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13. ABSTRACT *(Maximum 200*

Retinal imaging is key for diagnoses and treatment of various eye-sight robbing injuries and pathologies. Included are retinal detachments, laser damage, CMV retinitis, retinitis pigmentosa, glaucoma, tumors, and the like. Historically, "fundus" cameras were used for this function and these have been provided as physically large units requiring film, specially trained personnel, and generally only used by ophthalmologists or in hospital settings. The retinal camera of this project will revolutionize retinal imaging and bring quality ophthalmic care into routine medical settings. One version will be "field portable" and hand-held. Another will have additional capabilities and will be suitable for optometrists to be utilized for routine examinations as well as routine use in medical clinics. The unit for use in the clinics will be physically small and integrated into a slit-lamp type mounting. Primary aspects of improvement will be smallness of size, simultaneous imaging of the cornea and retina for ease of use, high-quality digital imaging, substantially lower capital and use costs, and a basic design which routinely implements Telemedicine.

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N.a. Mansi
Principal Investigator's Signature

4/3/97
Date

Table of Contents

Introduction. It is the first objective of this program to develop a field-portable retinal camera to visualize laser induced retinal damage in the battlefield. However, in the larger view of field ocular imaging requirements, it is well known that over 10% of injuries in the battlefield are of the eye, not even considering the laser damage modality. Therefore the imaging system will be used for visualizing a large number and variety of ocular injuries, both to the retina and the cornea.

Once a field camera is postulated there arise a host of additional opportunities for using the system to support field Telemedicine. To understand this consider that the camera can be divided into several sub-systems which would include:

1. The CCD imager.

2. The computer with frame grabber, image storage, and display.

3. The communication system.

4. The illumination source and system.

5. The imaging optics.

If the costs of items 1 through 4 can be amortized over additional uses then the entire system becomes considerably more cost-effective. For example, by proper modular design, optics can be provided to support visualization of skin problems, traumas, ENT problems, and even military hardware. As a result, a properly designed system will have a very large economic return as well as providing substantial opportunities for enhanced quality of medical care.

Ophthalmic equipment has historically been expensive as compared to commercial sector equipment performing a similar function. This is in part driven by the very small number of users and in part driven by the special requirements for imaging the eye. The low unit volume is driven by the fact that there are only an estimated 45,000 ophthalmologists world-wide. The number of optometrists is by comparison likely to be 140,000 world-wide and the number of general care physicians even larger. However, optometrists, in the past, have not commonly purchased imaging equipment.

New laws in the U.S. allowing therapeutic drug administration (TPA) by optometrists will likely change all of this. TPA, now enacted in nearly all states, will allow optometrists to treat simple glaucomas as shown in Fig. 1.

Many observers feel that once the O.D.'s understand the difficulties involved in diagnosing early glaucoma they will want to manage these cases with the support of ophthalmologists. Low cost imaging systems will be key to making this kind of co-management workable. Especially in the HMO setting, this kind of digital data acquisition for later expert review is likely to be the screening modality most appropriate in terms of quality care at a lower cost.

Therefore, major objectives of this program include establishing retinal and corneal imaging at the MASH unit level, bringing low-cost retinal and corneal imaging to the O.D. market, both civilian and military, and also for general Telemedicine. This is the genesis of the "clinical" retinal imaging unit which will share many components with the "field" unit but will be integrated into a digital slit-lamp for corneal imaging as well.

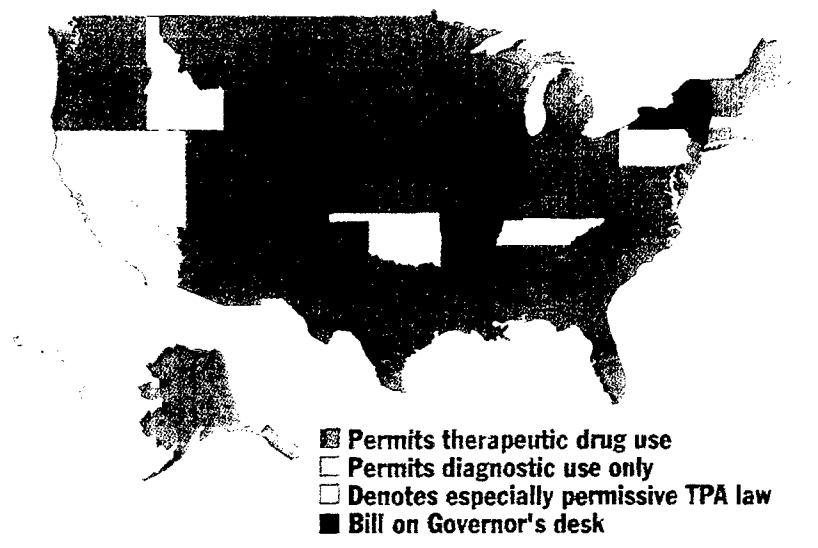


Fig. 1. Optometrists are being allowed to treat simple glaucomas in nearly all states.

A major benefit of this will be that reaching a much larger market (as compared to the small market for ophthalmologists alone) will access the economies of scale and dramatically reduce costs. For example, a Topcon Megapixel retinal camera currently sells for $80,000. Our wide-field retinal camera sells for $50,000, a substantial price break. We seek a price for the imager of this program of $20,000. At this price point, the economics and clinical benefits make this purchase absolutely compelling to the optometric market. For further information on digital retinal imagers currently on the market, see the summary in Fig. 2.

A. Results of the Phase I Work.

A.1. Modalities of use. As noted above, in our study of retinal imaging requirements, we identified basically two modalities of use. These are:

Field portable: Military: Field use and use in clinics. The field system will be hand-held and would also be useful for the non-ophthalmic imaging applications. Field Telemedicine uses are primary here.

Civilian: Field use could include paramedics and emergency rooms as well as use in general medical clinics with the non-ophthalmic imaging applications as well. Field and Clinic Telemedicine uses are primary here.

Clinical use: Military and civilian: This unit would become part of a slit-lamp installation and would include capability to image the retina in both narrow and wide field and the cornea. The primary applications would be for OD and MD and Telemedicine between various levels of medical service providers.

Potentially extensions of this imaging system could provide a more complete ability to asses visual function and to simultaneously perform objective and subjective refractions. Our analysis of the economics suggests that these enhanced features should be provided as options to maintain the lowest price for the basic system.

Topcon	"ImageNet" Features 1,024 CCD with FA and ICG FOV to 50 degrees	$79,990
Ophthalmic Imaging Systems	Features 1,024 CCD Price is $40,000 plus cost of retinal camera purchase. Net cost to customer is shown. FOV to 50 degrees	$65,000
Tomey	"ImageScape", features 1,024 CCD FA and ICG FOV to 50 degrees	$80,000
Massie Research Laboratories	RetCam 120 Features 3CCD color and FOV of 90 degrees and easy field acquisition	$49,950

Fig. 2. Ophthalmic cameras and costs.

A.2. Clinical performance requirements.

A.2.1. Requirements for field-of-view (FOV) and resolution. FOV requirements vary with pathology and the below is a summary of key pathologies and imaging requirements.

For laser damage: Laser damage can be quite small. However, even small damage spots can subsequently lead to retinal detachments. In general, the laser damage occurs in the central region and images of 30 degrees FOV are acceptable. In Fig. 3 I display a general summary of resolution vs. field for common retinal abnormalities.

For the direct and indirect ophthalmoscope, we are uncertain as to the actual practical resolution obtained. In theory, for "good" eyes on axis the human visual system is "diffraction limited." This acuity decreases with age and field angle and we note that the majority of clinical practitioners are old enough to have begun to lose their diffraction limited visual acuity. As a result, we have serious reservations about the actual resolution of the direct and indirect ophthalmoscope.

Such limitations do not exist for the camera as its optics do not age and obtaining high magnification is as simple as clicking a mouse. In the end, we feel that the resolution of the digital cameras will exceed that of the direct and indirect ophthalmoscopes, as will of course, the FOV. With this in mind and with the fact that the digital image can be studied with time and care, there is an excellent case to be made that the digital system will provide higher resolution, larger FOV, and better clinical information than the ophthalmoscopes. In conclusion, the location of the ophthalmoscopes on the resolution axis is only notional.

For glaucoma: High resolution color visualization of the optical disk is important. The issues are the cupping of the disk, its pallor, the cup-to-disk ratio, and any other abnormalities. It has been shown that accurate observations of the nerve fiber layer can be key to early assessment of glaucoma. Quigly and associates at John Hopkins claim up to five years earlier detection. It is also widely believed that the NFL can be hard to visualize and even harder to asses.

The disk only occupies a few degrees. However, given a realistic assessment of the users ability to point the imager, a field of view (FOV) of at least 15 degrees is required. For nerve fiber layer (NFL) assessment, a FOV of about 30 degrees is preferred and with red-free imaging to enhance the visibility of the NFL.

For tumors: Tumors frequently occur in the periphery. In fact, this is commonly the case. Observations to the boundary of the retina and actually into the interior angle is preferred. The tumors can be sufficiently large that narrow field retinal cameras cannot observe the tumor from edge to edge. Those centers treating tumors are forced to obtain many images of portions of the retina and then paste them together to complete the total image.

For detachments: Detachments can be quite large and extend across the entire retina. They can also be difficult to detect. Optometrists have confided with us that missed detachments are a major cause of lawsuits. Documentation of the lack of detachments can provide the clinician with vital protection from lawsuits.

CMV retinitis: This is a manifestation of AIDs and generally occurs in the mid-periphery. The lesions are not especially small, but with AIDs patients living longer, they are now subject to treatment.

Diabetic retinopathy: Screening for diabetic retinopathy is in general in the central to mid-periphery. The resolution requirements for diabetic retinopathy screening are higher and, as a result, we will provide a special camera for this application.

A.2.2. Color requirements. Fluorescein angiography (FA) and ICG angiography are imaged at a single wavelength and a monochrome imager is quite suitable for these applications. Virtually all other retinal imaging requires color. For example, in tumor treatment, the color of the tumor tells as to whether the specific area is calcified or is still growing. With glaucoma, the pallor of the disk is an important measure of the health of the disk. The consequence is that obtaining high quality color images is very important for all imaging modalities except the angiographies.

A.2.3. Angiography requirements. There are two generally used angiographies, flourescein and ICG. FA excites the dye at 480 nm and looks for fluorescence at 520 nm and ICG excites the dye at 790 nm and looks for fluorescence at 900 nm. Obtaining FA or ICG with the 3CCD is possible but, unfortunately, the currently available 3CCD's are fabricated with an IR blocking filter and are therefor not sensitive above 700 nm which is required for ICG. We have been unable to convince any of the manufacturers to supply a 3CCD without the IR blocking filter at this time but expect to get past this barrier in the future. In any case, it is likely that for angiography that the spatial resolution requirements will drive us to use a 1,024 square monochrome chip as opposed to the 3CCD and this will be discussed in detail below.

A.2.4. Field medicine needs. Laser pulses can generate very small damage spots. While these do not represent the direct loss of very much visual field, they can proceed to detachments. As a result, it is important to detect even the smaller ones.

Based on the slides provided to us by personnel at Brooks AFB, some of these smaller lesions are difficult to observe. As a result, high resolution is critical in this application. In fact, one should search for methods to make the smaller lesions stand out with greater contrast. Potential methods might include polarization imaging, differential color imaging,

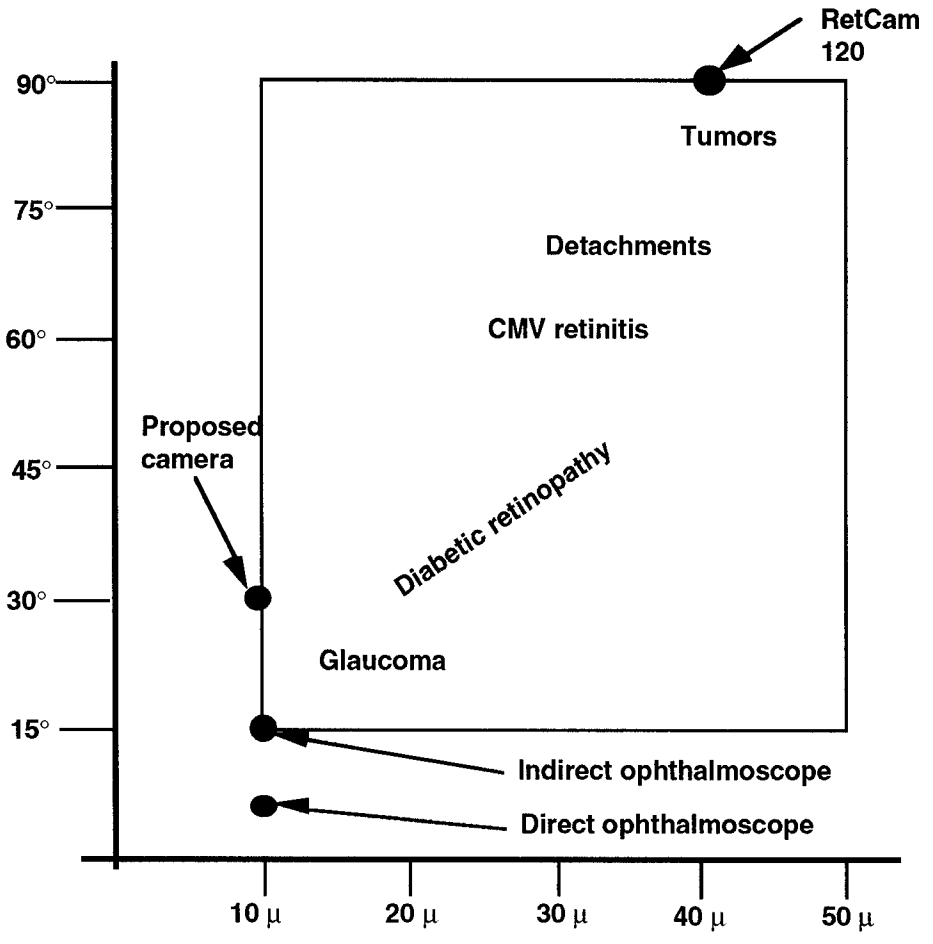


Fig. 3. FOV vs. resolution for various retinal pathologies.

and image processing. By differential color imaging we mean a concept where images are obtained at different colors and therefore different depths of the retina and then subtracted. From this "differential" image we may be able to catch the laser damages more easily but this concept needs further testing.

The inputs from personnel at Brooks are that we should consider that this modality of damage will only occur in the central visual field. This is taken to mean about 30 degrees in diameter with a little larger being desired. The counter to this is that laser damage could occur from a threat which came from a direction the soldier was not staring and that the lesion could occur in the mid-periphery and lead to retinal detachments. Note that at a glancing angle that the reflectivity of the light at the cornea increases dramatically and that the blur circle at the retina is increased so that the damage threshold will be increased.

Retinal detachments can be the result of physical trauma to the head. Physical blows to the head are a common experience in battlefield conditions and retinal detachments can result. However, detachments can be difficult to detect and it is likely that a skilled review of the image would be necessary in many instances.

Retinal bleeding from trauma to the eye or skull can occur at the disk or other locations.

Blunt traumas or penetrating wounds in most instances are so severe that imaging will not be a factor in the decision to transport. However, in some instances, there may be a foreign body lodged in the vitreous or retina and knowledge of this may be important.

Evaluation of the optical disk for hypertension or abnormal intracranial pressures is very critical and can represent a requirement for immediate medical intervention. The camera and its instant images could assist general medical personnel in making this determination or having it made for them through a Telemedicine consult with a general medical officer.

In the civilian use arena the hand-held retinal imager potentially can assist in evaluation of the optical disk for general medicine. For example, some ophthalmologists claim that general medical practitioners should evaluate the disks of their patients at risk for glaucoma. The generalists we have spoken with claim that this evaluation is difficult. If the camera were simple enough, inexpensive enough, perhaps general practitioners could become a more effective screener for early glaucoma.

A.2.5. Clinical medicine needs. Here it is important to recognize that the imaging must fit into the delivery of eye care, a process which involves clinical aspects other than the image of the retina. There are twenty-one items in a conventional eye exam as given by an optometrist. Primary among these in summary is visual system performance and correction and eye health. The retinal imaging is therefore an adjunct for evaluation of eye health. General medical practitioners are also concerned with eye health, visual acuity (but not refraction), and eye health as an indication of systemic problems.

A.3. Technical concepts.

A.3.1. Image quality and FOV for retinal imaging. There are various limiting factors for image quality and FOV and we discuss these in turn. Some of these are fundamental physical limits and cannot be circumvented, some are technology driven, and yet others are cost driven. We will conclude this section with a proposed imaging system selection based on our vision of acceptability of costs and clinical requirements and a potential optical system design.

Diffraction: This is the physical limit derived from the wavelength of the light, the focal length, and the pupil size. In Fig. 4 I draw a schematic cross section of a diffraction pattern from a circular aperture such as the eye pupil. The half width is given as shown and is a function of wavelength, focal length, and pupil size.

There are various ways to express resolution and various vendors use differing criteria and the purchaser of ophthalmic imaging equipment is frequently left without accurate and comparable information as to what can actually be expected in terms of image quality. A commonly quoted resolution criteria is the so-called Rayleigh limit and this occurs when two point sources are separated as shown in Fig. 5.

However, another method of portraying image quality is the modulation transfer function or MTF. A square wave of 100% modulation depth located at the object plane is examined at the image plane and its modulation depth is the MTF at that spatial frequency. If one selects the Rayleigh criteria as shown in Fig. 5 then the MTF at this resolution will only be 50%. Put in another way, the contrast will be low, and perhaps, in a system such as the eye where there are multiple sources for scattering and reduction of the effective MTF, the Rayleigh criteria is likely to be optimistic. As a result, we believe that two times the Rayleigh criteria is more realistic criteria as is depicted in Fig. 6.

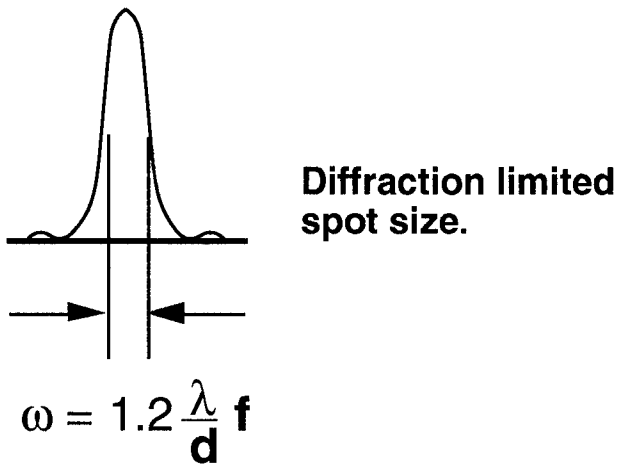


Fig. 4. Diffraction limited point spread function (PSF.)

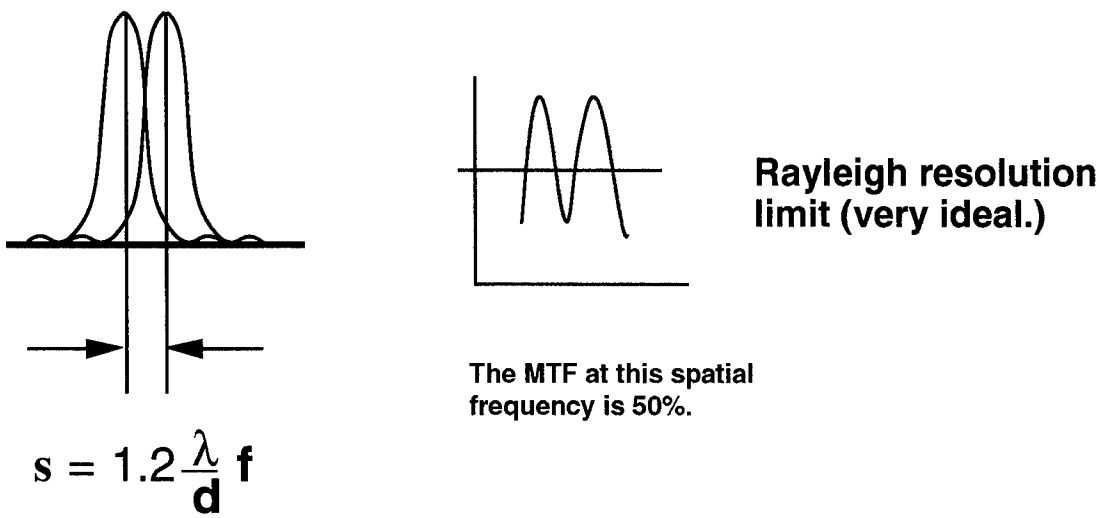


Fig. 5. Rayleigh resolution limit.

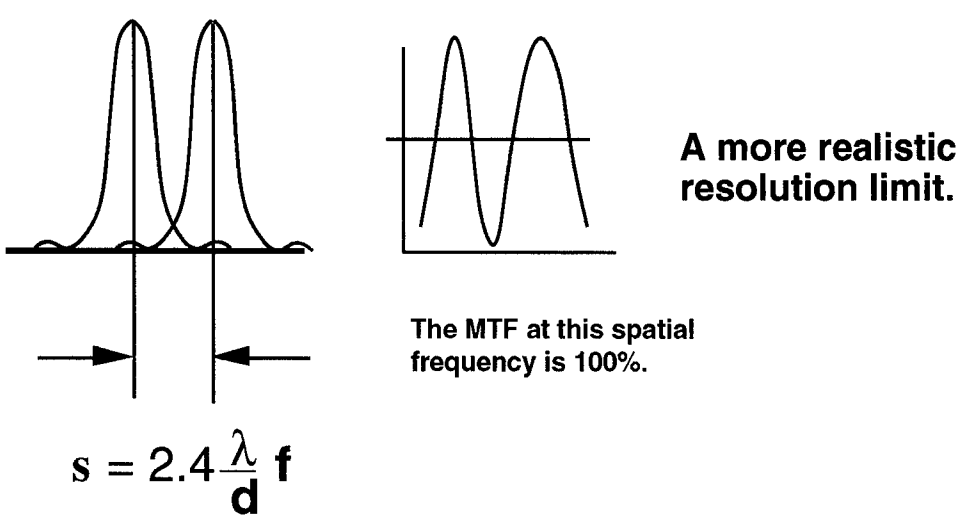


Fig. 6. A more realistic resolution criteria is where the MTF is essentially 100% without considerations of scattering.

A decision has to be made as to the pupil size to use for resolution calculations. For non-mydriatic, we assume a 3 mm iris opening and for mydriatic we assume a 6 mm iris opening. The iris diameter has to accommodate a ring of light entering the eye about the periphery of the pupil and this ring is the illumination light. We allow the ring to be 1 mm in width and this leaves a 1 mm entrance pupil for the imaging system. For the mydriatic camera, a 3 mm optical system pupil would be realistic. The numerical results for diffraction limit at the mid-wavelength of 600 nm and for non-mydriatic and mydriatic cameras are shown in Fig. 7.

f = 2 cm $\lambda = 0.6\ \mu$

	Optical system entrance pupil size		
	1 mm	**2 mm**	**3 mm**
ω	**14.4 μ**	**7.2 μ**	**4.8 μ**
Rayleigh limit	**14.4 μ**	**7.2 μ**	**4.8 μ**
More realistic	**28.8 μ**	**14.4 μ**	**9.6 μ**
	Non-mydriatic camera.		**Mydriatic camera.**

Fig. 7. Diffraction limited optical resolution for potential pupil sizes typical of non-mydriatic cameras.

The Nyquist sampling theorem then says that the highest sampling frequency the resels should be the order of 7 to 14 microns across for the non-mydriatic camera depending on your level of optimism. (This is based on a Nyquist sampling of two times.)

Geometrical optics: The eye lens is not a perfect imaging system and has substantial variations in size and optical properties, all of which vary with age. As a result, one designs the optical system based on a model eye and attempts to make guesses as to how the eye will vary between individuals and design the optical system to be as tolerant as possible.

We have evaluated the image resolution reduction sourced from astigmatism in the cornea and lack of perfect focus of the camera, sometimes caused by inadvertent accommodation of the subject or changes in the distance between the camera and the patient or lack of operator skill. These results are shown in Fig. 8 and 9 and can be summarized thusly:

A quarter of Diopter of focal error decreases the MTF times 0.70.

A quarter of Diopter of astigmatic error decreases the MTF times 0.80.

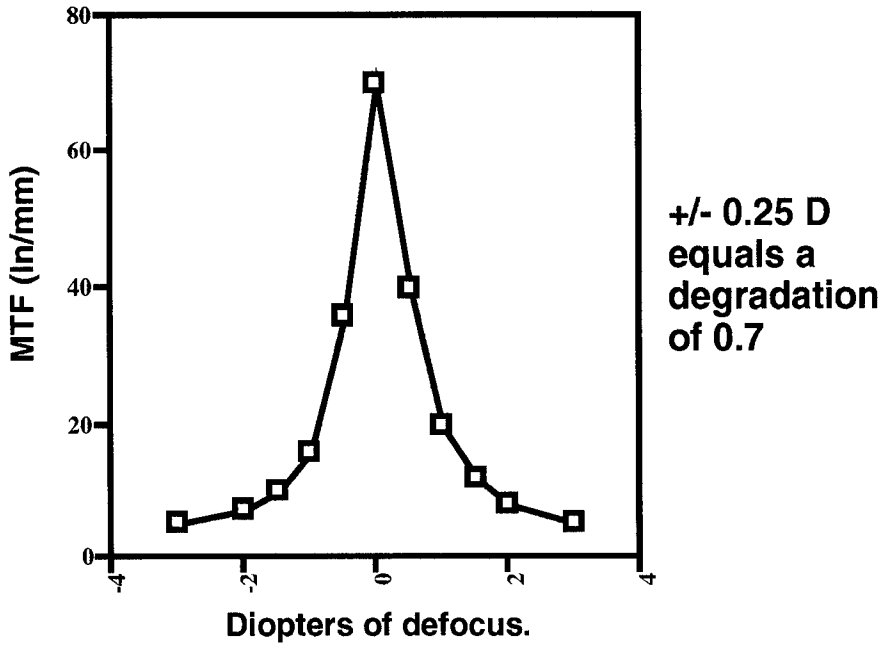


Fig. 8. MTF reduction vs. focal error.

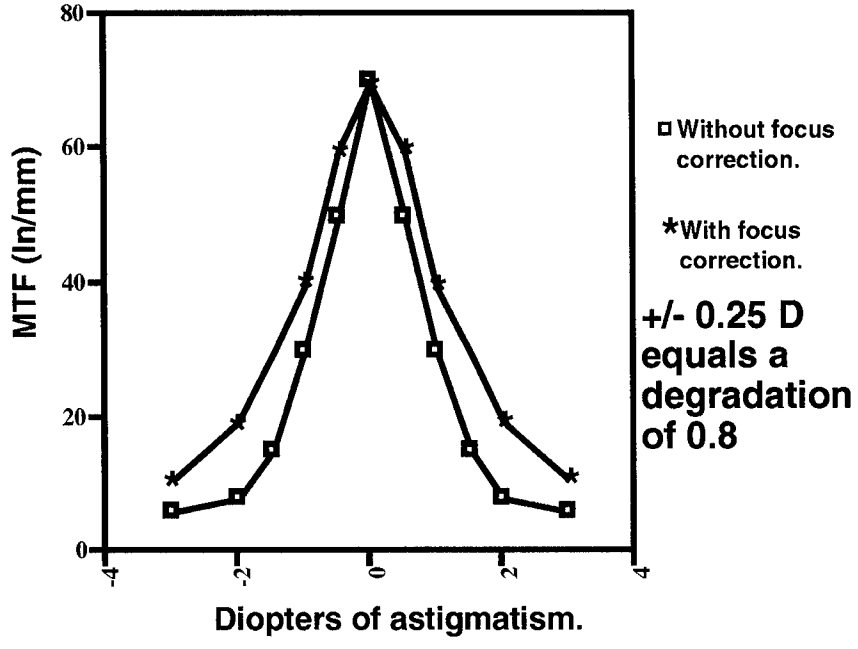


Fig. 9. MTF reduction for astigmatic error with and without focal correction.

It is unlikely that a typical operator will focus or correct astigmatism (when and if the capability is provided) by better than this so we are of the belief that the MTF given by the calculations herein will be reduced by a factor of (0.7)(0.8) or 0.56. In discussions with several professional retinal photographers they noted that the Zeiss camera produces the best images and that the Zeiss has the best astigmatism adjustment. Some retinal cameras either do not have an astigmatism adjustment or can only adjust astigmatism in large steps.

We have performed a calculation of geometrical blur circle up to 60 degrees for an ideal model eye and this is shown in Fig. 10. This plot is for the rms blur circle diameter without the corrections that we may be able to achieve using the external optics. This is the blur circle diameter as the un-aided eye would produce. The eye is nearly diffraction limited on axis for small pupils. The cross lines indicate the result at the typical 30 degree retinal camera. How well we can do with external optics is limited because of the variation in eyes and in the Phase II program this issue will be extensively studied.

Other geometrical optical errors occur when the optical axis of the subjects eye and that of the camera are laterally displaced or if the distance between the camera and the eye is not proper with the sum total conclusion that even with the best of optical system designs one will not obtain the theoretical resolutions on a routine basis.

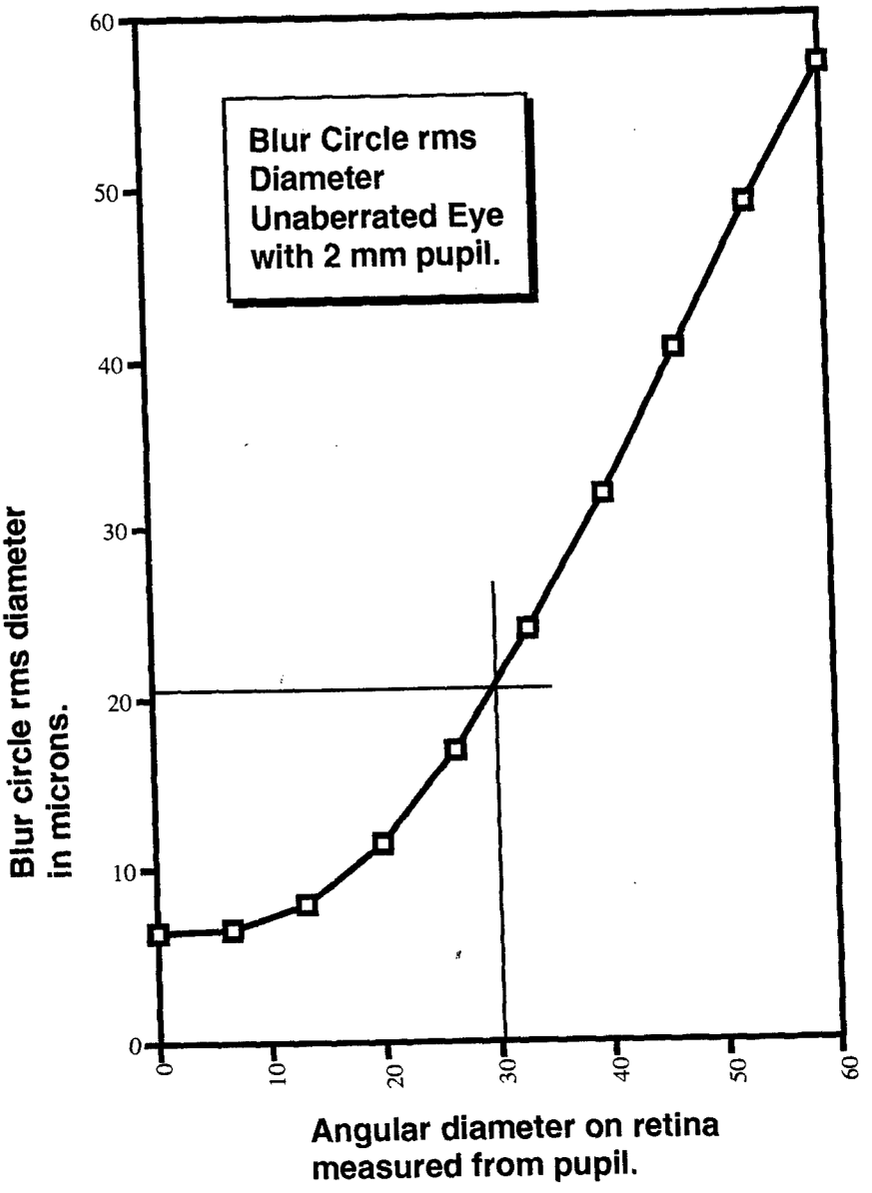


Fig. 10. Geometrical blur circle for model eye without external optical correction.

Field distortion: The mapping of the object onto the image may not be geometrically perfect. This is a major challenge for wide-field imaging but should be of little consequence for these cameras. In our wide-field camera, we have been able to reduce field distortion to below 10% at the edge of the field.

Color: Some objects require color for assessment and there are chromatic aberrations in the eye. In fact, the brain uses the lateral chromatic aberrations to assist in many optical functions. It is necessary to correct the color aberrations in the eye using external optics.

While color is important much of the information for the retina is in the red (However, red free images are used to obtain high contrast images of the nerve fiber layer for glaucoma and different wavelengths can emphasize different layers in the retina.) In experiments conducted here with our own wide-field camera, we truncated the digitization from 8 bits per color to 4. Since most of the color was located around a narrow range in the reds, the image took on a washed out blotchy nature and was considered clinically unacceptable.

To this end we will only consider the use of three-chip or 3CCD cameras. In a conventional CCD, a mask is placed over the chip which has a color filter pattern as shown in Fig. 11. Generally, the mask is organized to emphasize the green portion of the spectrum so that the resolution will not be cut times 0.33 but times 0.67 instead. Thus, the typical mask looks like this:

Green	Green	Red	Green	Green	Blue
Blue	Green	Green	Red	Green	Green
Green	Blue	Green	Green	Red	Green
Green	Green	Blue	Green	Green	Red

Fig. 11. Typical color mask pattern for color CCD imagers.

Note that only one pixel in six horizontally is red, so the red resolution is reduced by six times while the green resolution is only reduced by one third. This may be the best choice for typical TV schemes but it is a disaster for retinal imaging where red dominates.

A three chip camera uses a prism to split the light colors and to direct the colors to separate chips. Thus, at each and every resolution element there are three color measurements and there is no reduction in resolution at any of the colors as compared to the monochrome chip, as shown in Fig. 12.

Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue
Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue
Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue
Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue	Green Red Blue

Fig. 12. In the three chip CCD there is a red, green and blue measurement made at each resel.

For angiography, be it fluorescein or ICG, the wavelengths of emission are almost monochromatic. This will enhance the optical system resolution because the chromatic aberrations of the camera will not be relevant. A color imaging chip is not necessary. Also, a larger FOV is usually required, so to maintain high resolution from the CCD, a larger format single chip is used. Thus, for color, a 3CCD of 480 by 640 pixels is used with a total of about 1 megapixels of information. For angiographies, a 1,024 by 1,024 format monochrome chip is used, for about 1 megapixels of information.

Another challenge but one which is less glamorous is that of color control and matching throughout the system. The color balance of the CCD, its color control vs. light levels, the color temperature of the light source, the color quality of the monitor, and the printer, all conspire to make good color control challenging. The Company has extensive experience with dealing with this problem and has for example tested numerous monitors for their color and image quality. (The result is that there is a lot of variation.)

Dynamic range: Experimentally we have had satisfactory results with 8 bits of dynamic range. Note that many cameras and frame grabbers claim 8 bits of range when they do not actually achieve it. We however have a camera with a claimed 10 bits of dynamic range but the affordable and readily available RGB frame grabbers and processing software limit us to 8 bits at this time. The RGB output and frame grabbers will provide a higher quality image than that of NTSC.

A 10 bit system would be useful in that it would give the user more freedom in setting the light level. Also, it would be helpful if the system was smart enough to adjust the joules of light sent to the eye in real time for the best result. There is a difficulty however in displaying greater than 8 bits per color. These light level settings are challenging because the reflectivity of the retina tends to follow the reflectivity or coloration of the skin and hair and we have noted a factor of ten variation in the reflectivity of the retina and this corresponds to the open literature results as well. A system which automatically corrected for this would be of assistance to unskilled users and the extra bits of range reduce the accuracy to which this system must work. The higher dynamic range is also of assistance in eyes with a lot of scattering as will be discussed below.

Contrast: There is scattering in the eye and this lowers the image contrast. The scattering is a serious issue because of the low reflectivity of many retinas, around 1%. In fact, it is one of the objectives of the scanning laser ophthalmoscope (SLO) to circumvent the scattering by providing separate channels for the paths for the input and output light. In the design of our wide-field camera a great deal of practical knowledge has been obtained in obtaining high contrast retinal images. In fact, resolving the contrast or back-scatter/reflection issues were key to the success of the entire project. However, as the FOV narrows, many of the problems of reflections from the eye lens vanish.

However, electronic imaging provides other methods to reduce the effects of scatter. A cross-sectional profile of a retinal image with a lot of scattering is shown in Fig. 13 with a bias from scattering. The image on the right has the scattering bias removed. Even though we remove the bias we can not remove the noise of the bias which is the square root of the signal. Thus, this is not a perfect solution but a helpful one and one which could not be achieved with film. The improved contrast is an attractive feature of the scanning laser ophthalmoscope or SLO. However, the SLO suffers from high cost, large size, small FOV's, moving parts, and lack of convenient color imaging.

Motion blur: Seldom is the patient's eye perfectly motionless and the field portable system will be challenging to use due to motion of the camera itself as well. A motion of only microns during the image aperture time is sufficient to reduce image quality.

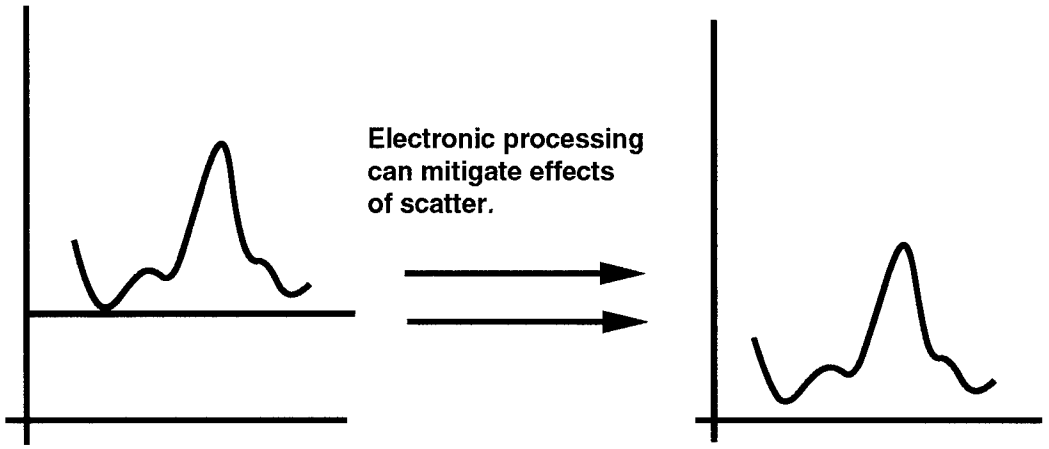


Fig. 13. Image profile with scattering and with scattering removed.

Unfortunately, current 3CCDs of the physical size required for these cameras work on the interlace process. This means that it requires two CCD captures/reads to obtain the image and since these are generally 17 milliseconds apart, one can suffer image blur. There is just now available a 3CCD which works in the progressive scan mode which avoids this problem. With this CCD, a very short flash will be used to freeze image motion. It is not yet available in a small physical size but we anticipate that it will be before the completion of the Phase II Program.

With a full frame sensor and a flashed lighting system there will be no practical issue with image blur. We note that this will be extremely critical for the hand-held device.

Light levels: We have experimented with imaging with our 3CCD in the red region above 600 nm but below 700 nm. Since the eye is of low sensitivity in this region, using a high light level is possible without patient discomfort. Since the camera has high sensitivity in the red, red light can be used for aligning and focusing to the desired portion of the retina and then a white flash can be used for the actual image acquisition. Since the red light reflects from a different layer of the eye than the rest of the light we may need a small longitudinal focal offset for the white light image. The current CCD has an ASA equivalent of 800 which compared to that of typically used film f 10, giving a eight times reduction in required light intensity.

Camera resel size: The camera resels when projected onto the eye are a finite size and this is the cost/technology limit to resolution. Currently, the best commercially available 3CCD cameras use a 480 by 640 element format. Empirically we have discovered a wide variation in sensitivity and especially in color quality between various vendors. Many 3CCD cameras are far too large physically, their size being the size of 10 inches long by 5 inches square. The 3CCDs that we feature in our current wide-field system are about 1.5 inches on a side and weigh the order of 1 oz.

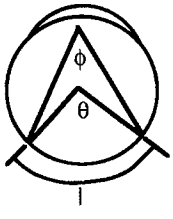
There is one 3CCD commercially available with a 1,200 by 1,500 format. The size for the head is about 5 inches on a side. It is thus too large and too heavy for the field camera. The current wholesale price is about $16,000 also placing it into the too expensive category. This camera may however be suitable for the high end clinical applications.

In the end, we believe that the 3CCD technology will improve each year concurrent with price reductions. We believe that there is a good chance that there will be an affordable 1,000 element square format 3CCD available in a small package at an affordable cost within

the next two years time frame. The designs herein will be able to accept this camera when it is available but the designs for Phase II described herein are based on the existing cameras until the larger format cameras are available.

Actually, the Company has the technical capability to build its own 3CCD camera at the larger format and may consider doing so. The barrier to this is not only the development costs but the manufacturing costs associated with limited quantities and the likelihood that a larger company will bring out the same 3CCD within the next two years and at a price which we cannot meet.

Before we discuss the trades of camera format, FOV, and resolution, we need to define angles as used in discussing retinal imaging. For historical reasons, retinal cameras are categorized by angular image width as measured from the iris or pupil of the eye. We prefer to work in terms of angular width as measured from the center of the eye as this is the natural angle to convert between the physical width of retinal features and the angle. In Fig. 14 we display these relationships and the ratio of the angles θ and φ is taken as approximately 0.7 to 1 and in Fig. 15 I show some numerical results for the sizes of various retinal features.



l (length along retina)
θ (angular extent measured from center of eye)
ϕ (angular extent measured from pupil)

Fig. 14. Relationship between the various angles in describing the eye and retinal imaging FOV.

Retina	**2.6 cm**
	235°
	176°
Disk	**0.1 cm**
	5.7°
	4.3°
Disk to fovea	**0.27 cm**
	15.5°
	11.6°

Fig. 15. Typical numbers for retinal features.

In Fig. 16 I show the FOV consequence for various selections of CCD chips and pixel size as projected onto the retina.

Format	Pixel size: 5 micron	10 micron	15 micron	40 micron
500 x 700	0.25 x 0.35 cm 14° x 20° 10° x 15°	0.50 x 0.70 cm 28° x 40° 20° x 30°	0.75 x 1.05 cm 42° x 60° 30° x 45°	2.0 x 2.8 cm 112° x 160° 80° x 120°
1,024 x 1,024	0.51 cm 29° 22°	1.02 cm 58° 44°	1.53 cm 87° 66°	4.08 cm 232° 176°

Fig. 16. Camera resolution and FOV options.

Note that the 10 micron pixel size gives an excellent FOV of 20 by 30 degrees and is close to the practical resolution limits discussed above. For the clinical camera, a switchable FOV between 14 by 20 degrees at 5 microns resolution and 30 by 45 degrees at 15 microns resolution would be a likely choice. For the angiographies, it is likely that a FOV of 44 degrees would be desired and this would give a resolution of 10 microns, likely to be quite sufficient. For example, Kaiser Permanente is conducting a clinical trial to determine if a resolution of 20 microns would be sufficient.

Another significant limit to FOV is the optical system. Consider that for a 30 degree FOV (as measured in the eye at the pupil) that the rays exit the eye at about 45 degrees due to the difference in refractive index between the eye and air. This means that the first lens of the optical system will have to have a diameter at a working distance of 3 cm (to just barely clear the nose) of 3 cm. That is, its diameter is equal to the distance from the eye. Larger FOV's require yet larger lens, and these are difficult and costly to fabricate and make the camera large and this is not likely to be applicable to the hand-held unit.

A.3.2. Quality imaging in practice. The major problems with conventional retinal digital imaging cameras are resolution and contrast. While many have noted the limitations of the resolution of the CCD we believe that blaming the CCD format for lack of resolution has frequently been a false conclusion. Certainly, when the retinal images of our wide-field camera are zoomed into on the screen, pixels are observed. However, if the image was "depixelated" or blurred slightly, one would not notice the pixels. The question remains as to would more pixels equal more resolution.

We have had the opportunity to discuss this with a number of high-end professional retinal imaging technicians. These persons are very professional in their approach, are certified, and run large imaging departments. In one instance, the individual supervises a department where 150,000 images are obtained each year.

The common thread from them was that the Zeiss retinal camera gave the best images and that even using the Zeiss requires a lot of care to get good images. It was necessary, as our calculations suggested, to be very careful to remove the astigmatic errors of the eye with the camera and to be very careful with alignment. We note that some retinal cameras do not even provide astigmatic correction capability, or if so, then only in large steps. In these instances, we question as to the limitations from the CCD or from the camera optical system and the capability of the user.

Our first thesis is that in practice the resolution of the images obtained on a routine basis is limited by the existing cameras and users abilities and not that of the CCD format. For the clinical camera, it is a major objective to make the camera easier to align and to provide astigmatic correction and to make this easy to use.

Another support for this view is that doctors have been extremely pleased with the resolution of our camera. It only has a 480 by 640 imager with 3CCD and the pixels are 40 microns in size, much larger because of the wide-field. However, the camera has a large depth of focus, making it almost impossible to acquire out of focus images, and since the camera touches the cornea, the optical aberrations of the cornea are essentially eliminated, thus supporting the view that technique and camera optics and not the CCD pixel count are the routine limit to clinically useful resolution.

The second major in-practice issue for image quality is that of contrast. The eye lens scatters and reflects light as does the media. Here is where the scanning laser ophthalmoscope has an advantage. However, high contrast images are obtained with our wide-field camera and wide-field imaging is especially subject to such limitations.

The key here is very careful attention to details in the optical system and the eye as to where the sources of scattering are and how to eliminate them. For example, for our wide-field camera we have developed a very special coating for the edge of the lens and the lens barrels. Simply painting these black will not suffice. Many so-called black paints are actually quite shiny when viewed on edge. We have a paint which contains special dyes which absorb the light for example.

The optical system must place the entrance pupil at the eye lens. Then, to at least first order, the reflections from the eye lens will not re-direct light into the camera. Attention must be placed to extraneous scatterings then from the iris, etc. Computer processing can also improve the image contrast. In the end, a carefully designed system can routinely obtain images of high contrast at all but the very most stressing requirements and eyes and a very low cost and small size as well and in color.

A.3.3. Design concepts for retinal and corneal imaging. A first challenge of this program is to produce a hand-held retinal imager for field use, and in particular to asses laser damage to the retina at the MASH unit level. There are challenges of every nature to achieve this, not the least of which is acceptance of the concept.

Perhaps the greatest is how to align and use the camera in a tense setting. To this end, we have studied the reasons as to why the existing cameras are considered difficult to use. In particular, we find that they are hard to align. Resting the hand-held unit against the forehead as opposed to placing the patients head in a rest (chin and forehead) is useful but difficult. Second, it is difficult to asses the image because in general the images are obtained on film and the final result is not known until the patient is long gone.

Two features of our concept are then key: an optical system which will allow the medic to visualize the cornea as seen by the camera and in real-time to ease the alignment problem

and a digital imaging system which will instantly display the retinal image for quality assessment. Further, a great deal of ergonomic work must be performed to assure the cameras pivots, control functions, etc. are designed for ease of use.

While resolving all of these issues will be central to the success of the program, it is actually in the clinical unit that the program will really begin. The clinical unit will have the optical system of the field unit and other optical systems as well,but it is in the clinical unit where the alignment can be tested quantitatively that we can accurately test our concepts. As a result, we will discuss its design in detail and will therefore reveal the design for the field unit as a subset.

I will discuss the clinical unit in detail first since within it are all of the technical issues for both cameras. The clinical unit is challenged to image the cornea, provide binocular corneal imaging as does the slit-lamp, provide the slit-lamp itself, and provide imaging of the retina. This is challenging to accomplish in a single package. In essence, we are providing the clinician with everything he has traditionally done with the slit-lamp type imaging system and we are providing him digital imaging capability of both the retina and cornea as well and in a package no larger than his current envelope. The hand-held unit will contain a subset of these features which only include the retinal and corneal imaging.

In summary, the clinical system will provide:

Binocular visual (through the eyepiece) images of the cornea.

All other features traditionally provided through a slit-lamp biomicroscope such as Goldmann tonometry, Hruby lens, etc.

Digital imaging of the cornea.

Digital imaging of the retina without mydriatic drops, with a 30 degree FOV, and in high-resolution color.

The retinal imaging system will be equipped to provide near-simultaneous imaging of the cornea as an aid for alignment and focal and astigmatic aberration correction. An artist's concept of the clinical imager used for corneal imaging is shown in Fig. 17 and for retinal imaging in Fig. 18. Similar drawings for the hand-held unit for corneal imaging is shown in Fig. 19 and for retinal imaging in Fig. 20.

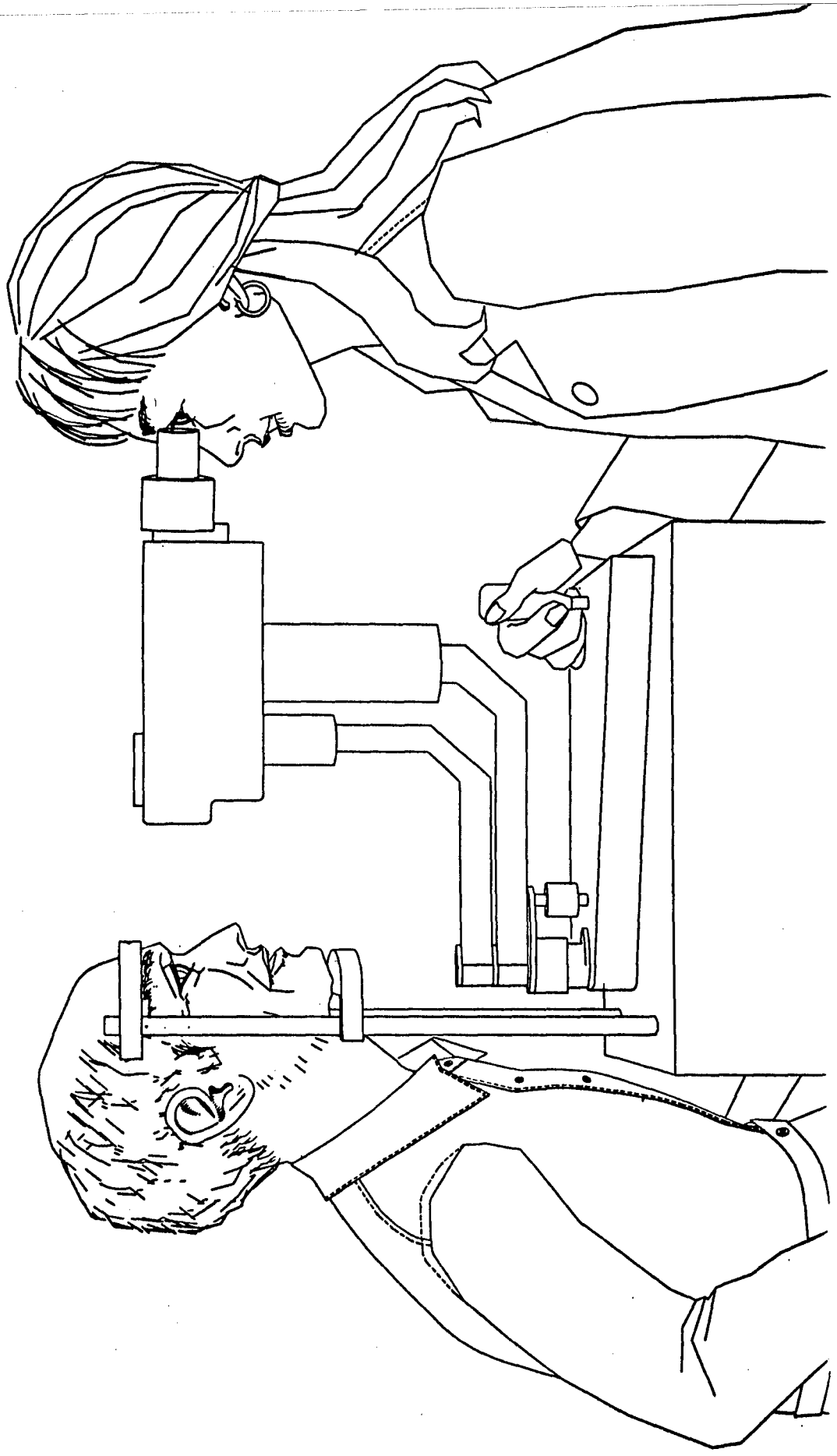


***Figure 17. Artists concept of clinical unit being used for corneal imaging.** Proprietary Information: Use or disclosure of the proposal data in the figure of this page is subject to the restriction on the cover page of this proposal.

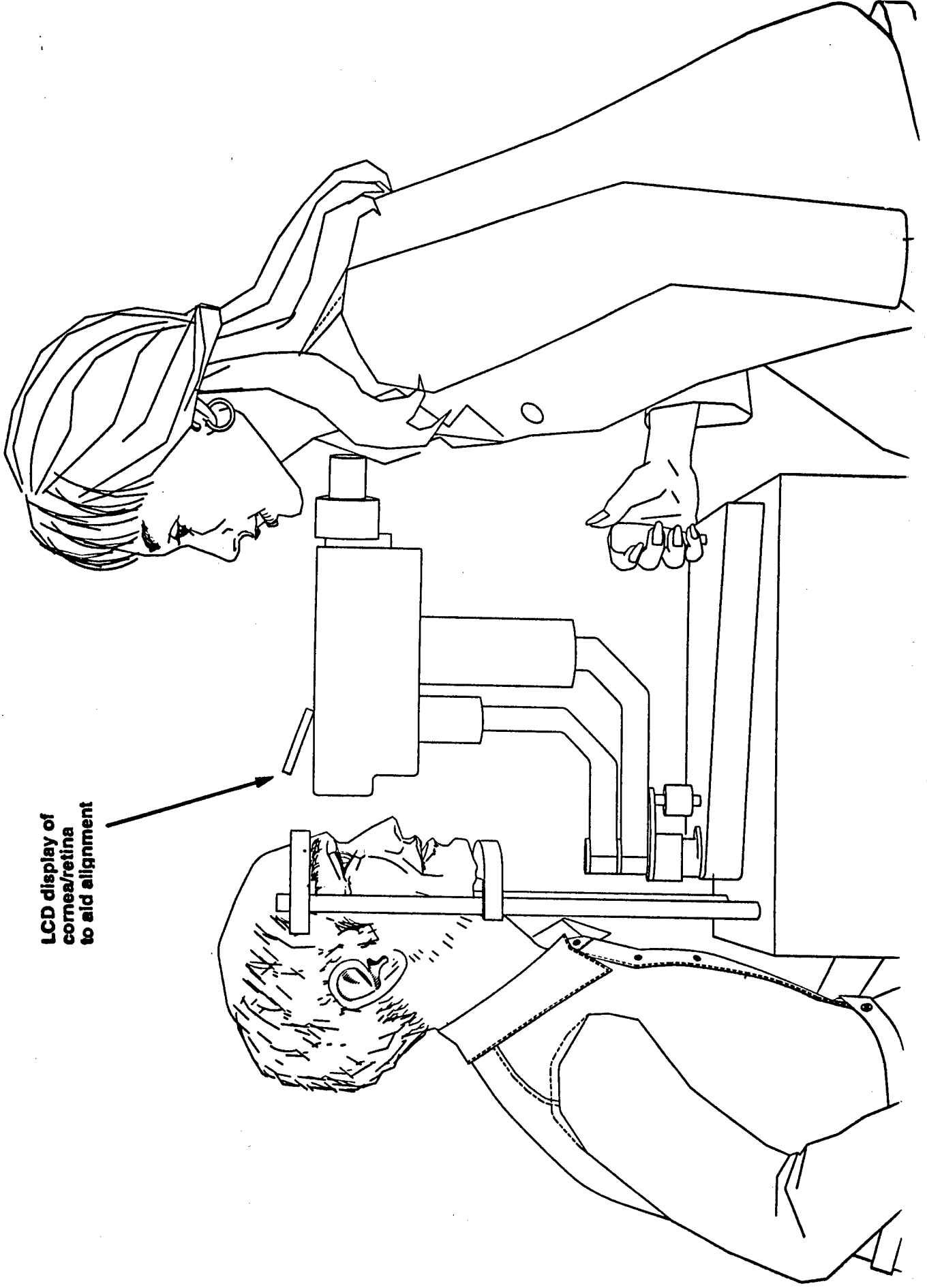


***Figure 18. Artists concept of clinical unit being used for retinal imaging.** Proprietary Information: Use or disclosure of the proposal data in the figure of this page is subject to the restriction on the cover page of this proposal.

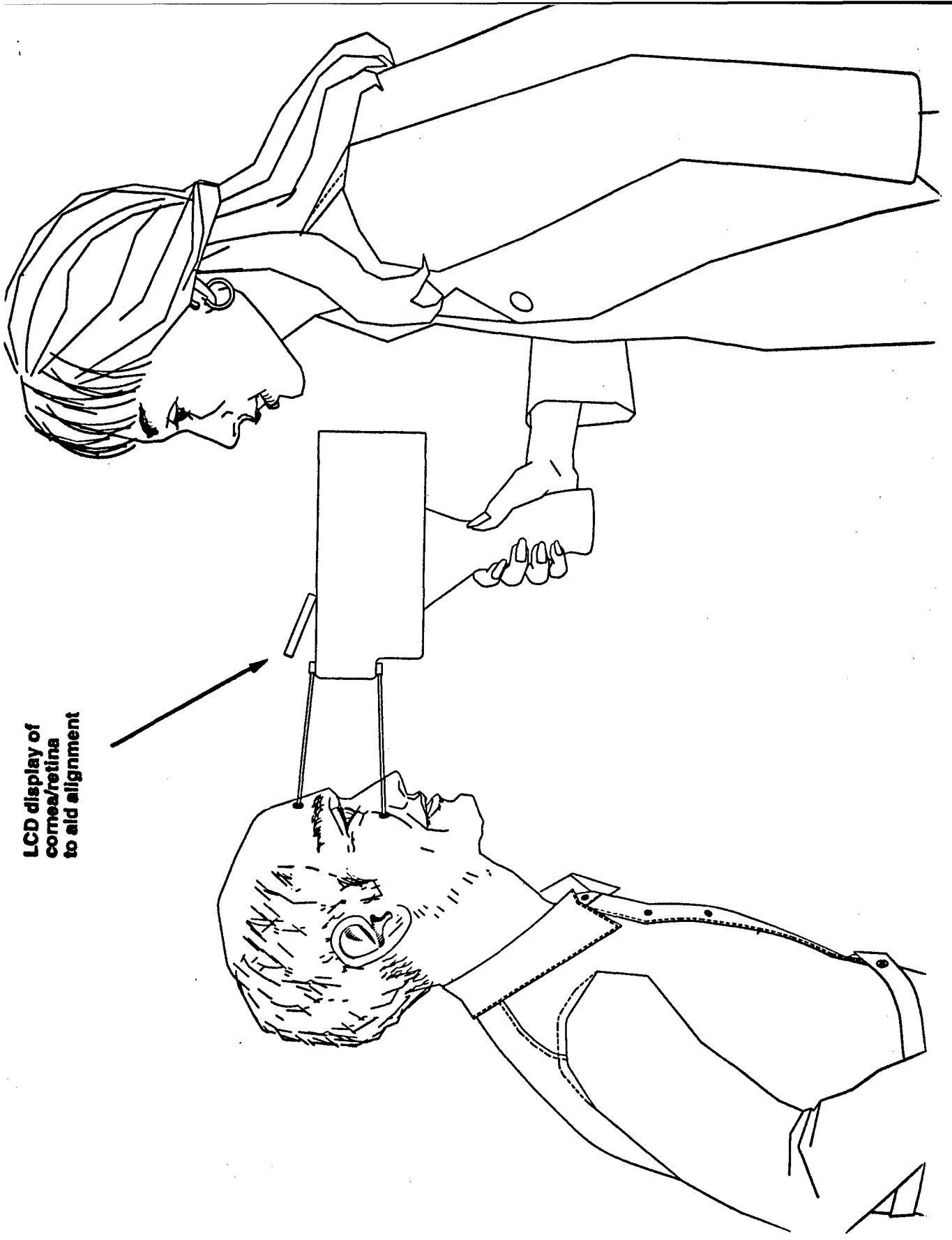


***Figure 19. Artists concept of hand-held unit being used for corneal imaging.**

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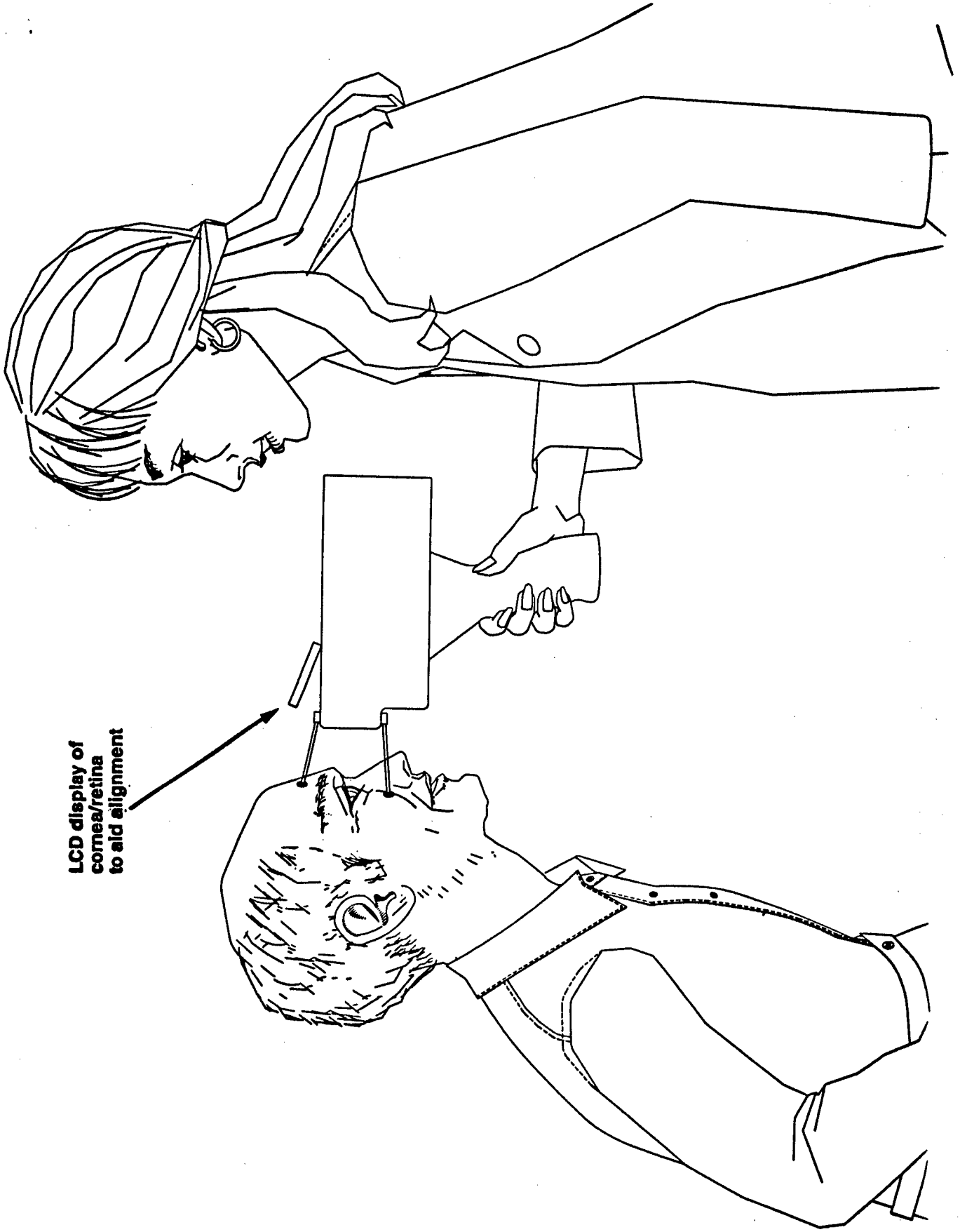

***Figure 20. Artists concept of hand-held unit being used for retinal imaging.**

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*A candidate optical system to achieve this is shown in Fig. 21. The patient's eye is designated as E1 and is meant to represent either the cornea and retina as object planes. The eyes of the clinician are noted as E2 and E3. The image of the cornea is visible at both E2 and E3 through the eye lens of the optical system, L6 and L7. A high eye point will be provided to allow the clinician to wear his or her eye glasses.

*A key feature of this optical design is the use of the so-called "landscape" lens as the objective lens, L1, which is used for both corneal and retinal imaging. The lens L1 is placed at a distance of approximately 3 cm for retinal imaging and entire apparatus is slid back for corneal imaging to a traditional distance of 8 cm. Because the entrance pupil of the entire system has to be located at the eye lens of the patient, the choice of the "landscape" lens helps in reducing the aberrations. As mentioned before, the diameter of the lens L1 is almost equal to the distance between the patient's eye and the lens. To image the retina, the focal length of the lens L1 has to be equal to that distance too. The result is a lens with a relative aperture of F/1 which is very difficult to design and manufacture. Furthermore, in order to decrease the scattering from the multiple optical surfaces, the number of lenses used between the L1 and the optical fiber must be minimized. It would be best if only one lens were to be used. We currently have three concepts for the lens design: a conventional multi-element design with emphasis on advanced AR coatings; a double aspheric lens design; and a spherical lens designed using gradient index glass.

*In the traditional slit lamp, two objective lenses are used. In our design, with the use of the "landscape" lens, an intermediate image is formed on the field stop S4. This image is then re-imaged by two subsequent lens systems beginning with apertures S5 and S6 for binocular imaging of the cornea. Due to this additional re-imaging stage, instead of using four Porro prisms as it is used in the traditional slit lamp, four simple mirrors M2, M3, M4, M5 will be used to redirect the image. The inverted telephoto type of lens will be used for L4 and L5 to achieve longer back focus length and balance the achromatic aberration. The lens L6 and L7 will be commercially available eyepieces to reduce the cost.

*For viewing the cornea through the CCD camera, the mirror M1 is moved into place to direct light to the CCD. Two different magnifications will be provided for both binocular and CCD viewing by sliding a meniscus lens in behind the lens L1. The lens L3 is used to compensate the chromatic aberration of lens L1 and re-image the intermediate image onto the CCD at the right size. The focusing of the image at the CCD is done by moving lens L3 along its axis. The use of 3 chip-CCD camera and the insertion of **beamsplitter BS1** demands a long focus length for L3. In addition, the aperture stop of the system, S3, has to be located about 2.5 cm in the front of lens L3 for easy installation of an illumination system for retinal imaging. These requirements can be accomplished with either an inverted telephoto or telecentric lens design. The illumination of the cornea is by mean not shown, but is traditionally through a slit lamp.

*For retinal imaging, the mirror L1 is held in place and initially, lens L2 is also moved into the beam train. This will provide an image of the cornea on the CCD and the illumination will be in the deep red to prevent an adaptive response of the patients iris. This retinal image will not be of the highest quality but will be of sufficient quality for alignment. This image will be displayed on the top of the retinal camera as shown below. By this means, the clinician can focus his eyes on the patients eyes and can also focus on the cameras image of the cornea as shown on the LCD to ascertain alignment.

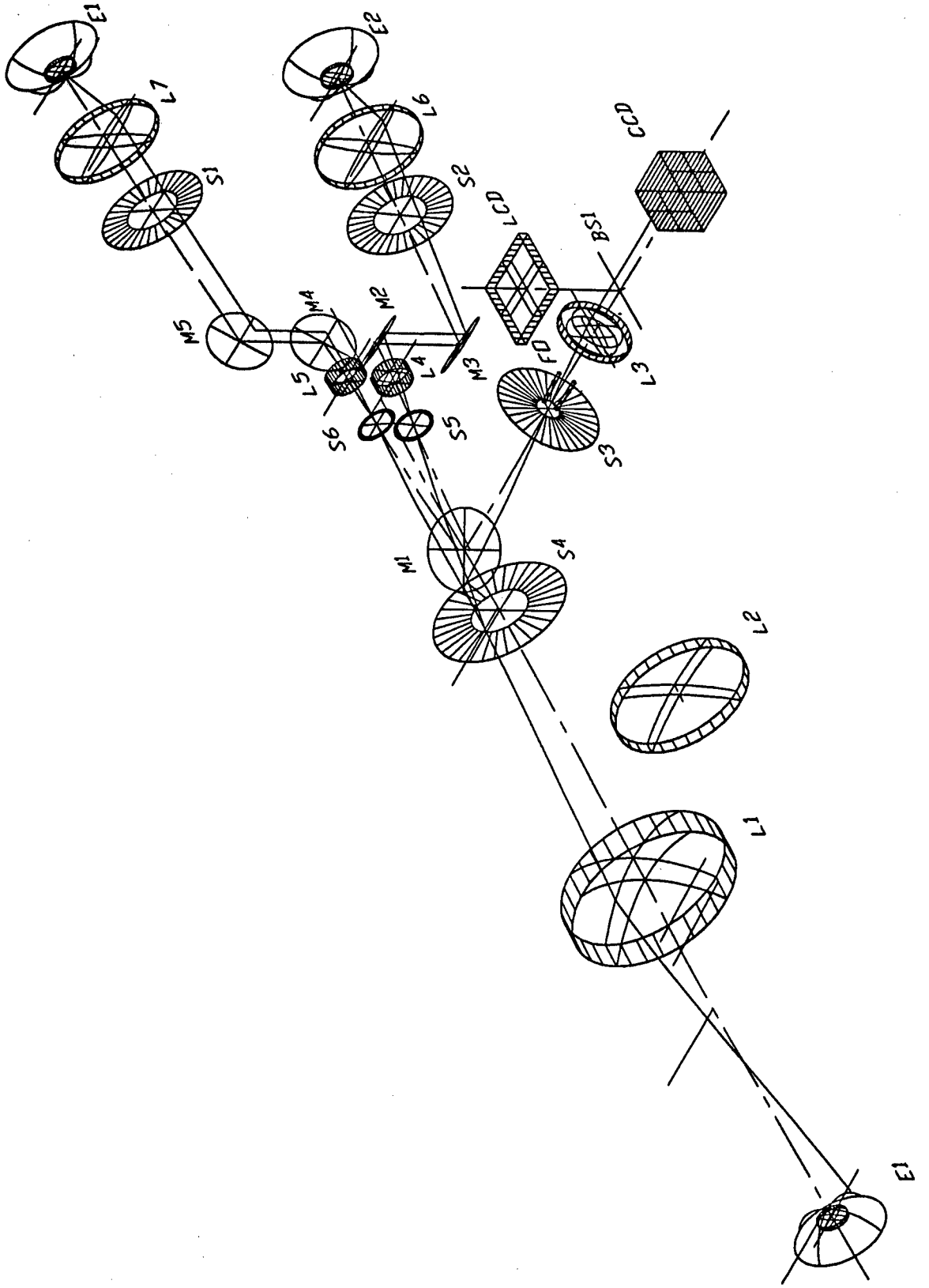

***Figure 21. Optical system for clinical unit.**
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*When the image of the retina is to be obtained the lens L2 is moved out of the beam train and the fiber optics labeled FO are illuminated with red light. The LCD display shows this deep red image and the clinician can now verify that the system is aligned and focused. We will separately discuss how the astigmatic error can be corrected.

*Finally, the clinician presses the image acquire button and a flash of white light is provided through the fibers to image the retina. The image is immediately displayed on a high-resolution monitor and can be evaluated for quality and appropriateness.

*A single 5 watt Halogen bulb can drive the imaging requirements and the slit-lamp. The previous use of very high joule strobes for retinal imaging was related to requirements for flourescein angiography, the use of film, and low-efficiency light collection and delivery systems.

*The system has numerous aperture stops labeled S1 through S2 and these are necessary for properly blocking unwanted light. The liquid crystal display (LCD) is labeled LCD. The LCD is back lit and has the important property that its transmission is programmable. That is, one can put a single point fixation light for the patient, can vary its intensity and location to do a modest central field perimetry, or can project various symbols to ascertain visual acuity. Also, for children, a dynamic object could be programed to keep their attention.

*Not shown in this beginning design is the astigmatic sensing and correction devices. In the location now occupied by lens L3 one would place a pair of cylindrical lens. Their spacing could be varied to vary the astigmatic power and then could be rotated to control the angle. The more serious problem to obtain a signal for the clinician to use to close the loop. There are several methods for this but for example we consider here the use of a single point source provided by programming at the LCD.

*At the best focus, an uncorrected astigmatism will provide a point spread function (PSF) which has the shape of a cross. Better that a solenoid is used to move the CCD to one side of focus where the astigmatism appears as an ellipse. The astigmatism correction system could then be turned to be best angle and the correction could be determined by that which makes the spot size the correct diameter as would be indicated on the display by the computer. Undoubtedly, a great deal of experimental evaluation of various schemes would be necessary because of the vagaries of working with real eyes and clinicians with minimal skills. The portable or hand held system would not have astigmatic correction because of the size and complexity of use associated with field use.

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A.4. Markets and marketing.

A.4.1. Obtaining adoption. Many new technologies, including those which have been extremely successful in the long term, have had difficulty with initial acceptance. Classic examples of this are the Xerox machine (will only be used by a few accountants) and the transistor (perhaps useful for hearing aids.) Obtaining acceptance for our new technology, and in particular, the new paradigm of delivering eye health care presented with this technology, will be a significant challenge and one which requires substantial calendar time.

The program would benefit greatly by obtaining an early "buy-in" by thought leaders in each of the key markets. For example, as discussed below, we have visited with leaders from large medical providers and the military. These individuals have agreed to participate in the specification, design, clinical testing, and adoption of this technology from its very inception. By the time the technology is on the market, they will have had time to sell their individual organizations.

In particular, we have asked these individuals the following question: Consider that we have the funding from the Army contract and our own funds to develop an advanced camera. How would the camera have to perform and at what price point for you to aggressively recommend its use to your organization.

The inputs from these individuals have been significant in selection of the performance and design requirements of the cameras of this report and proposal. Further, the organizations and individuals as discussed below have agreed to spend significant effort to test, evaluate, and demonstrate the cameras and to recommend to us how the cameras should be modified and configured for wide acceptance.

A.4.2. Military Telemedicine. Military Telemedicine will support eye care at remote sites, dependent care, ships, and battlefields. We have visited with a number of military medical officers who have expressed interest and opinions on the camera, its use in the military, and all have expressed an interest in supporting its development and testing.

We meet with twelve ophthalmologists at the Naval Medical Center San Diego. Our contacts there are Commander Peter H. Custis, M.D., Director, Vitreoretinal Service and Captain Russ Edwards, M.D., Co-Chair Telemedicine Working Group, Naval Medical Center, San Diego. Dr. Custis has recently been appointed Specialty Leader for Navy Ophthalmology to the Surgeon General. Both individuals have expressed an interest in conducting testing of the camera.

We meet with several M.D.'s at the recent Global Forum for Telemedicine at W.D.C. Included were Commander Forest Faison, M.D., and Scot Bower, M.D., U.S. Army of MATMO.

We also meet with Lt. Col., USAF, MC, FS, David K. Scales, M.D., Director, Ophthalmic Research, U.S. Army Medical Research Detachment, Walter Reed Army Institute for Research and currently stationed at Brooks AFB.

The picture which emerged is this: The cost of EVAC is enormous. There have been examples of costs exceeding $200K. At least 10% of the injuries are to the eye. The Navy puts medical officers on boats who have only completed Internship training. These officers may have no more than six weeks of ER training. They would be more grateful for Telemedicine than one would expect from physicians who have completed Residency training.

Not only is EVAC from the ships expensive, but EVAC from places such as Diego Garcia are expensive and difficult to judge the necessity of. On Navy missions which are classified, it may not be possible to EVAC but communication is possible.

Dependent care around the world is quite expensive. In many instances, great sums of money are expended to fly dependents from remote sites for evaluation and treatment.

A.4.3. Large organizations. We are holding discussions with both Kaiser Permanente (Dr. Berry Linder, M.D., Director Telemedicine, Oakland, CA) and Mayo

Clinic (Kevin E. Bennet, Strategic Alliances, Mayo Foundation, Rochester, Minnesota) for joint efforts to define clinical requirements, new paradigms for delivering eye health care, and utility testing of the cameras when completed.

Both institutions are greatly concerned with reduction of costs. For example, Kasier is currently testing Telemedicine for screening for diabetic retinopathy. They are using an OIS 1,024 imager with another retinal camera to verify that sufficient resolution will be available. Mayo Clinic has developed a diabetic management data base. We are in discussion with them as to how the data base would be modified to include retinal images.

Both institutions feel that the high cost of digital retinal imagers is a significant barrier to use. Both would like to move the retinal imaging to the medical clinics as opposed to the ophthalmic clinics. This of course pre-supposes that the cameras are sufficiently easy to use so that specially trained technicians would not be required to obtain good images.

B. Phase II Technical Objectives and Approach.

B.1. Basic program objectives: The objectives of this program primarily represent achieving improvements in functionality as opposed to basic technical capability. By this we mean that imaging of the retina is well established in an upscale clinical setting. This imaging is however accompanied by high capital equipment and operational costs, requirements for high skill levels, and is not "field portable" nor "Telemedicine ready."

What is not available and what is critically impeding a higher level of clinical care is imaging at an affordable cost, in remote locations, in the battlefield, and all of this using low-skill level personnel. Thus, the fundamental objectives of the program include achieving a large improvement in the functionality of retinal imaging. This will be achieved through:

Lower capital equipment costs.

Lower costs of operations.

Greater ease of use and use by individuals of lower skill levels.

Field portable imaging.

Integration of retinal imaging into ordinary and everyday clinical practice and with enhanced clinical features.

Subject to the particular application, the imager will perform additional functions such as corneal imaging, general medical imaging for wounds and dermatology, and ENT imaging.

Enhanced clinical utility.

All of this is to be designed with Telemedicine as a primary objective.

More specifically, we seek:

Capital equipment cost reduction: A factor of two to four reduction in capital equipment cost is being sought.

Ease of use: A substantial factor of improvement in ease of use is sought so that the requirement for a specially trained "Certified Ophthalmic Technician" will be a thing of the past.

Fully digital: The system will be designed from the beginning to be digital to eliminate the rather high operating costs associated with film systems.

Functional availability: By this we mean new designs so that the function of retinal imaging will be available in new venues. In particular, we seek to bring retinal imaging into the optometrists office on a routine basis and into the battlefield MASH units.

Enhanced clinical utility: This unit will hopefully provide improved diagnostic information, for example glaucoma. We select glaucoma because it is especially difficult to diagnose in its early phases. In this respect we seek enhanced stereo imaging of the optical disk. Another objective will be a means to detect laser damage through perhaps enhanced contrast by multiple wavelength differential images.

Multiple modalities in a single unit: The basic and most expensive elements of a system are the high-performance CCD, the light control box, and the digitization system including the computer, CD image storage, and the display and communication system. With these expenses covered one now naturally asks as to how the investment can be leveraged for enhanced return. The result is that a great deal of cost-effective value can be added by also making available various lens sets to image:

The retina.

The cornea.

The skin and various wounds and superficial infections.

The ear, nose, and throat and possibly the colon.

Perhaps other digitizing equipment should be made available such as a digital stethoscope, etc.

The initial program will not provide the resources to develop all of these imaging modalities at first. However, it will be possible to design the basic system so that they could be efficiently added to them at a later date. For example, the Company now has the ability to acquire ultrasound images into its current data archival system for the wide-field retinal camera.

Achieving all of these goals simultaneously will be technically stressing but is the basic challenge of this program. For example, obtaining digital images is stressing and costly but simultaneously obtaining them in a hand-held unit and at a lower cost is an even more stressing objective.

The objectives as enumerated above will shape the program in a fundamental way. It is not sufficient to simply design and fabricate a piece of imaging equipment. Achieving the goal of "ease of use" will require a lot of user testing. Achieving this goal and at low cost will require multiple re-design cycles, each one aimed at reducing parts count, using less expensive lens, etc. This is one of the reasons for the design/test looping in the program plan; that is, we will first build a bread-board system to demonstrate the basic principles on co-operative patients, then a first version operating system which will be subjected to a lot

of clinical testing, and then a second operating version which will essentially be the Beta site system, etc.

As an example of this type of design with testing and then modifications, our current wide-field camera has been through three complete design revisions, about 50 imaging sessions at six major medical centers, and we are now actually ready for the "real" usability testing. It is expected that this summer, after our first eight clinical centers are in full use, to make a round-robin with them to identify all of the "usability" issues and then stabilize the design for the larger production runs.

In the Phase I program we have identified the basic design and this process has lead us to recognize that there should be two cameras (but with the same basic imager within) and these are:

The field imager: This unit will be hand-held. It will be integrated into a fieldable computer which will have its own communication system or the ability to plug into the MASH units communication system for the military. For the private sector, it is possible that physicians and so-forth may use it in regular medical exam rooms, especially if integrated with other instruments such as a digital otoscope. Thus, one use will be field Telemedicine for the military and one use will be Telemedicine for the private sector. The private sector would use it for children's screening at schools, older persons in rest-homes, remote sites, paramedics, emergency rooms, general practitioners, etc.

The clinical imager: This unit is designed to be used when the patient is in an exam chair. It will be integrated into a slit-lamp type system. In fact, the slit-lamp and the retinal imager will both take advantage of the digital imaging capability. The target markets include routine optometric and ophthalmic examinations and Telemedicine. This system will be designed so that it can be readily used by a medical technician. We anticipate further that this unit will see use in general medical clinics, especially in rural areas where Telemedicine is appropriate and in HMOs where technicians will acquire the data.

Thus, the program is structured to develop both of these units but with many common components. For example, the CCD's, most of the lenses, the frame grabber, software, etc. will all be in common. This is not an issue of reduction in cost for the development schedule but is a major issue for cost reduction for the production units. These cameras will be the first digital ophthalmic product to ever be installed in large quantities.

B2. Phase II Work Plan. Accordingly, to accomplish "a lot of usability testing" the program will be divided into four major phases as depicted in Fig. 22.

I now discuss these tasks in detail with detailed sub-task phasing as described below.

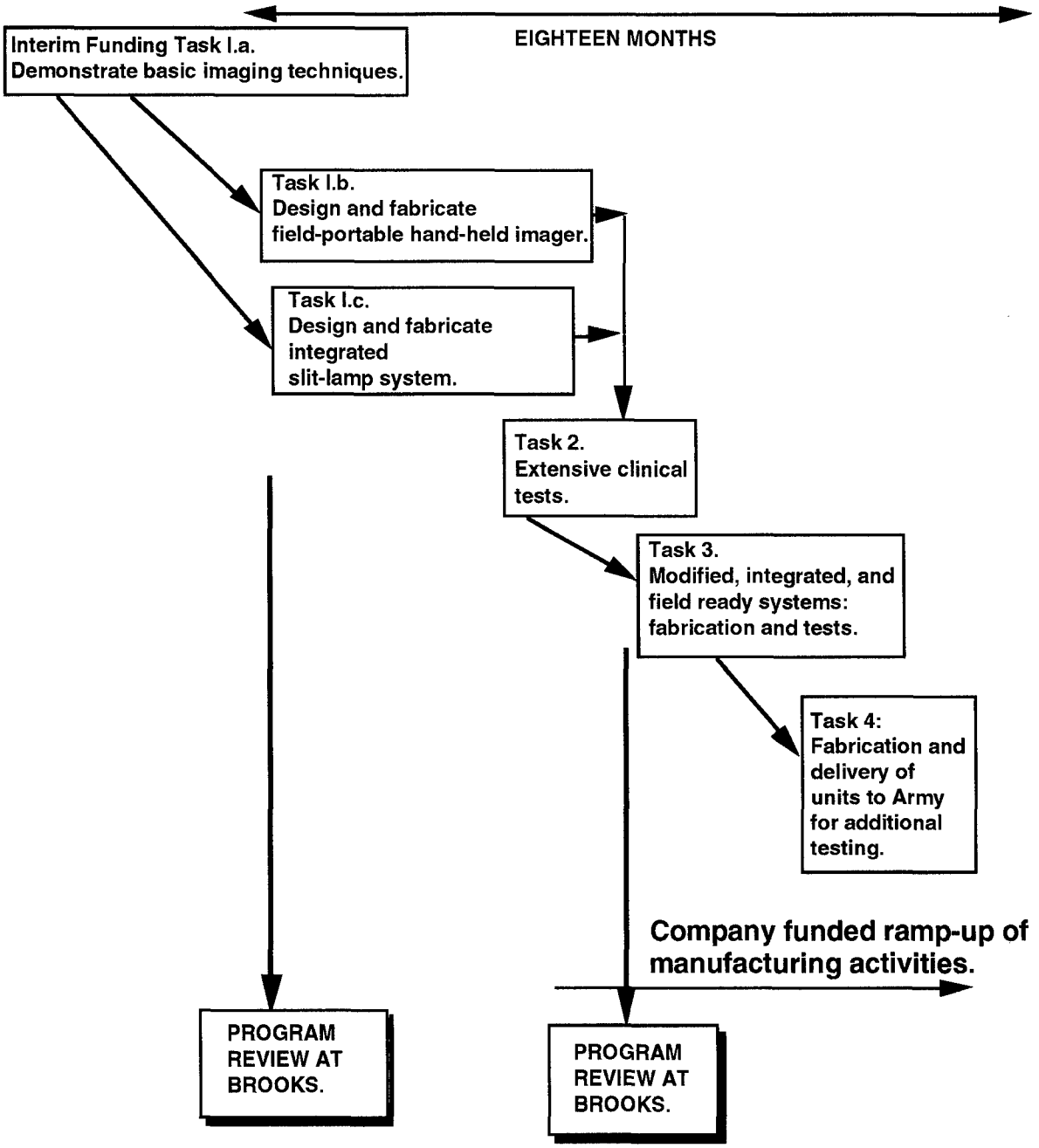


Fig. 22. Program phasing.

Task 1a. Demonstration of basic imaging techniques. Shown in Fig. 23 is the program time plan for Task 1.a.

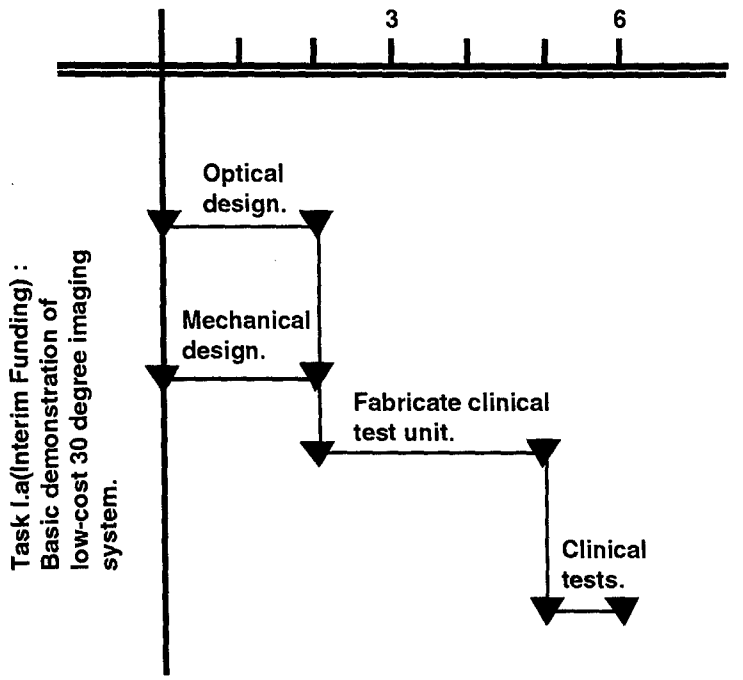


Fig. 23 Detailed task phasing for interim period between Phase I and Phase II.

A commonly mentioned difficulty in retinal imaging is the simultaneous alignment of the camera to the eye while focusing and aligning to the particular portion of the retina (as controlled by the patients glaze angle.) The clinician has to frequently move his/her head back and forth from looking through the camera eye-piece or looking over or around the camera head to see the eye. In fact, this alignment and focusing are the key aspects of quality ophthalmic photography. In particular, when the eye is mis-aligned (transverse or longitudinal) there are extraneous reflections from the cornea, the iris, the eye lens, and aberrations given by the mis-alignment of the optical axis of the eye and the camera.

Thus, it is a major objective of this project to overcome this alignment difficulty. We note that this problem is greatly exacerbated by making the camera hand-held and asking field medics to perform the imaging.

To achieve this ease of alignment, we will provide a simultaneous or near simultaneous image of the cornea and retina on an LCD screen at the front of the camera but rear-ward facing. This and other features will require a rather unique optical system which will include special methods for illumination, the use of multiple CCD's, LCD displays, etc. Specifically in this initial task:

It is the first objective to complete a working design of the basic imaging system which simultaneously presents images of the cornea and the retina.

It is the second objective to fabricate this system in a bread-board prototype and then test it clinically.

It is a third objective to complete preliminary designs for the cameras to be completed in subsequent tasks.

This system will be constructed on a bread-board in this task to allow for flexibility as we complete our imaging tests. By bread-board we mean "non-compact and non-packaged" but essentially the same system as one would eventually build.

Digital imaging will be obtained and compared for the same eyes with film images from conventional retinal cameras. The standard of quality in retinal imaging is clearly the Zeiss camera. The Company intends to purchase with its own funds a film-based Zeiss camera to use for quality comparisons.

Designing the camera in this short amount of calendar time is challenging. However, even more difficult will be the fabrication of a system with custom optics. The Company has established a relationship with a lens vendor who can supply custom lens with a four to five week turn-around. This is in contrast to the typical ten to twelve week turn-around. This is accomplished because they have the very latest in CNC diamond grinding/turning equipment. Using this equipment the vendor can quickly make near net shape lens and substantially reduce the time for fabrication. As a result, this very short calendar time schedule can reasonably be expected to be met.

The bread-board system would then be used extensively on humans. Within a few weeks we can test the operation on several hundred patients. Features to verify in these tests include:

Dealing with stray light as may reflect from the eyelens and the cornea.

Ease of alignment.

Resolution and contrast of the image.

Light levels as developed using various light sources.

The essential result of Task I.a. will be to clearly establish in practice methodologies for simultaneous or near simultaneous imaging of the retina and cornea for a non-mydriatic camera.

Task 1.b. Design and fabricate a field-portable hand-held imager. A detailed task phasing is shown in Fig. 24.

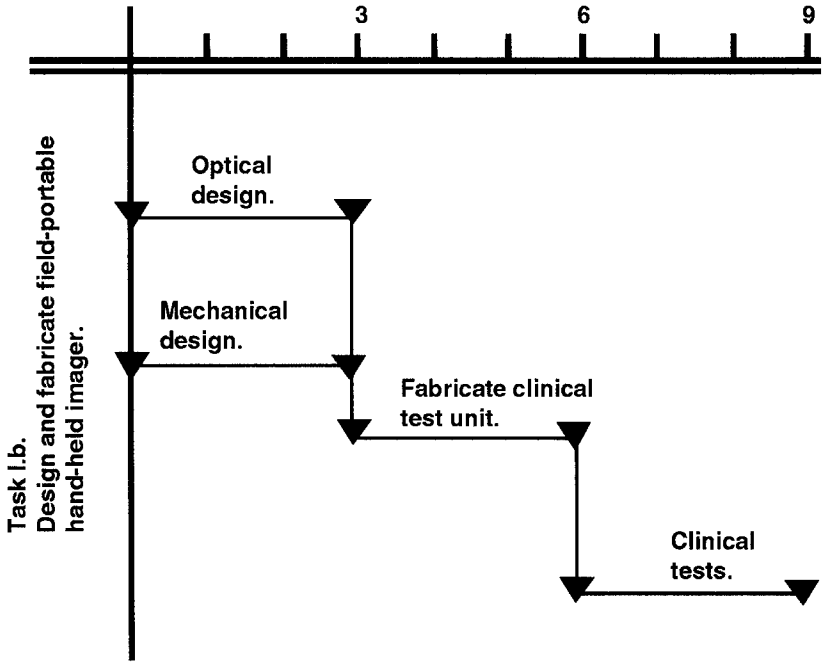


Fig. 24. Detailed task phasing for Task 1.b.

There currently exists a hand-held film based retinal imager. This is the Japanese Kowa Genesis system. We know of two institutions who use this camera and complain of its difficulty of use. Both of these institutions are replacing the Genesis with our wide-field camera.

The optical design for the hand-held camera is shown in the body of the report/proposal. Perhaps the key issue here will be packaging all of these small optics into a small case. Small optics are harder to fabricate than large optics and these will be extremely small by retinal camera standards. A great deal of attention has to be applied to details of stray light, light sources, battery power, cables, etc. However, while it is unique to simultaneously present the retinal and corneal images and it is quite stressing to achieve all of these functions in a small package.

Issues such as the shape of the handle, the nature of the pivots, the details of the feet which rest on the patients head, are in the final analysis going to dominate the utility of the camera. Keep in mind that even though the military command system may select the camera, purchase the camera, train troops to use it, in the end, it must be accepted by the extremely practical minded field medics.

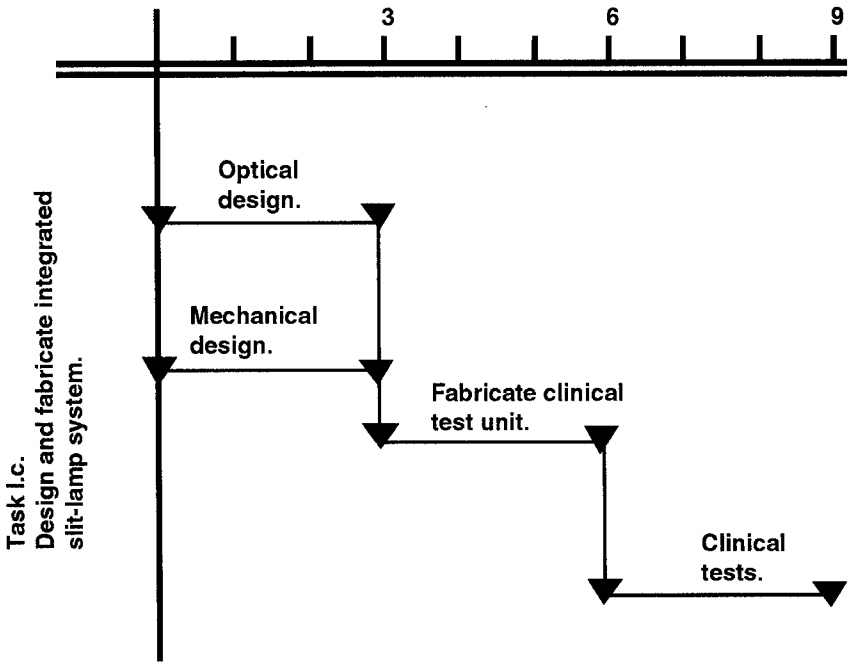
Consequently, a lot of effort must go into field testing. In parallel with the optical system packaging exercise we will design at least three different "man-machine" interface designs. It is likely that we will retain the services of an expert design shop here in Silicon Valley. For example, Frog design of Mountain View is well known for some of the Macintosh designs it has produced.

Several of these designs will be made as plastic mock-ups to test "useability." Then, final sections will be made and the units stuffed with the optical and electro-optical systems. We

will test and modify as necessary in our shop and then move on to testing in the offices of various optometrists. Arrangements will be completed with local HMO's to have the cameras used in general medical clinics.

From these "useability" tests we will then concentrate on a final design. By the end of this task it is the intention to have a fieldable design with considerable confidence in its practicality.

Task I.c. Design and fabricate an integrated slit-lamp system. The time plan for this task is shown in Fig. 25.



Task 25. Time plan for Task 1.c.

The integrated slit-lamp/retinal imager is a revolutionary aspect of this program. Various companies have added (generally low-quality) CCD imagers to existing slit-lamps or existing fundus cameras or ophthalmoscopes. No company has had the vision to integrate the retinal camera and the slit-lamp into one unit. By making this system digital, there are essentially no operational costs (as opposed to film based systems.)

The hand-held unit will sell to the military for field use and to general medical practices around the world. The slit-lamp based system will sell to all eye care professionals around the world.

Integration of the slit-lamp and retinal camera into a single unit is very hard when one is seeking compact size and rock-bottom costs. The system will occupy about 10% of the volume of the existing Zeiss retinal camera. As noted before, smaller is more difficult in these optical systems and great attention must be given to stray light rejection and costs.

There exist a number of packaging options. In particular, the basic functions provided by the system will include:

A binocular imager with eye pieces: Allows conventional

imaging of the cornea.

A 3CCD provided through one of binocular imager channels for digital imaging of the cornea.

A 30 degree retinal camera with a 3CCD imager.

A conventional slit-lamp light source.

Mountings for a tonometer, etc.

A separate 45 degree retinal imager with a 1,024 monochrome CCD for flourecein angiography which can be mounted on the stand in place of the other imager.

With this system, the eye care specialists can conduct a conventional visual exam and a digital exam. The exam should require the same or less time, add no operational costs, and provide the opportunity for documentation and Telemedicine.

The system packaging issues will not only relate to the packaging of the individual optical systems but also to:

How to switch between the stereo corneal microscope and the retinal camera.

How to make this switch and use only one 3CCD.

How to achieve this and provide cable access.

In this task a preferred concept will be selected and designed in detail. Then it will be constructed and tested first through selected doctors and patients and then put to the test of wider evaluations.

Task 2. Extensive clinical tests. This is the "last best" opportunity to work out the operational clinical performance, the user acceptance, and to identify modifications before going into production. This is the time when key players in the user community must complete their testing and produce for us their own views of the clinical and commercial value of the cameras. To this end we have sought and obtained the commitment from the following groups for utility testing: U.S. Army, Navy, Air Force, Kaiser, Mayo, and various independent medical practitioners.

It is not just an issue of clinical testing. History has shown that adoption of new technology, especially that which portends to introduce a major shift in operational procedures, is difficult. Classic examples include the transistor (It will find use in hearing aids and not much else.), the Xerox machine (Be used by accounts only; a small market.), and the Dodge Mini-van (We don't see any market surveys with people asking for Mini-vans.) As a result, it is a prime objective of the Phase II program to obtain the support and involvement of key institutions in the project.

These institutions have been involved in the Phase I in considering the format of the instruments. They have all agreed to participate in "utility" studies of the instruments. By this I do not mean the technology but I do mean does the technology fit a real need.

Keep in mind that the instrument portends a new way of delivering eye health care. Obtaining adoption by large institutions can be difficult. By involving them from the beginning we seek to obtain their early "buy-in" and identification with the project.

In the final analysis with large institutions, there are two customers. The first group are the individual care providers, the optometrists, ophthalmologists, nurses, physician assistants, and the technicians. The second group are the higher level systems analysts. These individuals include M.B.A.s, accountants, and time and motion study individuals. Their viewpoint may be quite antithetical to that of the care providers. The former may see technology as a threat to the need of the institution for their services and the later will see accomplishing more with fewer expensive care providers as an opportunity.

Task 3. Modified, integrated, and field ready systems: fabrication and tests. From the results of Task 2 new systems will be built and tested before construction of those systems to be delivered to Brooks and for the commitment for manufacturing tooling. Experiments will be conducted using the hand-held imager in field settings.

Task 4: Fabrication and delivery of units to Army for additional testing. Completed units will be provided to Brooks AFB for clinical demonstrations in the field.

Conclusions:

The proposed "Field-Portable Retinal Camera" can be built, will have the required performance, and will have an acceptable price. The camara will also see wide-spread use in a clinical setting.

Personnel

The following people worked on the Phase I Contract DAMD17-97-C-7012:

- Nobert A. Massie, CEO
- Greg Sprehn, **Chief** Scientist
- Wei Su, Optical Scientist

DEPARTMENT OF THE ARMY
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REPLY TO
ATTENTION OF:

MCMR-RMI-S (70-1y) 4 Dec 02

MEMORANDUM FOR Administrator, Defense Technical Information Center (DTIC-OCA), 8725 John J. Kingman Road, Fort Belvoir, VA 22060-6218

SUBJECT: Request Change in Distribution Statement

1. The U.S. Army Medical Research and Materiel Command has reexamined the need for the limitation assigned to technical reports written for this Command. Request the limited distribution statement for the enclosed accession numbers be changed to "Approved for public release; distribution unlimited." These reports should be released to the National Technical Information Service.

2. Point of contact for this request is Ms. Kristin Morrow at DSN 343-7327 or by e-mail at Kristin.Morrow@det.amedd.army.mil.

FOR THE COMMANDER:

Encl

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Deputy Chief of Staff for
Information Management

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