

Toward a miniaturized fundus camera

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1 Introduction

Retinopathy of prematurity (ROP) is a disease of developing blood vessels that affects about 50% to 60% of premature newborns weighing 1000 g or less at birth.¹ The retinal blood vessels begin to develop 3 months after conception and complete their development at the time of normal birth. Therefore the eye's development is disrupted when the child is born prematurely. If ROP develops, the blood vessels grow abnormally from the retina into the clear gel that fills the back of the eye, where they become fragile and often hemorrhage into the eye. This is followed by the development of scar tissue, which pulls the retina loose, leading to reduced vision or, in severe cases, to blindness.

ROP is classified in four stages of increasing severity. At stage I a line on the retina is visible which marks a border for blood vessels and hence prevents oxygen supply to the areas lying outside. At stage II the line becomes more dominant, rises above the surface of the retina, and becomes a ridge. In most cases, spontaneous healing without any complications is observed at this point. Many premature infants develop mild ROP, but in about 1 out of 10 cases, depending on the risk factors mentioned later, the pathological development continues. At stage III the line is even more pronounced since external tissue extends from the ridge through the internal limiting membrane of the retina into the vitreous gel and back over the surface of the vascularized retina. The blood vessels often show abnormal tortuosity as the state of shunt is approached. Stage IV finally is reached when the retina is de-

Abstract. Retinopathy of prematurity (ROP) describes a pathological development of the retina in prematurely born children. In order to prevent severe permanent damage to the eye and enable timely treatment, the fundus of the eye in such children has to be examined according to established procedures. For these examinations, our miniaturized fundus camera is intended to allow the acquisition of wide-angle digital pictures of the fundus for on-line or off-line diagnosis and documentation. We designed two prototypes of a miniaturized fundus camera, one with graded refractive index (GRIN)-based optics, the other with conventional optics. Two different modes of illumination were compared: transscleral and transpupillary. In both systems, the size and weight of the camera were minimized. The prototypes were tested on young rabbits. The experiments led to the conclusion that the combination of conventional optics with transpupillary illumination yields the best results in terms of overall image quality. © 2004 Society of Photo-Optical Instrumentation Engineers. [DOI: 10.1117/1.1631313]

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tached, causing severe impairment of the vision or blindness.^{1–4}

ROP is one of the most common causes of acquired blindness in infants, but if it is diagnosed in time and treated with laser or cryotherapy it is also one of the most treatable diseases.^{5–9}

Even though the causes of ROP are not fully understood, some factors are known that increase the incidence of ROP and the risk associated with it. They are extreme prematurity, extreme low birth weight, factors related to the cardiopulmonary system, especially pO_2/pCO_2 . In the past, excess use of oxygen to treat premature babies also stimulated abnormal vessel growth in the eye. However, on a result of better monitoring, the number of such cases has decreased.

Figure 1 shows an eye with clear signs of ROP in stage III. At this stage, treatment with a good chance for complete recovery is still possible. Figure 2 shows the final stage of ROP; part of the retina is detached and there is little chance of saving the sight. This is basically the picture of a blind eye.

Owing to improvements in neonatal care, the number of children in need of examination for ROP can be expected to increase, even though these improvements, especially in mechanical ventilation and monitoring and controlling arterial oxygen saturation and pO_2/CO_2 homeostasis, reduce the risk of ROP.^{10,11} Guidelines have furthermore been established according to which a systematic screening for ROP should be performed (see, e.g., American Academy of Ophthalmology homepage¹²).

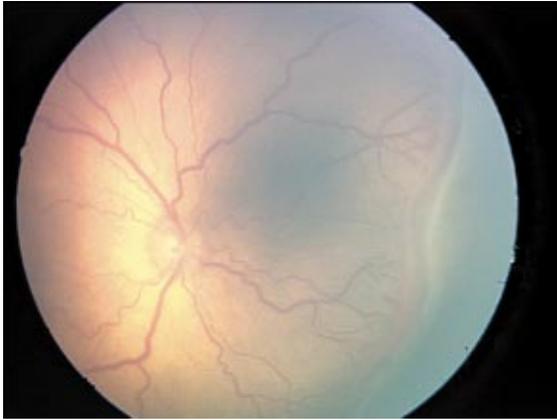


Fig. 1 ROP in stage III. The line of vascularization has become dominant. The blood vessels show an increased tortuosity. At this stage, successful treatment of ROP is still possible. (Image taken by J. Flynn.)



Fig. 5 Image of a pigmented rabbit's fundus taken with prototype A.

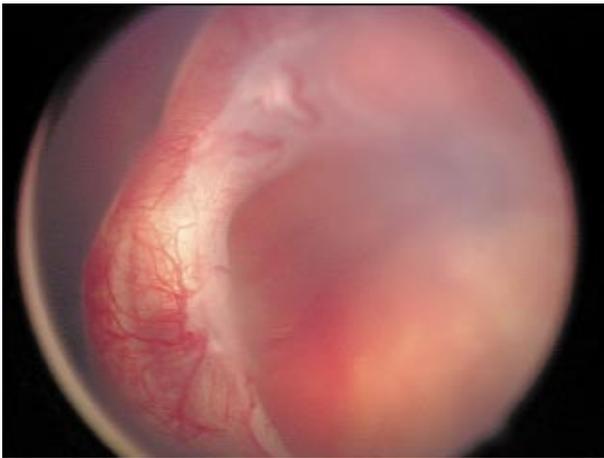


Fig. 2 ROP in stage IV, the final stage of ROP. Most of the retina is detached. At this point there is no chance for successful treatment. (Image taken by J. Flynn.)

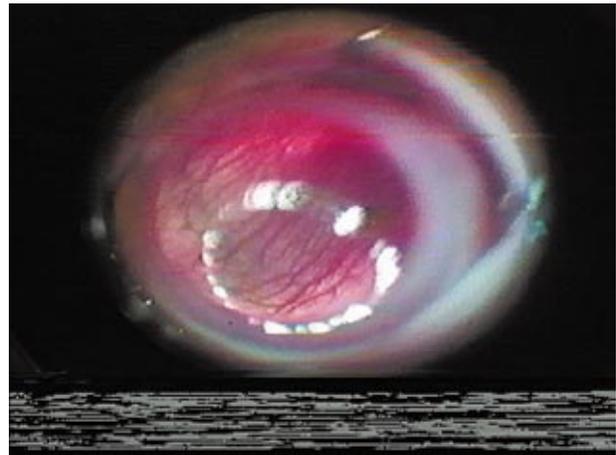


Fig. 6 Eye of an albino rabbit seen with prototype B. The reflections occurred because the contact glass is not yet in contact.

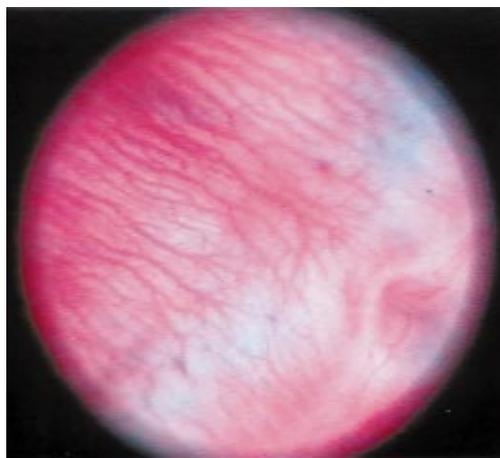


Fig. 7 Eye of an albino rabbit seen with prototype B. The contact glass is in contact with the eye. In the case of transscleral illumination, an image could only be taken with albino rabbits because the sclera of pigmented rabbits absorbed too much light.

In view of the extensive knowledge gained in the diagnosis and treatment of ROP, the problem is not primarily the screening procedure or the therapy per se, but the fact that even in highly developed countries there is no guarantee that an ophthalmologist experienced in ROP is available to perform the examination.^{13–17} A solution to this problem may be found in an approach based on telemedicine. Several telemedical studies in different countries have proven the possibility of a remote diagnosis of ROP that leads to satisfactory results.^{18–20} For a telemedical diagnosis, a small, lightweight and portable digital fundus camera is needed that covers the entire area of interest on the fundus. Also, an international network has to be established by which telescreening for ROP can be performed. The use of standard components enables us to connect the camera directly to a standard medical database that is widely used within Europe.²¹ This ensures compliance with the law and privacy on one hand and with medical standards on the other.²² Portability, safety, and ease of application thereby require that no bulky equipment be associated with the camera and network access.

2 System Requirements

Owing to the unstable health of prematurely born infants, the examination should be done with a maximum of care and a minimum of stress for the infant, i.e., with a minimum of images. Therefore, the envisaged fundus camera has to be equipped with a lens system that has a field of view (FOV, usually given in degrees of the opening angle) as large as possible. The camera also has to be designed for connection to a computer network so that images are available for on-line examination as well as for digital postprocessing over the network. Documentation for further analysis and archiving has to be implemented.

To avoid any unnecessary stress, the examination is often done at the bed of the patient. Since space in hospital rooms is usually quite limited, the camera equipment has to be small enough to be installed and carried around easily from one room to the next, sometimes between different buildings. For practical reasons, therefore, the entire system should not exceed the size of a small and light suitcase.

The devices and procedures for examining the fundus of prematures that have been in use so far appear to fail at least at one of these requirements. A large amount of general work on wide-angle fundus cameras, theoretically as well as practically, has been published by Pomerantzeff and his co-workers.^{23–25}

Standard fundus cameras require a cooperative patient. Obviously, these camera cannot be used for infants. The indirect ophthalmoscope that is used in many hospitals usually has no capability for saving an image, either on conventional film or digitally. A standardization of image acquisition by way of an indirect ophthalmoscope appears difficult. A camera with a contact glass that is in direct contact with the patient's eye seems to be more practical for the application envisaged here.

Currently, two digital fundus (contact) cameras exist for noncooperative patients: RetCam²⁶ and Medibell.²⁷ However, both camera systems are relatively large and heavy for practical use and transportation. In the case of a heavy camera head, the application is tiring and it is more difficult to contact

Table 1 Average size of the eye and average weight of premature infants.²⁸

Gestational Age (weeks)	Average Body Weight (g)	Diameter of Eye (mm)
25	550	10
29	1180	
35	2370	
39	3100	13
Full term		17

the eye without applying undue pressure to it. If a mechanical arm is provided for the camera, bulkiness increases and transportability is compromised.

When designing a fundus camera for ROP, one has to consider in particular the geometric constraints associated with the eyes of newborn infants. These eyes are significantly smaller than those of adults, and in the case of prematures, even more so. Their diameter can be less than half of that of an adult eye²⁸ (Table 1). Thus the radius of curvature of the contact glass has to be chosen accordingly.

Likewise, the pupil of a prematurely born infant is also smaller than that of an adult eye. The maximum diameter to which it can be dilated is about 6 mm, whereas a dilated pupil of an adult can reach a diameter of 12 mm. The small size of the eye and the small interpupillary tissue limit the size of the instrument. Therefore, the tip of the camera containing the contact glass plus eventual fibers for illumination should have a diameter of 6 mm at most. Table 2 summarizes the system requirements.

3 Materials and Methods

Two prototypes of miniaturized fundus cameras were designed. Prototype A was built using a graded refractive index

Table 2 Summary of system requirements.

Size of camera handpiece	Length < 100 mm
Weight of camera handpiece	< 250 g
Size of total instrument	Fit in small suitcase (e.g., carry-on luggage)
Weight of total instrument	< 10 kg
Diameter of contact glass	< 5 mm
Radius of curvature of contact glass	Approx. 6 mm
Diameter of transpupillary illumination ring (if used)	< 6 mm
Field of view	> 70 deg
Frame rate	> 15 frames/s
Resolution	> 640 × 480 pixels

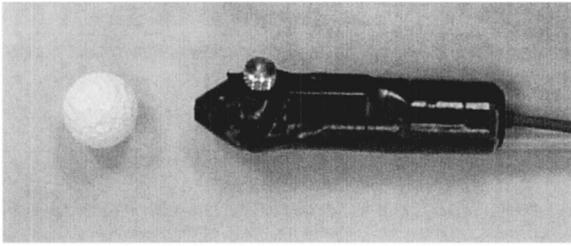


Fig. 3 Photo of prototype A compared with a Swiss coin (size of the coin in front of the prototype = 20 mm) and compared with the Ret-Cam.

(GRIN) lens, based on previous experience,^{29–31} in prototype B, conventional optics were used. While the GRIN lens (diameter 0.5 mm) of prototype A was surrounded by a fiber bundle for transpupillary illumination, the lenses of prototype B were too large for this type of illumination. Instead, transscleral illumination was used.

The prototypes were tested on young rabbits whose eye geometry is similar to that of newborns. Prototype A was tested on both pigmented and albino rabbits and prototype B was tested only on white New Zealand rabbits. The rabbits had a pupil diameter of 9.4 mm (rabbit 1) and 8.07 mm (rabbit 2), a limbus diameter of 10.5 mm (rabbit 1) and 12.7 mm (rabbit 2), and a globe diameter of 16 mm (rabbit 1) and 16.5 mm (rabbit 2). Thus the eyes of these young New Zealand rabbits were approximately of the same size as the eye of a newborn child (Table 1). The eye of a prematurely born child can be even smaller, however (see Table 1). All tests were made at the Bascom Palmer Eye Institute in Miami according to the regulations relating to animal experiments. The rabbits were anesthetized during the experiments.

Prototype A (Fig. 3) had the following characteristics:

- Owing to the extremely small diameter of the system, no contact glass was used, but the 0.23 P GRIN rod lens touched the eye directly. The optical part of the system had a diameter of 1.8 mm, which was determined by the GRIN lens.
- The optics consisted, apart from the GRIN lens, of the same conventional optics used in the eye endoscope supplied by Volpi AG, Schlieren, Switzerland.³¹
- The fiber ring for illumination had a diameter of 2.5 mm.
- The illumination of an endoscopic system (Volpi AG) was used. This system had a maximum power of 80 mW. Owing to the lack of precision associated with the prototyping fabrication process, the maximum power transmitted by the ring was limited to 5 mW.

Prototype B was configured as follows:

- As contact glass, a wide-angle contact glass from Haag Streit AG, Berne, Switzerland, with a diameter of 13.7 mm was used (see Fig. 4 for a schematic drawing).
- The optics consisted of an $f = 11.1$ -mm biconvex coated lens (Volk 90-D) and an $f = 40$ -mm biconvex lens (field lens); an $f = 5.6$ -mm camera objective was used to image the retina onto a 1/3 in. CCD color image sensor.

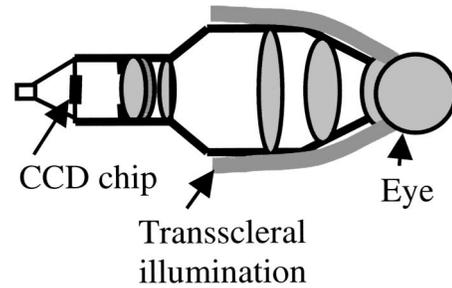


Fig. 4 Schematic drawing of prototype B, using transscleral illumination and conventional optics.

- A black sealing ring held 36 flat-polished plastic fibers in place (fiber diameter, 0.5 mm; fiber ring diameter, 15.5 mm; outer diameter of the sealing ring, 17 mm).
- For illumination, the lamp of an endoscopic system (Volpi AG) was used. A maximum power of 240 mW was measured at the end of the fiber bundle and a maximum power of 120 mW was measured exiting the illumination ring.

Prototype B was geometrically outlined to image the eye of an adult. For premature children, accordingly, the diameter as well as the radius of curvature of the contact glass will need to be adapted to the eye of a prematurely born infant. This requires rescaling the whole system without changing its quality or functionality. In its present form, the contact glass is too large in relation to the eyelid opening of a rabbit, so the rabbits' eyes had to be somewhat protruded. As a result, the contact between the glass and the cornea of the eye was not optimal.

Standard TV cameras were used in both prototypes. In spite of the relatively low resolution of standard TV, this technology has been used because it allows an uninterrupted observation. In addition, conventional TV images have a worldwide standard, allowing low-cost cameras to be used. Imaging systems with a higher resolution, in particular complementary metal-oxide semiconductor (CMOS)-based sensors (1000 × 1000 pixels or more), will be applied whenever a useful framing rate (at least 15 frames/s) can be achieved at reasonable cost. Table 3 shows some of the main design parameters of the two prototypes as well as those for an existing camera.

4 Results

Figures 5–7 show characteristic images taken with the prototypes. The image quality of prototype B in Fig. 6 is clearly better than that achieved with prototype A in Fig. 5. Especially at the edge, chromatic aberration of the GRIN lens is visible. The overall haze in prototype A might be due to the relatively large GRIN lens diameter (in comparison, e.g., with the endoscopic imaging system of Volpi AG, which is designed for endocular applications based on work by Rol's group.^{29–31})

Even though a relatively large GRIN lens was used, the GRIN system is still substantially smaller than the system equipped with conventional optics in prototype B. Owing to the extremely small size of prototype A, this camera could also be used to image the fundi of other and smaller animals,

Table 3 Some design parameters of the two prototypes and RetCam.

Parameters	Prototype A	Prototype B	RetCam
Lens system	GRIN	Conventional optics	Conventional optics
Angle of view (degrees, measured in air)	60	75	Approximately 80
Illumination type	Transpupillary	Transscleral	Transpupillary
Weight (g)	50	90	675
Size of contact glass or lens	1.8	13.7	5.0
Approximate length (mm)	40	60	>150

even those as small as mice. A number of pictures were taken of the eyes of a rat with good success in order to verify the applicability of the system for extremely small eyes.

For prototype A, 5 mW were available for transpupillary illumination, as mentioned earlier. When comparing these values, one should keep in mind that with prototype B (transscleral illumination), only the fundi of albino rabbits could be recorded with good image quality because the sclera of pigmented rabbits absorbed too much of the light (Fig. 7). The following intensities were used for illumination with albino rabbits: For prototype B, good image quality could be obtained with 10 mW when using the illuminating ring. When using a fiber bundle of either 1 or 4 mm diameter to illuminate the fundus transsclerally from one side, 1 mW was found to be sufficient.

Even though transscleral illumination is used in several ophthalmologic applications, e.g., Refs. 32–34, when our requirements are compared with those relevant for the applications described in the cited publications, it is found that the methods of transscleral illumination applied so far, although sufficient for other applications, are insufficient for our purpose. In particular: (1) As pointed out in the publications mentioned, only the major blood vessels can be seen with transscleral illumination, which is clearly not enough for an examination of ROP. (2) Only a small area is illuminated; thus, compared with our application, a correspondingly small field of view is available, which is not compatible with a wide-angle lens system. (3) Light is focused on the sclera, which can be done only when the patient is not moving (i.e., cooperative), which is not the case for children and newborns. (4) Light is applied from one side only, which leads to inhomogeneous illumination.

5 Conclusions

So far, it has been impossible to obtain images of a good quality using transscleral illumination. The transmission of the sclera is too low to illuminate a large FOV sufficiently for a wide-angle lens system. To obtain good image quality and wide-angle characteristics, a lens optics design similar to that used in endoscopes could be advantageous.

Although prototype A was small and lightweight and had a small contact area, the GRIN lens system performed unfavorably with respect to image quality. However, if an extremely small-diameter contact area (and easy to mount optics) is re-

quired, the GRIN design would nevertheless be preferred. Based on the present results, it appears to be desirable to design a system that combines transpupillary illumination with conventional optics.

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References

1. D. Hunter, S. Mukai, and T. Hirose, “Advanced retinopathy of prematurity,” in *Principles and Practice of Ophthalmology*, Vol. II, D. M. Albert and F. A. Jakobiec, Eds., pp. 782–791, W. B. Saunders, Philadelphia, PA (1994).
2. Committee for the Classification of ROP, “An international classification of ROP,” *Arch. Ophthalmol. (Chicago)* **102**, 1130–1134 (1984).
3. Committee for the Classification of Retinopathy of Prematurity, “II. The classification of retinal detachment. An international classification of ROP,” *Arch. Ophthalmol. (Chicago)* **105**, 906–912 (1987).
4. Association of Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften) <http://www.uni-duesseldorf.de/WWW/AWMF/II/index.html> (2003).
5. R. Axel-Siegel, M. Snir, D. Cotlear, A. Maayan, R. Frilling, I. Rosenblatt, D. Weinberger, I. Kremer, and L. Sirota, “Diode laser treatment of posterior retinopathy of prematurity,” *Br. J. Ophthalmol.* **84**, 1383–1386 (2000).
6. A. R. O’Connor, T. Stephenson, A. Johnson, M. J. Tobin, M. J. Moseley, S. Ratib, Y. Ng, and A. R. Fielder, “Long-term ophthalmic outcome of low birth weight children with and without retinopathy of prematurity,” *Pediatrics* **109**, 12–18 (2002).
7. C. Gilbert and A. Foster, “Childhood blindness in the context of VISION 2020—The Right to Sight. WHO,” **79**, 227–232 (2001).
8. L. J. Elsas *et al.*, “Multicenter trial of cryotherapy for retinopathy of prematurity—ophthalmologic outcomes at 10 years,” *Arch. Ophthalmol. (Chicago)* **119**, 1110–1118 (2001).
9. S. Clemens, C. Eckardt, H. Gerding, A. Grote, C. Jandek, U. Kellner, B. Lorenz, J. Petersen, V. Seiberth, N. Stark, M. W. Ulbig, A. Zubcov, G. Jorch, and F. Pohlandt, “Augenärztliche screeninguntersuchung von frühgeborenen,” *Ophthalmologie* **96**(4), 257–263 (1999).

10. M. Wolf, M. Keel, K. von Siebenthal, H.-U. Bucher, K. Geering, Y. Lehareinger, and P. Niederer, "Improved monitoring of preterm infants by fuzzy logic," *Technol. Health Care* **4**, 193 (1996).
11. M. Wolf, G. Duc, M. Keel, P. Niederer, K. von Siebenthal, and H.-U. Bucher, "Continuous noninvasive measurement of cerebral arterial and venous oxygen saturation at the bedside in mechanically ventilated neonates," *Crit. Care Med.* **25**, 1579–1582 (1997).
12. American Academy of Ophthalmology, <http://www.aao.org/aao/education/library/information/rop.cfm>.
13. C. B. Onofrey, W. J. Feuer, and J. T. Flynn, "The outcome of retinopathy of prematurity—screening for retinopathy of prematurity using an outcome predictive program," *Ophthalmology* **108**, 27–34 (2001).
14. A. K. Hutchinson, R. A. Saunders, J. W. O'Neill, A. Lovering, and M. E. Wilson, "Timing of initial screening examinations for retinopathy of prematurity," *Arch. Ophthalmol. (Chicago)* **116**, 608–612 (1998).
15. D. B. Roth, D. Morales, W. J. Feuer, D. Hess, R. A. Johnson, and J. T. Flynn, "Screening for retinopathy of prematurity employing the RetCam 120—sensitivity and specificity," *Arch. Ophthalmol. (Chicago)* **119**, 268–272 (2001).
16. M. H. DeJonge, P. J. Ferrone, and M. J. Trese, "Diode laser ablation for threshold retinopathy of prematurity—short-term structural outcome," *Arch. Ophthalmol. (Chicago)* **118**, 365–367 (2000).
17. A. R. Davis, H. Jackson, D. Trew, J. D. A. McHugh, and W. A. Aclimandos, "Transscleral diode laser in the treatment of retinopathy of prematurity," *Eye* **13**, 571–576 (1999).
18. B. Lorenz, M. Bock, H. M. Müller, and N. A. Massie, "Telemedicine based screening of infants at risk for retinopathy of prematurity," *Stud. Health Technol. Inform.* **64**, 155–163 (1999).
19. University of Regensburg, Department of Children's Ophthalmology (Abteilung für Kinderophthalmologie, Stabismologie und Ophthalmogenetik), <http://www.uni-regensburg.de/Fakultaeten/Medizin/Paedophth/projekte.htm#L2> (2002).
20. K. Yogesani, M. Cuyppers, C. J. Barry, I. J. Constable, and L. Jitskaia, "Tele-ophthalmology screening for retinal and anterior segment diseases," *J. Telemed Telecare* **6**(Suppl. 1), 96–98 (2000).
21. <http://www.imagic.ch/> (2003).
22. <http://medical.nema.org/> (2003).
23. O. Pomerantzeff, "Equator-plus camera," *Invest. Ophthalmol.* **14**(5), 401–406 (1975).
24. O. Pomerantzeff, R. Webb, and F. Delroi, "Image formation in fundus cameras," *Invest. Ophthalmol. Visual Sci.* **18**(6), 630–637 (1979).
25. O. Pomerantzeff, "Wide-angle noncontact and small-angle contact cameras," *Invest. Ophthalmol. Visual Sci.* **19**(8), 973–979 (1980).
26. <http://www.retcam.com/> (2003).
27. <http://www.medibell4vision.com> (2003).
28. V. Ozanics and F. A. Jakobiec, "Prenatal development of the eye and its anexa," in *Ocular Anatomy, Embryology and Teratology*, F. A. Jakobiec, Ed., pp. 12–57, Harper and Row, Philadelphia, PA (1982).
29. P. Rol, M. Sasoh, F. Manns, F. Edney, P. Niederer, and J.-M. Parel, "Experimental interocular laser surgery with a GRIN laser endoscope," *Proc. SPIE* **2673**, 50–53 (1996).
30. P. Rol, P. Edney, A. Hottinger, and P. Niederer, "Microendoscope as invasive ocular microscope," *Proc. SPIE* **2971**, 40–43 (1997).
31. P. Rol, R. Jenny, D. Beck, F. Frankhauser, and P. Niederer, "Optical properties of miniaturized endoscopes for ophthalmic use," *Opt. Eng.* **34**(7), 2070–2077 (1995).
32. A. Bradley, H. Zhang, R. Applegate, L. Thibos, and A. Elsner, "Entropic image quality of the retinal vasculature," *Vision Res.* **38**(17), 2685–2696 (1998).
33. R. Ronnerstam, "Fundus examination using transscleral illumination," *Graefes Arch. Clin. Exp. Ophthalmol.* **201**(3), 295–296 (1977).
34. V. Seiberth, "Transsklerale und transpupilläre laserkoagulation bei proliferativer sichelzellenretinopathie," *Ophthalmologie* **98**, 199–202 (2001).