Developing Femtosecond Laser for Vitreo-Retinal Surgery

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Background

❖ Vitreo-retinal diseases (i.e., DR) are common causes of visual blindness.

❖ A recent Meta analysis of 35 population-based studies showed that the prevalence of DR among individuals with diabetes is 35% (Yan, Rogers, et al, Diabetes Care. 2012), which indicates that, globally, case of DR will likely grow from 145 million in 2015 to 224 million by 2040, and 70M may suffer sight loss.
Current treatment: Primarily vitrectomy.

Can High Energy lasers improve current methods?

![Diagram of eye with vitreoretinal traction](image)

- Laser focal point
- Vitreoretinal traction (i.e., epiretinal membrane)
- Femtosecond laser
- Lens
Laser Terminology

For Ophthalmic laser applications, **spot size, flux density, pulse duration, and wavelength** are the most important properties.

- **Spot size**: the diameter measured between the two points at which the intensity is half the peak. Better focus results in smaller spot size.

- **Flux density (irradiance)**: Defined as energy per area (\(\text{uJ/mm}^2\)). Critical for determining laser impact on tissue.

- **Pulse duration**: Time interval between the two points at which the energy is half the peak. Ultra-short pulses are able to produce smaller shock waves and cavitation bubbles, thus less collateral tissue damage.
Wavelength:

The site of photon absorption is determined by the wavelength and the transmission properties of the ocular media.

Examples:

- **Excimer lasers (193 nm):** are used for corneal photoablation (T=0%)

- **NIR lasers (800nm):** are used for vitreo-retinal surgery (T=95%)
Mechanism of FS induced Photodisruption:

❖ FSL energy is absorbed by the tissue, resulting in plasma formation.

❖ This plasma of free electrons and ionized atoms rapidly expands, creating cavitation bubbles.

❖ The force of the cavitation bubble creation separates the tissue.

This is an example of corneal tissue, but same principle applies to vitreal traction.
Ophthalmic Applications of Femtosecond laser

Because of its ability to deliver laser energy deep into the eye with minimal collateral damage (1μm), FS pulses have been widely used in treating anterior segment diseases:

❖ Refractive and corneal surgery (Keratoplasty)
❖ Cataract surgery (capsulotomy and fragmentation)
❖ Glaucoma surgery (trabeculoplasty)
❖ What about Vitreo-Retinal Surgery??

Vitreo-retinal traction is so close to the retina, high energy NIR laser pulses may pose a special hazard to the photon opaque retina.

Vitreoretinal traction (i.e., epiretinal membrane)
The Good:

**Plasma:** an ionized gas consisting of positive ions and free electrons

Two key characteristics of plasma that amplify the multiple photon absorption effect:

1. A plasma created from a transparent material becomes opaque, absorbing more and transmitting fewer photons (Noack & Vogel, 1999).
2. Free electrons can contribute energy to bound electrons further increasing the number of free electron (cascade ionization). (Noack & Vogel, 1999)

The above two effects offer some protection to the tissue behind the location where the plasma is being generated, and thus lower the risk to the retina even though the beam will not have expanded much by the time it reaches the retina.
The Bad:
Achieving flux densities sufficiently high to create local ionization fields puts tissues near the laser focal point at risk, which is amplified in low transparency tissue (i.e., retina).

Challenge 1: Flux density at the retina is proportional to $1/d^2$ ($d =$ distance from the laser focal point to the retina). Therefore, as the laser focal point approaches the retina, flux density at the retina increases, preventing routine use of femtosecond lasers in the posterior segment of the eye (e.g. to relieve vitreoretinal traction).

Challenge 2: the aberrated optics of the eye will play a significant role in defocusing the laser, which will produce a larger point spread function. Therefore, it require increased pulse energy to achieve the same focal point flux density at the target tissue.
Solutions to the above obstacles:
Developing a customized aberration-free femtosecond laser delivery system which will allow us to correct ocular aberrations introduced by the anterior eye AND minimize laser focal diameter. *i.e.*, *spot diameter decreases by a factor of 3, flux density increases by a factor of 9, total energy required decreases by x9 and thus reduce risk of retinal damage.*
Two Big Qs:
Is it Effective?
Is it Safe?

Summary of our approaches

- AO-guided Femtosecond laser vitreolysis
- Dissected pig eye
  (Fresh pig eyes will be purchased from local houses)
- Dissected donor human eyes with Hx of vitreoretinal traction
  (Donor eyes will be offered by Nebraska Eye bank)
- Plastic model eye with pig retina
  (laser setup and model eye are ready)
- Clinical use on patients with vitreoretinal diseases
  (AO-OCT combined with AO-femtosecond laser vitreolysis, UNL team with help from Dr. Yoon)
Approaches

#1: Optimize delivery of ultrashort pulse in a model eye.

How will the cutting quality and localization of the ultrashort pulse, and potential retinal damage be affected by the focal point position along z-axis (z-location)?

For each z-location, the spatio-temporal controlled ultrashort pulses with varying energy levels will be focused into a model eye.

The postop retina will be examined with confocal laser microscopy (CLM) and scanning electron microscopy (SEM).
Experimental setup

**Standard laser parameters:** 1 mJ, 1 kHz (800 nm), 30 fs

**Optional capability:** <10 fs, 0.5 mJ
Approach 2: Vitreo-retinal cavitation effects in pig eyes.
Can aberration-corrected femtosecond laser achieve the laser energy levels required for cavitation of vitreoretinal traction without damage to the retina?

We will use equatorially bisected pig eyes (aberration-free optics) to quantify the axial and lateral spread of tissue damage as a function of z-location and laser energy levels. Retinal tissue will be examined with CLM and SEM.

For comparison, customized phase plates with aberrations will be introduced to simulate the typical aberrated human eyes.
Approach 3: Vitreo-retinal cavitation and retinal damage thresholds in donor eyes. Can an aberration-free femtosecond laser release the traction or generate local detachment of vitreous from the retina without collateral retinal damage in donor human eyes?

We will use **bisected donor eyes** with a history of vitreoretinal traction (i.e., DRD) from Nebraska Eye Bank.
Can aberration-free femtosecond laser pulses generate cavities at the target tissue (above cavitation threshold), without damaging the retina (below retinal damage threshold)?

We will compute the flux absorption (flux density × optical density) by vitreoretinal traction tissue and by the retina respectively, with and without aberration correction.
Approach 5: Configure OCT with adaptive optics guided femtosecond laser vitreolysis on real patients.

Femtosecond laser

Laser source – Femtopower
40 fs, 50 nm bandwidth
5 mm beam diameter

Micrometer axial resolution OCT for corneal imaging

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Conclusions

Non-externally invasive femtosecond laser vitreolysis is a promising new technology to overcome limitations of current vitrectomy procedures. To ensure the success of technology, our project is focusing on the following objectives:

❖ Determine the safety of femtosecond lasers on retinal tissue while focusing on vitreoretinal traction;
❖ Evaluate the range of retinal distances (z-locations) for cutting while maintaining safety
❖ Incorporate AO technology to minimize the risk.

More results are coming ...

Thank you!