Phantoms and Standardization in Ophthalmology

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when and how standardization is useful
Ophthalmology
Why a standard phantom?

• To have a common platform for:
  ✓ Drug dosing
  ✓ Surgical benchmark
  ✓ Surgeon’s training
  ✓ Ensure that patients have access to high quality, safe and effective medical devices
What an eye phantom should be

- Transparent
- Easy to fabricate, to handle, and to use
- Not expensive
what is going on in Europe and internationally

Ophthalmology
Common models in Ophthalmology

- **Ex vivo tissues**: human donor not suitable for transplants, animal
- **In vitro cells** (epithelial cells, endothelial cells, keratocytes, etc): drug delivering, corneal transparency study
- **Software**: mainly biomechanical, phothermal, multiphysics in general
- **Animals**: rats, rabbits, pigs...
Ex vivo tissues

Anterior part of a bovine eye

... they are EX VIVO!!!!

And physical properties of eye tissue degrade immediate after death
Cell lines

Phenotypic characterization of the SIRC (Statens Seruminstitut Rabbit Cornea) cell line reveals a mixed epithelial and fibroblastic nature

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SIRC cells, often described as of epithelial origin, are used as a corneal epithelial barrier model to study the permeability of ophthalmic drugs.

SIRC cells show a hybrid nature, fibroblast/epithelial!

- long-term in vitro cultivation of cell lines leads to a derangement of their specific phenotype, most likely due to genetic and epigenetic factors.
Optically inspired biomechanical model of the human eyeball

Anvil-profiled penetrating keratoplasty: load resistance evaluation.
A. Canovetti, F. Rossi et al., Biomechanics and Modeling in Mechanobiology
doi:10.1007/s10237-018-1083-y
Animals

• Incongruities between eyes of lab animals (dimensions, functionality...)
• Expensive
• ... And the 3Rs (ethical issues):

1. Replace the need for animal experiments
2. Reduce the numbers of animals used to an unavoidable minimum
3. Refine any procedures necessarily used, so as to minimize any pain or distress suffered by animals
What’s new?

New eye phantom for ophthalmic surgery

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Input from literature
Multidisciplinary

Consider healthy and pathological eye!

Table 1 Materials chosen for mimicking human eye.

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Material</th>
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<tbody>
<tr>
<td>Bone</td>
<td>Plexiglas</td>
</tr>
<tr>
<td>Sclera</td>
<td>5% (w/v) PCL in chloroform</td>
</tr>
<tr>
<td>Choroid</td>
<td>Polydimethylsiloxane</td>
</tr>
<tr>
<td>Retina</td>
<td>4% (w/v) Gelatin in deionized water + 0.2% (w/v) gelatin</td>
</tr>
<tr>
<td>Vitreous</td>
<td>31.5% (w/v) polyvinyl alcohol in deionized water</td>
</tr>
<tr>
<td>Humor</td>
<td>water + gelatin 2.5% (w/v) in deionized water</td>
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</tbody>
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Fig. 2 Sketch of the various parts composing the phantom: (a) View of the covers used for making the different eye parts. As explained in the text an eye part is made for compression moulding of polymer between the base and a specific cover: (b) various phantom parts: sclera (yellow), choroid (purple), retina (green), and vitreous (gray). The BASE (Plexiglas) represents the ocular bone cavity.

Fig. 3 Phantom versus eye. As it is possible to see the insertion scheme of trocar and vitrectomies in the eye phantom (a) is the same than in real eye (b).
What’s new?

3D-printing human corneas

Article by Amanda Doyle

Seeing eye to eye: Steve Swioklo and Che Connan from Newcastle University with a 3D-printed cornea
What's new?

3D Printed Phantoms of Retinal Photoreceptor Cells for Evaluating Adaptive Optics Imaging Modalities
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ABSTRACT
Adaptive optics-enabled optical coherence tomography (AO-OCT) and scanning laser ophthalmoscopy (AO-SLO) devices can resolve retinal cones and rods in three dimensions. To evaluate the improved resolution of AO-OCT and AO-SLO, a phantom that mimics retinal anatomy at the cellular level is required. We used a two-photon polymerization approach to fabricate three-dimensional (3D) photoreceptor phantoms modeled on the central foveal cones. By using a femtosecond laser to selectively photoproduce precise locations within a liquid-based photosensitive via two-photon absorption, we produced high-resolution phantoms with \(\mu\)-level dimensions similar to true anatomy.
In this work, we present two phantoms to evaluate the resolution limits of an AO imaging system: one that models only the outer segments of the photoreceptor cells at varying retinal eccentricities and another that contains anatomically relevant features of the full-length photoreceptor. With these phantoms we are able to quantitatively estimate transverse resolution of an AO system and produce images that are comparable to those found in the human retina.

Keywords: phantoms, photoreceptor phantom, retinal phantom, adaptive optics, direct laser writing, additive manufacturing, 3D printing, optical coherence tomography, scanning laser ophthalmoscopy

Fig. 1. Model eye setup for phantom imaging. (a) Individual components used for model eye and phantom assembly. (b) Photograph of the front end of the system.

Fig. 8. Full-length photoreceptor phantom (a) design and (b) corresponding AO-OCT B-scan.
possible common EU strategy

Ophthalmology
An idea from US

“To expedite the use of 21st-century science to protect and improve public health, federal agencies and stakeholders will work together to build a new framework to enable development, establish confidence in, and ensure use of new approaches to toxicity testing that improve human health relevance and reduce or eliminate the need for testing in animals.”
An idea from US

3 strategic goals:

1. Connect end users with the developers of NAMs (New Approach Methodologies)
   a. Identify anticipated testing requirements.
   b. Encourage the establishment of grant review criteria.
   c. Develop mechanisms to improve communication between end users and researchers

2. Foster the use of efficient, flexible, and robust practices to establish confidence in new methods.
   a. Clearly delineate testing requirements and context of use.
   b. Promote the use of new approaches for establishing confidence.
   c. Utilize public-private partnerships to promote cross-sector communication and cooperation.

3. Encourage the adoption and use of new methods and approaches by federal agencies and regulated industries.
   a. Provide clear language regarding the acceptance of NAMs.
   b. Collaborate with international partners to facilitate global harmonization and regulatory acceptance.
   c. Explore processes to incentivize and promote the use of NAMs.
   d. Identify appropriate metrics for prioritizing activities, monitoring progress, and measuring success
Conclusions

• There is a convergence of medical, scientific and safety needs
• Common EU strategy is needed

Key factors to success:

- Multidisciplinary
- Clear Communication and Collaboration within different stakeholders
- Contacts/comparison with extra EU Countries
- Support from EC (we need 1 ref, not 10s...
Thank you for your attention