

# Intraocular tamponades

## Present – Future trends

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I HAVE NO RELEVANT FINANCIAL INTEREST WITHIN THE  
PRODUCTS DESCRIBED IN THIS PRESENTATION

# Vitrectomy

- Diseased and dysfunctional vitreous is removed
- Vitreous does not regenerate
- Replaced with **artificial substitutes**
- Must mimic the natural vitreous chemical and functional characteristics.

keeps retina in place

ensure retinal adherence after laser or cryo

control intraocular hemorrhage

maintain intraocular pressure

prevents phthisis bulbi

- Vitreous substitutes are one of the most interesting and challenging topics of research in ophthalmology !

# Vitreous substitutes classification

- According to their **molecular status**
- According to their **functional and surgical application**

# According to their molecular status

- Conventional Vitreous substitutes

  - Air

  - Gases ( SF<sub>6</sub>, C<sub>3</sub>F<sub>8</sub>)

  - Liquids

    - Balanced salt solution,

    - Perfluorocarbon liquids

    - Silicone oils

- Newer Vitreous substitute

  - Semi Fluorinated Alkanes

  - Silicone Oil/ Semi Fluorinated Alkanes combinations

# According to their functional and surgical application

(i) vitreal substitutes as **temporary fillers** of vitreous cavity during the surgical procedure to maintain the ocular tone;

(Balanced salt solution)

(ii) vitreal substitutes used as **surgical tools** themselves during different phases of vitreoretinal surgery, requiring a short intraocular permanence; ( Perflourocarbon liquids)

# According to their functional and surgical application

(iii) vitreal substitutes as more **permanent fillers** of the vitreous cavity after vitreoretinal surgery with different permanence time

- gases

- and silicone oils (conventional SO – Heavy oils)

# Drawbacks

## GASES

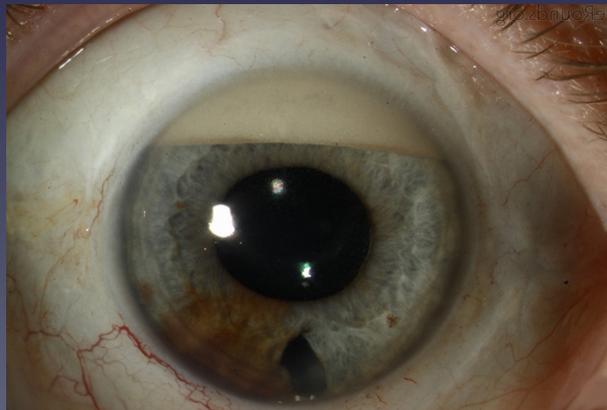
- Not for long term tamponade
- Not for inferior pathology
- Cataract
- Raised IOP > CRAO

## SILICONE OIL

- Overall success rate RD 70%
- Handling difficulties (inject-extrude)
- Cataract / glaucoma / keratopathy / silicone retinopathy

# EMULSIFICATION of SILICONE the big problem!!!!

(tendency of a substance to disperse into droplets)

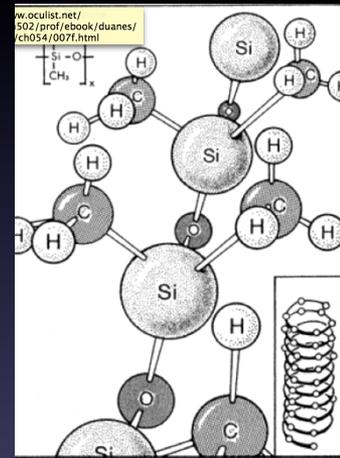


# Emulcification tendency

- Several factors promote emulcification
  - **viscosity** (the physical property of a fluid which measures its resistance to gradual deformation by shear stress)
  - interfacial surface tension,
  - chemical composition
  - content of low molecular weight (MW) siloxane compounds
  - other impurities,
  - and absorption of various biological substances from intraocular fluids and tissues (named emulsifiers)

# Emulcification / viscosity

- Viscosity depends on the length of the polymers that silicones are made of (greater the length, greater the viscosity.)
- (The less viscous a substance, the lower the energy that is required to disperse a large bubble of the substance into small droplets. )

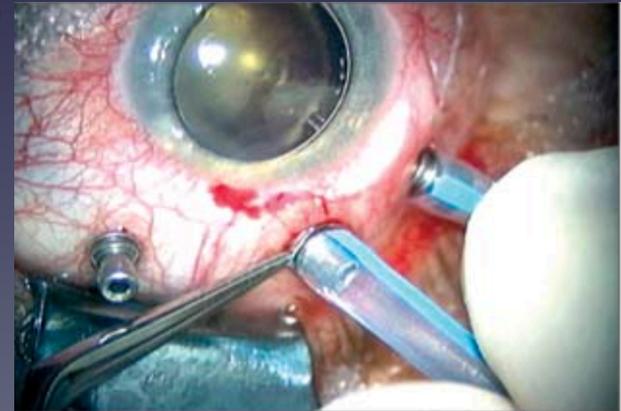


# Which silicone oil emulsifies more?

- The less viscous a silicone oil , the more it emulsifies.
- For a given viscosity,
  - the silicone oil with the lowest MW average will emulsify faster
  - A purified silicone oil with higher MW average will exhibit a higher resistance to the emulsification .

# Current silicone tamponade agents

- 1000 cs silicone oil that **is known to emulsify** in the eye and cause adverse effects for the patient
- 5000 cs silicone oil that is very viscous and **difficult to inject**, making surgery more difficult.



- Since the appearance and increased use of smaller- gauge instruments, the choice between **ease of oil handling** (low-viscosity oils) **versus its resistance to emulsify** (high-viscosity oils) has proven to be a difficult issue.

# Siluron XTRA (Fluoron GmbH)

- Relative new product (2014)
- It's a modification of standard clinical grade silicone oil tamponade agent (Siluron® 1000, Fluoron GmbH) mixed with 10% of a very high molecular weight (423k) polymer of the same chemistry



# Siluron XTRA (FluoronGmbH)

- The extensional viscosity of the oil has been increased and its emulsification has been reduced.
- Furthermore, this silicone oil blend has a lower shear viscosity than Siluron® 5000 (Fluoron GmbH), facilitating oil injection
  - (\* Under pressure, it shear thins and flows much better. The reason is that the very high molecular weight molecules line up in the same direction. The extensional viscosity however as high as normal 5000 under shear stress, this extensional viscosity increases even more.)

*\*personal communication Mr. David Wong*

# Anyway we still need a better vitreous tamponade agent

- New approaches has led research toward **functional biomimicry** : the use of synthetic molecules that
  - mimic the rheological function of the vitreous
  - interact with the intraocular structure without time-dependent degradation or optical transparency loss

# Current substitutes under investigation

- Natural Polymers
- Biosynthetic materials
  - polymeric Hydrogels
  - Smart hydrogels

Acta Biomater. 2011 Mar;7(3):921-35. doi: 10.1016/j.actbio.2010.10.030. Epub 2010 Nov 2.  
Baino F. Towards an ideal biomaterial for vitreous replacement: Historical overview and future trends.

# Natural polymers

- Natural Polymers

- Hyaluronic acid

- Collagen derivatives

- (gelatine, polygeline, chitosan)

Have been studied /poor results

# Polymeric Hydrogels

- Represent the first biomaterials ever synthesized for human use
- The concept is to inject them in an aqueous state and be transformed into gel in situ by light exposure or air oxidation ( cross linking processes)

# Polymeric Hydrogels

- Hydrophilic polymers / form a gel network when cross-linked
- Absorb water and swell
- They present good
  - Transparency
  - Biocompatibility
  - And viscoelastic properties
- They allow oxygen nutrients and growth factors to be implanted or pass through

# Smart hydrogels

- New class of stimuli – sensitive hydrogels
- Could respond better to signals such as
  - temperature
  - laser lights, pH etc
- Could interact better with the environment such as:
  - retinal tissue
  - Injected drugs etc
- That means **less emulsification** (increased gelification ,and viscosity )combined with **easier injection and handling**.

# Hydrogels – smart hydrogels

## Disadvantages

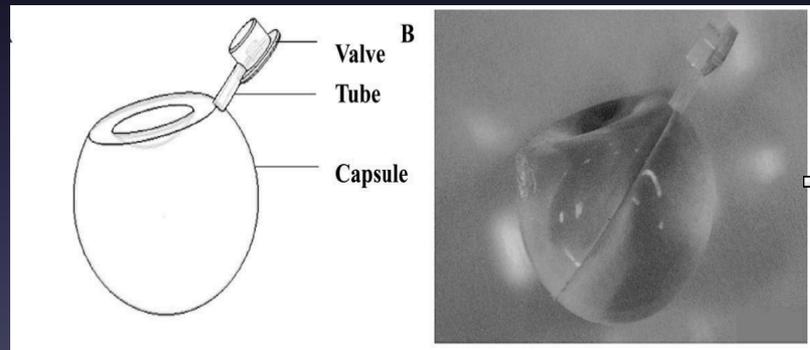
- **Injection problems** when injected in already gel form (rupture of polymeric chains)
- **Increased tendency to drift under retina** through tears before complete gelification because of their reduced degradation time
- **Biocompatibility issues** (can trigger immune reactions)
- **Other safety issues** (retinal toxicity, increased IOP, and the formation of opacities still need to be addressed.)

# Other ideas under investigation

- Retinal implants
- Vitreous regeneration

# Retinal implants

- Inspired by structure of natural vitreous
- Researchers have made Foldable capsular vitreous bodies (FCVB)
- Silicone rubber elastomer
- They consist of
  - Capsule
  - drain tube
  - valve.
- Filled with saline solution or SO and recently with Smart Hydrogel



Gao Q, Mou S, Ge J, et al. A new strategy to replace the natural vitreous by a novel capsular artificial vitreous body with pressure-control valve. *Eye* 2008; 22:461-8.

# Retinal implants

Theoretical advantages are

- They do not flow into the anterior chamber and subretinal regions or other sites.
- They do not emulsify or damage the media over time nor cause it to be isolated in the capsule.
- They have the capability to support retina all around the 360-degree solid arc.

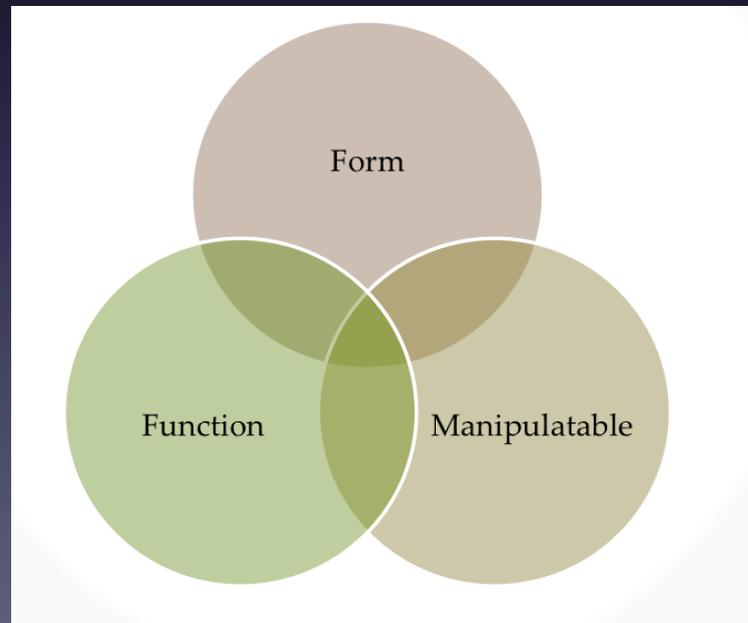
Preliminary results were good (although cataract / retinal damage from prolonged usage have been reported)

# Vitreous regeneration

- Recently Hyalocyte Cultures have been developed
- Which produce hyaluronic acid /other vitreous components
- Vitreous synthesis could be stimulated by hyalocyte proliferation,
- Could possibly lead to artificial generation of vitreous in vitro !

Y. Kashiwagi, K. Nishitsuka, H. Takamura, T. Yamamoto, and H. Yamashita, "Cloning and characterization of human vitreous tissue-derived cells," *Acta Ophthalmologica*, vol. 89, no. 6, pp. 538–543, 2011.

- THE IDEAL VITREOUS SUBSTITUTE HAS TO BE FOUND!



# Ideal vitreous substitute must resemble as much as possible of natural vitreous chemical and functional characteristics

- Mimic the native vitreous
- Be easily manipulable during surgery
- Have similar viscoelastic properties
- Be hydrophilic and insoluble in water
- Be able to maintain normal IOP
- support the intraocular tissues
- Allow movement of ions and electrolytes
- maintain the concentration of certain substances (oxygen, lactic acid, and ascorbic acid)
- Be clear and transparent
- Have refractive index and density similar to native vitreous
- Be biologically and chemically inert
- Not induce toxic reactions
- Be biocompatible
- Be easily available, stable, and injectable through a small syringe
- Be able to maintain its light transparency post-op without undergoing opacification

# Five-year view

- Over the next five to ten years, we can expect a movement toward developing **biomimetic compounds** that:
  - will maintain retinal apposition
  - will utilize novel materials and biotechnology concepts to control metaplasia of cells in contact with various materials
  - inhibit PVR formation, and promote the survival of retinal cells.

William Joseph Foster, MD, PhD

Expert Rev Ophthalmol. 2008 Apr; 3(2): 211–218.

# Five-year view

- Utilization of a variety of different physical concepts, including osmotic swelling to re-approximate the retina, will allow
  - faster visual rehabilitation,
  - improved patient comfort and compliance, and
  - better surgical outcomes.
- Finally, by combining physical reattachment of the retina with long-term drug delivery, retinal therapeutics can be delivered over sustained intervals to maintain retinal health.

William Joseph Foster MD, PhD

Expert Rev Ophthalmol. 2008 Apr; 3(2): 211–218.

Thanks for your attention!

*Dr E Manousakis*