# Comparative Ophthalmology - scientific discovery and innovation create synergies for veterinary and human medicine

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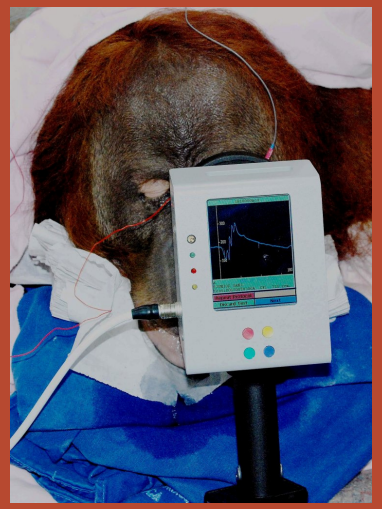
# Comparative Ophthalmology

- Comparative ophthalmology is the study of similarities and differences between human and various animal species' vision.
  - Evolutionary – mammals share many similarities
    - Developmental Biology
    - Genetics
    - Anatomical
    - Physiological



# Human / Animal Relationship

- Our understanding of these comparisons has yielded many breakthroughs in eye and neurological research of diseases and other causes of vision loss.
  - Leber Congenital Amaurosis (LCA)
    - RPE65 mutation
    - Congenital Stationary Night Blindness (CSNB) in animals
  - Retinitis Pigmentosa
    - Spontaneous animal model (Progressive Retinal Atrophy)
  - Glaucoma
    - Spontaneous and induced animal models

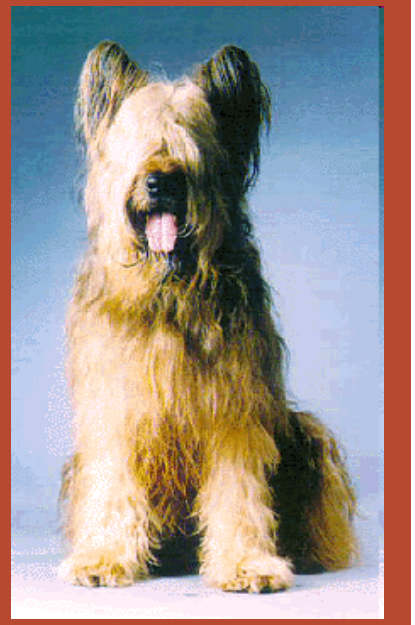
# Examples of Benefits

- Leber Congenital Amaurosis (LCA)
  - *Successful RPE65 Gene Replacement and Improved Visual Function in Humans*

    Ophthalmic Genetics 2008, Vol. 29, No. 3, Pages 89-91

  - *Gene therapy restores vision in a canine model of childhood blindness*

    Nature Genetics May 2001, Vol. 28, Pages 92-95



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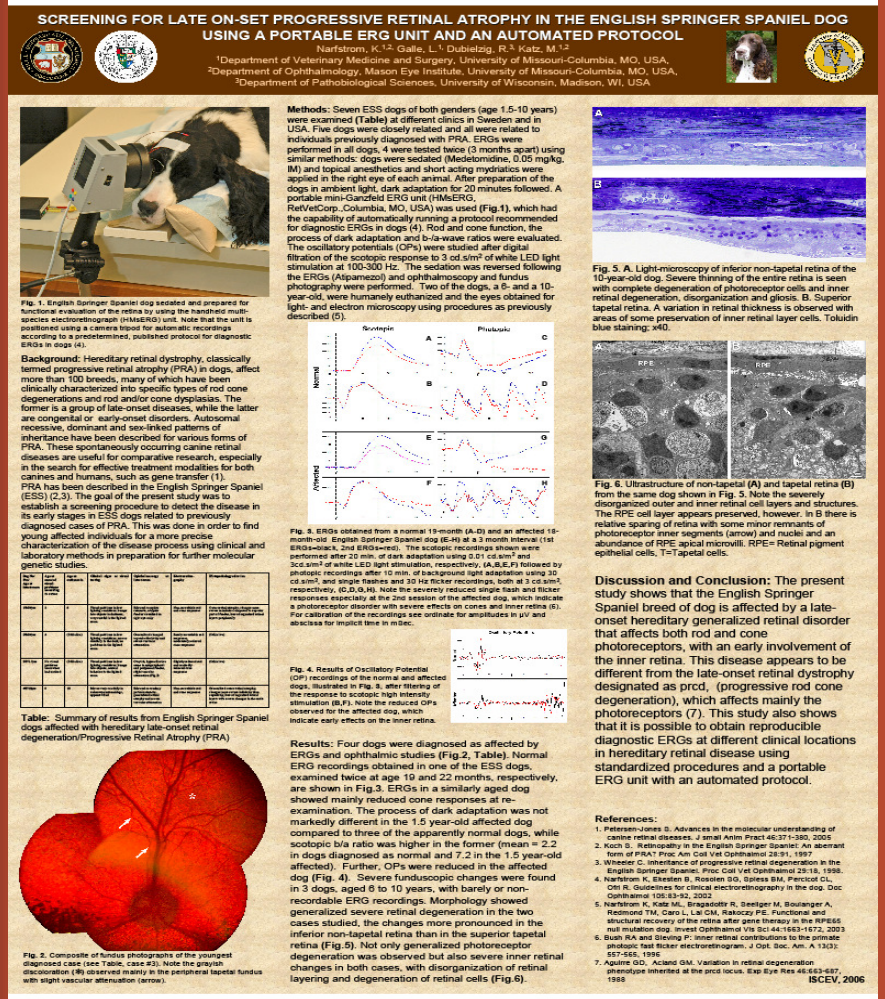
# Examples of Benefits



SCREENING FOR LATE ON-SET PROGRESSIVE RETINAL ATROPHY IN THE ENGLISH SPRINGER SPANIEL DOG USING A PORTABLE ERG UNIT AND AN AUTOMATED PROTOCOL

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Fig. 1. English Springer Spaniel dog sedated and prepared for functional evaluation of the retina by using the handheld multi-species electroretinograph (HMsERG) unit. Note that the unit is positioned using a camera tripod for automatic recordings according to a predetermined, published protocol for diagnostic ERGs in dogs (4).

**Background:** Hereditary retinal dystrophy, classically termed progressive retinal atrophy (PRA) in dogs, affect more than 100 breeds, many of which have been clinically characterized into specific types of rod cone degenerations and rod and/or cone dysplasias. The former is a group of late-onset diseases, while the latter are congenital or early-onset disorders. Autosomal recessive, dominant and sex-linked patterns of inheritance have been described for various forms of PRA. These spontaneously occurring canine retinal diseases are useful for comparative research, especially in the search for effective treatment modalities for both canines and humans, such as gene transfer (1). PRA has been described in the English Springer Spaniel (ESS) (2,3). The goal of the present study was to establish a screening procedure to detect the disease in its early stages in ESS dogs related to previously diagnosed cases of PRA. This was done in order to find young affected individuals for a more precise characterization of the disease process using clinical and laboratory methods in preparation for further molecular genetic studies.

Table: Summary of results from English Springer Spaniel dogs affected with hereditary late-onset retinal degeneration/Progressive Retinal Atrophy (PRA)



Fig. 2. Composite of fundus photographs of the youngest diagnosed case (see Table, case #3). Note the grayish discoloration (☆) observed mainly in the peripheral tapetal fundus with slight vascular attenuation (arrow).

**Methods:** Seven ESS dogs of both genders (age 1.5-10 years) were examined (**Table**) at different clinics in Sweden and in USA. Five dogs were closely related and all were related to individuals previously diagnosed with PRA. ERGs were performed in all dogs, 4 were tested twice (3 months apart) using similar methods: dogs were sedated (Medetomidine, 0.05 mg/kg, IM) and topical anesthetics and short acting mydriatics were applied in the right eye of each animal. After preparation of the dogs in ambient light, dark adaptation for 20 minutes followed. A portable mini-Ganzfeld ERG unit (HMsERG, RetVetCorp.,Columbia, MO, USA) was used (**Fig.1**), which had the capability of automatically running a protocol recommended for diagnostic ERGs in dogs (4). Rod and cone function, the process of dark adaptation and b-/a-wave ratios were evaluated. The oscillatory potentials (OPs) were studied after digital filtration of the scotopic response to 3 cd.s/m$^2$ of white LED light stimulation at 100-300 Hz. The sedation was reversed following the ERGs (Alfpamezol) and ophthalmoscopy and fundus photography were performed. Two of the dogs, a 8- and a 10-year-old, were humanely euthanized and the eyes obtained for light- and electron microscopy using procedures as previously described (5).




Fig. 3. ERGs obtained from a normal 19-month (A-D) and an affected 18-month-old English Springer Spaniel dog (E-H) at a 3 month interval (1st ERGs=black, 2nd ERGs=red). The scotopic recordings shown were performed after 20 min. of dark adaptation using 0.01 cd.s/m$^2$ and 3cd.s/m$^2$ of white LED light stimulation, respectively, (A,B,E,F) followed by photopic recordings after 10 min. of background light adaptation using 30 cd.s/m$^2$, and single flashes and 30 Hz flicker recordings, both at 3 cd.s/m$^2$, respectively, (C,D,G,H). Note the severely reduced single flash and flicker responses especially at the 2nd session of the affected dog, which indicate a photoreceptor disorder with severe effects on cones and inner retina (6). For calibration of the recordings see ordinate for amplitudes in µV and abscissa for implicit time in mSec.



Fig. 4. Results of Oscillatory Potential (OP) recordings of the normal and affected dogs, illustrated in Fig. 3, after filtering of the response to scotopic high intensity stimulation (B,F). Note the reduced OPs observed for the affected dog, which indicate early effects on the inner retina.

**Results:** Four dogs were diagnosed as affected by ERGs and ophthalmic studies (**Fig.2, Table**). Normal ERG recordings obtained in one of the ESS dogs, examined twice at age 19 and 22 months, respectively, are shown in Fig.3. ERGs in a similarly aged dog showed mainly reduced cone responses at re-examination. The process of dark adaptation was not markedly different in the 1.5 year-old affected dog compared to three of the apparently normal dogs, while scotopic b/a ratio was higher in the former (mean = 2.2 in dogs diagnosed as normal and 7.2 in the 1.5 year-old affected). Further, OPs were reduced in the affected dog (**Fig. 4**). Severe funduscopic changes were found in 3 dogs, aged 8 to 10 years, with barely or non-recordable ERG recordings. Morphology showed generalized severe retinal degeneration in the two cases studied, the changes more pronounced in the inferior non-tapetal retina than in the superior tapetal retina (**Fig.5**). Not only generalized photoreceptor degeneration was observed but also severe inner retinal changes in both cases, with disorganization of retinal layering and degeneration of retinal cells (**Fig.6**).




Fig. 5. A. Light-microscopy of inferior non-tapetal retina of the 10-year-old dog. Severe thinning of the entire retina is seen with complete degeneration of photoreceptor cells and inner retinal degeneration, disorganization and gliosis. B. Superior tapetal retina. A variation in retinal thickness is observed with areas of some preservation of inner retinal layer cells. Toluidin blue staining; x40.




Fig. 6. Ultrastructure of non-tapetal (A) and tapetal retina (B) from the same dog shown in Fig. 5. Note the severely disorganized outer and inner retinal cell layers and structures. The RPE cell layer appears preserved, however. In B there is relative sparing of retina with some minor remnants of photoreceptor inner segments (arrow) and nuclei and an abundance of RPE apical microvilli. RPE= Retinal pigment epithelial cells, T=Tapetal cells.

**Discussion and Conclusion:** The present study shows that the English Springer Spaniel breed of dog is affected by a late-onset hereditary generalized retinal disorder that affects both rod and cone photoreceptors, with an early involvement of the inner retina. This disease appears to be different from the late-onset retinal dystrophy designated as prcd, (progressive rod cone degeneration), which affects mainly the photoreceptors (7). This study also shows that it is possible to obtain reproducible diagnostic ERGs at different clinical locations in hereditary retinal disease using standardized procedures and a portable ERG unit with an automated protocol.

**References:**
1. Petersen-Jones S. Advances in the molecular understanding of canine retinal diseases. J small Anim Pract 46:371-380, 2005
2. Koch S. Retinopathy in the English Springer Spaniel: An aberrant form of PRA? Proc Am Coll Vet Ophthalmol 28:91, 1997
3. Wheeler C. Inheritance of progressive retinal degeneration in the English Springer Spaniel. Proc Coll Vet Ophthalmol 29:18, 1998.
4. Narfstrom K, Ekesten B, Rosolen SG, Spiess BM, Percicot CL, Ofri R. Guidelines for clinical electroretinography in the dog. Doc Ophthalmol 105:83-92, 2002
5. Narfstrom K, Katz ML, Bragadottir R, Seeliger M, Boulanger A, Redmond TM, Caro L, Lai CM, Rakoczy PE. Functional and structural recovery of the retina after gene therapy in the RPE65 null mutation dog. Invest Ophthalmol Vis Sci 44:1663-1672, 2003
6. Bush RA and Sieving P: inner retinal contributions to the primate photopic fast flicker electroretinogram. J Opt. Soc. Am. A 13(3): 557-565, 1996
7. Aguirre GD, Acland GM. Variation in retinal degeneration phenotype inherited at the prcd locus. Exp Eye Res 46:663-687, 1988

ISCEV, 2006

- Retinitis Pigmentosa
  - Understanding Progressive Retinal Atrophy helps our understanding of RP
  - Treatment options include transplantation, gene, and stem cell therapy
  - Potential cures for animals and humans

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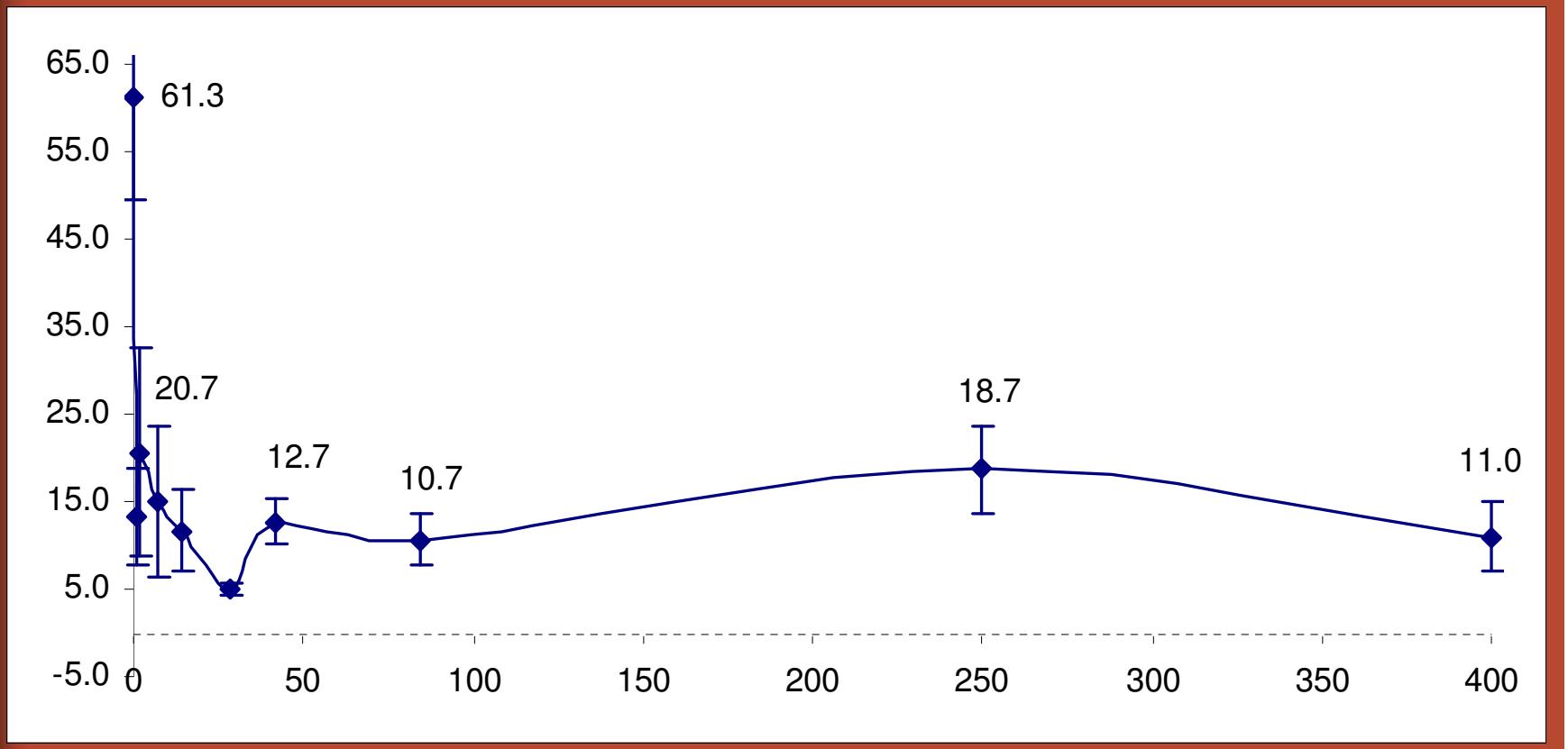
# Examples of Benefits

## Glaucoma

# Glaucoma

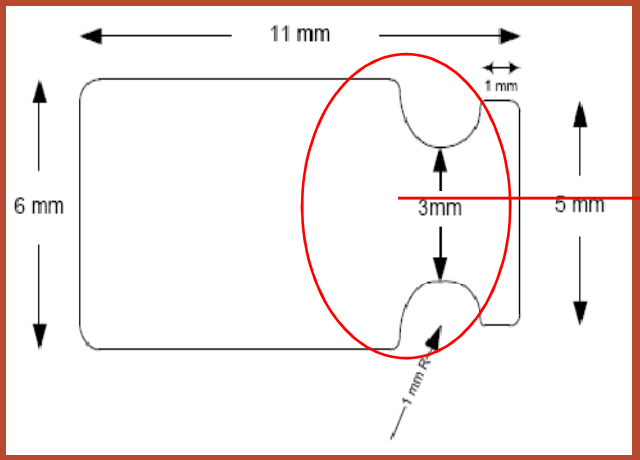
## Ongoing Results; Pilot Study (3 eyes)

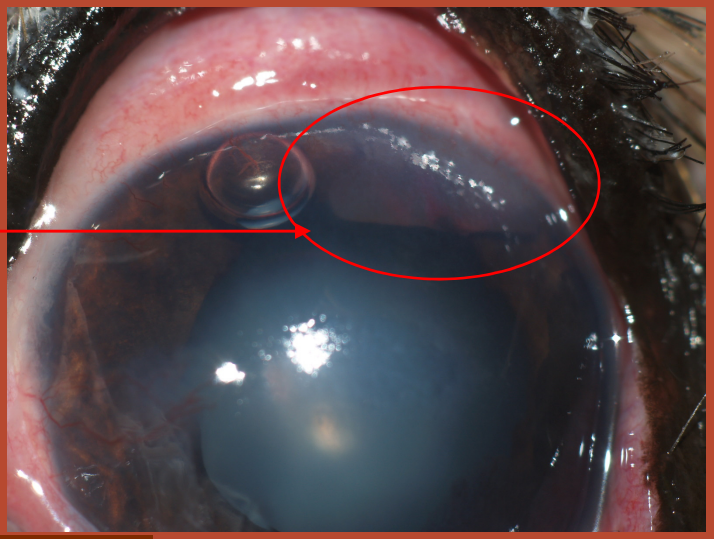


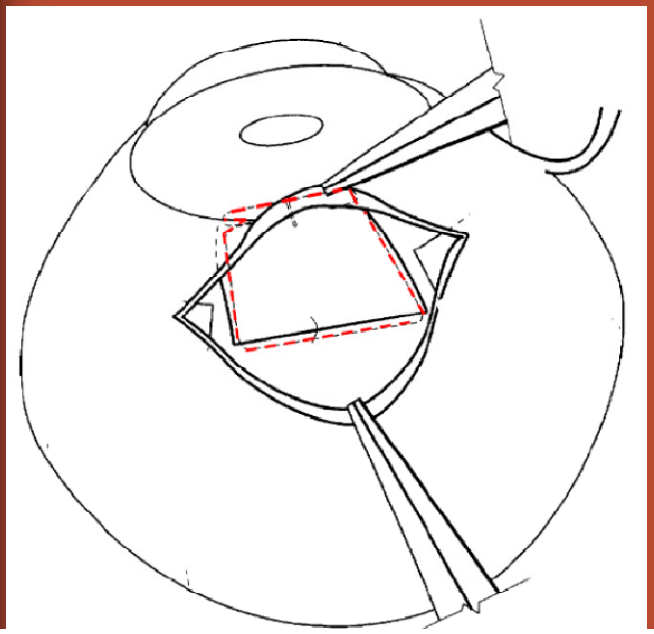

Original Data Presented at ACVO 2008:
Roberts SW and **Woods, CW**. "The Use of a Novel Porous Implant for Refractory Canine Glaucoma".
Abstract Presentation; Am. College of Vet. Ophthalmologists 2008; Boston, MA

# Glaucoma

# Implant and Surgical Approach





Anterior Chamber

- Create a limbal based flap
- Introduce implant through a 3mm incision
- Place implant body adjacent to choroid
- Close sclera

# Innovative Technologies

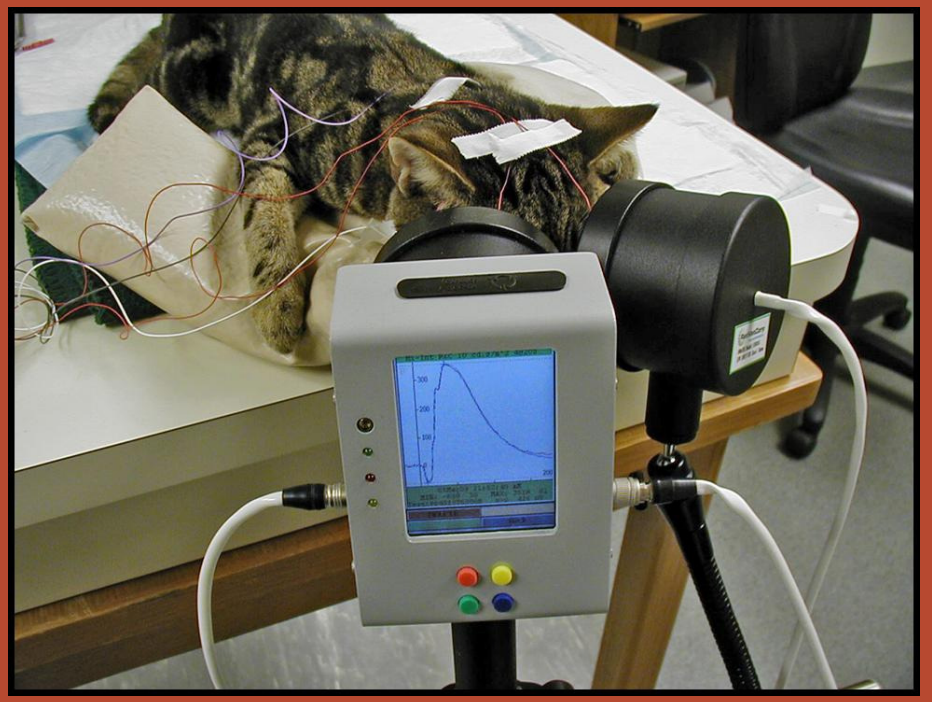
- Electrophysiology of Vision
  - Diagnostic Medical Device
  - Research began in 1930's
  - Quantifiable analysis of retinal "function"
  - Diseases and drugs affect the function of the retina before "structural" changes occur.

# Innovators


Dr. Kristina Narfström, DVM, PhD, and Diplomate of the European College of Veterinary Ophthalmology (ECVO), is Professor Emeritus at the University of Missouri-Columbia. She was the Ruth M. Kraeuchi Missouri Endowed Professor of Veterinary Ophthalmology. She holds adjunct professorships at the Mason Eye Institute, Department of Ophthalmology, and at the Faculty of Biomedical Engineering at the University of Missouri-Columbia. Her research work concerns primarily hereditary retinal disease processes of animal models, including retinal functional testing, using electroretinography. She is also engaged in comparative research concerning treatment modalities for hereditary retinal blinding diseases such as the use of gene therapy, stem cell implantation and retinal prosthetics. Narfström is cofounder and scientific director of RetVetCorp.

# HMsERG™

- Handheld Multi-species Electroretinogram
- Scotopic / Photopic
- Single / Dual Stimulator
- Flash ERG / VEP
- Battery operated
- Automated Protocols
- Truly portable
- Mini Ganzfeld dome
- ISCEV guidelines
- Analytical software
  - Amplitudes / Implicit Times
  - Oscillatory Potentials



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# Collaboration

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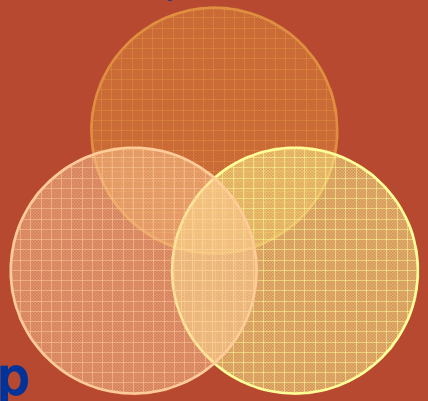
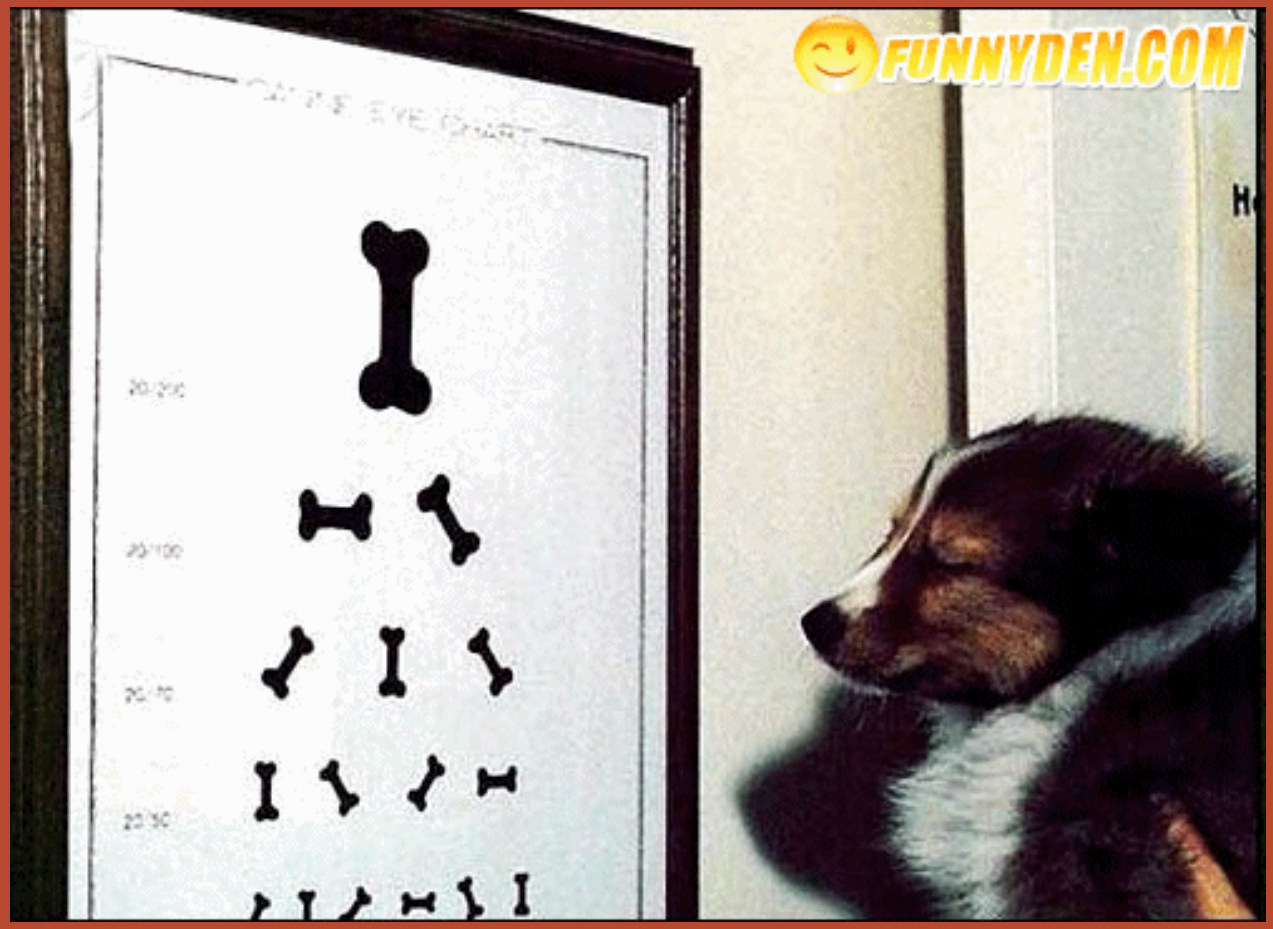


**RetVetCorp**

**Linscan**

# Non-communicative Patient

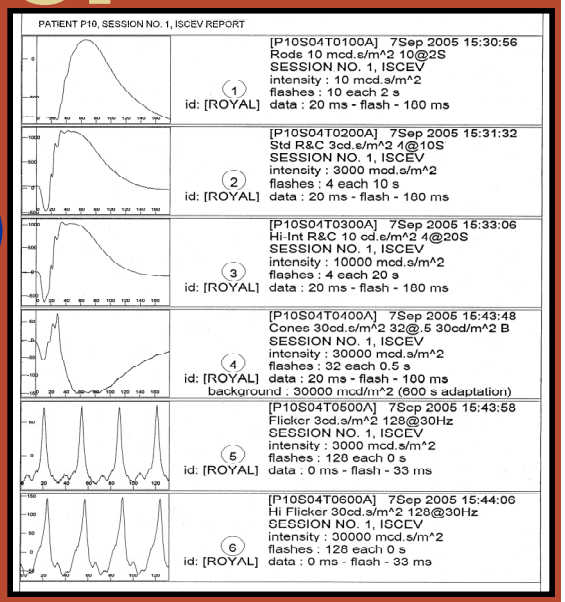


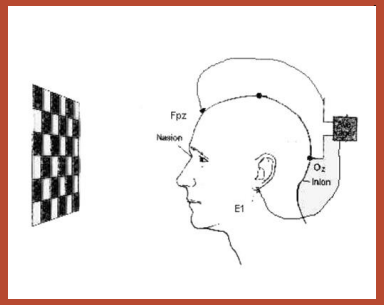
# Electroretinogram – Definition

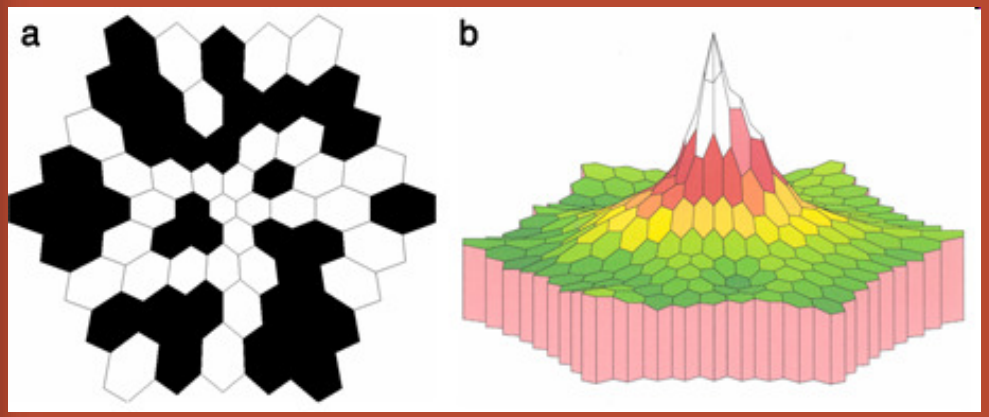
- The electroretinogram (ERG) is a tracing of the summed electrical changes of a large number of retinal neurons and glia in response to a light stimulus.

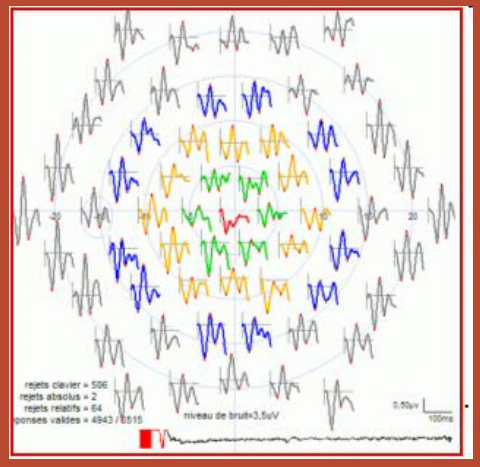
# Electrophysiology of Vision

- Flash Electroretinography (ERG)
- Focal ERG
- Vision Evoked Potential (VEP)
- Pattern ERG
- Multi-focal ERG

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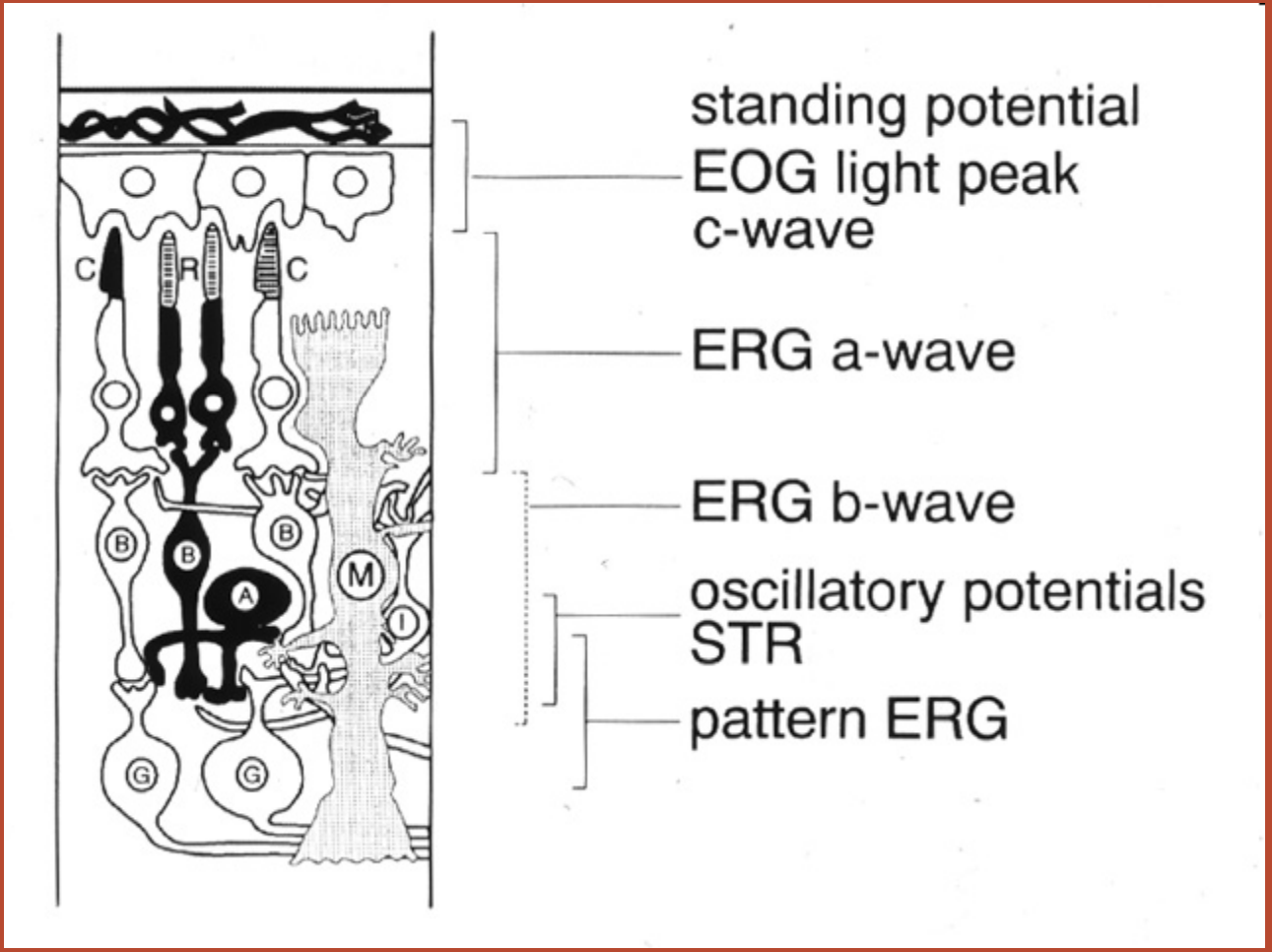
# Cellular Structure and Electrophysiology of Vision




Selective Rod- and Cone-ERG Responses in Retinal Degenerations
Digital Journal of Ophthalmology 1998 Volume 4, Number 10

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# HUMAN VISUAL ELECTRODIAGNOSTICS

**A Guide To Procedures**



| PROVISIONAL DIAGNOSIS | EOG | ERG | BRIGHT FLASH ERG | PATTERN ERG | FLASH VEP | PATTERN VEP | SPECIAL VEP |
|---|---|---|---|---|---|---|---|
| Inherited retinal dystrophies | + | + | | | | | |
| Vascular diseases including diabetes | | + | | + | | + | |
| Opaque media or trauma | | + | + | | + | | |
| Retrobulbar neuritis* | | | | + | | + | |
| Unexplained visual loss | | + | | + | | + | |
| Infant with questionable vision | | + | | | + | | + |
| Albinism | | +** | | | | | + |
| Toxic and nutritional eye disease | + | + | | + | + | | |
| Glaucoma | | X | | + | | | |
| Suspected intracranial lesion | | | | + | | + | + |

* not helpful during active phase but rather to monitor the recovery

** to exclude other conditions associated with nystagmus

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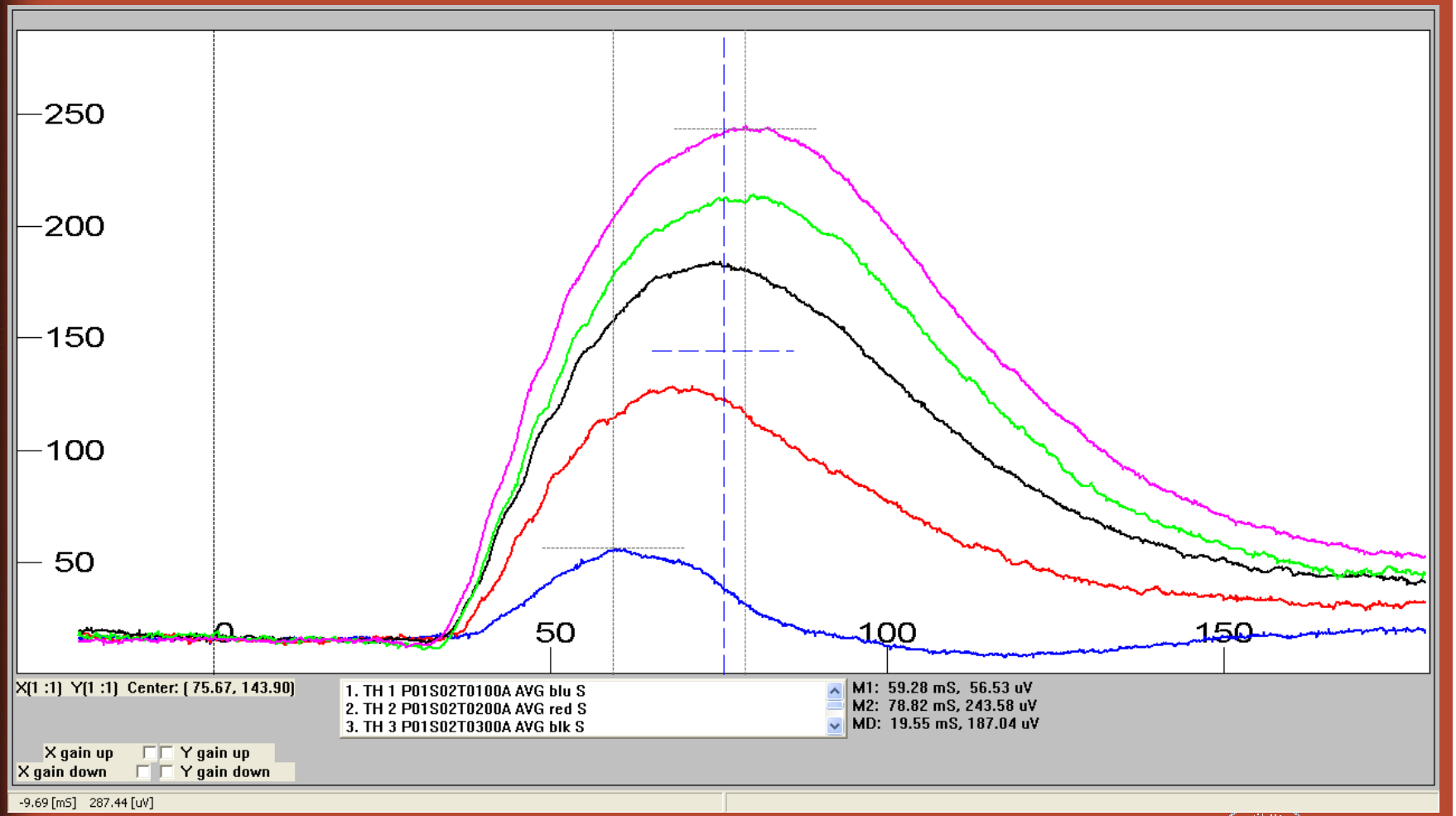
# Changing Paradigms

- In the Lab
  - Basic Research
    - Transgenic
    - Safety / Efficacy
    - Animal Models of Human Diseases
    - Detection / Diagnosis
  - Clinical Research Organizations
- In Surgery
  - Retina function check
- By the Bedside
  - Pediatric
  - Trauma (Sudden Vision Loss)
- In the Clinic
  - Retina (RP, Glaucoma, CRVO, Diabetic Retinopathy, Uveitis)
  - Cataract/Refractive (Screening, Endophthalmitis)

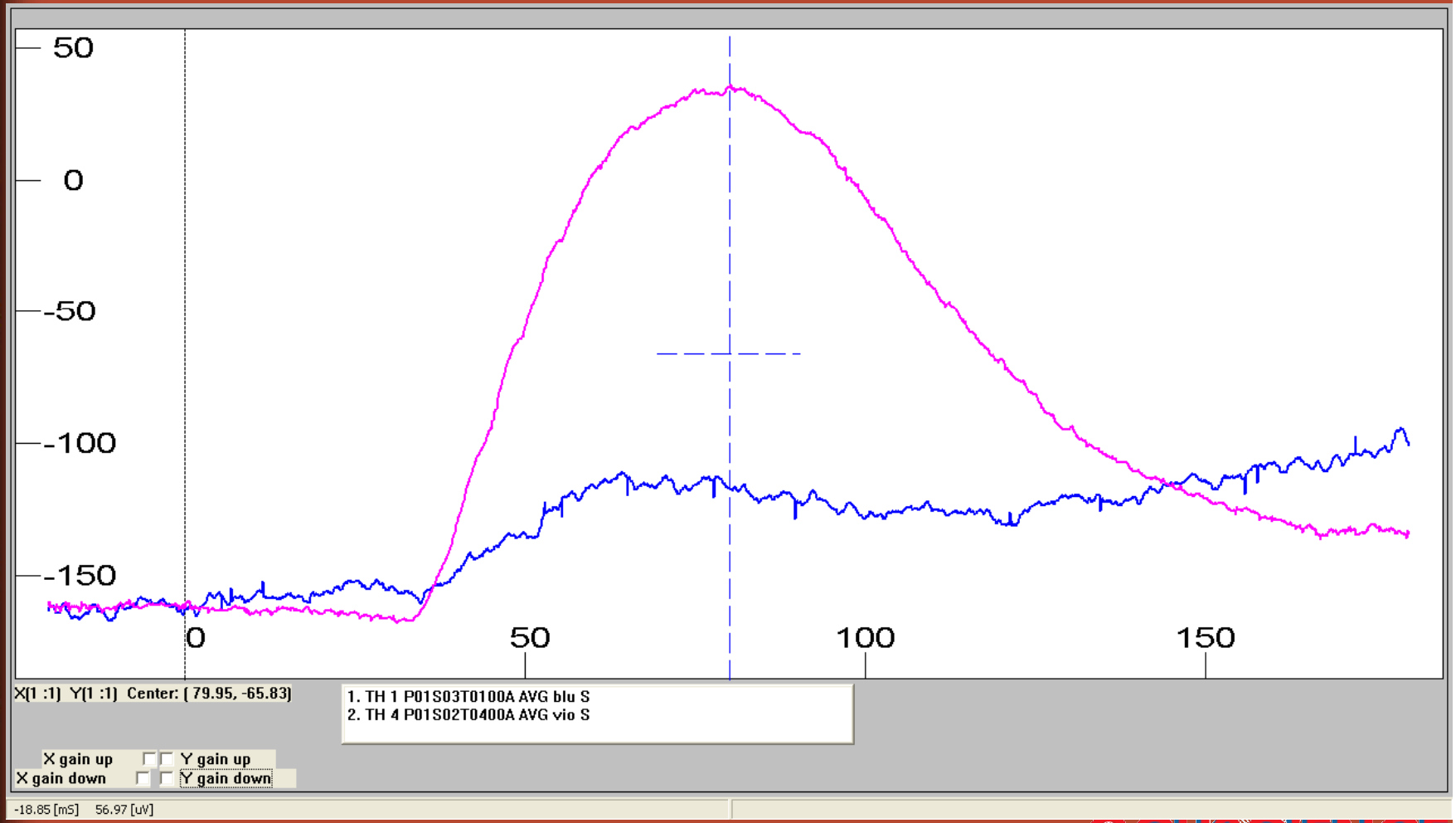
# ERG in Research

- Pharmaceutical Development
  - Safety
  - Efficacy
- Transgenic animal model phenotype
- Does it effect the Retina?
- What in the retina is being effected?
- Quantification
- Use in complementary diagnostic tools FA/SLO/OCT

# Rod Dark Adaptation



# Abnormal Rod Only B wave



# Scientific literature

- ARVO 2006
  - Jeong et al.
- ISCEV 2006
  - Narfstrom et al.
- ACVO 2007

  - Jeong et al.: Comparison of 2 ERG systems used in dogs: the HMsERG and the RETIcom
- Upcoming Publications:

  -Katz et al.: Retinal pathology in a canine model of late infantile neuronal ceroid lipofuscinosis, Accepted IOVS, 2008

  -Ropstad & Narfstrom: The obvious and more hidden components of the electroretinogram. In Press, European Journal of Companion Animal Practice, 2008

  -Norman et al.: The effects of medetomidicne hydrochloride on the ERG of normal dogs, Submitted, 2008

  - Jeong et al. : Comparison of 2 ERG systems used in canine electrophysiology: the HMsERG and the RETIcom. Submitted

# Commercial opportunity

- Clinically compared to larger, more expensive systems
- Early Detection / Progression
- Making ERGs easier to obtain
- Use in a variety of environments
- Data collection simpler
- EMRs and Information Sharing

# Comparison of two electroretinography systems used in dogs: the HMsERG and the RETIcom

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[1]Dept of Veterinary Surgery and Ophthalmology, Seoul National University, Korea, [2]Dept of Veterinary Medicine and Surgery, University of Missouri-Columbia, USA

**Purpose.** To compare two different electroretinography (ERG) instruments used on the same animal in a clinical practice.

**Methods.** Retinal function in both eyes of 12 healthy Miniature Schnauzers was evaluated under general anesthesia using medetomidine (60 μg/kg, IM) and Ketamine (5 mg/kg, IM). Scotopic and photopic ERGs were recorded by a compact, portable mini-Ganzfeld ERG unit (HMsERG, RetVet Corp Inc., MO, USA) and a contact lens electrode with a built-in light-emitting diode (LED) stimulator, part of a commercial ERG equipment (RETIcom, Roland Consult, Brandenburg, Germany), respectively, following published Guidelines for Clinical Electroretinography in the Dog[1] **(Fig.1)**. Light intensity used with the two different ERG equipments is showed in **Table 1.** The ERG waveforms, a- and/or b-wave amplitudes and implicit times of recordings by the two ERG units were compared. For statistical analysis, a paired student *t*-test, and median, and 5th and 95th percentiles were employed. In addition, the results were then fitted into a graphical representation of reference ranges for both ERG systems.

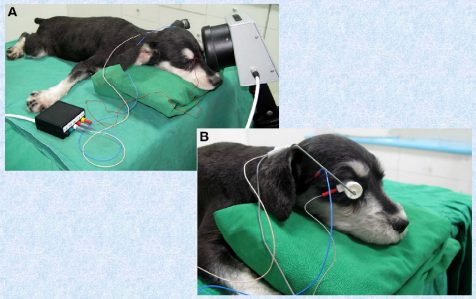


**Fig. 1**. ERGs using the **HMsERG (A)** and the **RETIcom (B)** in Miniature Schnauzers. Note the difference between the portable LED mini-Ganzfeld stimulator employed in the HMsERG and the LED with a built-in contact lens electrode (LED-electrode) used in the RETIcom. The entire HMsERG unit is shown **(A)**, while for the RETIcom **(B)**, only the contact lens with the built-in stimulator is shown.

**Table 1**

| | | | Light stimulation intensity (cd·s/m²) | |
|---|---|---|---|---|
| | HMsERG (signal averager) | | | RETIcom (single flash) |
| Scotopic ERG | Low light intensity | S1 | 0.01 | 0.025 |
| | | S2 | | |
| | | S3 | | |
| | | S4 | | |
| | | S5 | | |
| | Standard light intensity (S-ST) | | 3.0 | 2.5 |
| | Higher light intensity (S-H) | | 10 | 7.9 |
| Light Adaptation (cd/m²) | 30 | | | 25 |
| Photopic ERG | Single flash (P) | | 3.0 | 2.5 |
| | 31 Hz flicker (P-FL) | | 3.0 | 2.5 |

**Results.** The waveforms of the ERGs obtained by the two ERG units were identical to those of previous studies[1] **(Fig. 2)**. Except for the amplitude of the b-wave for scotopic low light intensity stimulation, the overall changes of ERG parameters recorded by the HMsERG unit in response to changes in the protocol as to light stimulation were very similar to those recorded by the RETIcom equipment. This was found most clearly for the photopic single flash and 31 Hz flicker responses **(Fig. 3 A, B, C, and D)**. There was a greater increment in b-wave amplitude and implicit times recorded by the HMsERG than those of RETIcom during dark adaptation **(Fig. 3 E)**. Mean b/a ratio for the HMsERG were higher than those for the RETIcom, but the differences were not significant **(Fig. 3 F)**. The results demonstrate that both ERG systems are comparable. As illustrated in **Fig. 4**, some major differences between the two units were shown by using 95% confidence intervals.

**ACVO, Hawaii 2007.**
**Supported by BK 21 Program for Veterinary Science and BK 21 Global Internship**

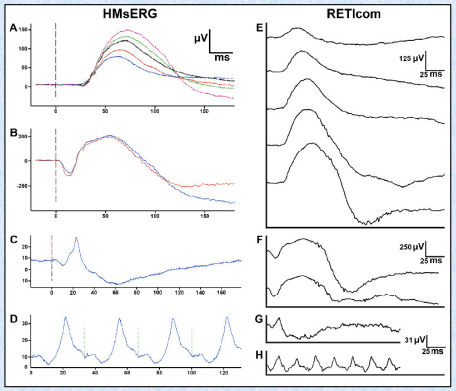


**Fig. 2**. Representative ERG waveforms recorded by the two ERG units. Scotopic ERGs **(A and B; E and F)** and photopic ERGs **(C and D; G and H)** are shown. Scotopic low intensity responses **(A and E)**, which was subdivided into S1, S2, S3, S4, and S5 (from bottom to top in A; from top to bottom in **E**), scotopic standard intensity responses (blue line in **B**; upper line in **F**), and scotopic higher intensity responses (red line in **B**; lower line in **F**); Photopic single flash response **(C and G)** and 31 Hz flicker response **(D and H)**. The light stimulus is shown by the vertical dashed line for the HMsERG, while the light stimulus is shown at the beginning of each recording for the RETIcom.

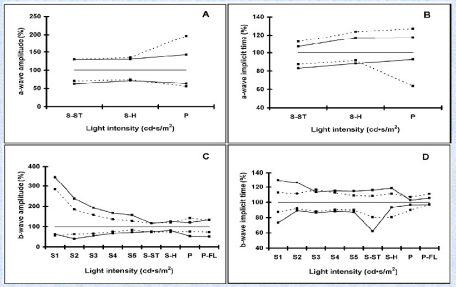


**Fig. 4**. Graphical illustration of the reference ranges depicting ERG differences between the HMsERG **(a solid line)** and the RETIcom **(a dotted line)** using the median set at 100% and 95 % confidence intervals. Amplitude and implicit time values on the y-axis for the a- and b-waves, respectively, are shown as percentages of the values obtained by the two ERG units.

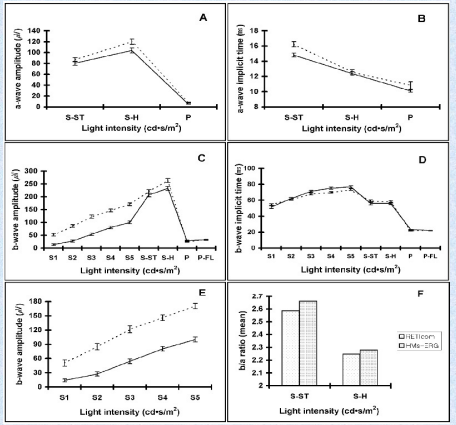


**Fig. 3.** The comparison of mean (±SEM) amplitude **(A, C, and E)** and implicit times **(B, D)** of a- and b-waves recorded by the HMsERG **(a solid line)** and the RETIcom **(a dotted line)**. The b/a ratio for the two ERG equipments are shown in **F**. The changes in a- and b-wave amplitude and implicite time parameters obtained during a recording session using both ERG units are very similar in ERG responses except for amplitudes of the b-wave for scotopic low light intensity stimulation.

**Conclusions.** Both ERG units are appropriate for routine veterinary clinical use. It is recommended, however, to establish ERG system-specific reference ranges for each laboratory and clinic using a 95% confidence interval in order to obtain reliable results especially when evaluating hereditary retinal degenerative disease processes.

**Reference.**

1.Narfström, K., Ekesten, B., Rosolen, S.G., Spiess, B.M., Percicot, C.L., Ofri, R., 2002. Guidelines for clinical electroretinography in the dog. *Documenta Ophthalmologica* 105, 83-92.

# The efficacy for functional evaluation of feline hereditary rod cone degeneration using a portable mini-Ganzfeld electroretinography unit

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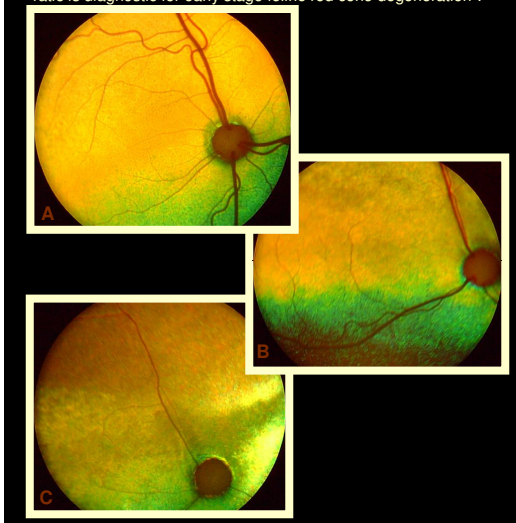
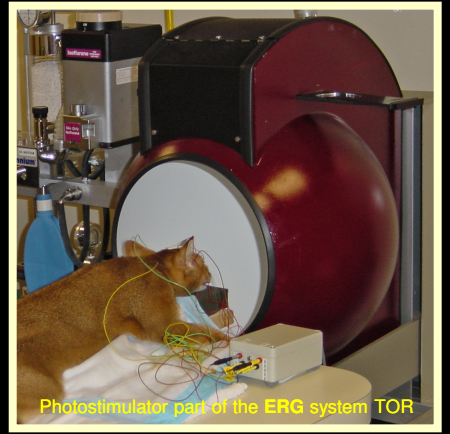
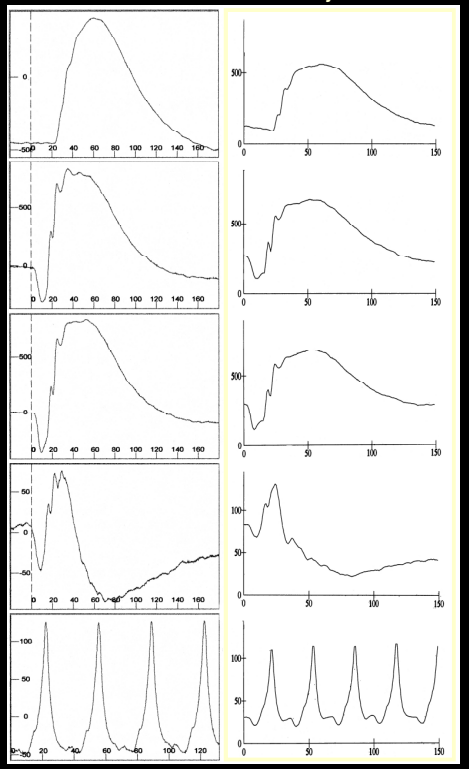
**Background**: Objective evaluation of retinal function is often needed in the clinical and research environment. We studied normal cats and cats affected with different stages of inherited rod cone degeneration[1] to evaluate the efficacy for obtaining a diagnosis with a new portable mini-Ganzfeld ERG unit, using it in parallel with a conventional table-top Ganzfeld ERG. Previous studies, with large ERG equipment and extended protocols, have shown that a significant reduction in scotopic high intensity a-wave amplitude[2-4] together with a corresponding increase in b/a wave ratio is diagnostic for early stage feline rod cone degeneration[5].




**Methods**: Eleven affected cats in different stages of disease (S2 - S4; early (**A**), moderate (**B**) and advanced (**C**)), and four normal controls were anesthetized using a combination of medetomidine (0.09 mg/kg, IM) and ketamine (5 mg/kg, IM) and studied using the protocol recommended by ISCEV for diagnostic ERGs[6] in humans. Cats were dark-adapted overnight and prepared under red lights. Scotopic ERGs were first obtained using a conventional tabletop unit (ERG System **TOR**, Global Eye Program, Rejmyre, Sweden). Before light adaptation, the units were switched and the small, portable ERG (Handheld multispecies ERG; **HMsERG**, RetVet Corp. Inc., Columbia, MO) was used, with the ISCEV protocol, followed by photopic recordings using the larger unit. A- and b-wave amplitude and implicit times were evaluated along with waveform shape, b/a-wave ratios and oscillatory potentials (OPs). The latter were obtained from responses to high intensity stimuli under scotopic conditions through digital filtering at 100 to 300 Hz. The **table** shows light stimulation parameters used with the two different ERG units.


**HMsERG**

| Light intensity / Stimulation (white LEDs) | Mean amplitude µV (Standard Deviation) |
|---|---|
| Scotopic 0.01 cd.s/m² | b-wave: 774.8 (341.8) |
| Scotopic 3.00 cd.s/m² | a-wave: 197.3 (82.2)<br>b-wave: 1118.5 (344.9)<br>b/a-wave ratio: 6.3 (1.8) |
| Scotopic 10.00 cd.s/m² | a-wave: 247.4 (103.8)<br>b-wave: 1159 (344.6) |
| Photopic 3.00 cd.s/m² with 30 cd/m² background | a-wave: 43.0 (18.5)<br>b-wave: 123.3 (59.8) |
| Photopic 30Hz at 3.00 cd.s/m² with 30 cd/m² background | b-wave: 136.0 (47.9) |

**ERG System TOR**

| Light intensity / Stimulation (Xenon flash) | Mean amplitude µV (Standard Deviation) |
|---|---|
| Scotopic 0.01 cd.s/m² | b-wave: 467.5 (156.5) |
| Scotopic 1.00 cd.s/m² | a-wave: 116.0 (44.0)<br>b-wave: 662.8 (172.8)<br>b/a-wave ratio: 4.7 (1.1) |
| Scotopic 4.00 cd.s/m² | a-wave: 126.8 (56.3)<br>b-wave: 676.9 (213.4) |
| Photopic 1.00 cd.s/m² with 30 cd/m2 background | a-wave: 8.9 (5.1)<br>b-wave: 60.2 (36.6) |
| Photopic 30 Hz at 1.00 cd.s/m² with 30 cd/m2 background | b-wave: 70.4 (33.6) |

Light stimulation parameters and mean ERG a- and b-wave amplitudes (**µV**) ±SD for the **HMsERG** and for the ERG System **TOR**, respectively, in early stage of feline rod cone degeneration.

Commercial relationships: Narfstrom K; Provisional patent application for the HMsERG through RetVet Corporation, Inc.

**Results:** Figure (left) shows results of ERG tracings using the HMsERG and the TOR units, respectively, in a case of early stage hereditary retinal degeneration. In affected animals, the mean amplitude of the scotopic a-wave using 3 (HMsERG) and 1 cd.s/m² (TOR) respectively, of white light stimulation was significantly lower already in early disease: 197 ± 82 µV using the **HMsERG** (p=0.004) and 116 ± 44 µV for the **TOR** unit, when compared to results of controls: 559 ± 115 µV and 307 ± 65 µV, respectively. Similarly, significant differences between affected early stage cats and controls were found for the b-wave amplitudes, although not as marked (p=0.014 for the HMsERG) when using this level of light stimulation. For the b/a-wave ratios of affected cats, these were also significantly increased (p=0.037 for HMsERG) in early disease compared to those of normal cats using both units. A- and b-wave implicit times, were not found to be diagnostic when comparing early stage affected and normal cats using either equipment, and 3 and 1 cd.s/m², respectively, of light intensity stimulation. OPs were reduced in affected cats in comparison to those of normal cats (data not shown) using both instruments. The ERG waveform shapes obtained using the portable unit were comparable to those of the conventional tabletop unit (Figure, left).

**Conclusion**: The portable mini-Ganzfeld **HMsERG** provided results that were remarkably similar to the conventional tabletop full-field ERG System **TOR** in normal and affected animals. Although subject to further evaluation, this study shows the efficacy of the portable unit in the diagnosis of generalized photoreceptor disorders. Additional work is underway to establish reference ranges using the portable ERG for research and in the clinical practice.

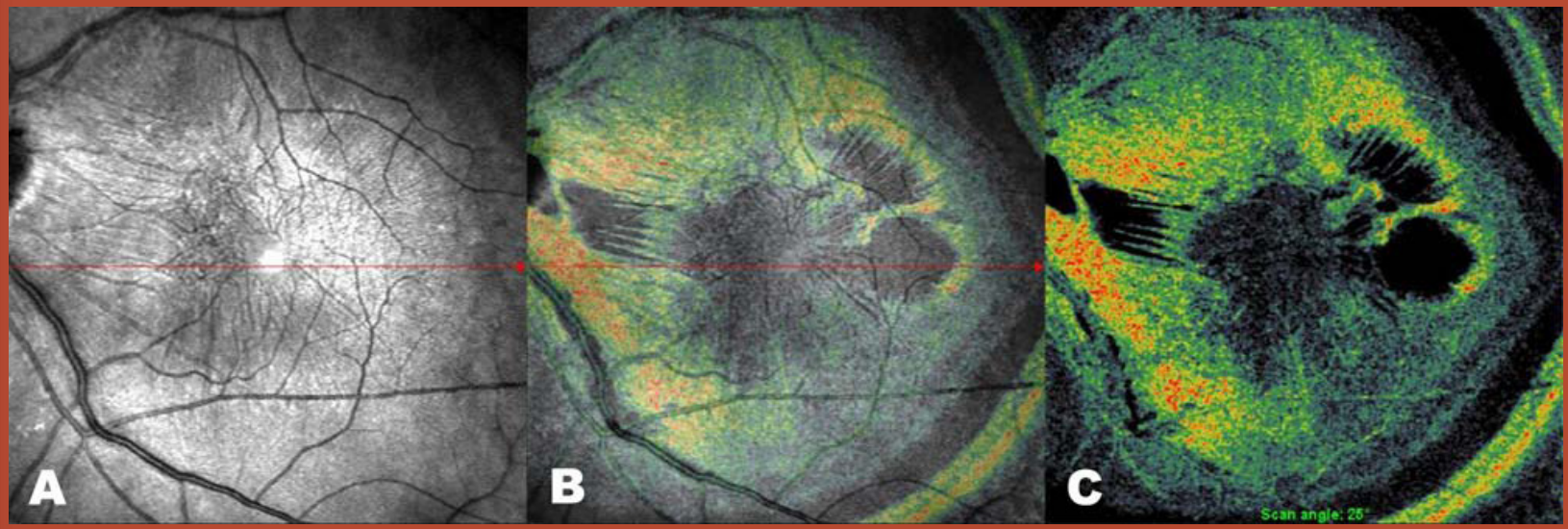
**References:**
1. Narfstrom K. Progressive retinal atrophy in the Abyssinian cat. Clinical characteristics. *Invest Ophthalmol Vis Sci*, 1985;26:193-200.
2. Vaegan, Narfstrom K. Optimal discrimination of an Abyssinian cat recessive retinal degeneration: a short electroretinogram (ERG) protocol is more efficient than a long one. *Clinical and Experimental Ophthalmology*, 2004: 32:619-625.
3. Vaegan, Narfstrom K. Amax is the best a-wave measure for classifying Abyssinian cat rod/cone dystrophy. *Doc Ophthalmol*, 2005:111 (1):33-38.
4. Kang Derwent J, Padnick-Silver L., McRipley M., Giuliano E., Linsenmeier RA, Narfstrom K. The electroretinogram (ERG) components in Abyssinian cats with hereditary retinal degeneration. *Invest Ophthalmol Vis Sci*, In Press, 2006.
5. Hyman J, Vaegan, Lei B, Narfstrom K. Electrophysiologic differentiation of homozygous and heterozygous Abyssinian-crossbred cats with late-onset hereditary retinal degeneration. *Am J of Vet Research*, 2005: 66 (11):1914-1921.
6. Marmor MF, Holder GE, Seeliger MW, Yamamoto S. Standard for clinical electroretinography (2004 update). *Doc Ophthalmol*, 2004: 108:107-114

**ARVO 2006**

# Structure and Function

- Imaging, Histology provide data of retina cellular organization, interactions, and structural integrity
- Electrophysiology assesses the function of the retina / visual pathway

# SLO and OCT




Analysis of topographic features in macular pucker. A, Grayscale SLO image of the fundus in a subject's left eye. B, Overlay of the coronal OCT image (color photo C) superimposed on the SLO fundus image (grayscale photo A) with point-to-point registration. C, Coronal plane OCT image, in color. The overlay image (B) was used to characterize the macular hole and/or macular pucker (as in this case) for topographic analysis.

MACULAR HOLES AND MACULAR PUCKER: THE ROLE OF VITREOSCHISIS AS IMAGED BY OPTICAL COHERENCE TOMOGRAPHY/SCANNING LASER OPHTHALMOSCOPY
BY Jerry Sebag MD FRCOphth,* Priya Gupta, Richard R. Rosen MD, Patricia Garcia MD, AND Alfredo A. Sadun MD PhD

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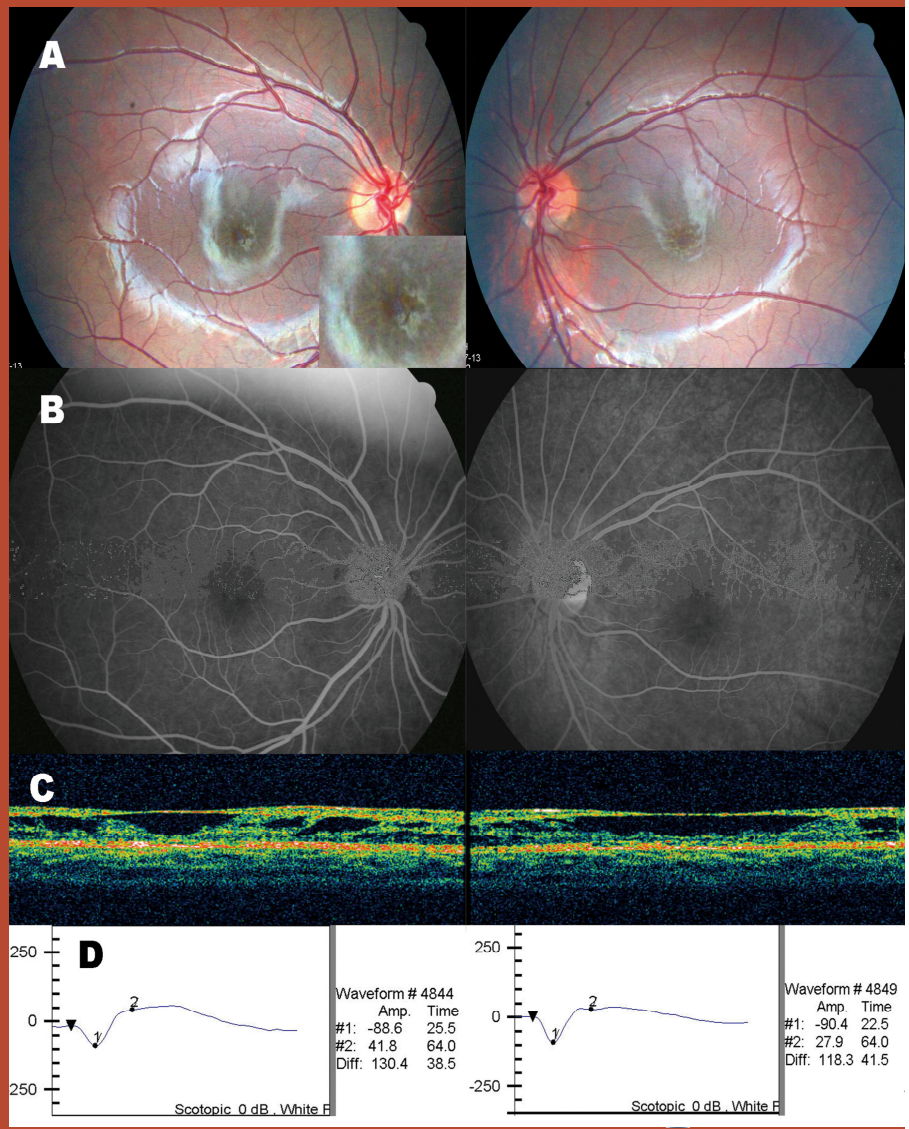
# Combining Structure and Function

Ocular findings in a Korean XLRS patient (case 16). **A:** Fundus photograph of the both eyes showed typical stellate pattern of schisis cavities in the macula. The inset presents an image of the macula magnified twofold. **B:** Fluorescein angiogram showed no definite leakage from the cystic cavities. **C:** Optical coherence tomography showed the schisis in the nerve fiber layer. **D:** Electroretinogram showed markedly decreased amplitude of b-wave and relative preservation of a-wave, which are key features of XLRS.

Kim, Mol Vis 2009; 15:833-843.

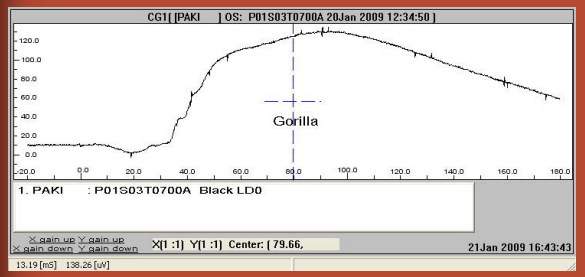


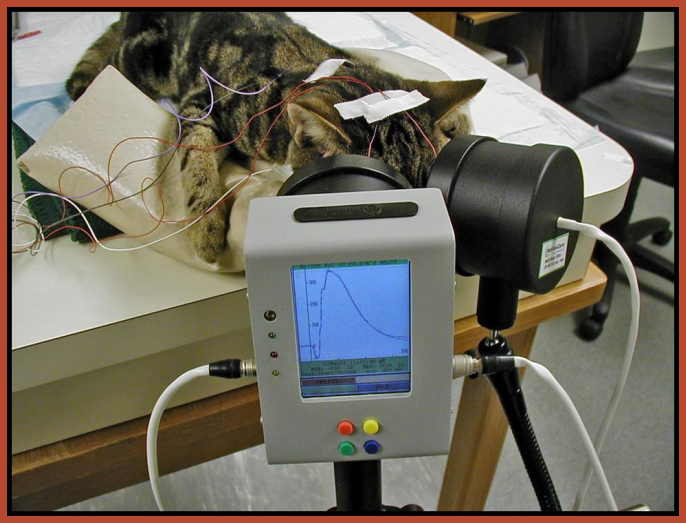
# Multi-modal Imaging

- Integration of Structure and Function in Real-time
  - "Synergising optical coherence tomography and ERG enhances retinal phenotyping in rodents"
    M Seeliger
  - "Determination of optimal recording parameters for multimodal imaging using combined OCT/SLO and micro-mfERG"
    S Walker
  - "Diabetic macular edema: correlations between retinal thickness, micro-perimetry and mfERG"
    S Coupland

# Thank You

Contact:
info@ocuscience.us

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