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# Laser Photocoagulation for Peripheral Retinal Capillary Hemangioblastoma in von Hippel-Lindau Disease

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***Purpose:*** To study the efficacy and limits of laser photocoagulation for retinal capillary hemangioblastoma (RCH) of various sizes in von Hippel-Lindau disease.

***Design:*** Retrospective study.

***Patients:*** The records of 176 patients with von Hippel-Lindau were reviewed retrospectively. Seventy-four patients with 304 RCHs in 100 eyes were treated primarily with laser photocoagulation. Eyes with concomitant rhegmatogenous or tractional retinal detachment or with papillary RCH were excluded.

***Methods:*** The treatment consisted of inactivating RCH using direct green laser photocoagulation with long-duration laser burns (0.1−0.7 seconds).

***Main Outcome Measures:*** The number of RCH lesions per eye, RCH size in disc diameter (DD) at diagnosis, the presence of retinal lipid exudation or subretinal fluid, and visual acuity were recorded. Final outcomes included RCH inactivation, posttreatment complications, and final visual acuity.

***Results:*** Patient mean age was 28 years (range, 8−62). Mean follow-up duration after treatment was 4.5 years (range, 0.4−17.5). Median RCH size was 0.25 DD (range, 0.25−3.00). Laser alone inactivated 97% of RCHs. A mean number of 1.6 laser sessions (range, 1−8) were needed to achieve RCH inactivation. A single laser session allowed coagulating 77% of RCHs. Their median size was 0.50 DD (range, 0.25−1.50). More than 1 laser session was needed to inactivate 23% of RCHs. Their median size was 1 DD (range, 0.25−3.00). Among them, 29 (10% of all RCHs) needed additional laser session during the first 48 hours. Their median size was 1.5 DD (range, 0.5−3). Subretinal fluid transiently increased in 7 eyes after the first laser session and was controlled promptly by additional photocoagulation. Additional cryotherapy was needed only in 7 eyes with large RCH partially inactivated by laser. In all eyes, visual acuity remained stable during the follow-up.

***Conclusions:*** In the absence of tractional retinal detachment, laser photocoagulation allowed inactivating most RCHs up to 3 DD, even when they were associated with subretinal fluid. Laser photocoagulation alone inactivated 100% of RCHs up to 1 DD, and 73% of larger RCHs. In such cases, additional cryotherapy increased RCH inactivation to 94% so that 99% of all treated RCHs were finally inactivated. *Ophthalmology Retina 2016;■:1−9 © 2016 by the American Academy of Ophthalmology*

von Hippel-Lindau (VHL) disease is a rare, autosomal-dominant multisystem cancer syndrome resulting from mutations in the tumor suppressor gene VHL on chromosome 3.[1−3] In the retina, the disease is characterized by the proliferation of retinal capillary hemangioblastomas (RCHs). The prevalence of RCHs in VHL patients is approximately 50% and patient mean age at diagnosis is 25 years.[4,5] Retinal capillary hemangioblastomas may be found anywhere in the retina and involve the optic disc in about 15% of cases.[6] RCHs are bilateral in one-half of cases and multiple in one-third of eyes.[6] Despite being slow growing and sometimes quiescent, RCHs may cause significant visual loss over time[5] owing to their exudative or tractional effects on the surrounding retina.[7] Large tumors tend to develop extensive exudation and tractional retinal detachment more often than smaller tumors.[5]

Treatment is based on ablative therapy unless RCHs are located on the optic disc or too close to the macula. The efficacy of laser photocoagulation has been well established in several publications since Annesley et al in 1977.[8−10] However, the treatment technique, maximum size of RCH suitable for laser photocoagulation, and definition of a successful treatment differ from 1 publication to another. Only a few large case series have been published.[8−14] Other treatment modalities have been proposed as a complement or an alternative to laser therapy, including trans-conjunctivoscleral cryotherapy,[13,15] dynamic photo-therapy,[16] transpupillary thermotherapy (TTT),[13] and anti-vascular endothelial growth factor injections.[17−19] In extremely severe cases with retinal detachment, treatment options include vitreoretinal surgery[20,21] or radiotherapy.[7,22] The aim of this study was to update data on the efficacy,



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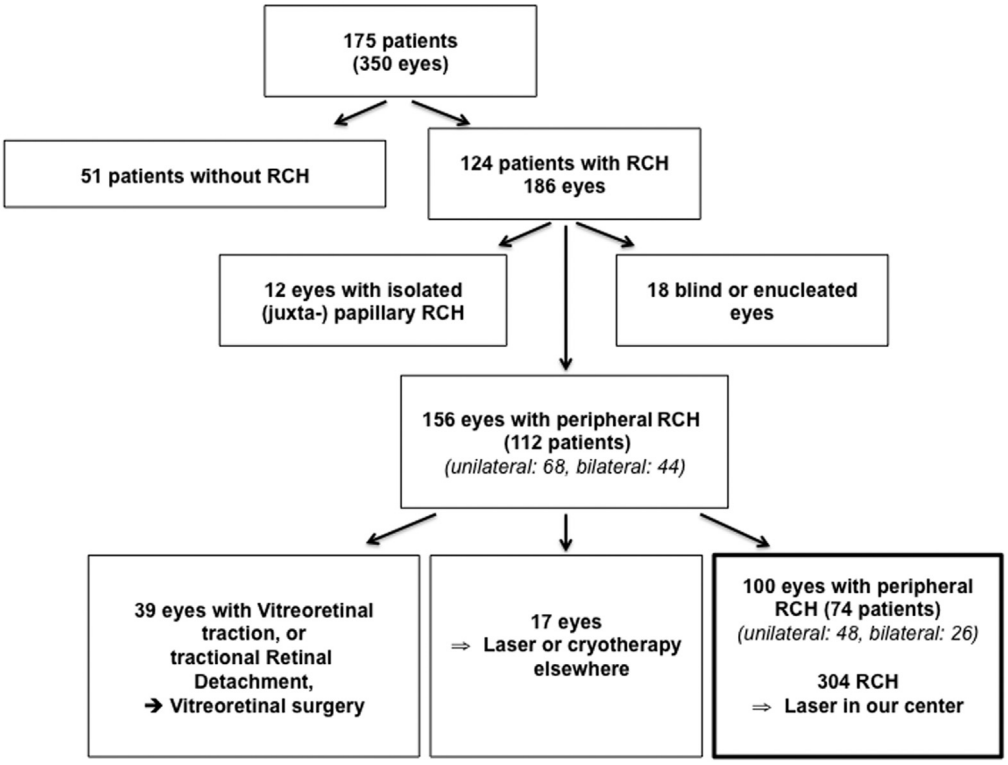


**Figure 1.** Flow chart of the studied population of patients with retinal capillary hemangioblastomas (RCHs) of von Hippel-Lindau disease. Initially, 304 peripheral RCH in 100 eyes of 74 patients were treated with laser photocoagulation in our department.

safety, and limits of laser photocoagulation for RCH of various sizes in VHL disease and to define the conditions for a clinically optimal treatment.

## Patients and Methods

This retrospective study was approved by the institutional review board of the French Ophthalmology Society. The records of 175 patients with VHL disease were reviewed retrospectively. Patients were followed over the 1997−2015 period in our Reference Center for rare vascular diseases of the brain and the eye (CERVCO) in collaboration with the "PREDIR" center (Reference Center for rare cancers, PREDIspositions aux tumeurs du Rein).

The diagnosis of VHL disease was based on clinical findings and a positive genetic test for mutations in the VHL gene in all cases. The diagnosis of RCH was based on the fundus appearance of a circumscribed, roundish red vascular retinal lesion, supplied by dilated retinal vessels. However, in very small RCH, the feeder vessels were not significantly dilated; in contrast, large RCH could be partially white owing to the formation of fibrosis at their surface. In this cohort (Fig 1), 51 patients had no RCH and 124 had RCH in $\geq$1 eye so that a total of 186 eyes were included in this analysis. Eighteen eyes of 18 patients were excluded from the study because, at initial examination, they had no light perception or had already been enucleated. Twelve additional eyes of 12 patients were also excluded because they had only papillary or juxtapapillary RCH. Among 112 patients, 156 eyes had $\geq$1 peripheral RCH at initial examination or during follow-up. Among these eyes, 39 eyes of 37 patients presented with retinal detachment, vitreoretinal traction, and neovascularization over the RCHs or the optic disc, and had undergone primary vitreoretinal surgery. In 17 eyes, the RCHs had previously been treated elsewhere. Thus, the records of 74 patients (25 women and 49 men; mean age, 28 years; range, 8−62) who received primary therapy via laser photocoagulation in our center were reviewed, corresponding with 304 peripheral RCHs treated in 100 eyes (Fig 1).

All patients underwent an initial ophthalmologic evaluation, including slit-lamp examination with contact wide field lens or indirect ophthalmoscopy. Color fundus photographs were taken (Topcon, TRC50, Tokyo, Japan, and OPTOS, 200Tx, Malborough, MA), and fluorescein angiography (FA) was performed (HRA, Heidelberg Engineering Heidelberg, Germany, or Topcon TRC50, Tokyo, Japan). Optical coherence tomography was performed either with the Spectralis (Heidelberg Engineering) or Cirrus optical coherence tomography (Carl Zeiss-Meditec, Inc, Dublin, CA).

The number of RCHs per eye, the RCH size at diagnosis, and the presence of complications such as subretinal fluid, hard exudates, hemorrhage, vitreoretinal traction, and macular involvement were recorded. RCH size was assessed via fundus imaging by measuring the ratio of the mean axis of the RCH to the mean diameter of the optic disc. The largest tumor dimension was used as a measure of tumor size. The characteristics of patients and eyes are shown in Table 1. The number of laser photocoagulation sessions needed to achieve RCH destruction was recorded. The effect of laser was monitored by fundus photography or FA. Outcome assessment included tumor regression, posttreatment complications, intraretinal exudation, and best-corrected visual acuity. The treatment was considered successful when subretinal fluid and exudation had completely resorbed and the RCH was inactivated. The signs for inactivation were RCH narrowing and flattening with whitening or pigmentation of its surface, return to a normal diameter of the feeding vessels, and no leakage on FA when performed.