EVALUATION OF THE TOXICITY OF INTRAVITREAL CARBOPLATIN INJECTION IN A RABBIT MODEL

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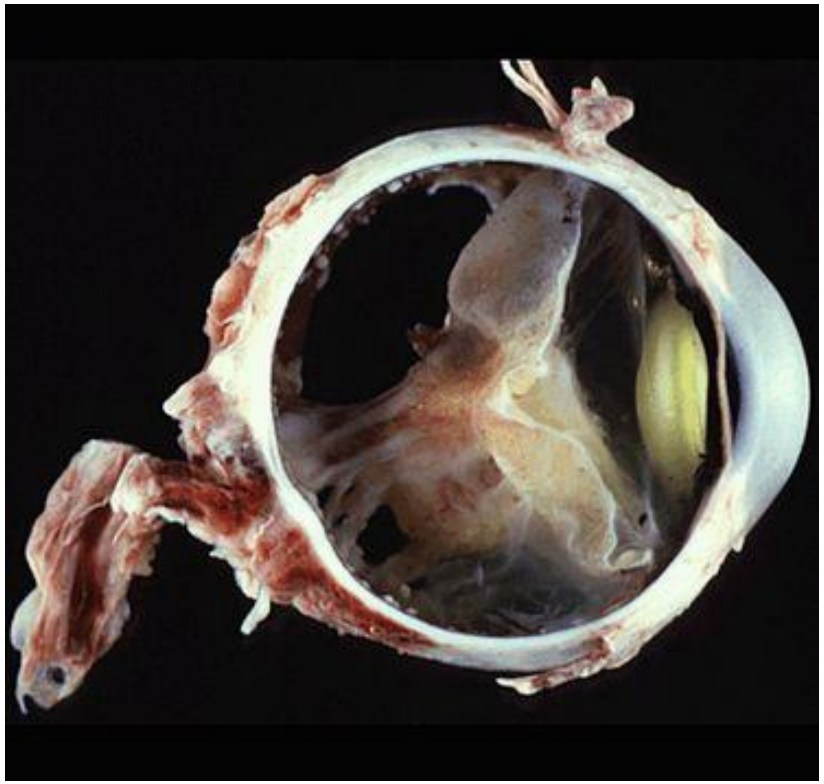
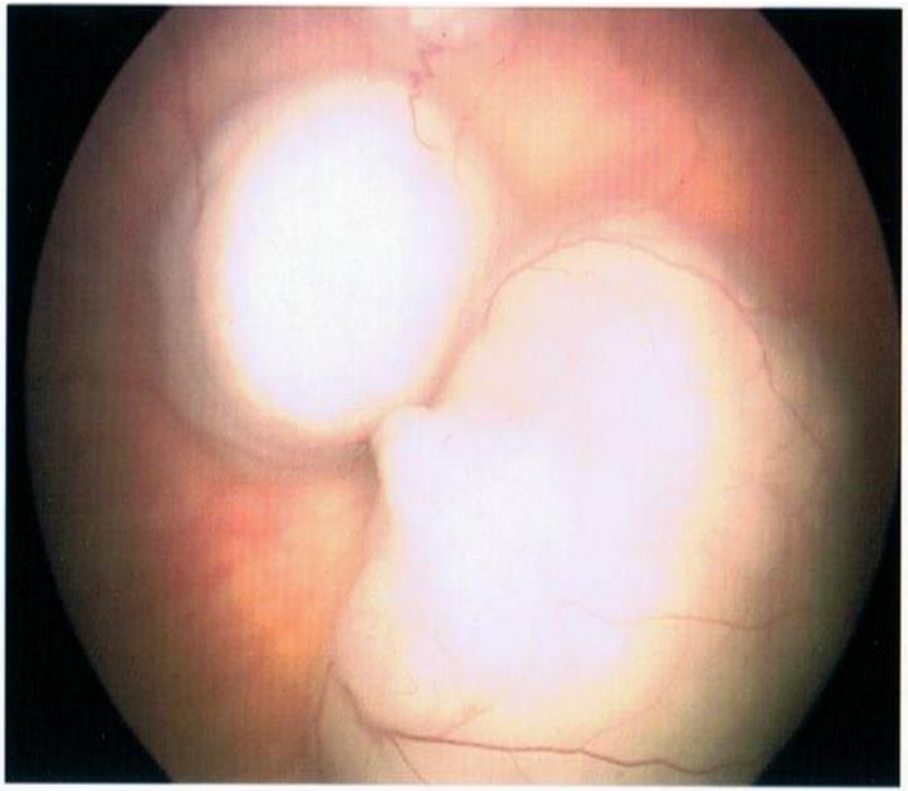
Carboplatin

- **Carboplatin:**
  - belong to the group of platinum based antineoplastic agents
  - chemotherapy drug used in a variety of cancers
  - Carboplatin is a widely used chemotherapy agent in the treatment of retinoblastoma

Retinoblastoma





Retinoblastoma

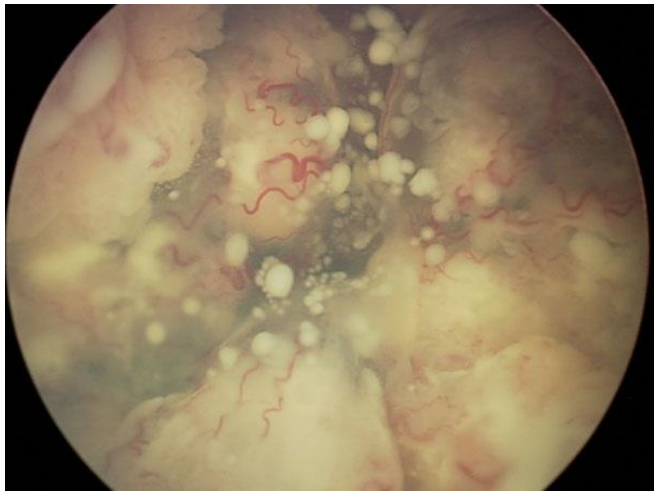
- **The leading treatment for retinoblastoma is:**
  - Intravenous chemotherapy
  - Intra-arterial chemotherapy

Retinoblastoma

- **<u>Vitreous seeding-</u>** a limiting factor in the success of globe-preserving therapies

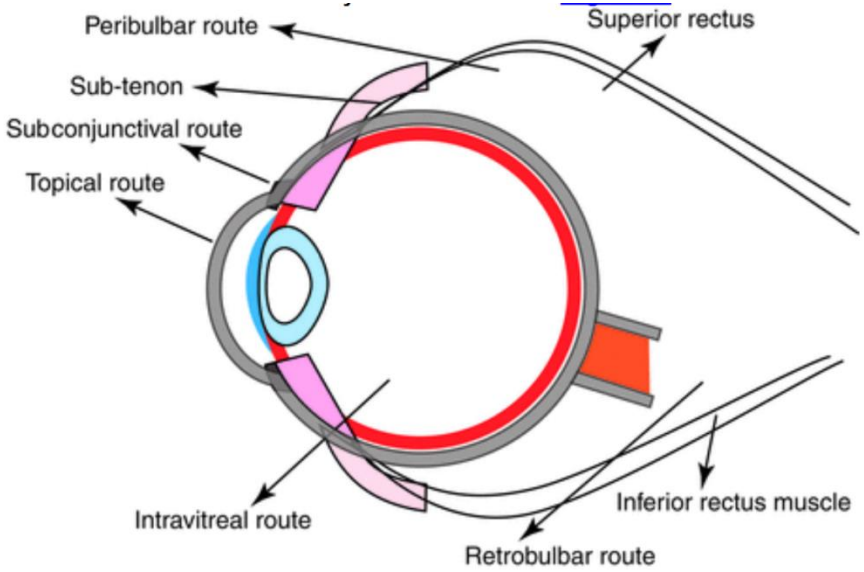
  melphanan:

  - Toxicity
  - Instability
  - cost



Carboplatin

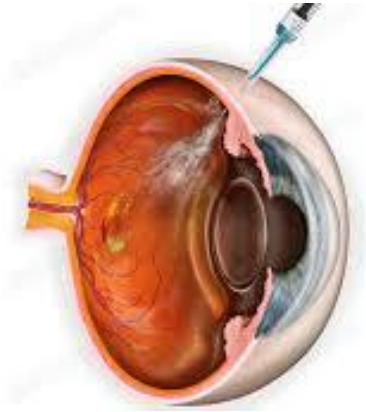
- **Carboplatin Delivery methods in retinoblastoma:**
  - Intravenous
  - Periocular
  - Intra-arterial



  - Intravitreal carboplatin administration toxicity was not examined to date

PURPOSE:

The purpose of this study was to evaluate the toxicity of intravitreal carboplatin injection in a rabbit model

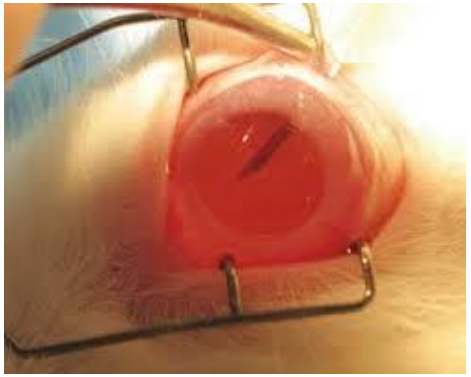


Methods :

- The study included Ten New Zealand albino male rabbits
- Weighing 1.8 to 2.2 kg each
- Handled according to the association for research in vision and ophthalmology (ARVO) Statement for the use of Animals

Methods :

- The rabbits were given a single carboplatin intravitreal injection
- In varied dosage (3-8µg) / 0.1 ml in one eye
- The second eye was used as control

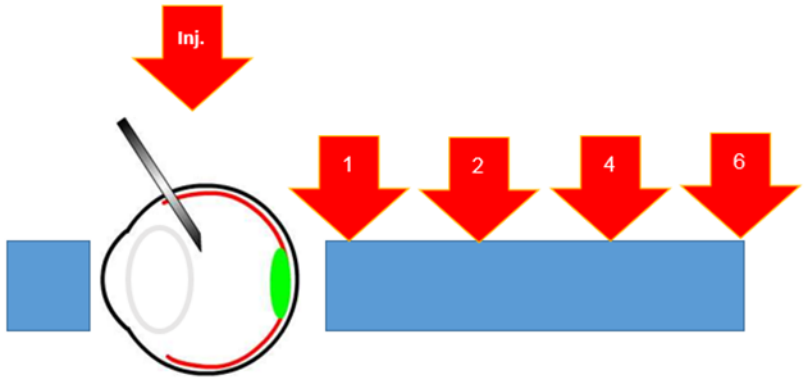


Methods

- **Outcome methods:**
  - Anatomical evaluation
  - Functional evaluation
  - Histopathological evaluation

Methods - clinical evaluation :

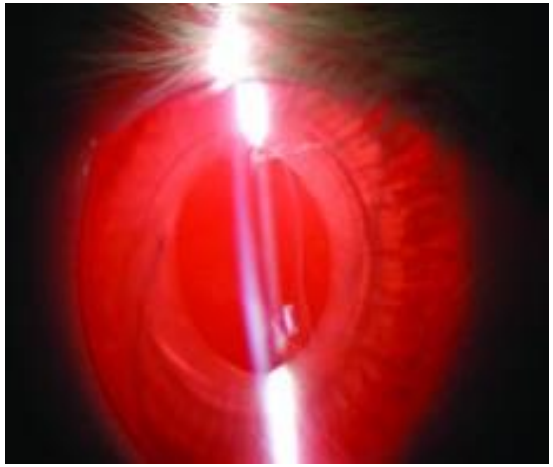
- Evaluation of changes in cornea, lens, vitreous, retina, and optic nerve Under Anesthesia

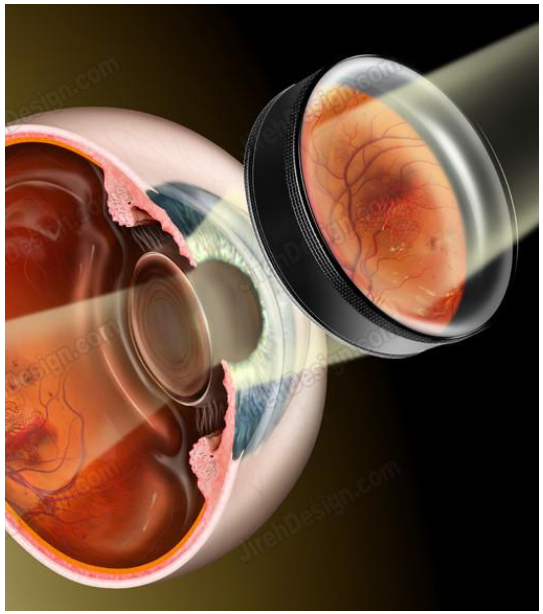


*Baseline day, Weeks 2, 4 ,6

Methods - clinical evaluation :

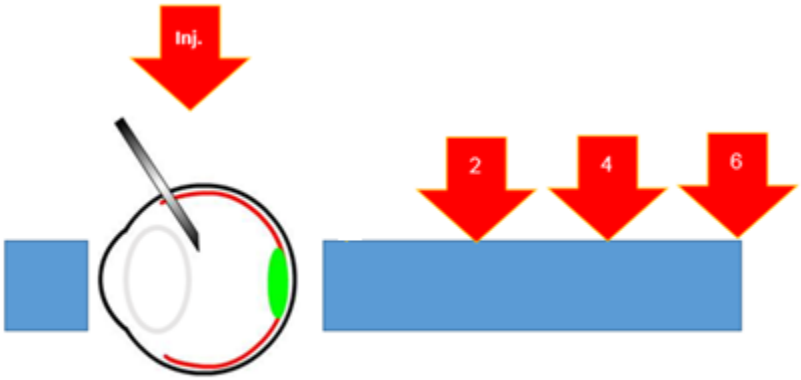
- Intraocular pressure measurement
- Slit lamp examination
- Indirect ophthalmoscopic fundus examination





Methods - toxicity evaluation:

- **Anatomical (in vivo) :**
- Optical Coherence Tomography (OCT)
- Ultrasound (US) anterior and posterior examinations



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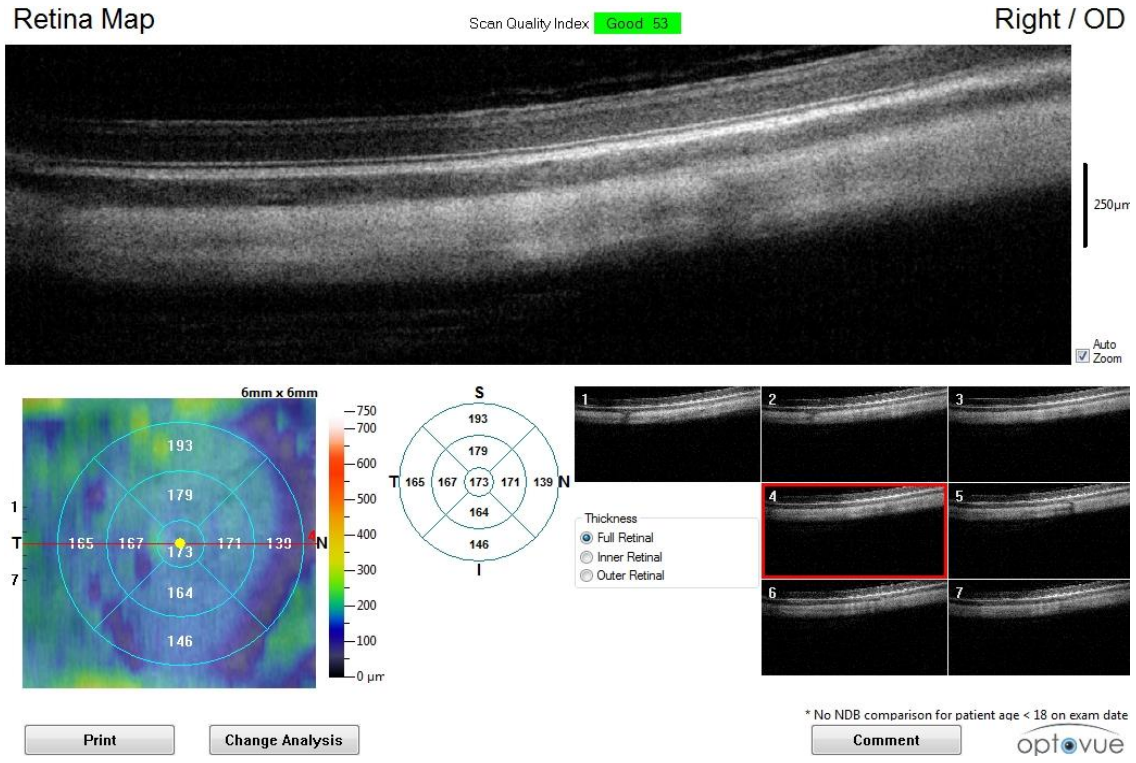

Methods - toxicity evaluation:

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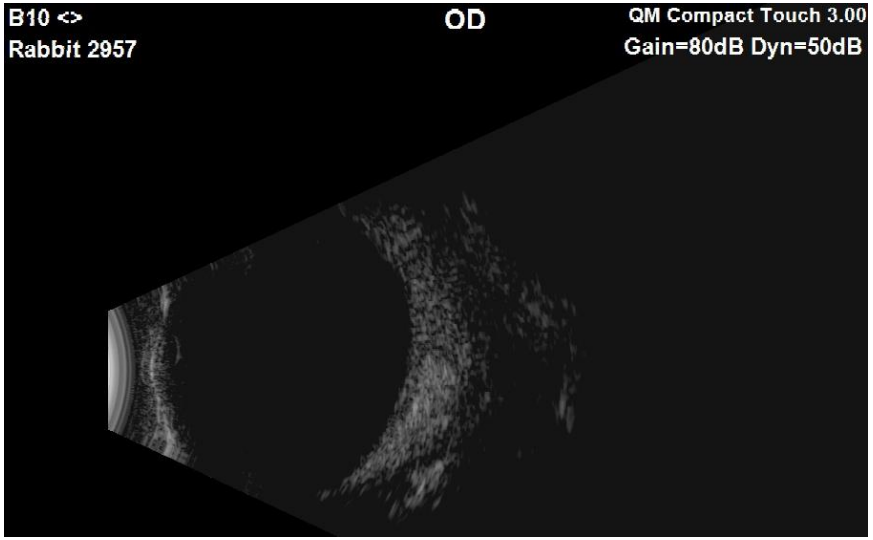
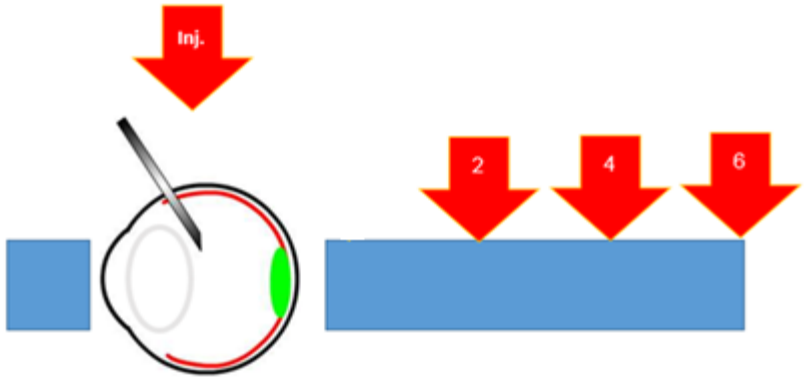


Methods - toxicity evaluation:

- **Functional:**
- The electroretinogram (ERG) is a diagnostic test that measures the electrical activity generated by the cells in the retina in response to a light stimulus
- Repeated electroretinogram (ERG) under photopic and scotopic conditions.



*Baseline day, Weeks 2, 4 ,6

Methods - toxicity evaluation:

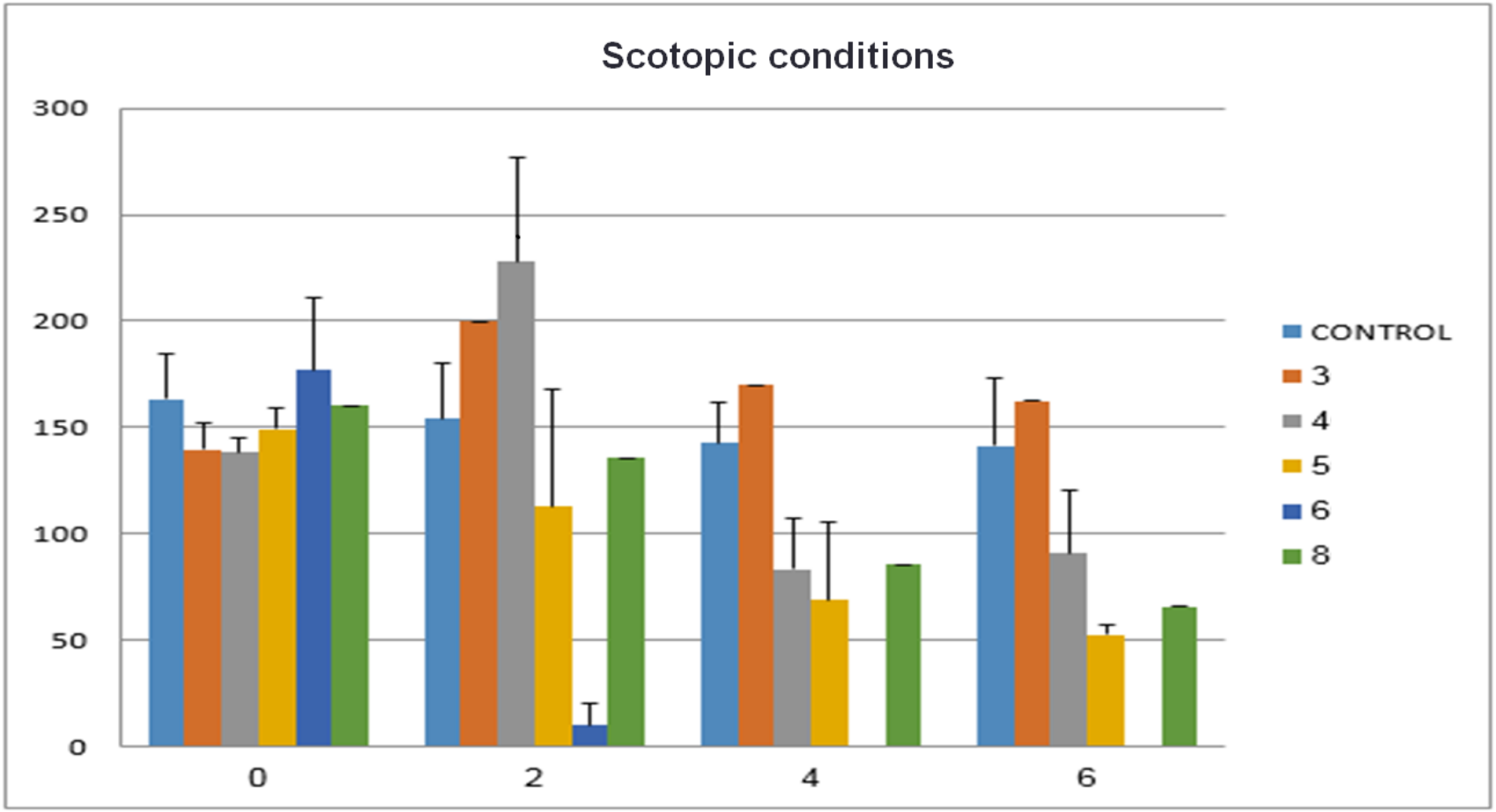
- **Histology:**
- After euthanasia the eyes were fixated and submitted for histopathological evaluation

Results:

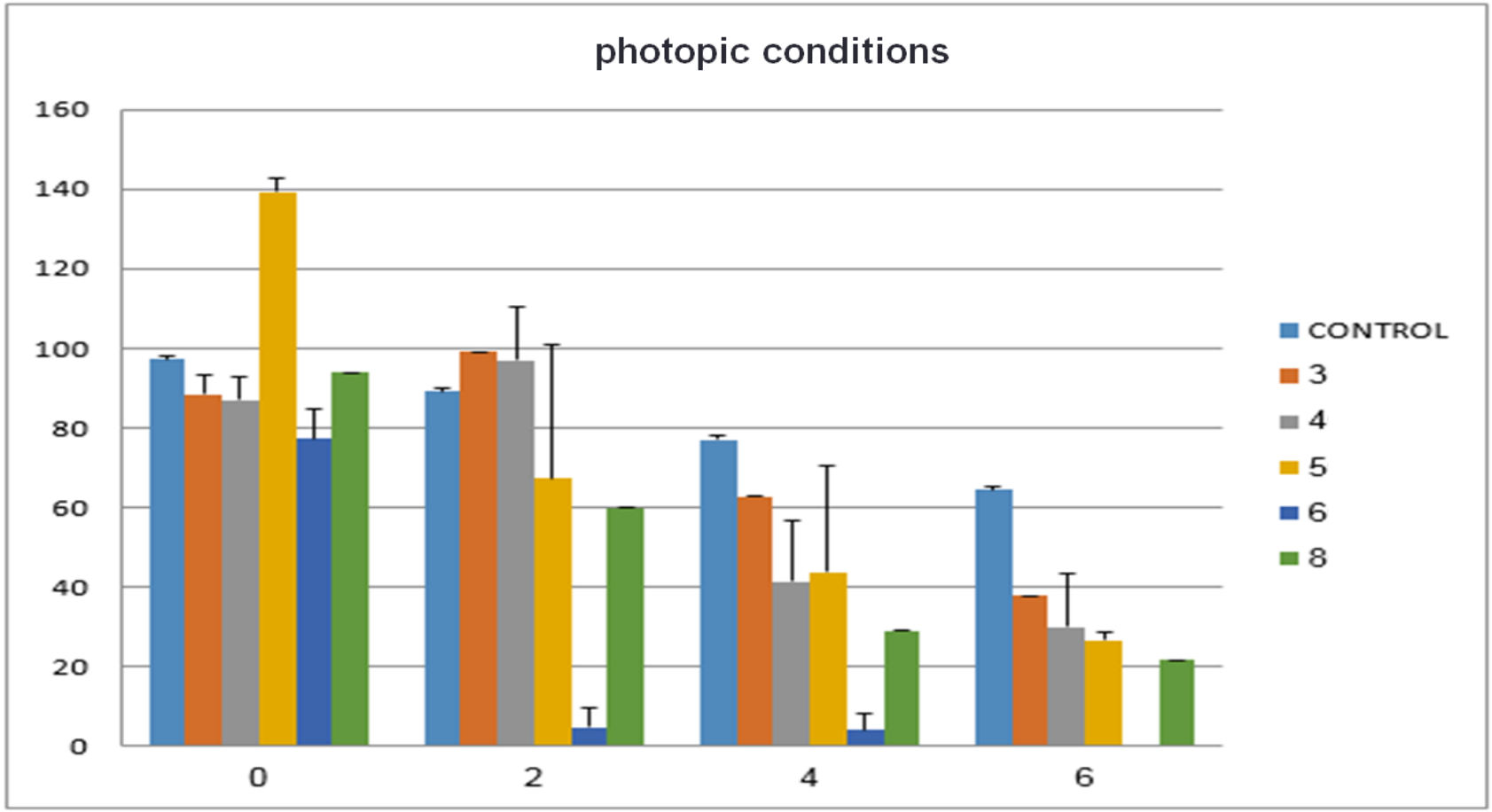
- All the eyes (study and control) had Normal:
  - ✓IOP examination
  - ✓anterior segment examination
  - ✓fundus examination
  - ✓OCT examination
  - ✓US examination

    at all the examination points
  - ✓histopathological evaluation

ERG Results:

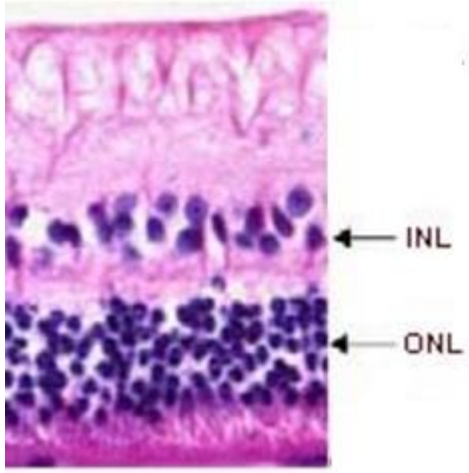

Scotopic conditions
300
250
200
150
100
50
0
0
2
4
6
CONTROL
3
4
5
6
8

ERG Results:


photopic conditions
160
140
120
100
80
60
40
20
0
0
2
4
6
CONTROL
3
4
5
6
8

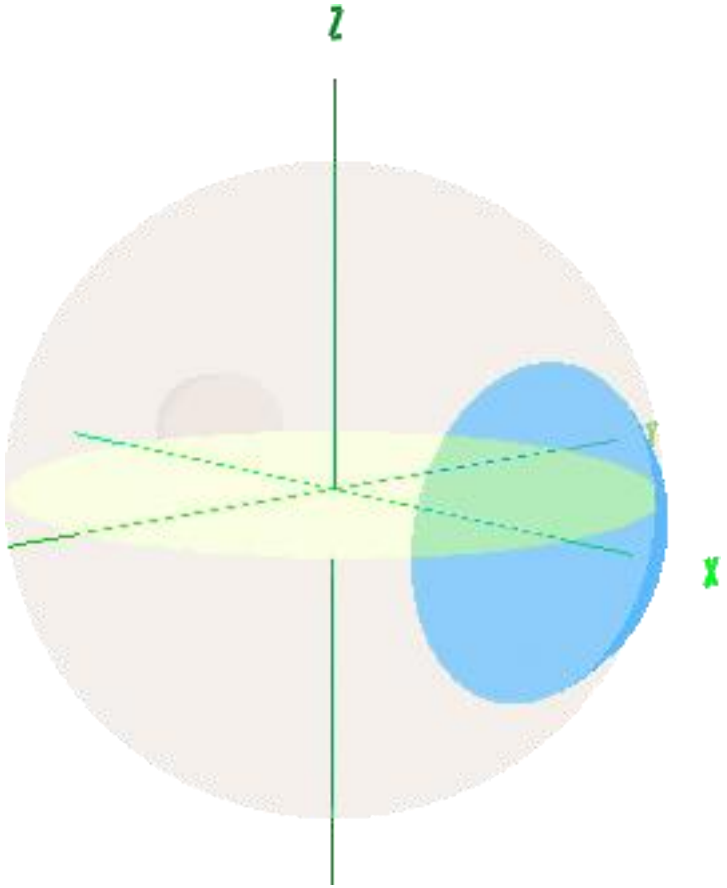
Methods- toxicity evaluation:

- Cell toxicity or cell death
- Retinal cell count:
  - Outer nuclear layer
  - Inner nuclear layer

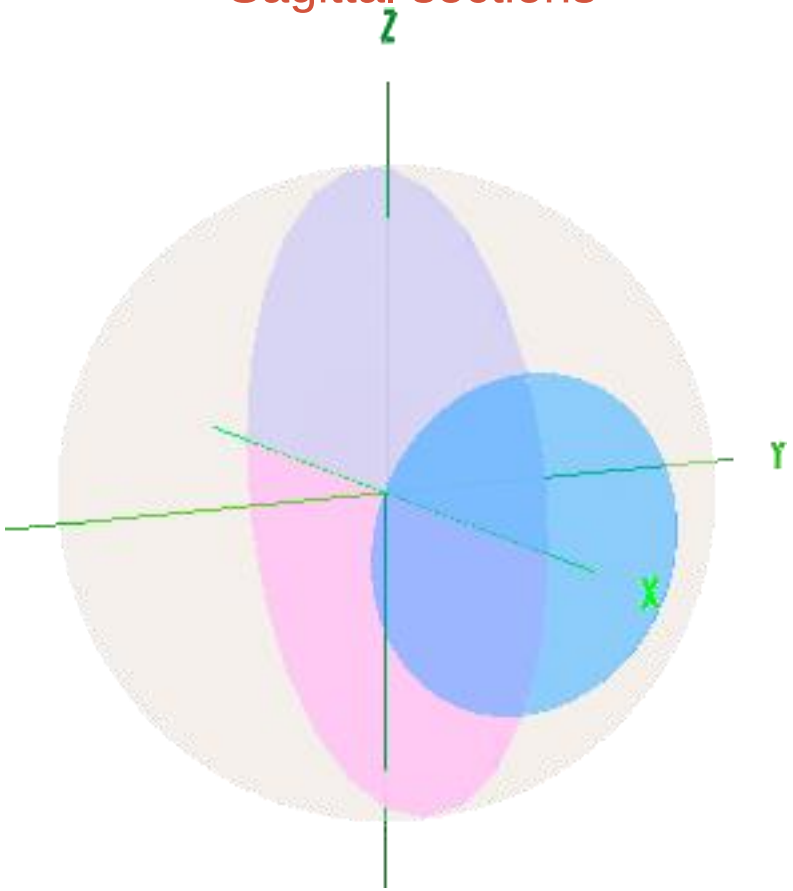


Methods - toxicity evaluation:

(A) Axial section



(B) Upper & (C) lower
Sagittal sections



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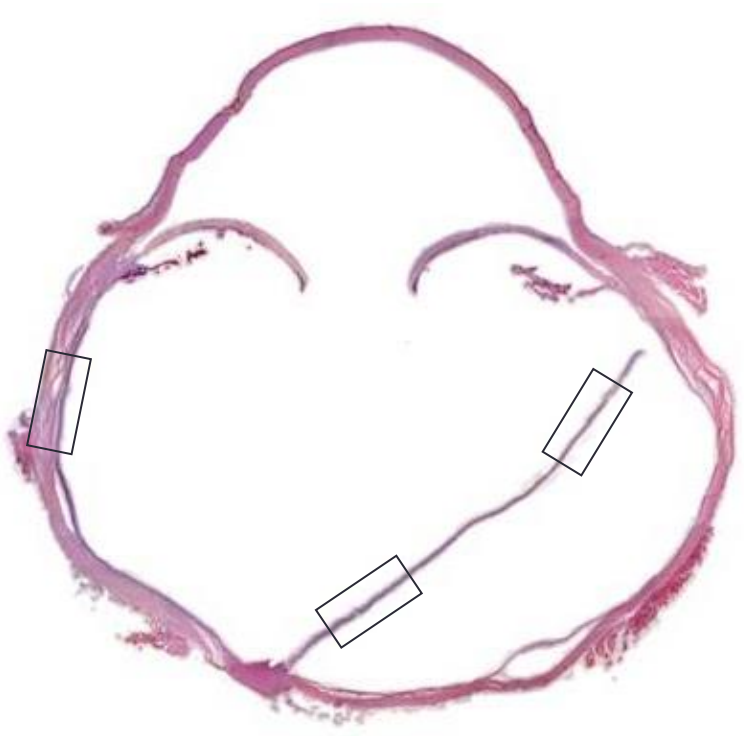

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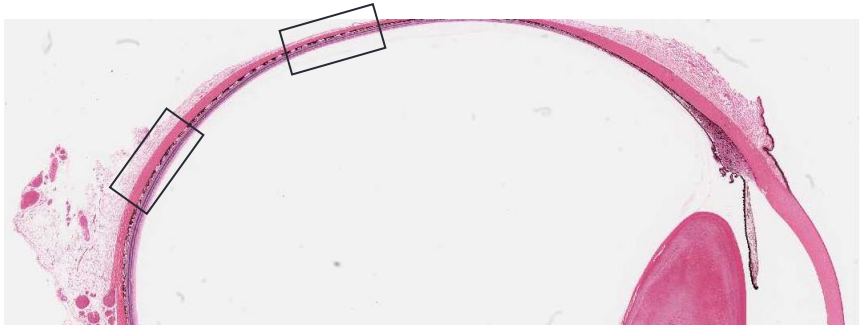
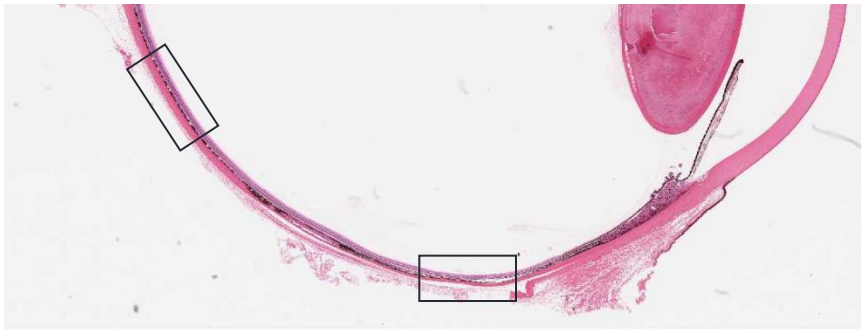
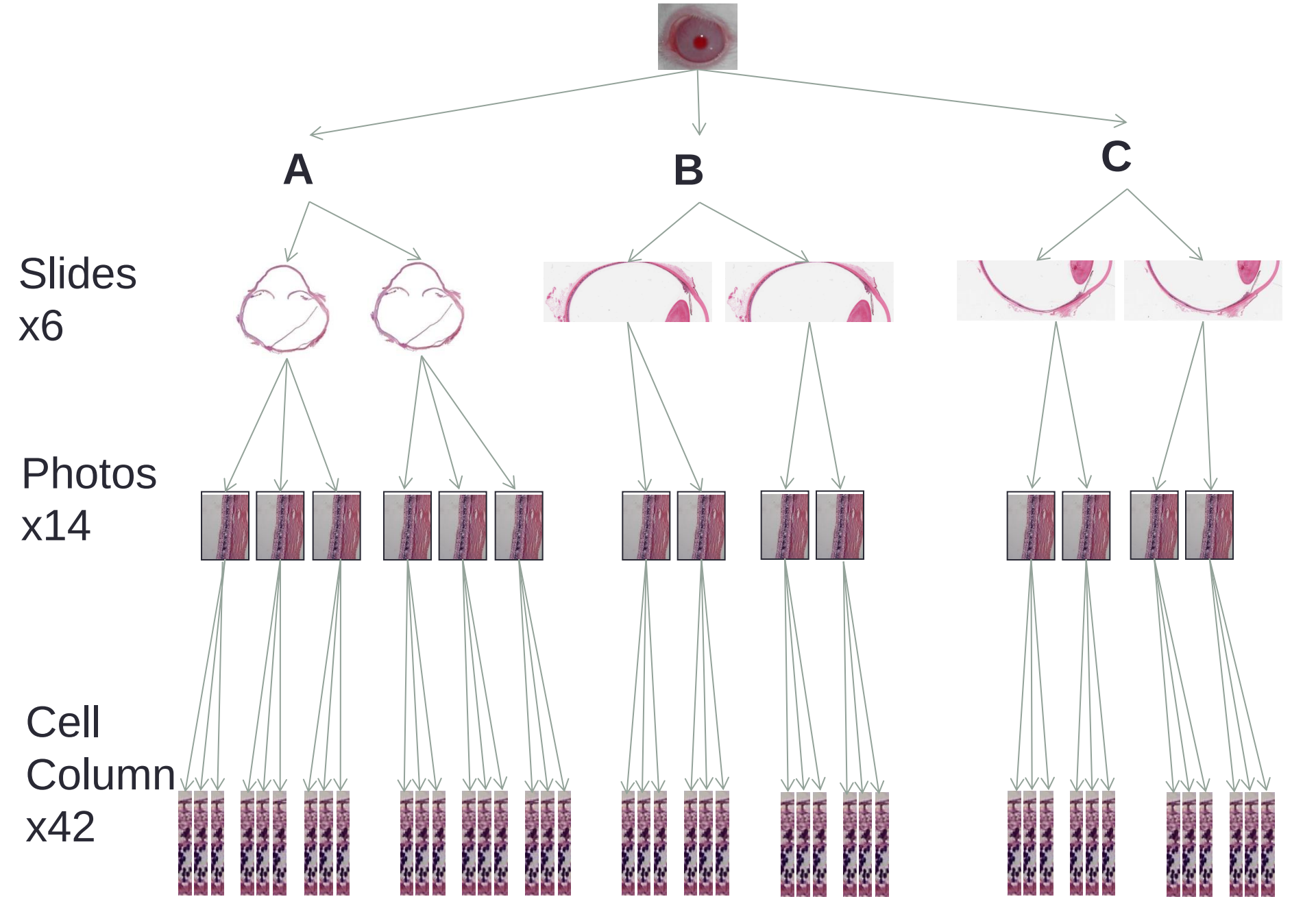
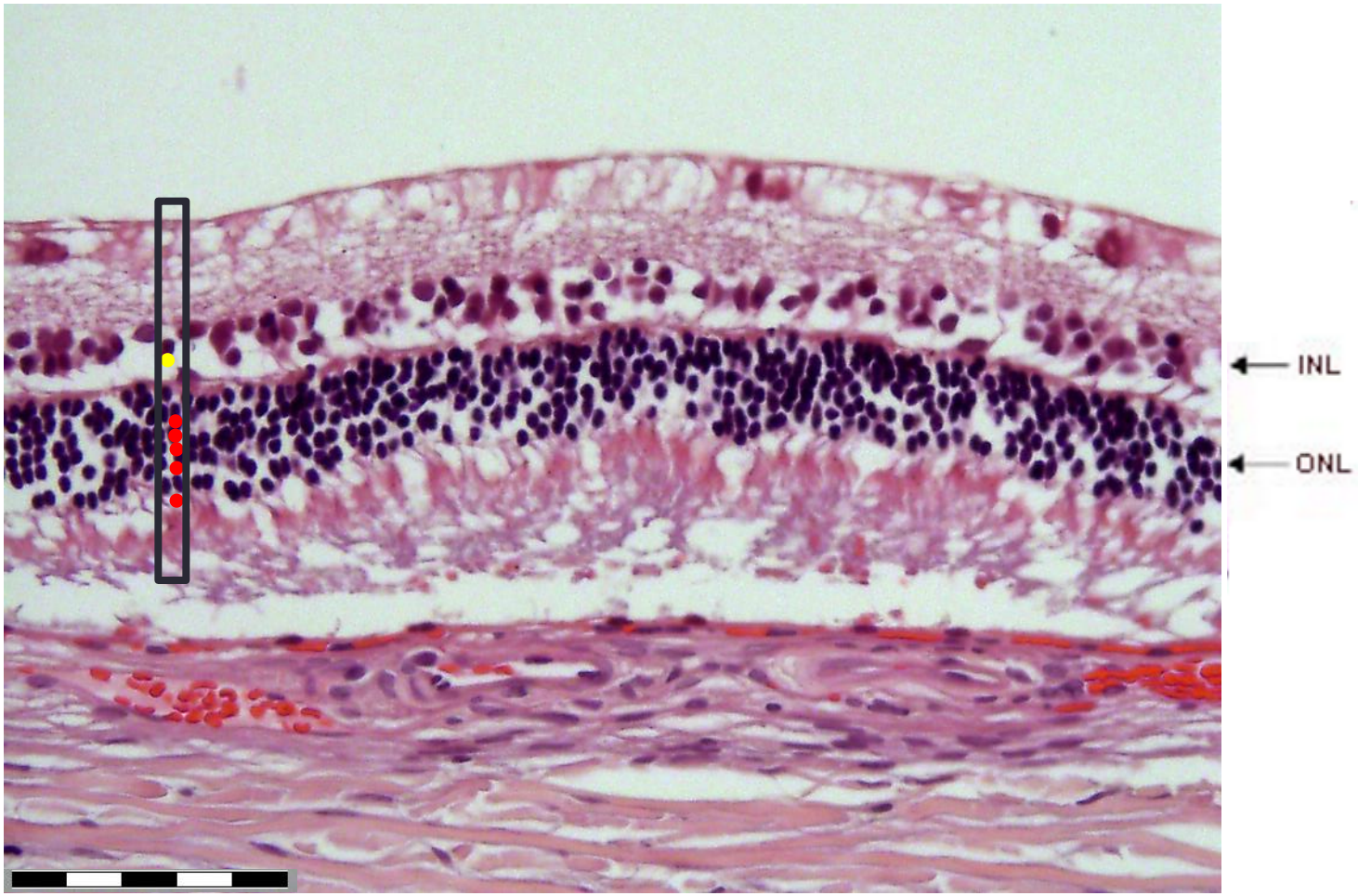


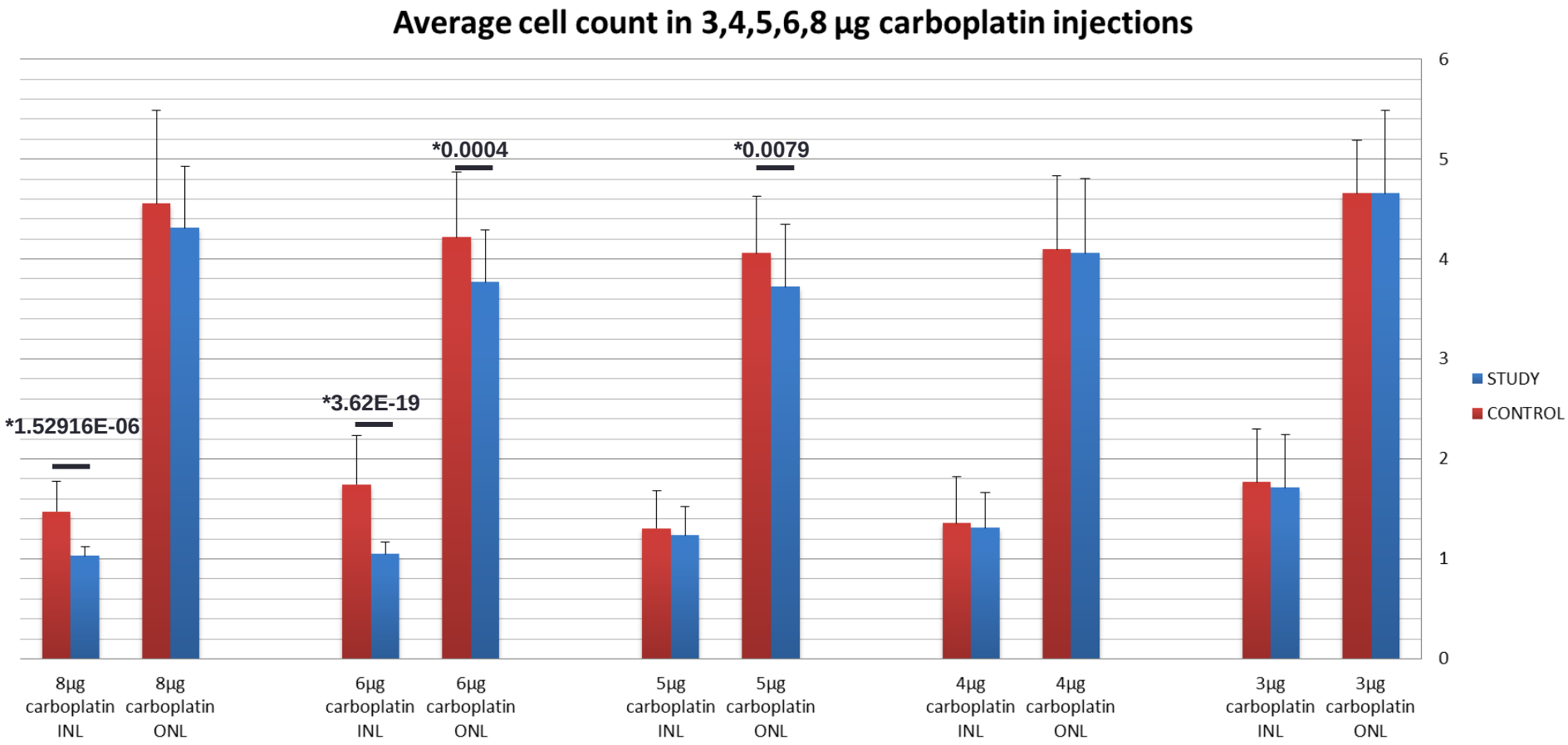



A
B
C
Slides
x6
Photos
x14
Cell
Column
x42

Methods - toxicity evaluation:



Retinal cell count results



Conclusions:

- Intravitreal carboplatin injection appears to be safe in the dosage of 3- 4 µg/0.1 ml in a rabbit model
- Dosage of 5-8 µg/0.1 ml lead to amplitude decline of the ERG reading and decrease in the average retinal cell count but resulted in no anatomical ocular changes
- Future studies are needed to examine the efficacy of 3- 4 µg/0.1 ml Intravitreal carboplatin injections

My personal experience with animal studies

“Ethical use in lab’s animal”
Tel-Aviv university

TEL AVIV UNIVERSITY אוניברסיטת תל-אביב
SACKLER FACULTY OF MEDICINE הפקולטה לרפואה ע"ש סאקלר

כתב הרשאה לניסויים בבעלי חיים למטרות מחקר והוראה

מספר **TAU-R-1011345**

בהתאם לסמכות שניתנה לי על ידי האוניברסיטה במסגרת פעילותה לפי
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המועצה לניסויים בבעלי חיים, הריני מסמיך

את החוקר/ת גב' דנה לוברמן

ת"ז 300962909

לבצע ניסויים מדעיים בבעלי חיים מסוג מכרסמים וארנבות.

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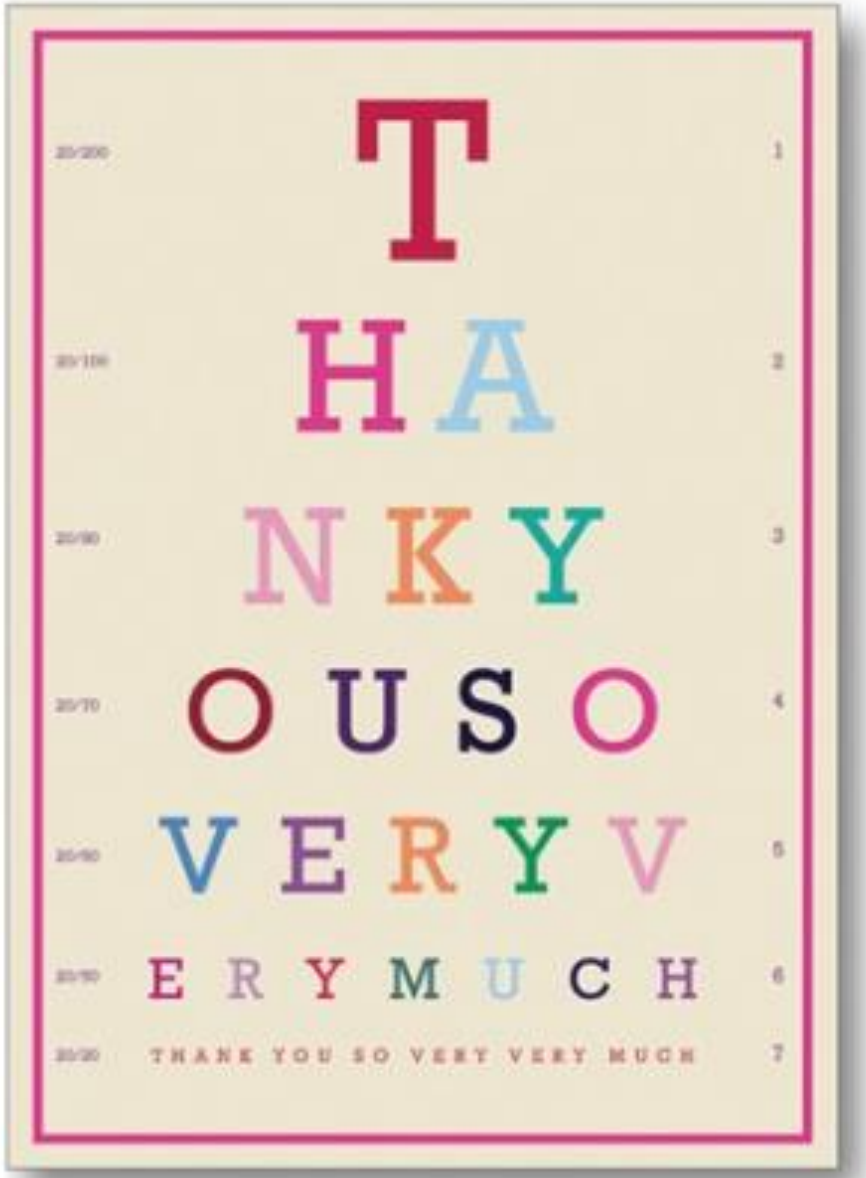
פרופ' רונית סצ'י פיינארו
יו"ר הועדה האוניברסיטאית לאתיקה של טיפול וניסויים בבעלי חיים

תאריך 01/06/2016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HA
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ERYMUCH
THANK YOU SO VERY VERY MUCH