhaut
Zentrum

Arabella
Klinik
München

VOLUME 28 · NUMBER 32 · NOVEMBER 10 2010

JOURNAL OF CLINICAL ONCOLOGY

DIAGNOSIS IN ONCOLOGY

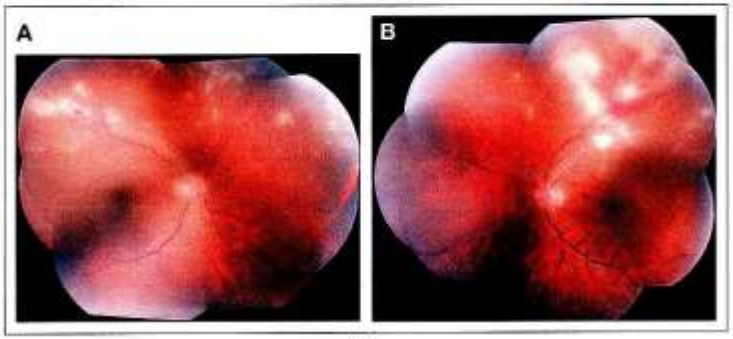
Cytomegalovirus Retinitis During Chemotherapy With Rituximab Plus Hyperfractionated Cyclophosphamide, Vincristine, Doxorubicin, and Dexamethasone

A 50-year-old man with a history of acute T-cell lymphoblastic leukemia developed changes in vision during cycle 4a of chemotherapy with rituximab plus hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (R-hyperCVAD). The patient was receiving routine antibacterial (ciprofloxacin), antifungal (fluconazole), and antiviral (acyclovir) coverage during hyperCVAD, as described in the literature.[1] Initially, he was administered dexamethasone eye drops for possible cytarabine toxicity, but his vision did not improve. The visual changes progressed, and he described the visual compromise as "the world appearing blurry" or as if he were "looking at the world through water." He also complained of black spots in his visual field. Lumbar puncture demonstrated no evidence of infection. Ophthalmologic examination (Figs 1A, 1B) showed yellow-white areas of necrotizing retinitis and intraretinal hemorrhages in both eyes, diagnostic of cytomegalovirus (CMV) retinitis. The patient was treated with oral valganciclovir. The retinitis resolved in a few weeks, with improvement of visual symptoms.

Elucidating the cause of visual problems in patients with hematologic malignancies receiving chemotherapy can be problematic. With leukemic involvement of the eye, retinal infiltrates and hemorrhages—sometimes white-center hemorrhages—are commonly seen. When opportunistic infections such as CMV retinitis invade the eye, acute retinal necrosis and progressive outer retinal necrosis are seen. Serologic testing methods for CMV, such as pp65 antigenemia and CMV DNAemia, are routinely used to monitor patients for reactivation and response to treatment in the transplantation setting. However, with CMV retinitis, positive findings on ophthalmologic exam in the proper clinical setting are diagnostic. Other differential diagnoses include herpes simplex, varicella zoster, toxoplasmosis, syphilis, and intraocular lymphoma. In the case of intraocular lymphoma, vitreous fluid examination or retinal biopsy may be necessary for diagnosis.[2]

CMV infection is infrequently encountered in general hematology or oncology patients, but it is a major issue for patients after allogeneic stem-cell transplantation. CMV reactivation can be seen in oncology settings other than transplantation, and therefore clinical vigilance is essential. The incidence of CMV infections in nontransplantation settings is thought to be minimal. Recent studies have challenged that perception and suggested that the incidence of CMV reactivation is on the rise in patients with hematologic malignancies. This is likely a result of the use of more immunosuppressive agents such as alemtuzumab. In a recent retrospective review,[3] Australian investigators reported that the rate of CMV reactivation over a 5-year period at a single referral center was especially high in patients receiving alemtuzumab (50%). The event rate for patients receiving hyperCVAD was 9.7%; denileukin diftitox, 6.1%; autologous stem-cell transplantation, 4.2%; fludarabine-containing regimens, 4.6%; and rituximab, 2.6%. The event rate for other standard-dose chemotherapy regimens was less than 1%.[3] Other reports have confirmed that the incidence of CMV reactivation in patients with cancer undergoing nonallogeneic transplantation and receiving chemotherapy is significant.[4]

Alemtuzumab (Campath; Genzyme, Cambridge, MA) is a humanized monoclonal antibody against the CD52 antigen. The CD52 antigen is expressed on the surface of normal and malignant B-lymphocytes, T-lymphocytes, natural-killer cells, monocytes, and macrophages. Patients enrolled onto phase I/II studies of this drug developed a significant number of CMV infections likely because of lymphopenia and T-cell depletion. Purine analogs such as fludarabine



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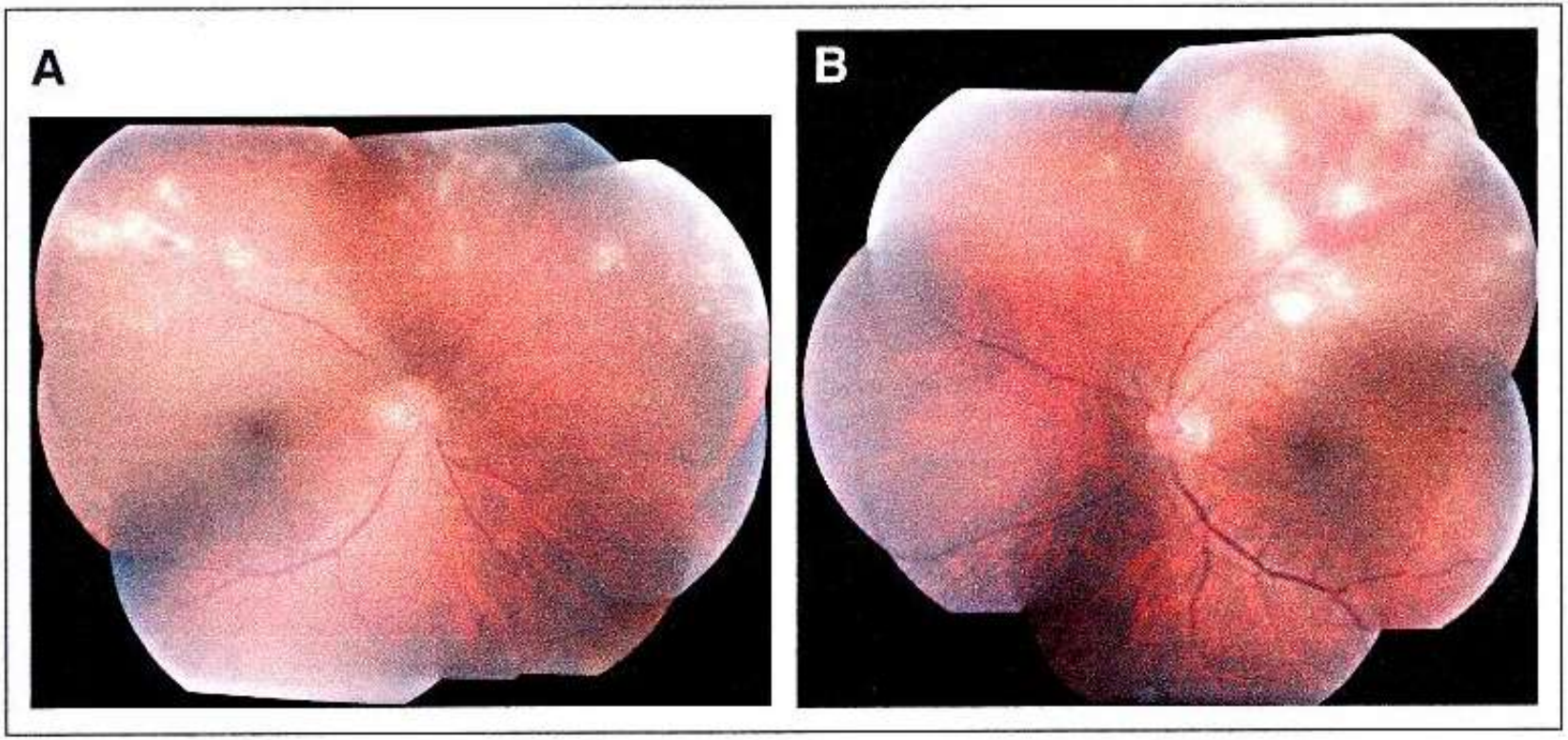
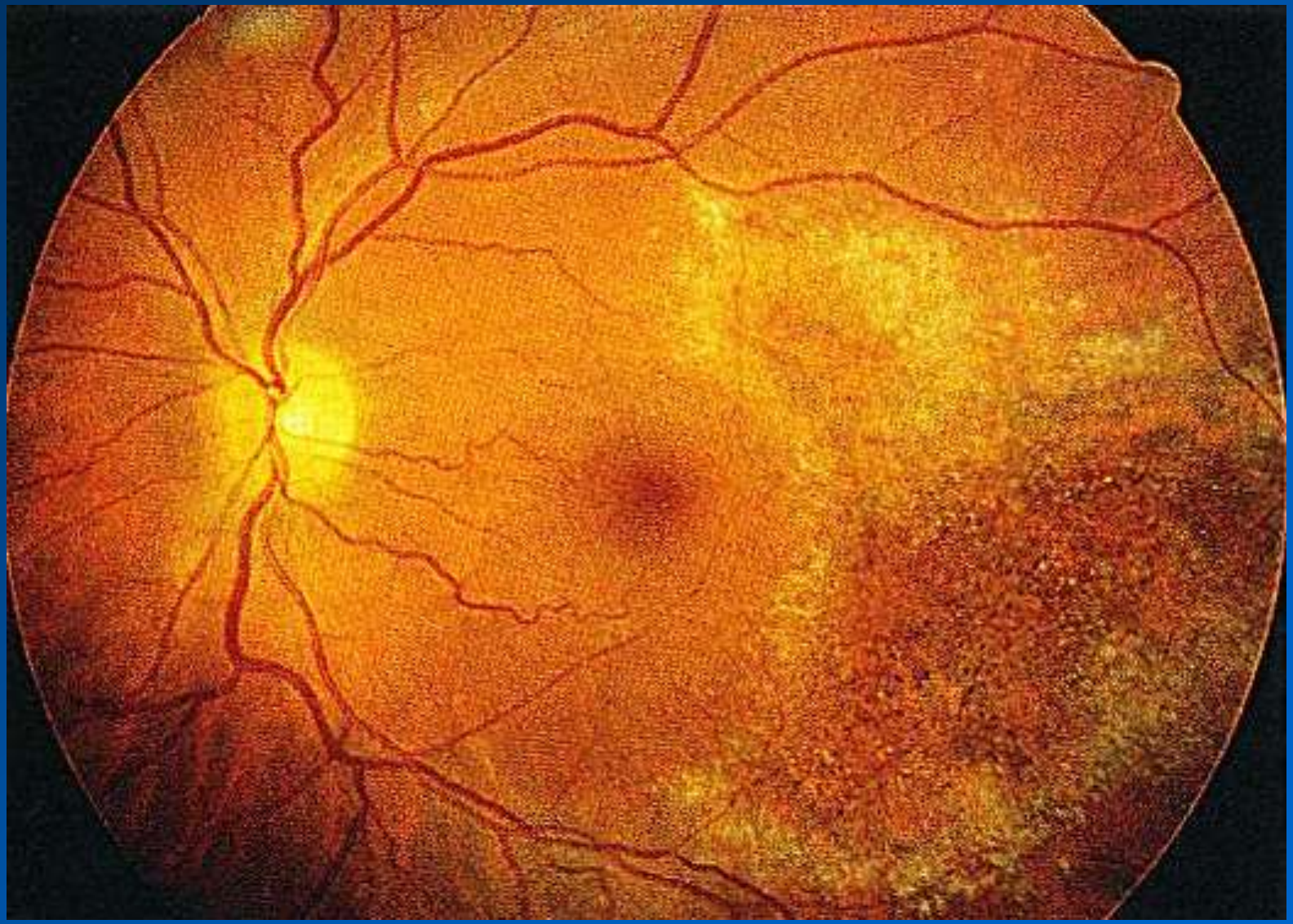

A
B

CMV-Retinitis

- „fovea sparing disease“
- Beginn in der mittleren Peripherie und nach peripher voranschreitend
- „Flächige“ Läsionen mit satellitenartigen Herden am peripheren Rand
- Abheilung unter Hinterlassen großer Pigmentepithelnarben mit Skotomen

Abgeheilte CMV-Retinitis



Diagnose

- Pseudo-Retinitis pigmentosa bei Verdacht auf abgelaufene opportunistische Infektion während des sechsten Zyklus der Chemotherapie
- Vermutlich stabiler Zustand
- Verlaufskontrolle, Serologie und Elektrophysiologie sind noch geplant