

Recent Advances in Tissue Biomechanics Using Dynamic Optical Coherence Elastography

Presented by:



Therapeutic
Laser Applications
Technical Group

Executive Committee



Chair: Elina A. Vitol

Advisor: David R. Busch, UT Southwestern Medical Center at Dallas

Committee Member: Yannis M. Paulus, Assistant Professor, University of Michigan

Committee Member: Guido Perrone, Associate Professor, Politecnico di Torino

Committee Member: Felix Fanjul-Velez, Associate Professor, University of Cantabria

Industry Liaison: Robbie Thomas, Photon Force, Ltd.

Social Media Liaison: Mariia Shutova, Texas A&M University

Where to find information about the group



Screenshot of the OSA website showing the 'Get Involved' section for the Therapeutic Laser Applications (BA) Technical Group.

The URL in the browser bar is https://www.osa.org/en-us/get_involved/technical_groups/bmo/therapeutic.

The page includes the OSA logo, a '100 Since 1916' anniversary banner, and a navigation menu with links to Journals & Proceedings, Meetings & Exhibits, Explore Membership, Industry Programs, Get Involved, Foundation & Giving, and Living History.

A red box highlights the 'Get Involved' button in the navigation menu.

The main content area shows the 'Therapeutic Laser Applications (BA)' page under the 'Get Involved' section. It features a photo of people at a conference, a description of the group's focus on lasers in surgery, and a heading for 'Upcoming Technical Group Webinars'.

A red box highlights the 'Therapeutic Laser Applications (BA)' link in the sidebar under the 'Bio-Medical Optics' section.

The sidebar also lists other technical groups: Microscopy and Optical Coherence Tomography (BM), Molecular Probes and Nanobio-Optics (BP), Optical Biosensors (BB), Optical Trapping and Manipulation in Molecular and Cellular Biology (BT), Photoacoustic Imaging of the Eye, Hosted By: Therapeutic Laser Applications Technical Group, 24 October 2019, 10:00 AM - 11:00 AM, Register Now, and Work in Optics.

The right sidebar includes an 'Announcements' section, a 'Join our Online Community' section with links to LinkedIn and Facebook, and a 'Work in Optics' section.

We want you to join us!



- Select **Therapeutic Laser Applications** as one of 5 technical groups of interest at your OSA membership account page
- Attend our networking events, webinars and poster sessions
- Join us on LinkedIn and Facebook to keep in touch  
- Look out for emails from the committee about group activities
- Interested in presenting your research? Have ideas for technical group events? Want to reach out to your fellow group members?
 - Contact us at elina.vitol@gmail.com or TGactivities@osa.org

Recent and upcoming webinars



Therapeutic
Laser Applications
Technical Group

24 October 2019

Photoacoustic imaging of the eye

Yannis M. Paulus, M.D., F.A.C.S., University of Michigan

Recording is available from OSA website

https://www.osa.org/en-us/get_involved/technical_groups/technical_group_webinars/#ondemand

21 January 2020, 11am EST*

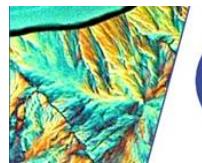
Thermomechanical effect of infrared laser for cartilage regeneration

Yulia M. Alexandrovskaya, PhD

Registration will open in December

Institute of Photon Technologies, Federal Scientific Research Centre “Crystallography and Photonics” of the Russian Academy of Sciences (RAS)

Welcome to today's webinar!



OSA

Therapeutic
Laser Applications
Technical Group



RECENT ADVANCES IN TISSUE BIOMECHANICS USING DYNAMIC OPTICAL COHERENCE ELASTOGRAPHY

Kirill V. Larin, Ph.D.
Professor, Department of Biomedical Engineering
University of Houston

November 1, 2019

Recent Advances in Tissue Biomechanics Using Dynamic Optical Coherence Elastography

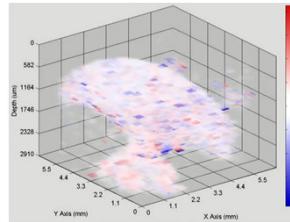
Kirill V. Larin

Professor
Fellow SPIE, Fellow OSA

University of Houston



Biomedical Optics Laboratory

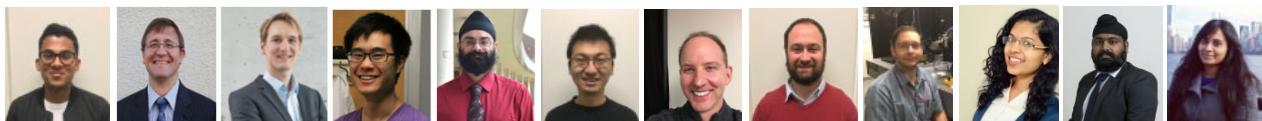


Major Projects in Biomedical Optics Lab

Optical
Elastography/Biomechanics

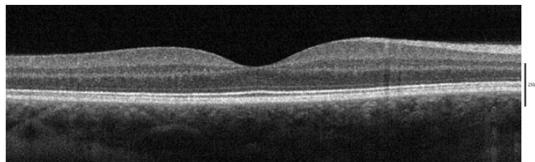


Developmental
Biology



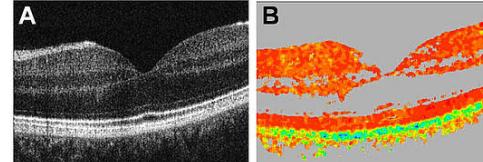
Major Breakthroughs in OCT Functional and Contrast Enhanced Imaging

Morphological Imaging



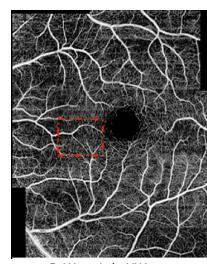
Introduced by Fujimoto et al in 1991

Polarization sensitive OCT



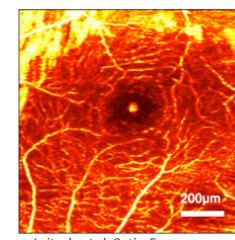
Hitzenberger, et al. Optics Express, 2001

OCT Angiography



R. Wang Lab, UW

Doppler OCT



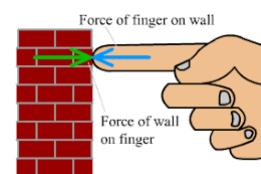
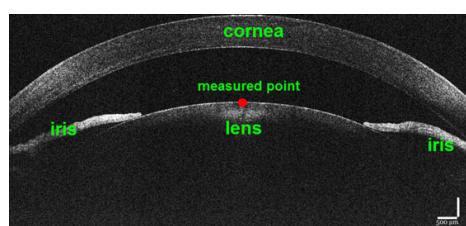
Leitgeb, et al. Optics Express, 2003

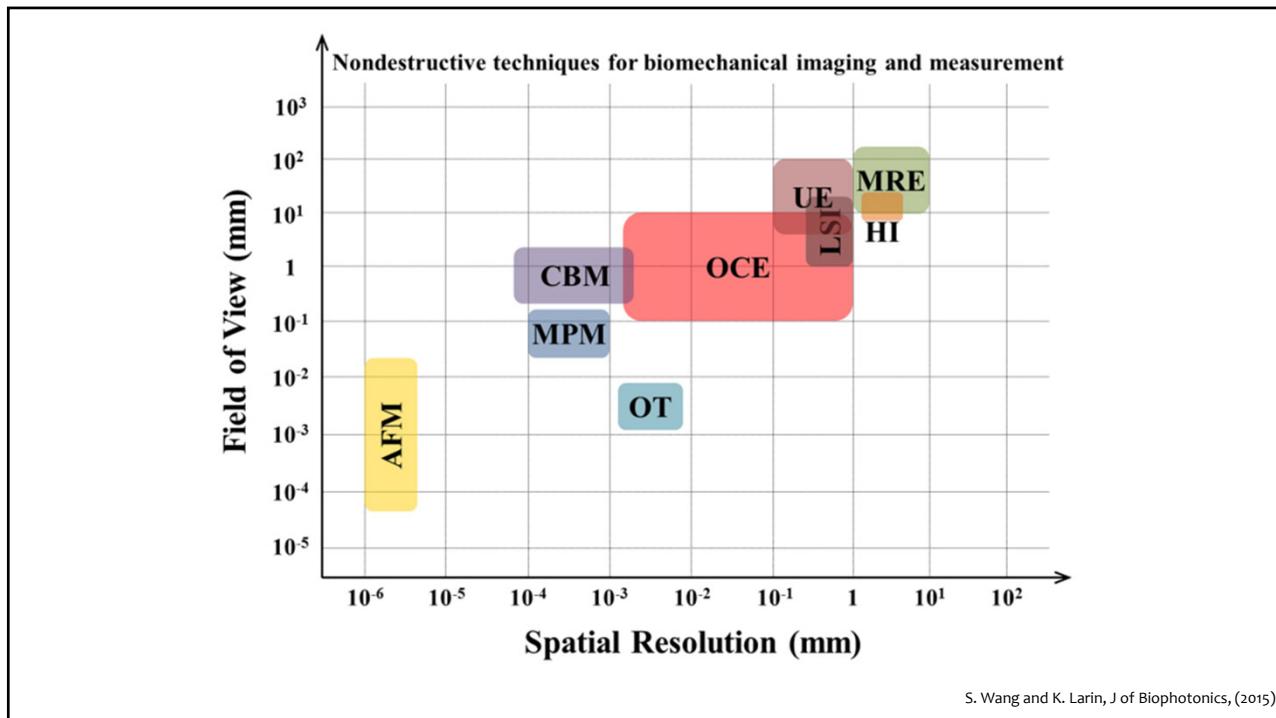
?



Optical Coherence Elastography:

OCT + Force





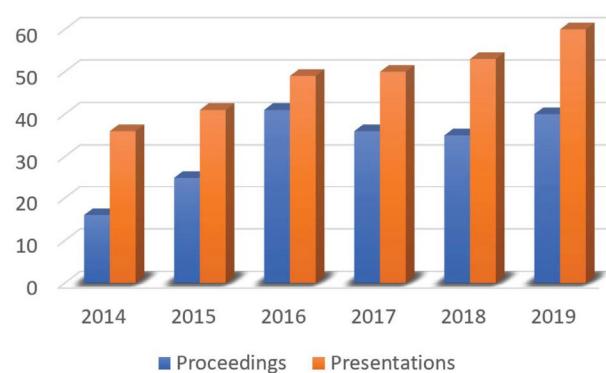
Optical Elastography and Tissue Biomechanics Photonics West, 1 - 6 February 2020

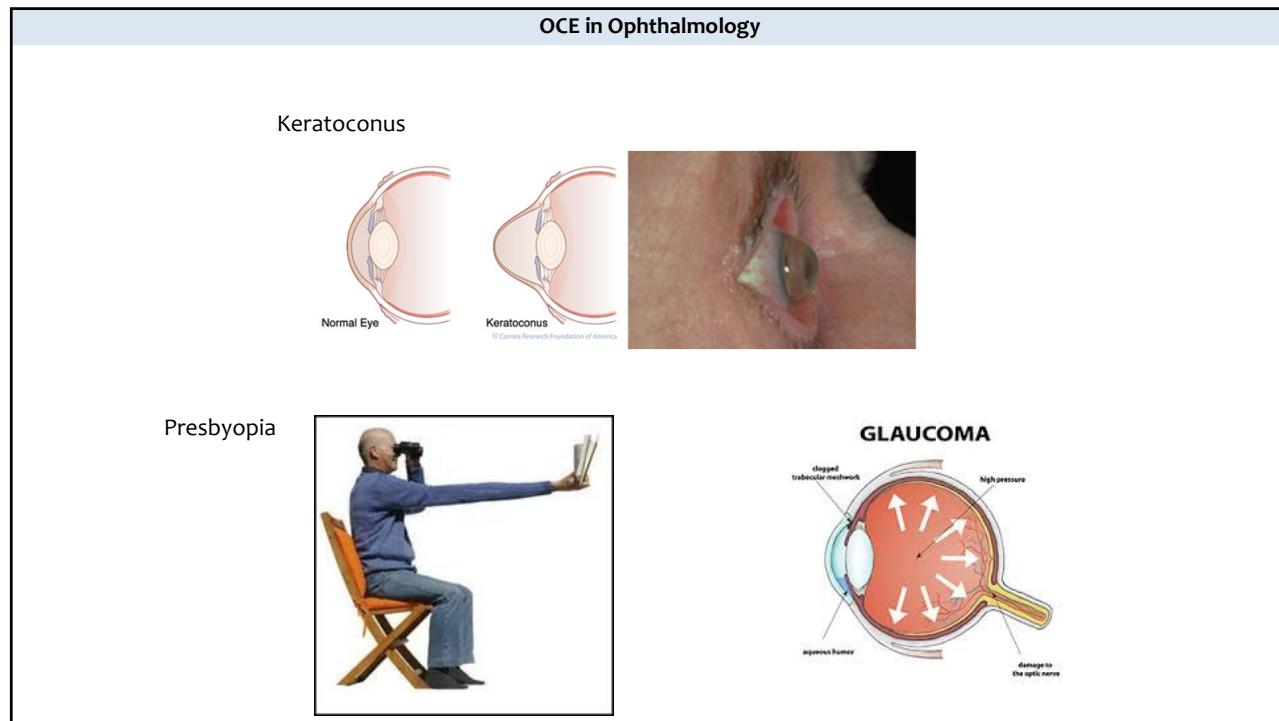
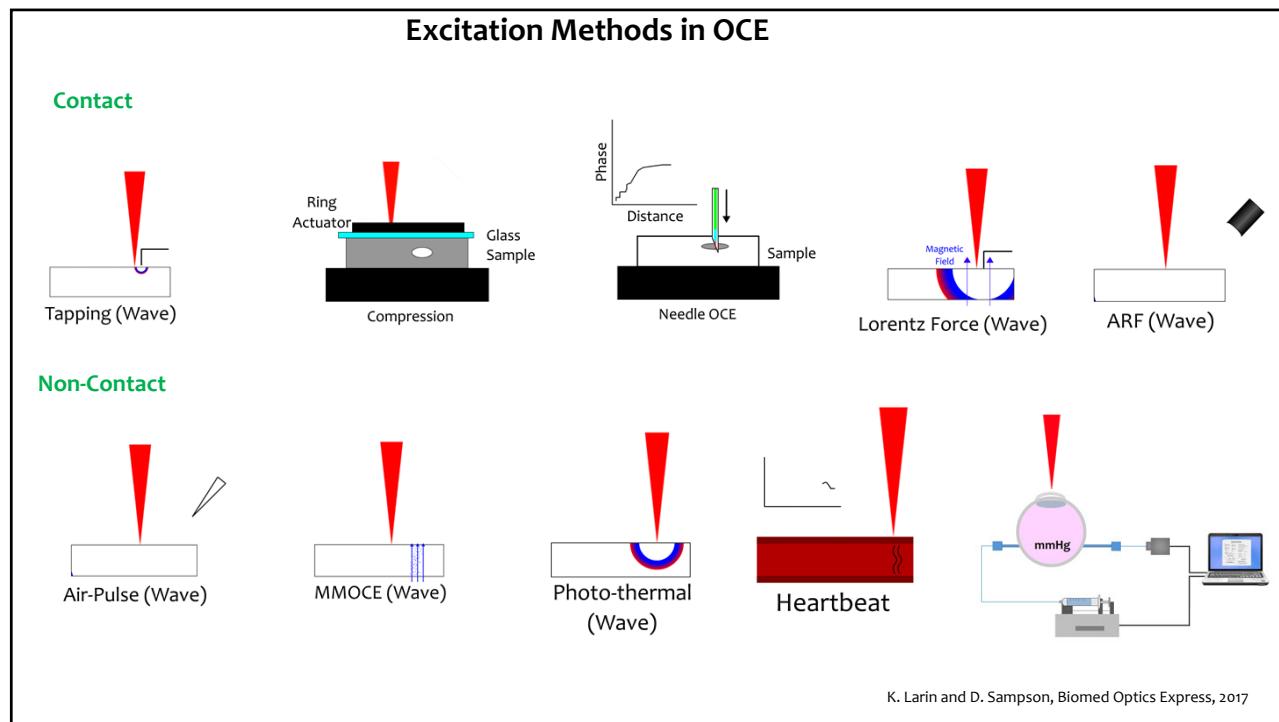
Conference Chairs

- Kirill V. Larin, Univ. of Houston (United States)
- Giuliano Scarnelli, Univ. of Maryland, College Park (United States)

Program Committee

- Steven G. Adie, Cornell Univ. (United States)
- Albert Claude Boccara, Institut Langevin Ondes et Images (France)
- Brett E. Bouma, Wellman Ctr. for Photomedicine (United States)
- Stefan Catheline, Institut National de la Santé et de la Recherche Médicale (France)
- Zhongping Chen, Beckman Laser Institute and Medical Clinic (United States)
- Jürgen W. Czarske, TU Dresden (Germany)
- Kishan Dholakia, Univ. of St. Andrews (United Kingdom)
- Christine P. Henton, Columbia Univ. (United States)
- Davide Iannuzzi, Vrije Univ. Amsterdam (Netherlands)
- Brendan F. Kennedy, The Univ. of Western Australia (Australia)
- Sean J. Kirkpatrick, Michigan Technological Univ. (United States)
- Matthew O'Donnell, Univ. of Washington (United States)
- Amy L. Oldenburg, The Univ. of North Carolina at Chapel Hill (United States)
- Gabriel Popescu, Univ. of Illinois (United States)
- Jannick P. Rolland, The Institute of Optics (United States)
- David D. Sampson, Univ. of Surrey (United Kingdom)
- Ian A. Signal, Univ. of Pittsburgh (United States)
- Kandice Tanner, National Cancer Institute (United States)
- Peter Török, Imperial College London (United Kingdom)
- Ruikang K. Wang, Univ. of Washington (United States)
- Tianshi Wang, Erasmus MC (Netherlands)
- Vladislav V. Yakovlev, Texas A&M Univ. (United States)
- Seok Hyun A. Yun, Wellman Ctr. for Photomedicine (United States)
- Vladimir Y. Zaitsev, Institute of Applied Physics of the RAS (Russian Federation)
- Qifa Zhou, The Univ. of Southern California (United States)





Biomechanics of the Cornea

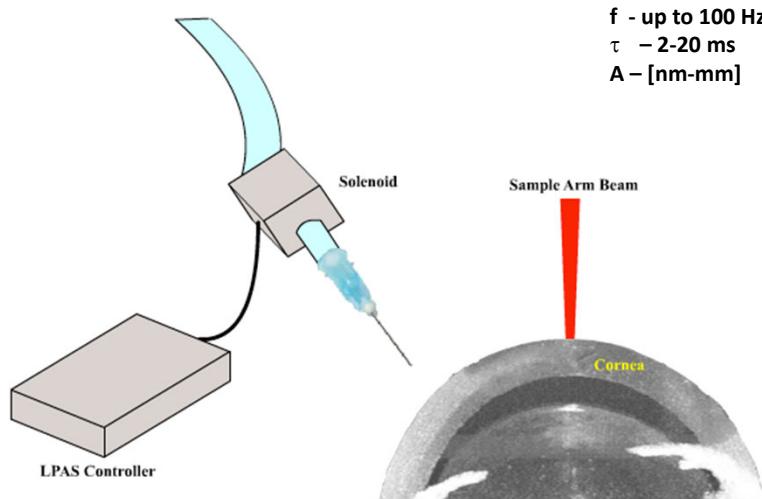


Michael Twa, Ph.D., O.D.
Professor, Dean of the College of
Optometry,
University of Houston

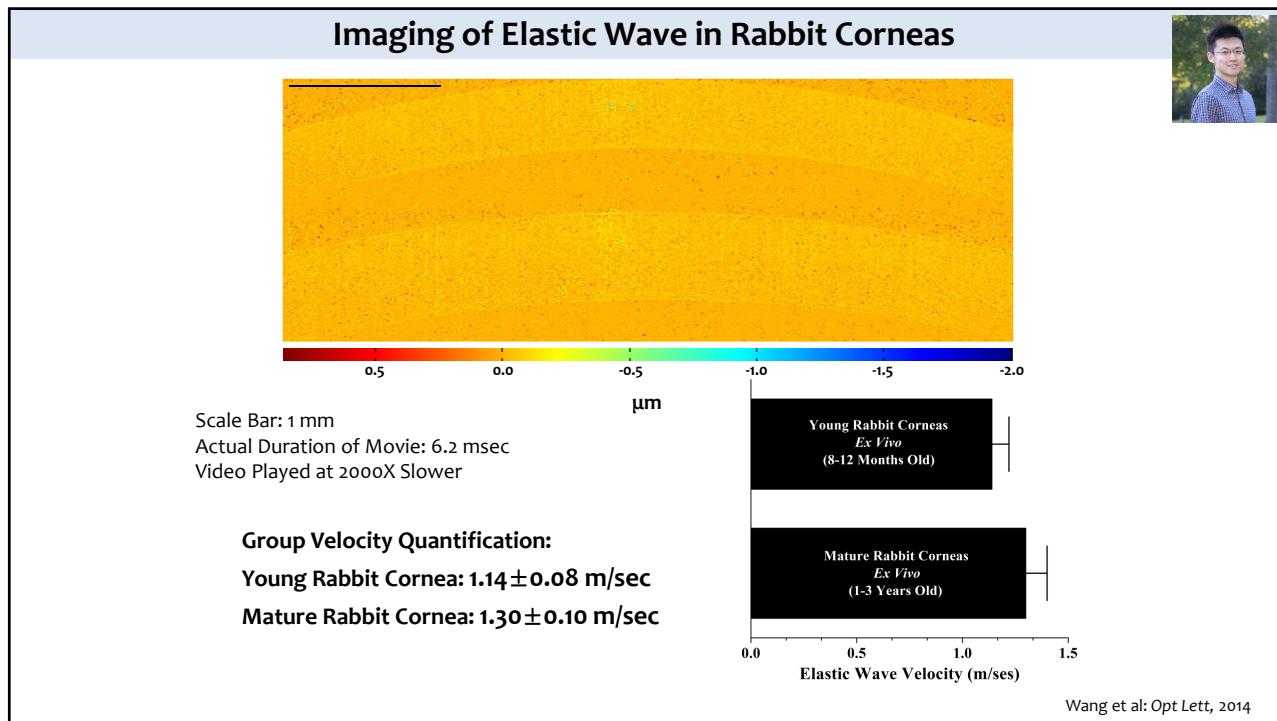
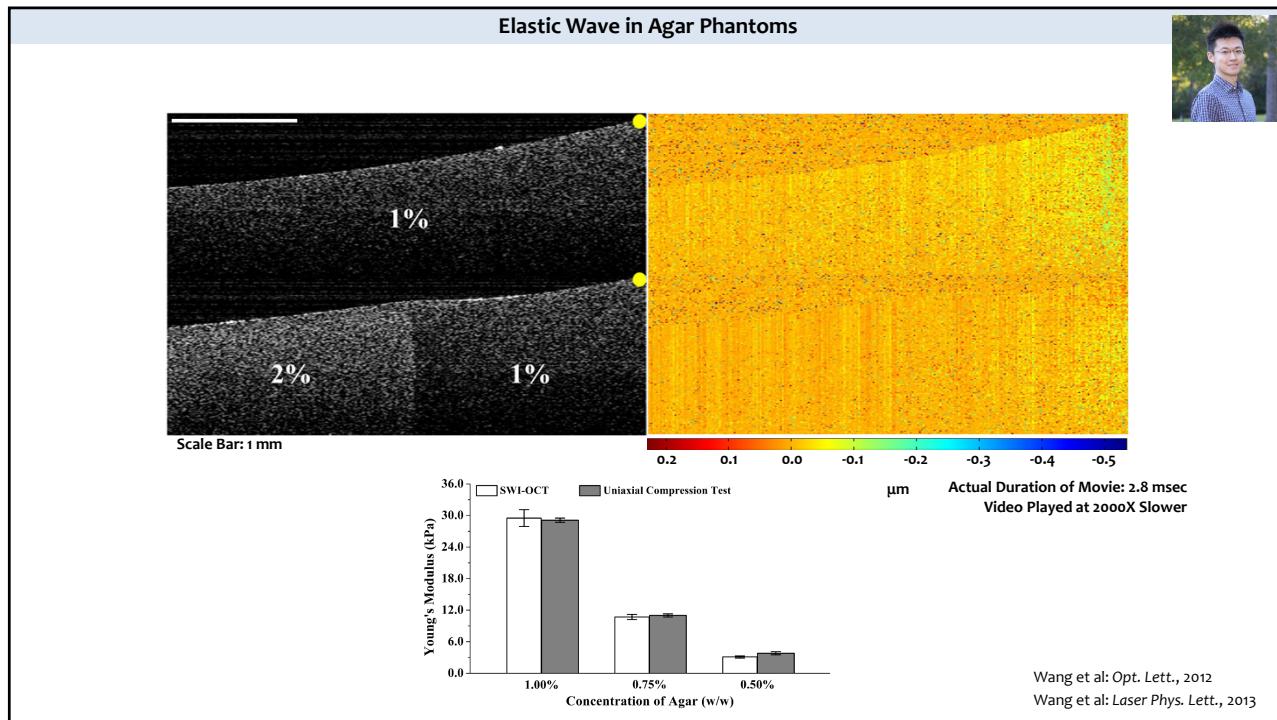


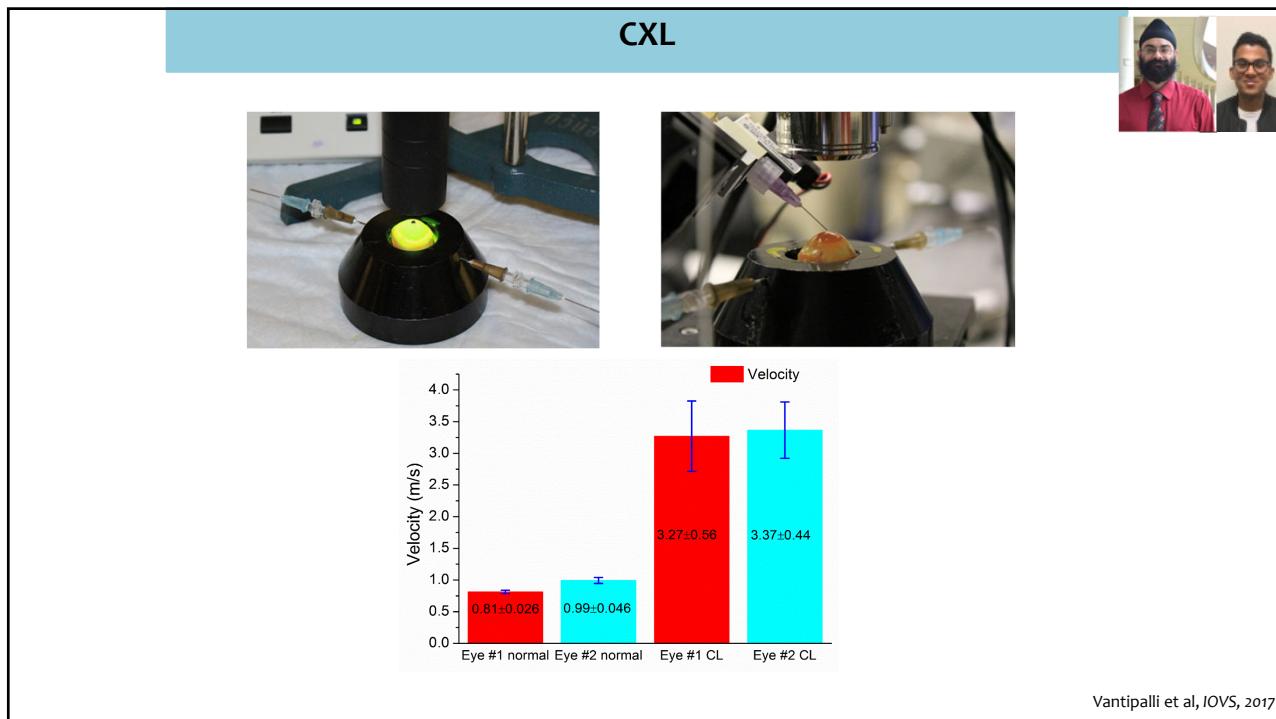
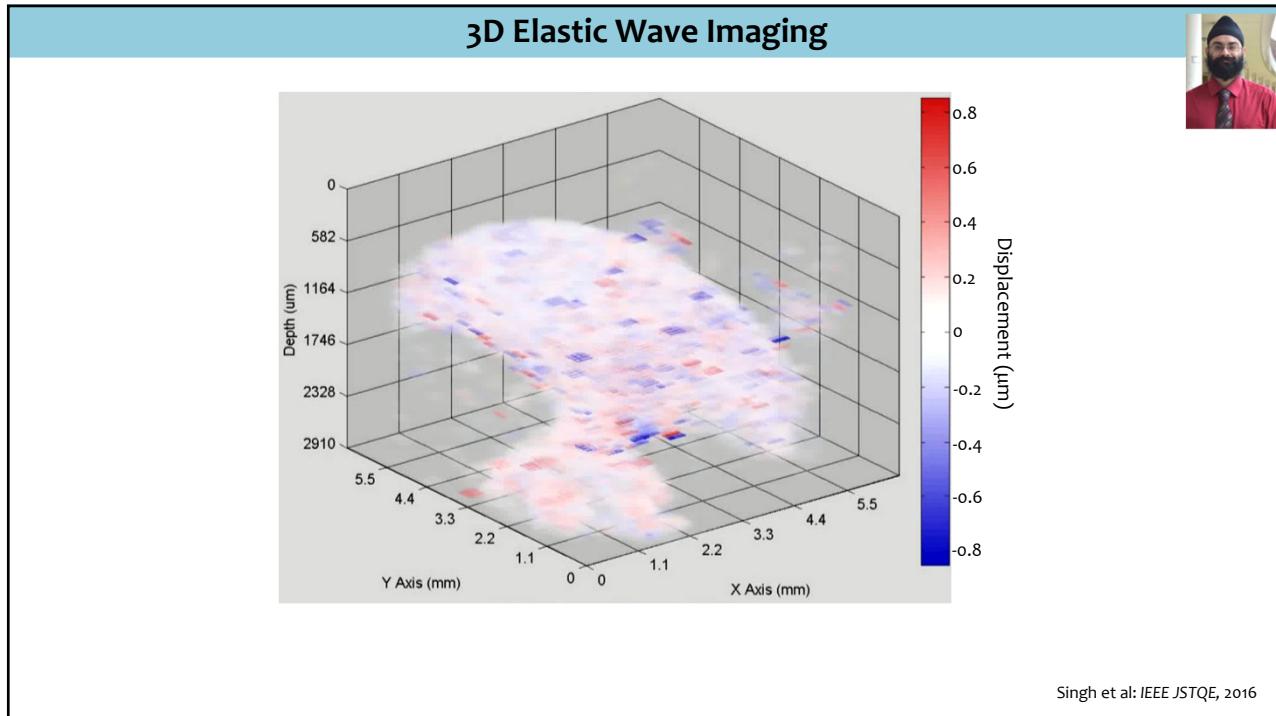
Stanislav Emelianov, Ph.D.
Professor, Department of
Biomedical Engineering,
Georgia Tech

Excitation Method: Focused Air Puff



Wang et al: Opt. Lett., 2012
Wang et al: Laser Phys. Lett., 2013



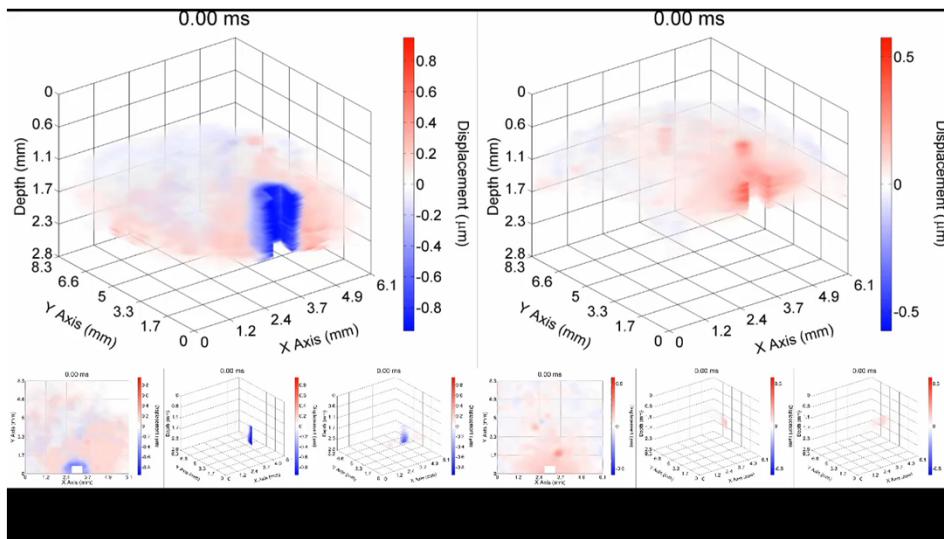


3D elastic wave propagation in cornea



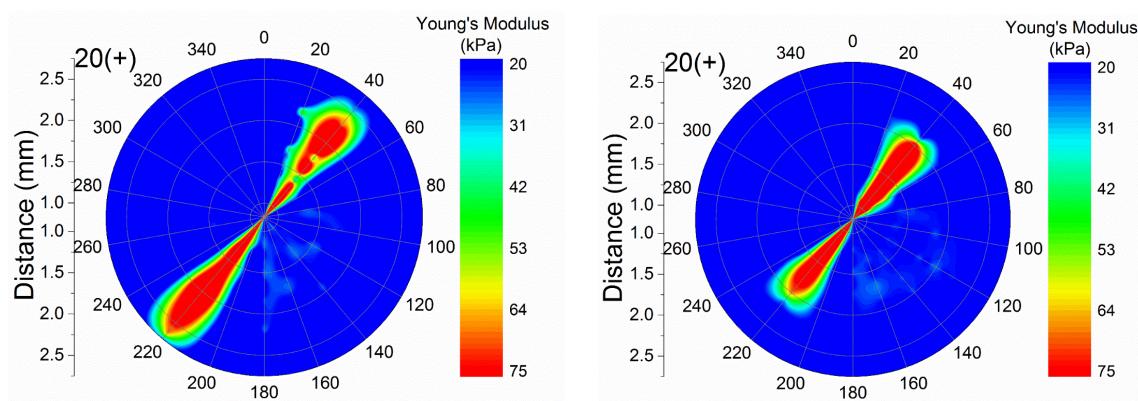
Untreated

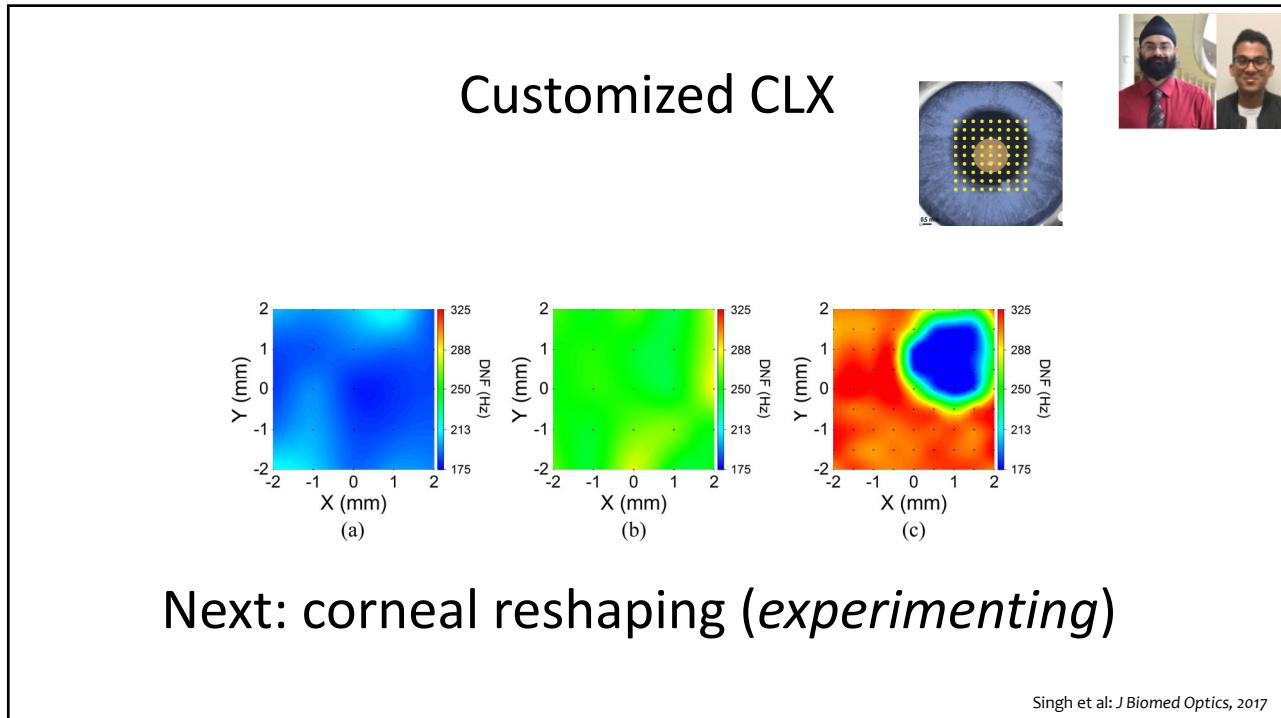
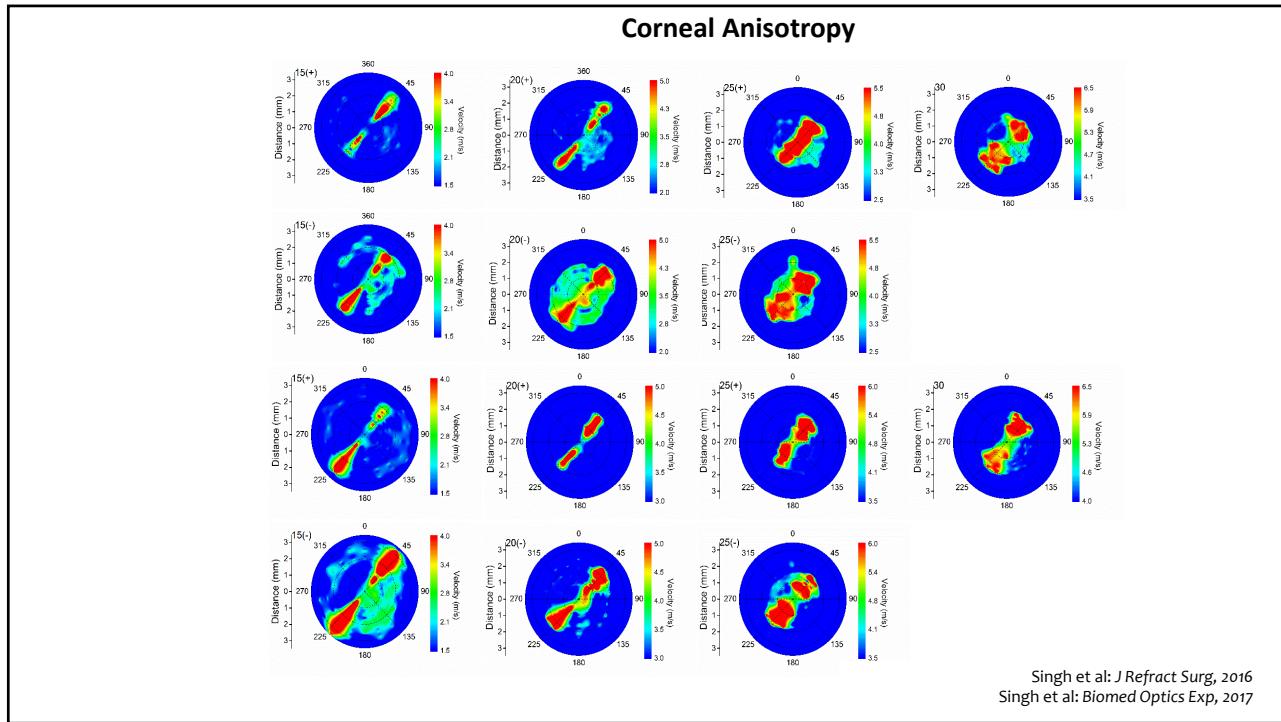
CXL



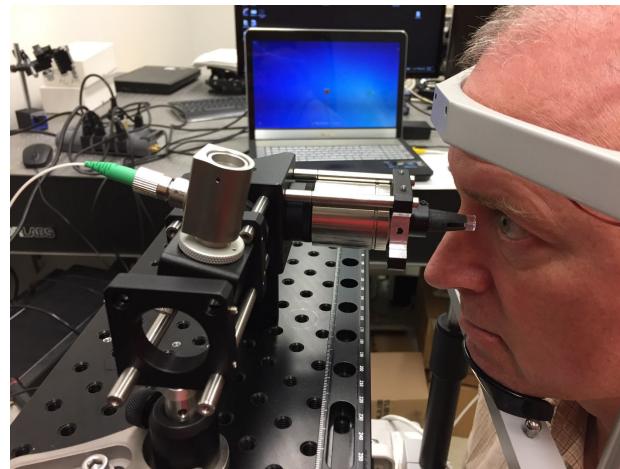
Singh et al: IEEE JSTQE, 22, 2016

Corneal Anisotropy

Singh et al: J Refract Surg, 2016
Singh et al: Biomed Optics Exp, 2017



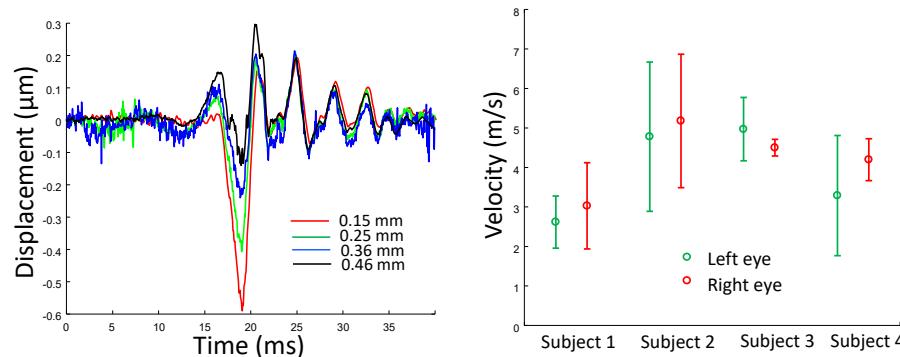
Pilot Human Studies



Twa et al, IOVS, 2017

Human Corneal OCE *in vivo*

n=11

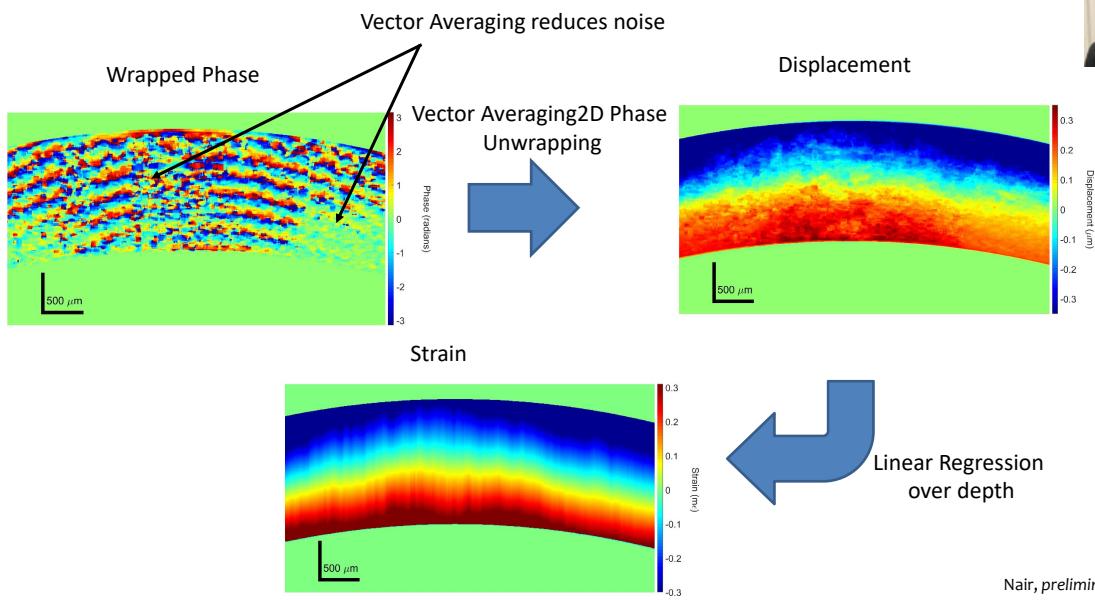


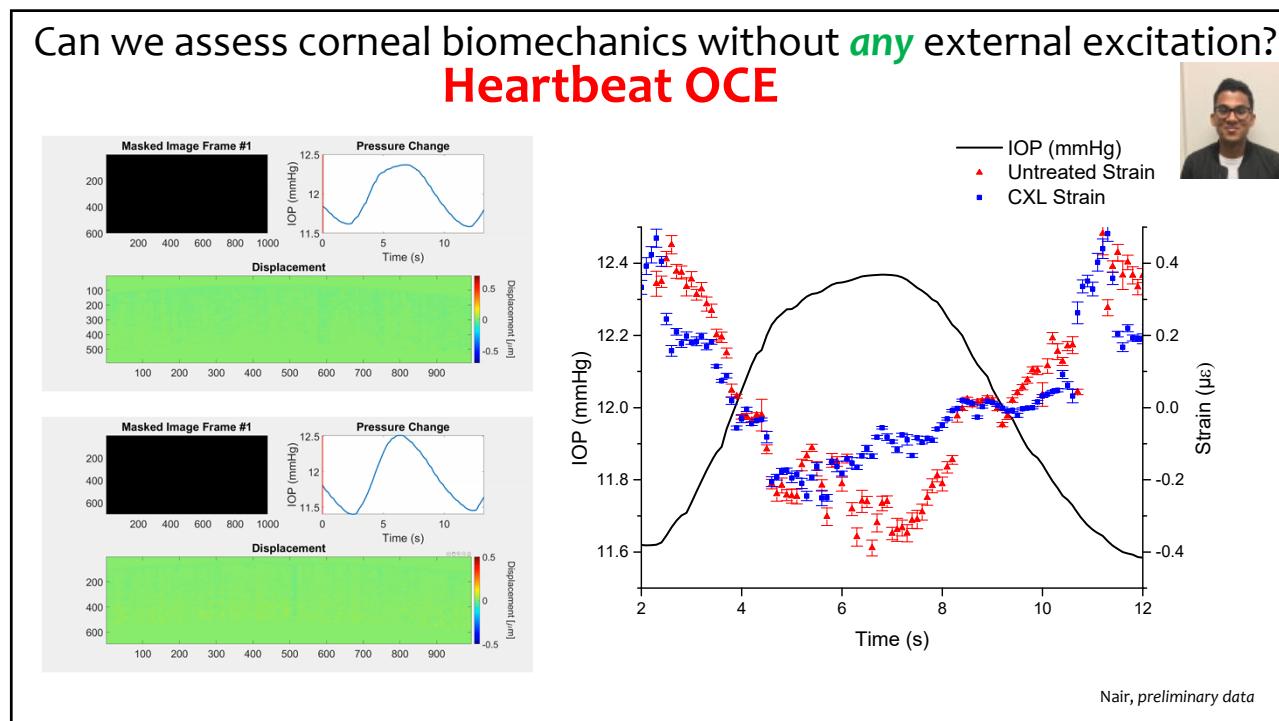
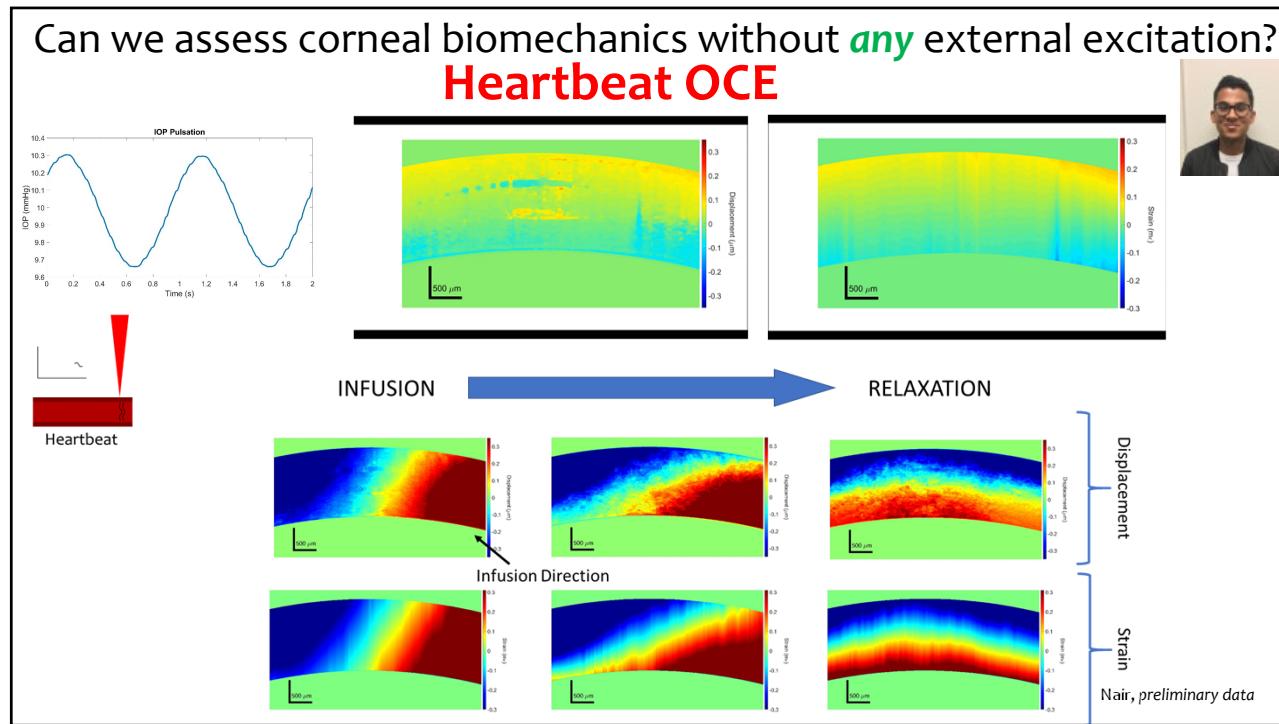
Twa et al, presented at ARVO, 2019

Can we assess corneal biomechanics without **any** external excitation?

Can we assess corneal biomechanics without **any** external excitation?

Heartbeat OCE



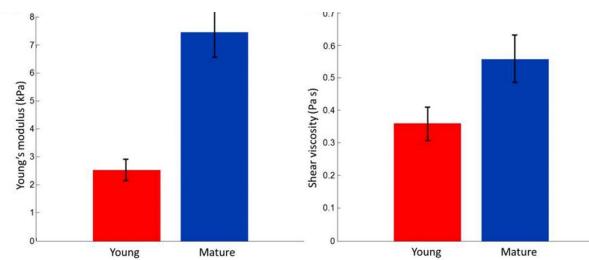
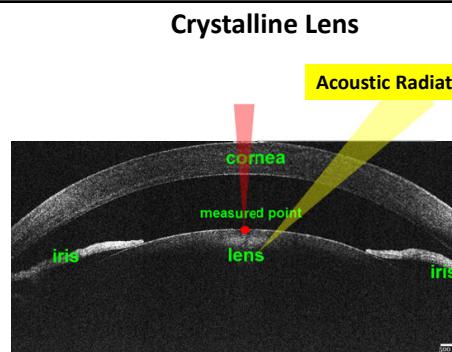


Biomechanics of the Lens

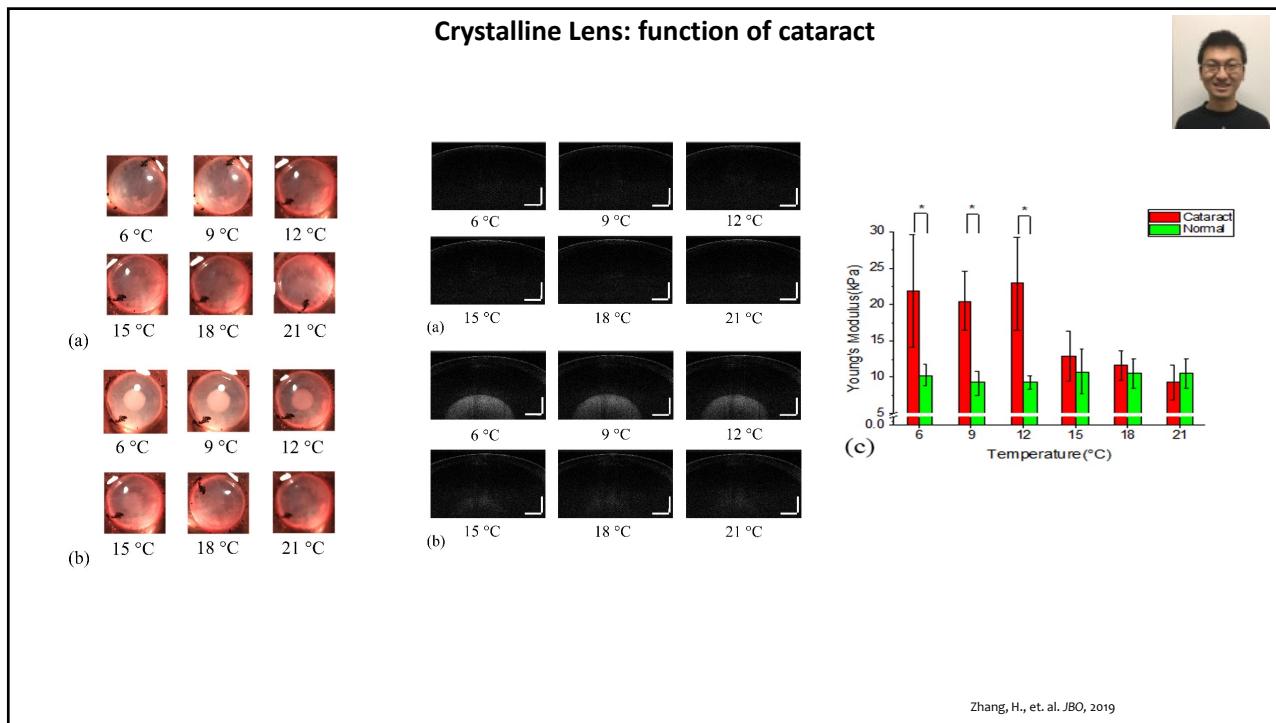
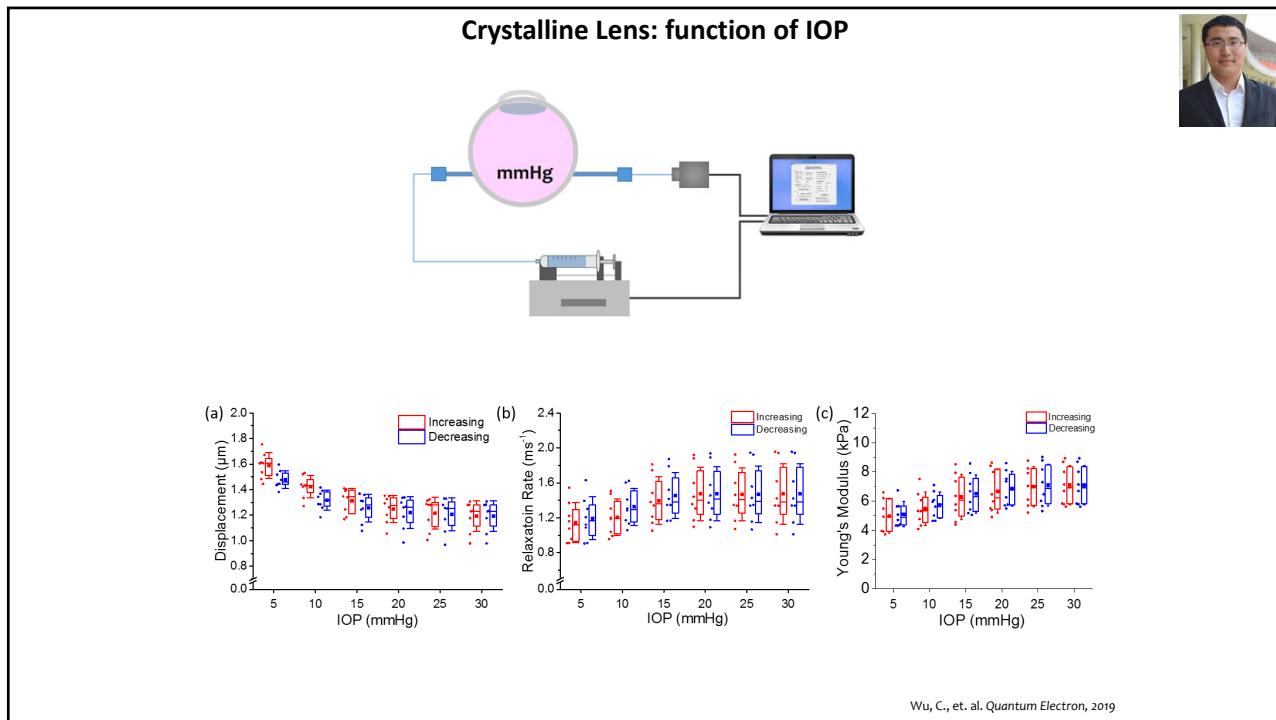


Giuliano Scarelli, Ph.D.
Assistant Professor, Fischell
Department of Bioengineering,
University of Maryland

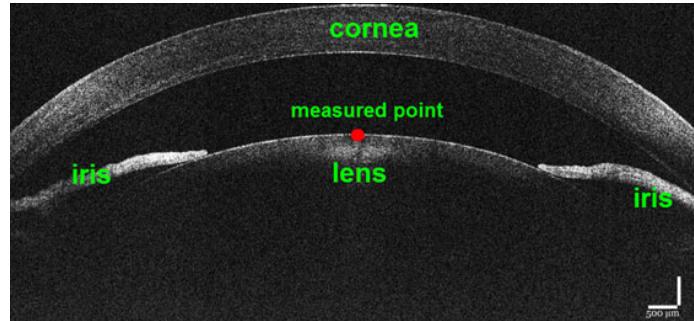
Fabrice Manns, Ph.D.
Professor, Department of
Biomedical Engineering,
University of Miami and Bascom
Palmer Eye Institute



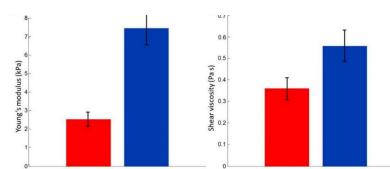
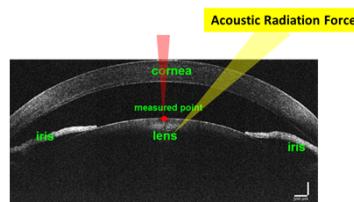
Wu, C., et al. Investigative ophthalmology & visual science, 56(2), 2015



Crystalline Lens: can we measure mechanical properties in 3D?

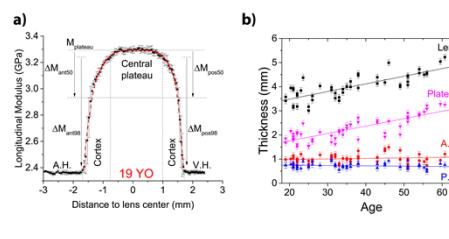
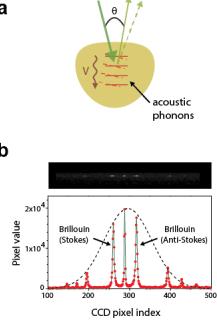


OCE:



Pros: Quantitative
Cons: Lens surface only

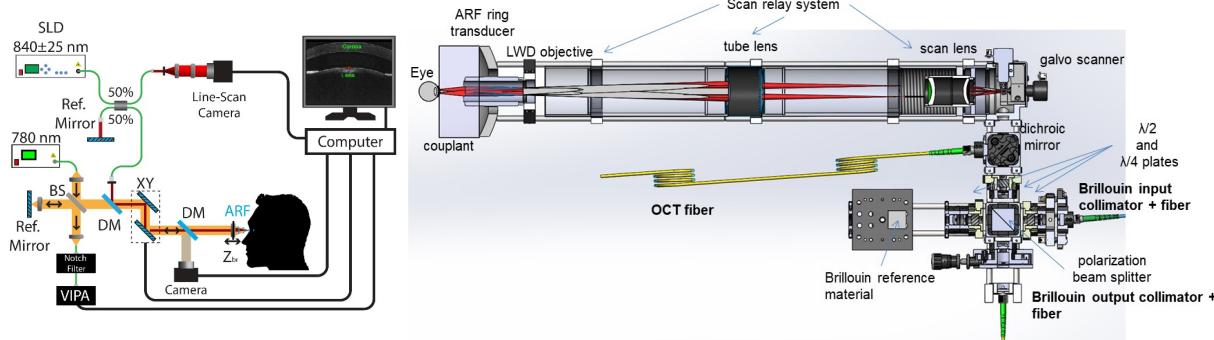
Brillouin Spectroscopy:



Pros: 3D ready
Cons: Qualitative

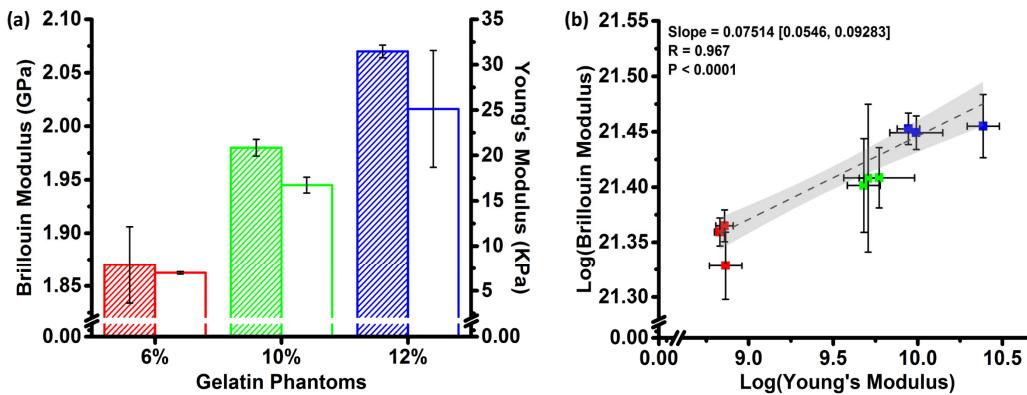
OCE + Brillouin Spectroscopy

For truly **quantitative** elastography of the Lens in 3D



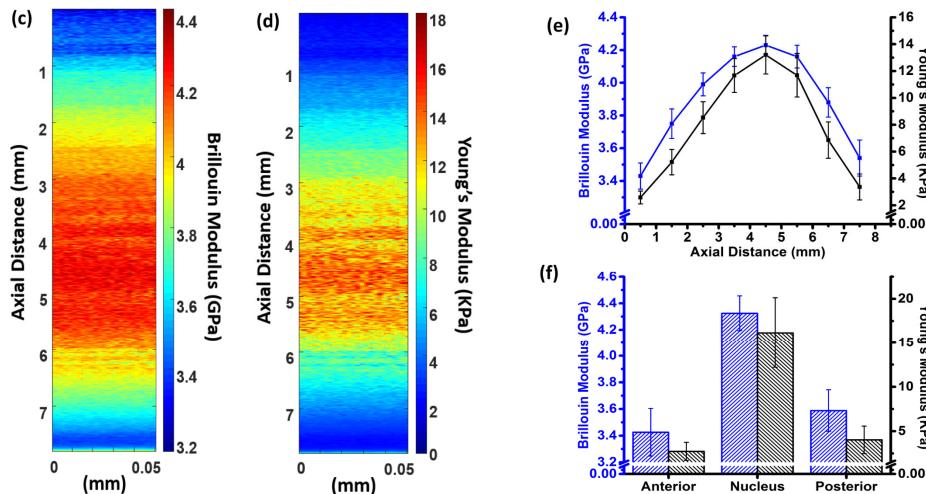
Can we **quantify** mechanical properties of the lens in 3D?

OCE + Brillouin Spectroscopy



Ambekar et al (in preparation)

Can we *quantify* mechanical properties of the lens in 3D? OCE + Brillouin Spectroscopy

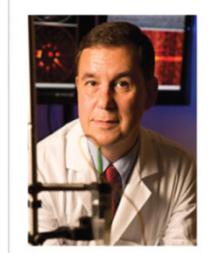


Ambekar et al (in preparation)

Biomechanics of the Cardiac Muscle



James Martin, M.D., Ph.D.
 Professor, Department of
 Physiology and Biophysics,
 Baylor College of Medicine



Stanislav Emelianov, Ph.D.
 Professor, Department of
 Biomedical Engineering,
 Georgia Tech

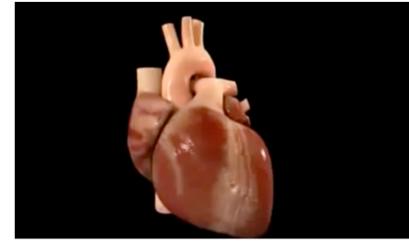


Xingde Li, Ph.D.
 Professor, Department of
 Biomedical Engineering,
 John Hopkins University

Mechanical Properties of Cardiac Muscle

Myocardium and the beating of the heart

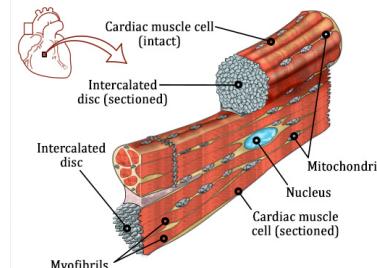
- ❖ Dynamic process: relaxation and contract;
- ❖ The elasticity of the cardiac muscle determines the normal function of the heart;
- ❖ Spatial heterogeneity: mechanical strength of the muscle fiber and between the muscle fiber.



Recovery of the heart after ischemic disease

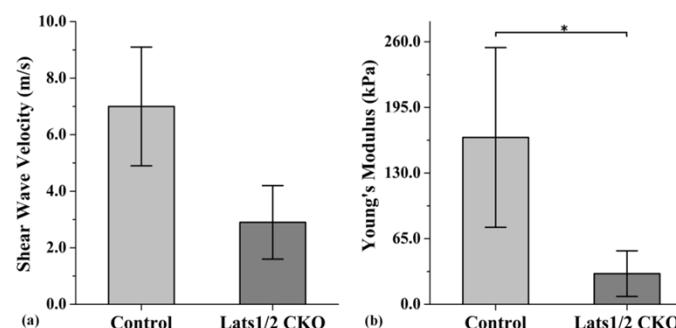
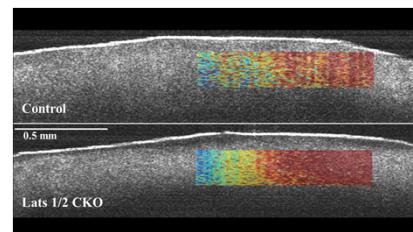
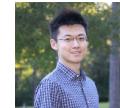
- ❖ Self-regeneration of cardiomyocytes.

Stiffness of the cardiac muscle increases with age



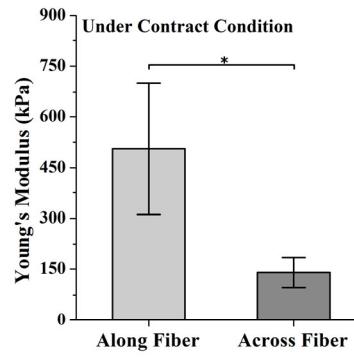
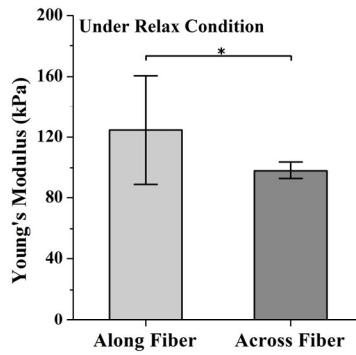
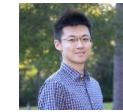
From Buzzle.com
<http://www.buzzle.com/articles/cardiac-muscle-structure.html>

Biomechanics of the Cardiac Muscle



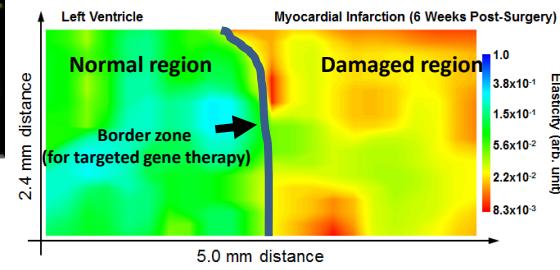
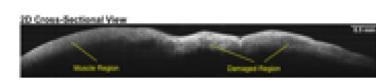
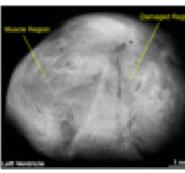
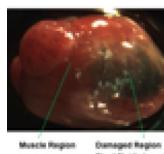
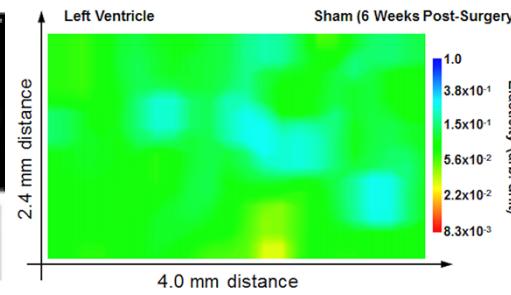
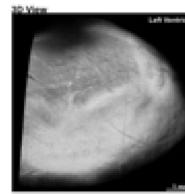
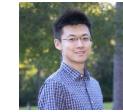
Wang et al: Biomedical Optics Express, 2014

Biomechanics of the Cardiac Muscle



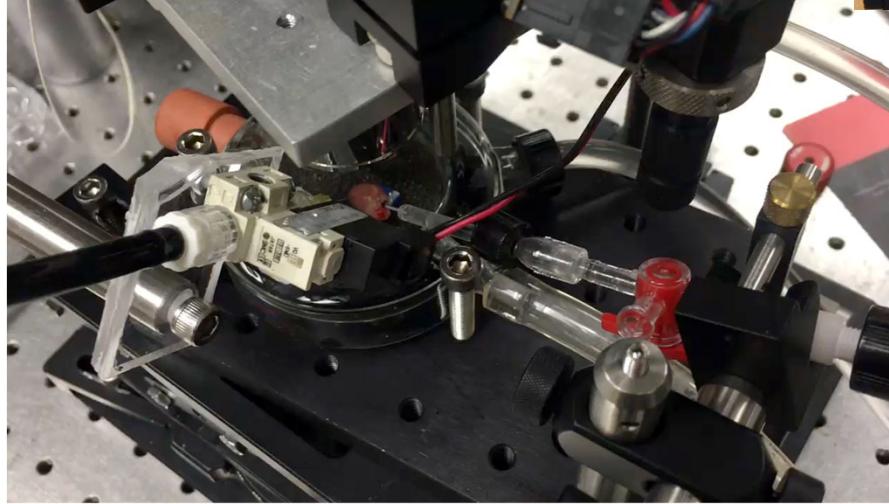
Wang, et al: (unpublished)

Biomechanics of the Cardiac Muscle during MI



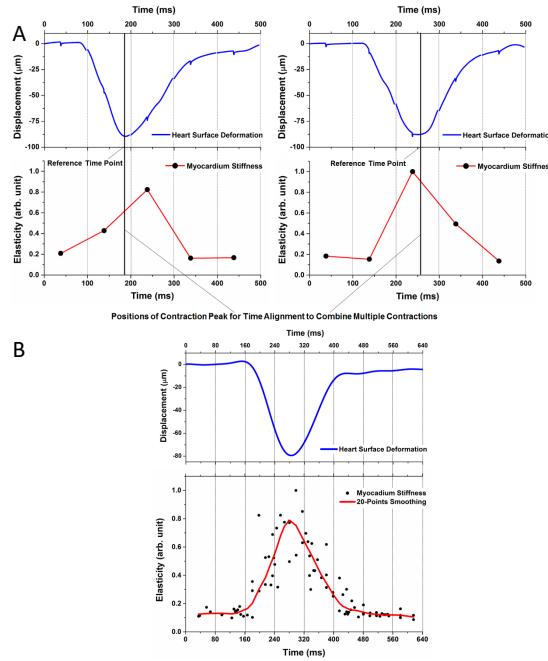
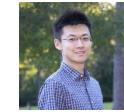
Wang, et al: Biomed Opt Express, 2018

Biomechanics of the Cardiac Muscle



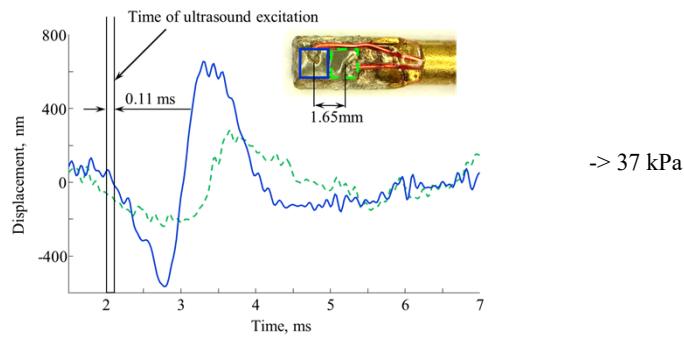
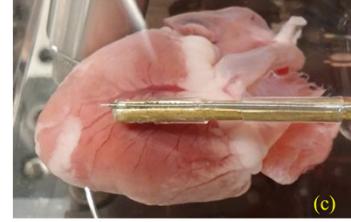
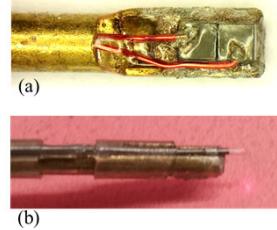
Lopez, Wang, et al, et al: unpublished

Biomechanics of the Cardiac Muscle



Wang, et al: (unpublished)

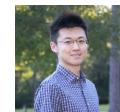
Biomechanics of the Cardiac Muscle: toward *in vivo*



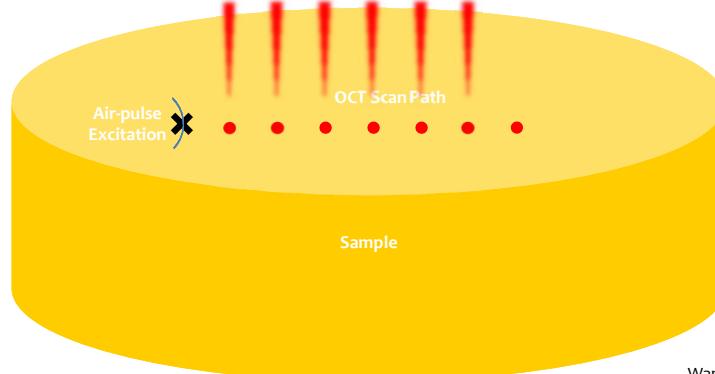
Karpouk, et al: J Biomed Optics, 2018

Pushing limits of the technology

M-B mode OCE Imaging Methodology



- Synchronize successive M-mode images with focused air-pulse [1]
 - Excite, acquire M-mode image
 - Move to next position
 - Excite, acquire M-mode image
 - Repeat

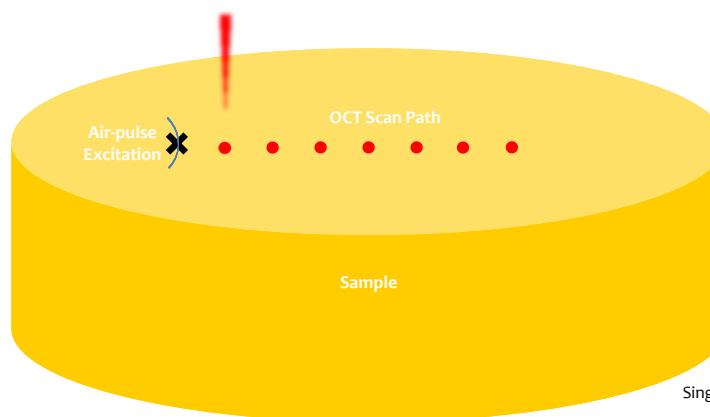


Wang et al: Optics Lett, 2014

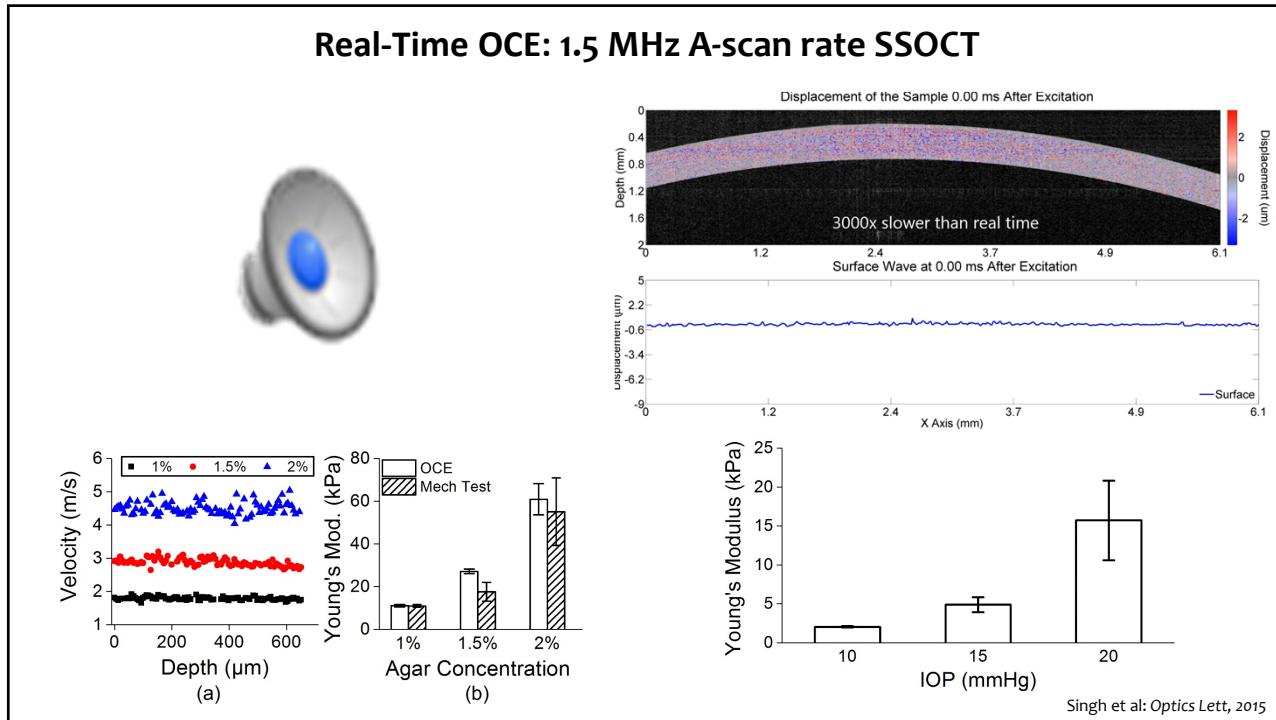
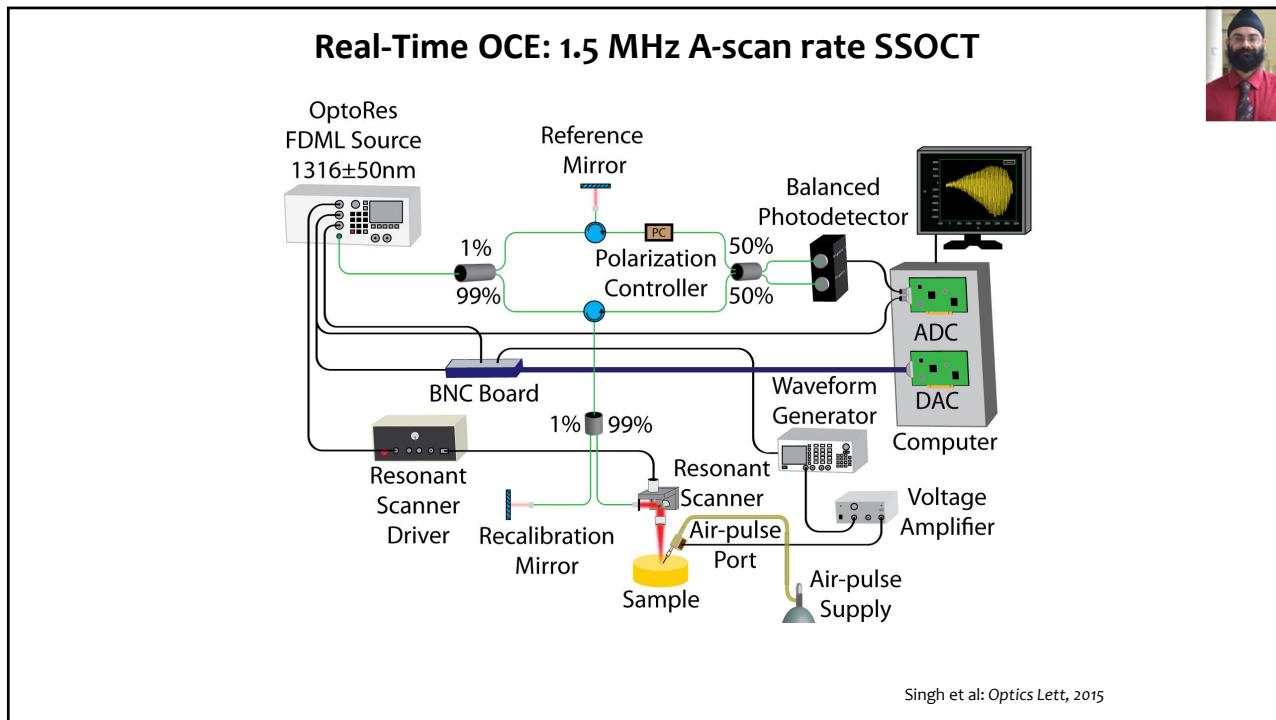
B-M mode OCE Imaging Methodology



- Fast B-mode imaging **during** wave propagation

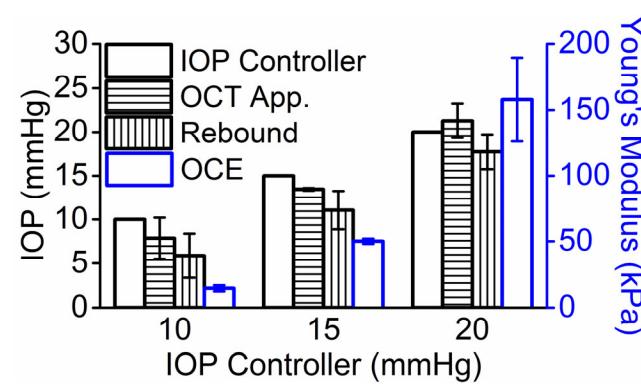
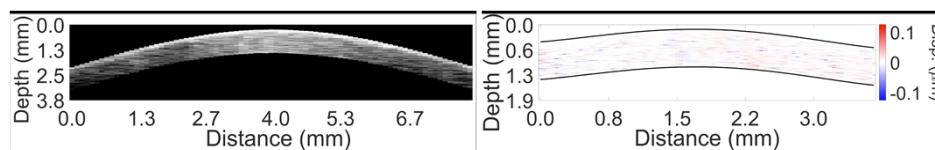


Singh et al: Optics Lett, 2015



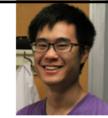
Can we measure **IOP** and **corneal stiffness** using **ONE** instrument?

Intraocular Pressure and Cornea stiffness in **ONE** instrument Applanation-OCE

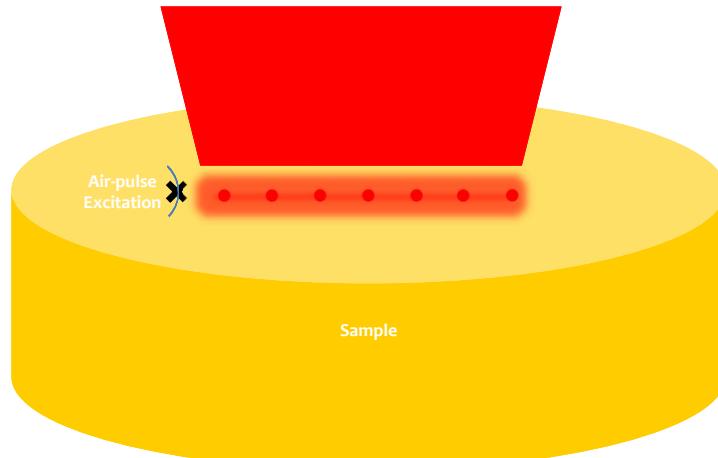


Singh et al: J Biomed Opt, 2017

Line-Field OCE Imaging Methodology

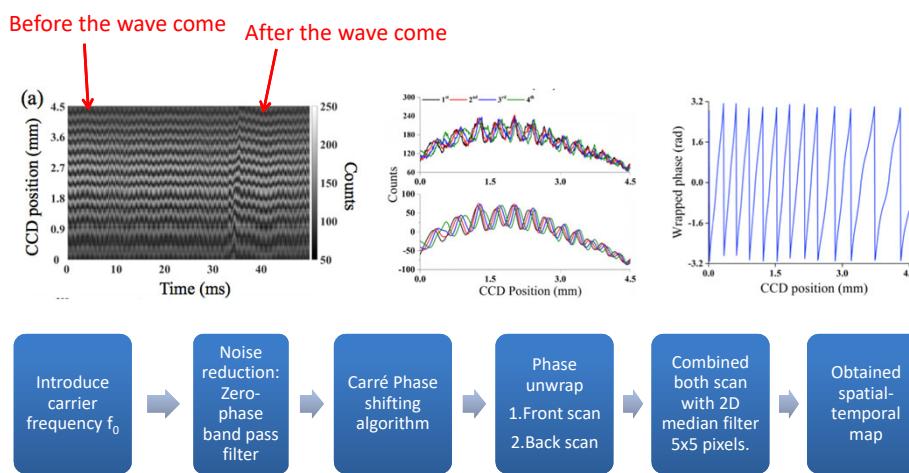


- Line imaging **during** wave propagation



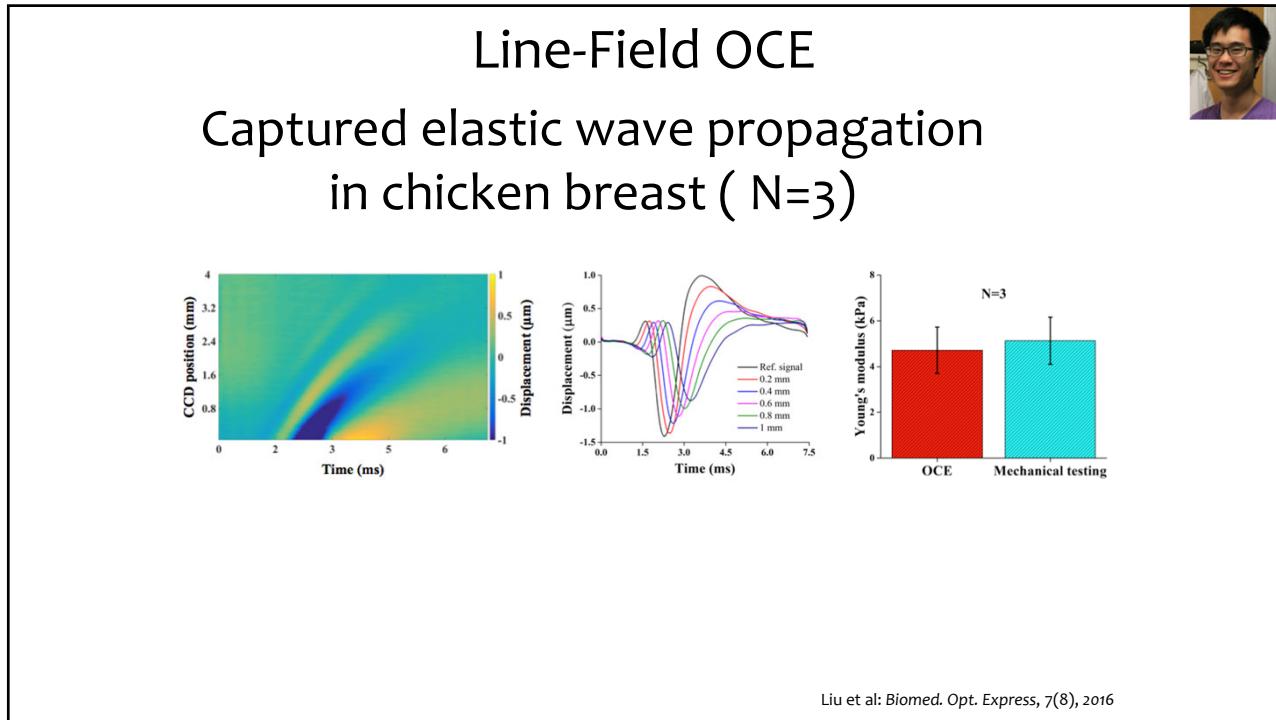
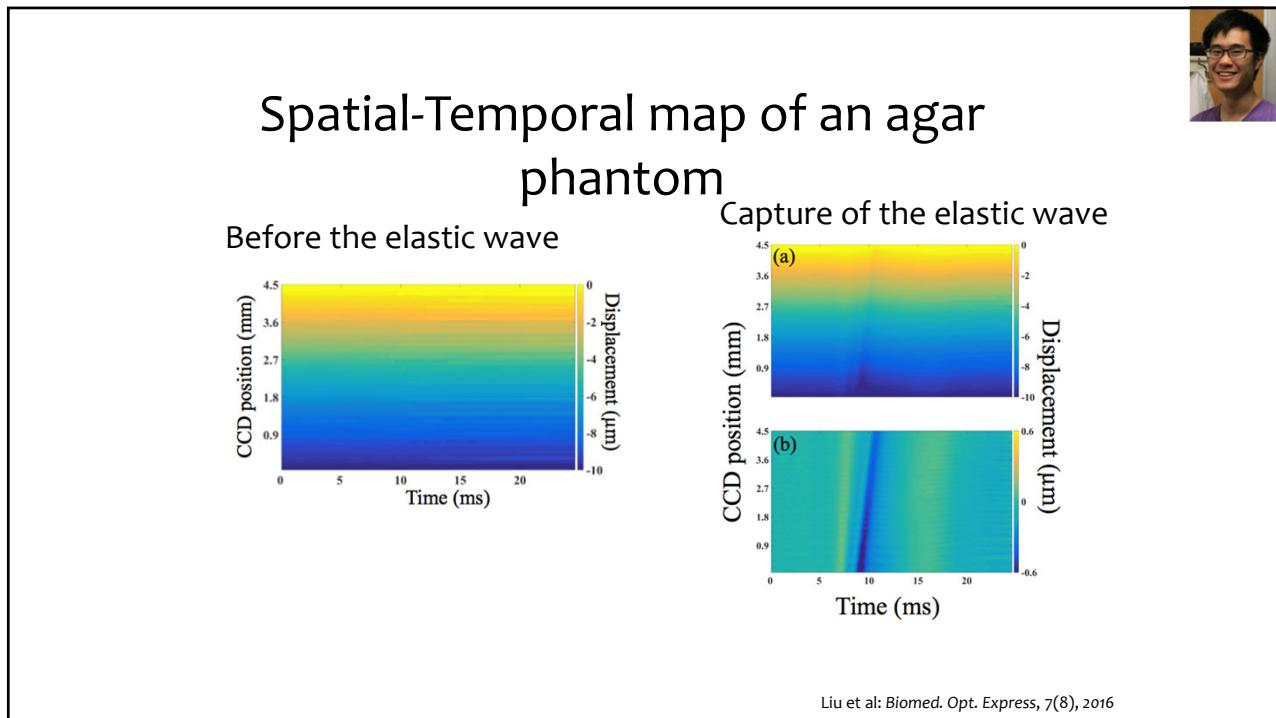
Liu et al: Biomed. Opt. Express, 2017
Liu et al: Biomed. Opt. Express, 2016

Line-field OCT methodology



Equivalent to **72 MHz** acquisition rate – fastest demonstrated speed in elastography

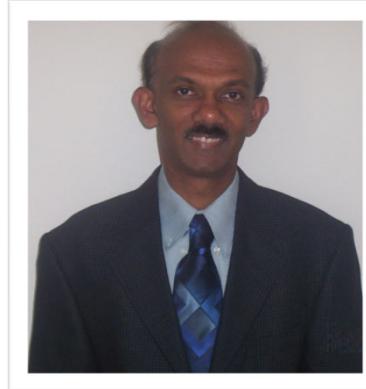
Liu et al: Biomed. Opt. Express, 7(8), 2016



The first clinical studies: Systemic Sclerosis



Shervin Assassi, M.D., M.S.
Associate Professor,
Rheumatology And Clinical
Immunogenetics,
UT Health



Chandra Mohan, M.D., Ph.D.
Professor, Department of
Biomedical Engineering,
University of Houston

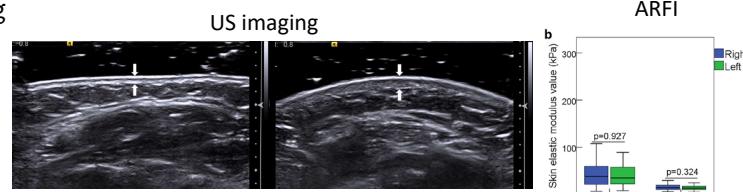
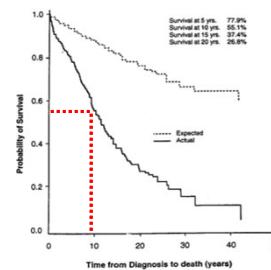
Systemic Sclerosis



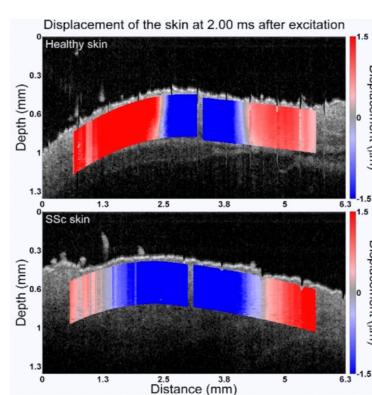
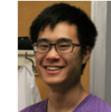
Systemic sclerosis (SSc) is a systemic connective tissue disease. Characteristics of systemic sclerosis include essential vasomotor disturbances; fibrosis; subsequent atrophy of the skin, subcutaneous tissue, muscles, and internal organs (eg, alimentary tract, lungs, heart, kidney, CNS); and immunologic disturbances accompany these findings.

Traditional systemic sclerosis examination

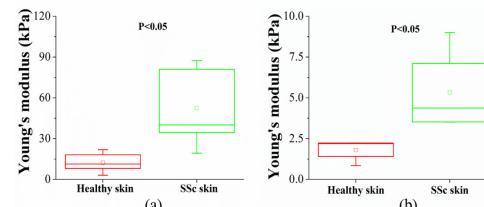
- 10-year survival rate: 58%
- Disease feature of SSc: Skin thickening
- Modified Rodnan score system (mRSS)
 - Limited sensitivity to subtle changes of the skin
 - Inter- and intra- observer variability (ICC:~0.76)
- Ultrasound imaging (US)
 - Dermal thickness detection
 - Acoustic radiation force impulse (ARFI)
 - Elastography assessment (Shear wave)
 - But, insufficient resolution for Imaging
 - Epidermal and dermal structures
 - especially dermal-epidermal junction.



Systemic Sclerosis – mice study



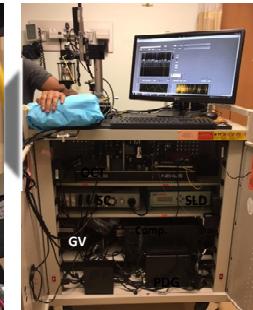
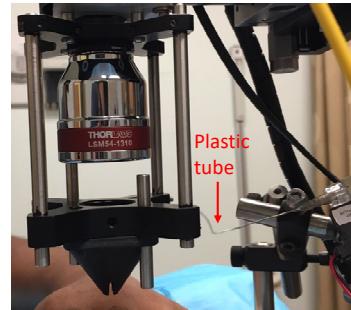
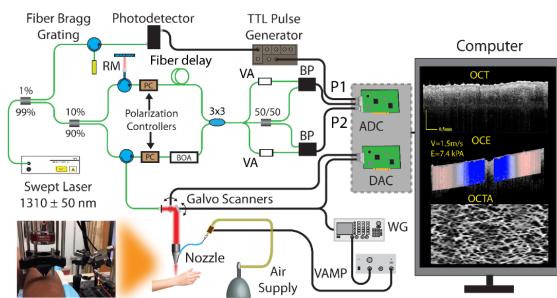
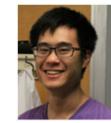
Elastic wave propagation in skin, as assessed by OCE in a typical healthy (top) and SSc (bottom) skin sample, measured at 2 ms after excitation in vivo



In vivo and in vitro OCE-assessment of skin involvement in the peripheral regions of SSc-affected skin. Plotted are the Young's modulus recorded in healthy skin and BLM-SSc afflicted skin at the periphery of the diseased region, from (a) in vitro and (b) in vivo OCE measurements (N = 4-9 mice per study group).

Du et al: JBO, 2016

Clinical OCE detection for SSc patients

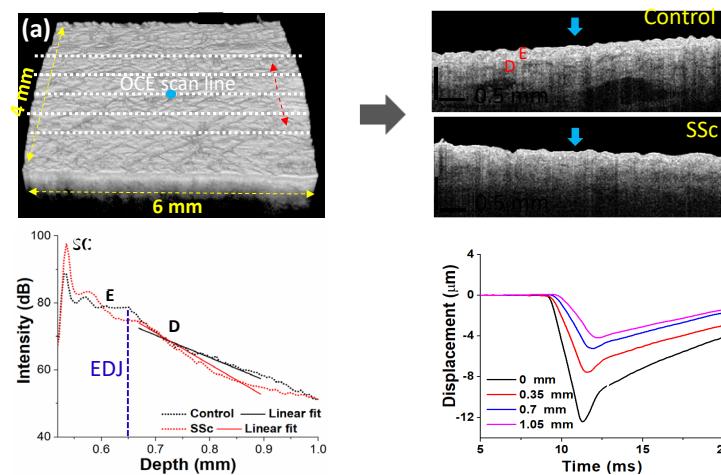
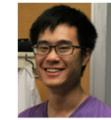


- Spectral domain OCT: $1310 \pm 45 \text{ nm}$
- Line rate: 70k Hz
- Pixel resolution: 8 μm in air
- Acquisition time: 3D OCT scan + 5 OCE scan
 - 15 min with 5 min break
- Site specific mRSS
- Skin biopsy

Liu et al: J. Biophotonics, (2019)

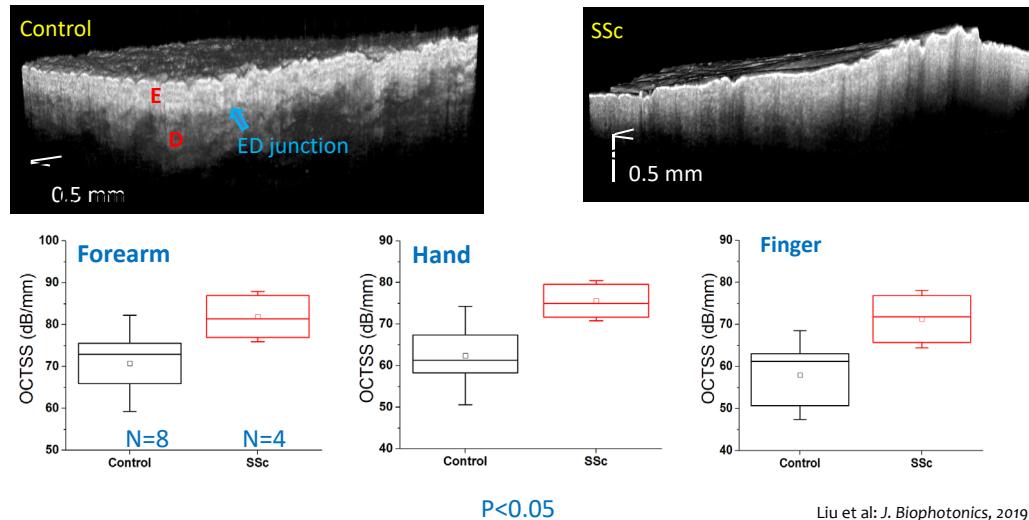


Experimental procedure

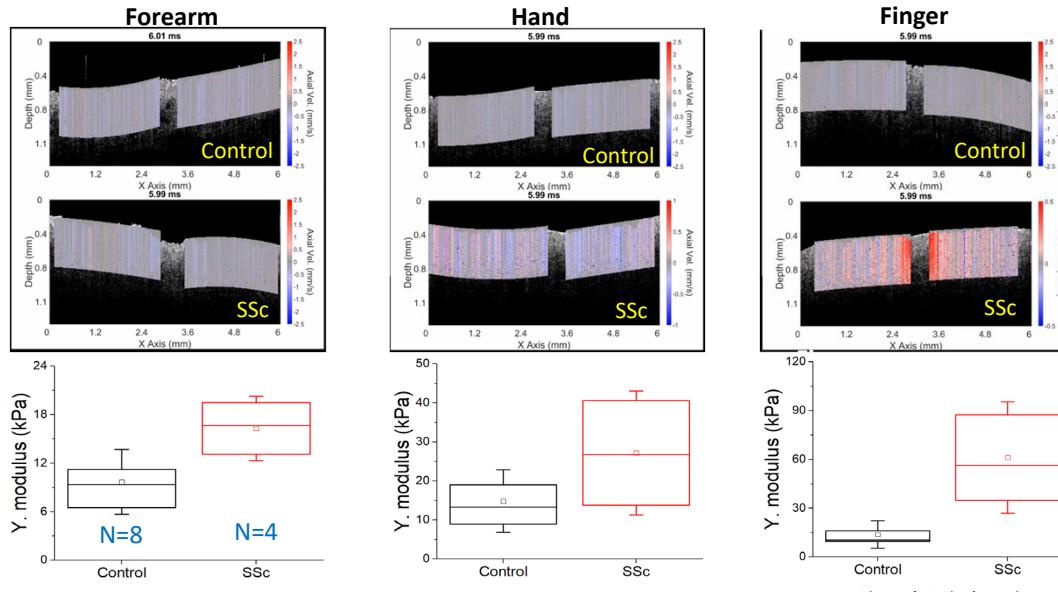


Liu et al: J. Biophotonics, 2019

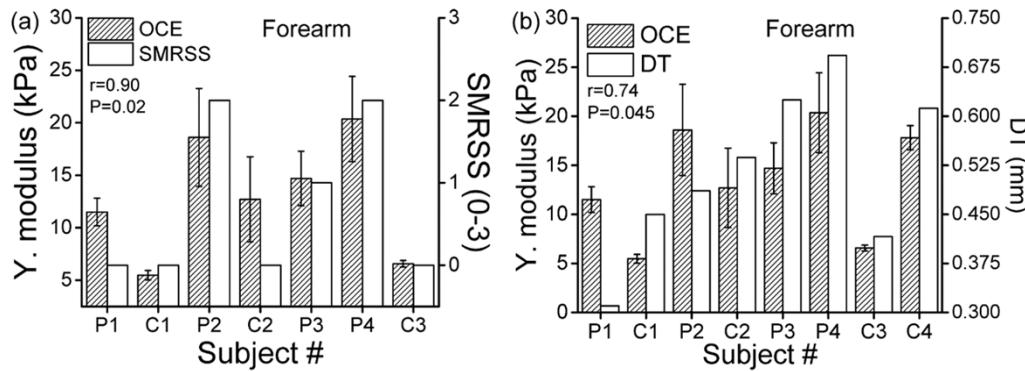
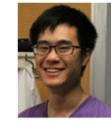
OCT analysis



OCE assessment



Clinical Summary

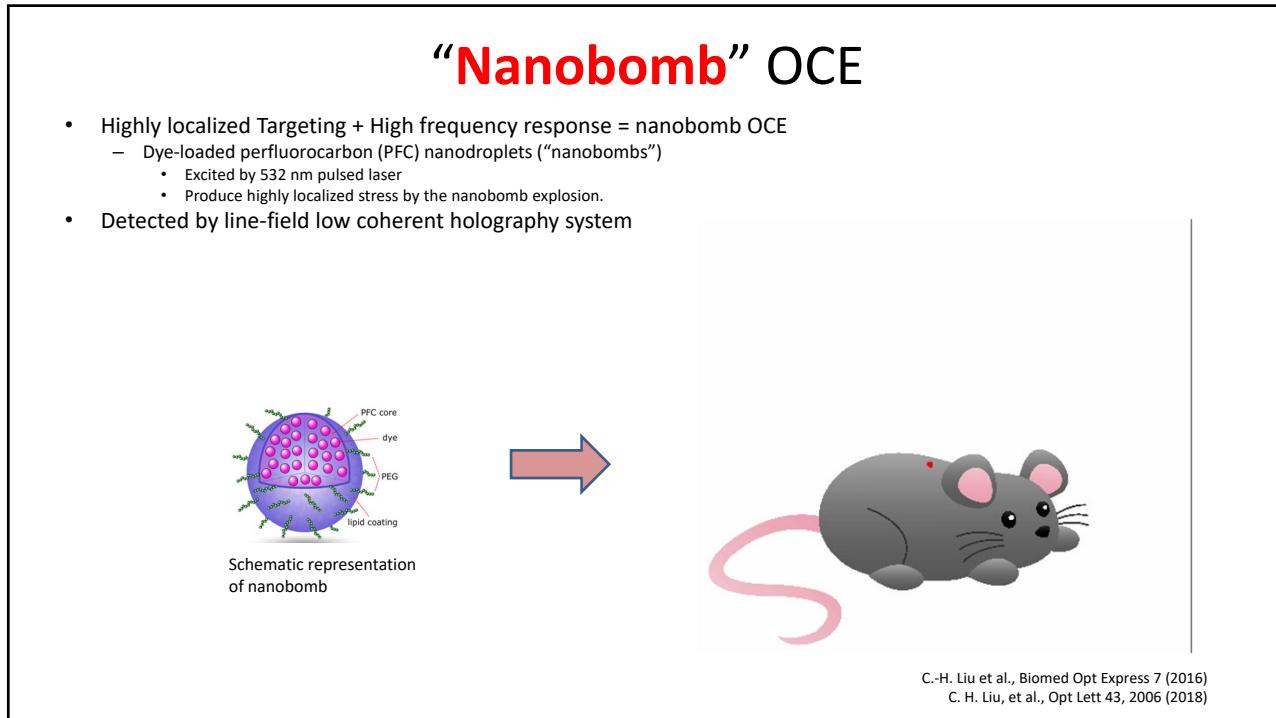
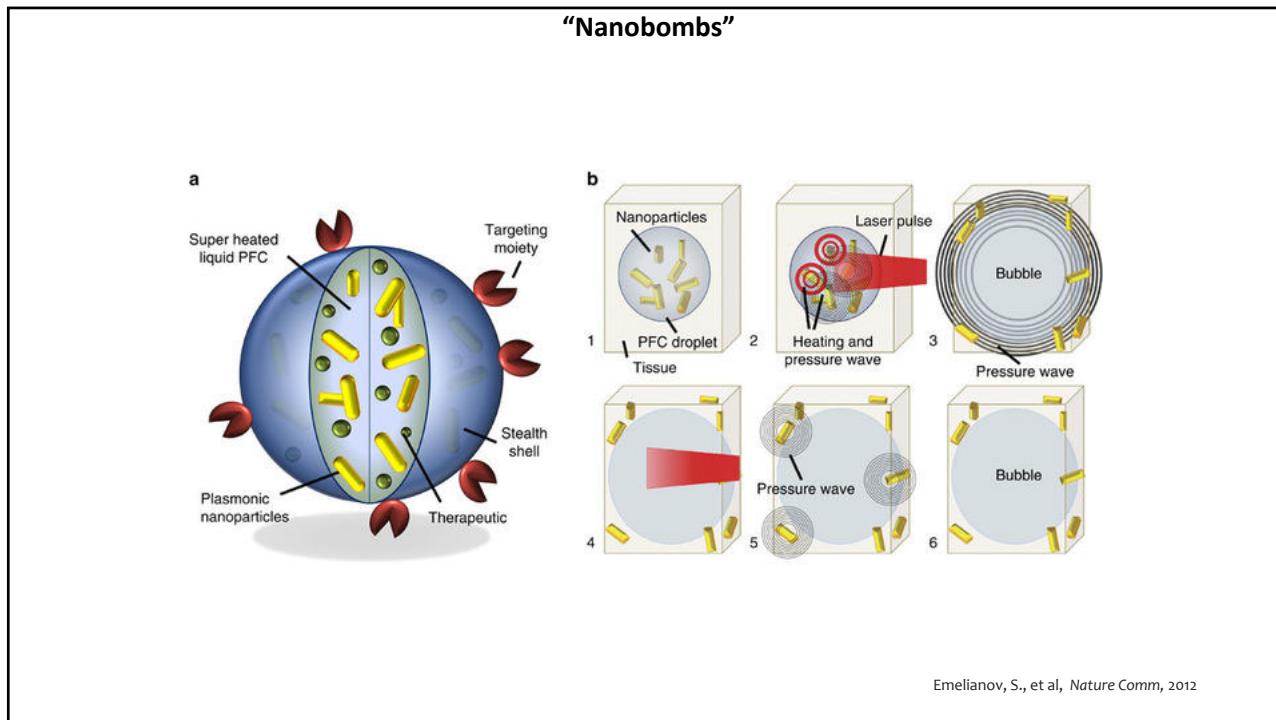


Liu et al: J. Biophotonics, 2019

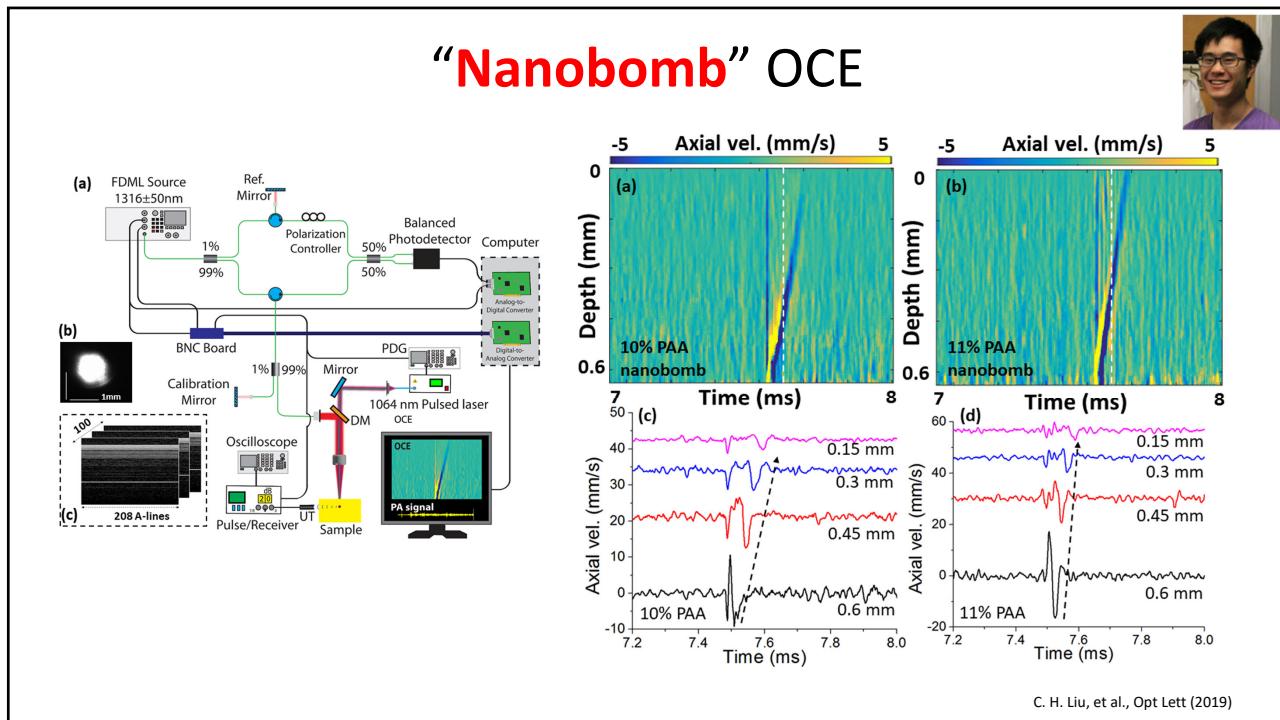
“Nanobomb” Optical Coherence Elastography



Konstantin Sokolov, Ph.D.
Professor, Department of
Imaging Physics,
M.D. Anderson Cancer Center



“Nanobomb” OCE



C. H. Liu, et al., Opt Lett (2019)

OCE: Summary and Conclusions

- OCE is a new emerging technique for tissue assessment: gives **biomechanical** contrast
- OCT structural images comes “for free”
- Allows 3D imaging and biomechanical assessment of various tissues
- Provides highly localized mechanical information of tissues with micrometer spatial resolution
- Holds a great promise for *in vivo* detection of various tissue diseases and quantitative evaluation of therapeutic interventions

Collaborators:

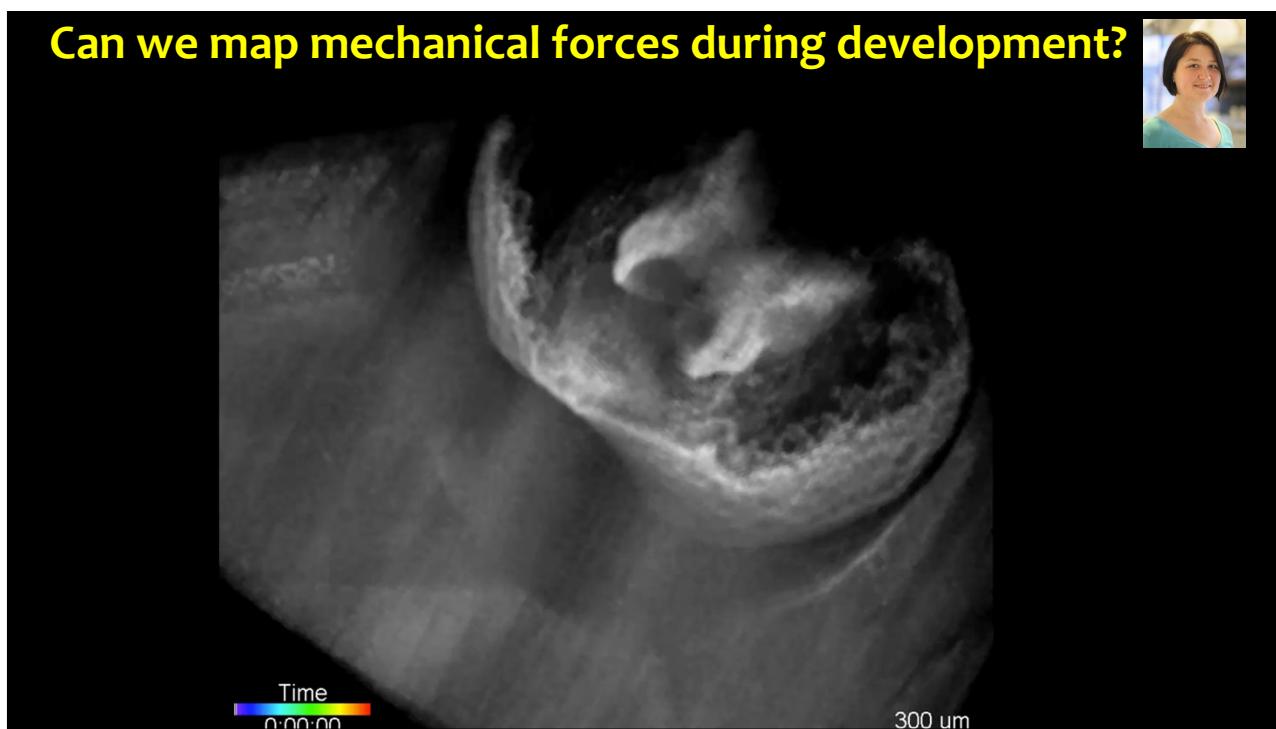
- Irina Larina – BCM
- Michael Twa – UH Optometry
- Salavat Aglyamov – UH
- Stas Emelianov – G. Tech
- Fabrice Manns – U. Miami
- Konstantin Sokolov - MDACC
- Shervin Assassi– UTH
- Chandra Mohan– UH
- Valery Tuchin – SSU
- Mary Dickinson – BCM
- Bruce Butler – UTHSC
- Michael Allon – HFC
- Xingda Li, JHU
- James Martin– BCM
- Rajesh Miranda– TAMU
- Mohamad Ghosn – Methodist
- Pradeep Sharma – UH
- Matthew Franchek – UH
- Richard Willson – UH
- Paul Ruchhoeft – UH
- Alexei Sobakin – UW, Madison
- Marlowe Eldridge – UW, Madison
- Raph Pollock – MDACC
- Giuliano Scarcelli, UMD
- Richard Finnell, BCM

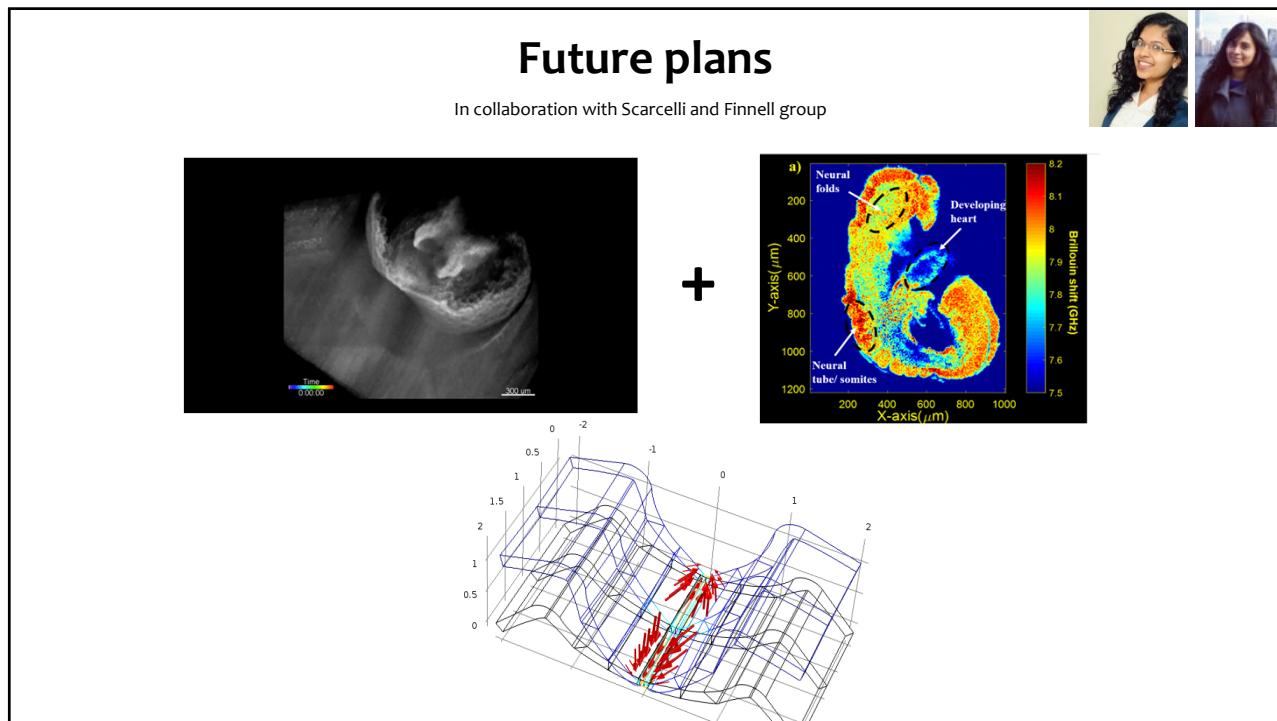
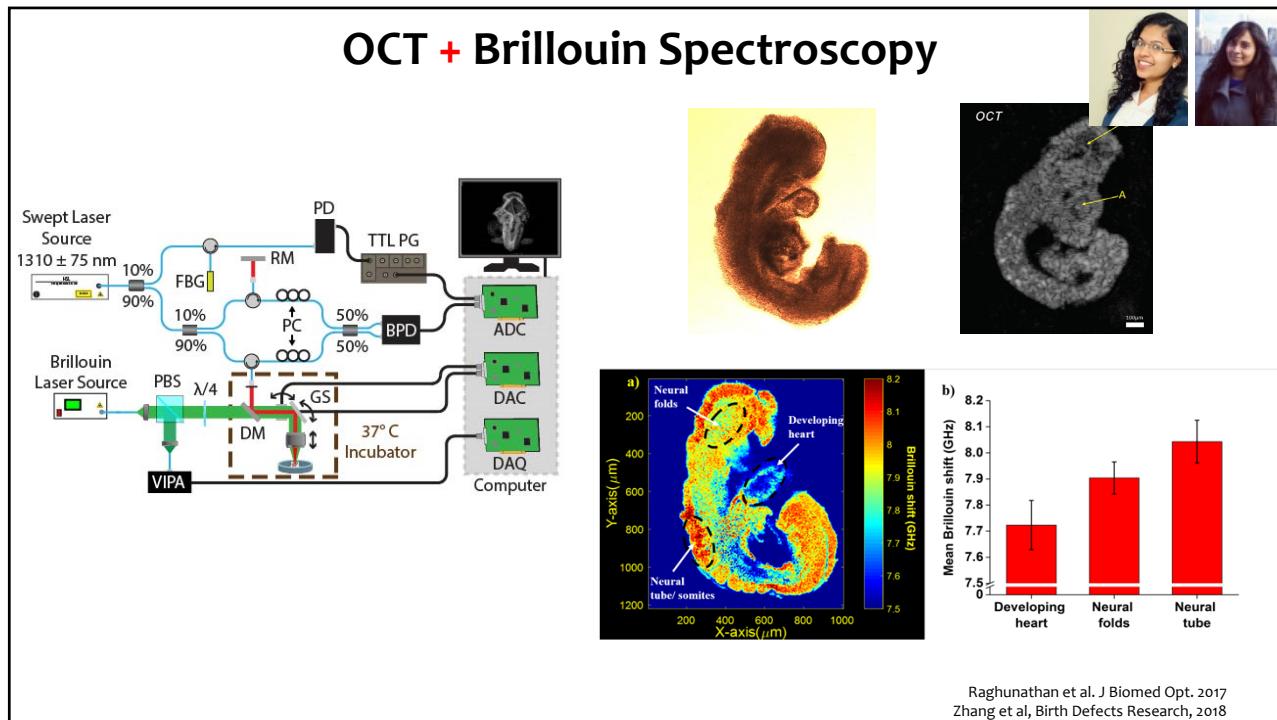
Current Funding:

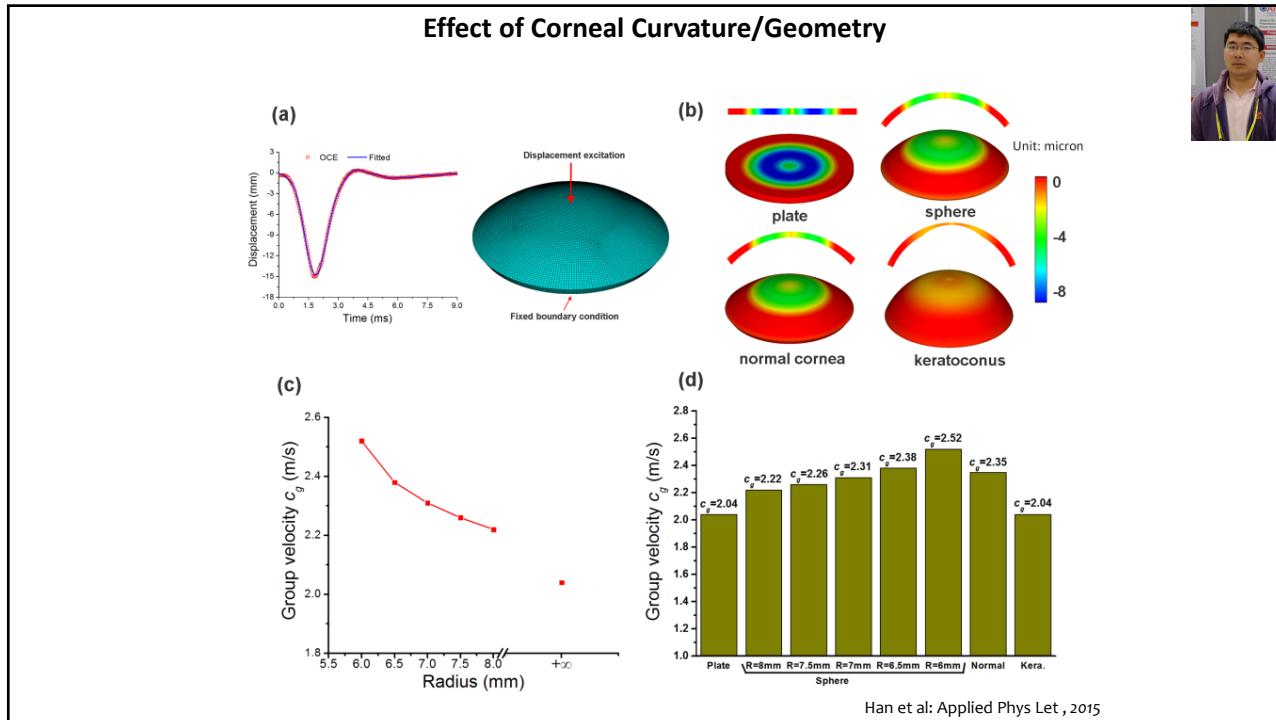
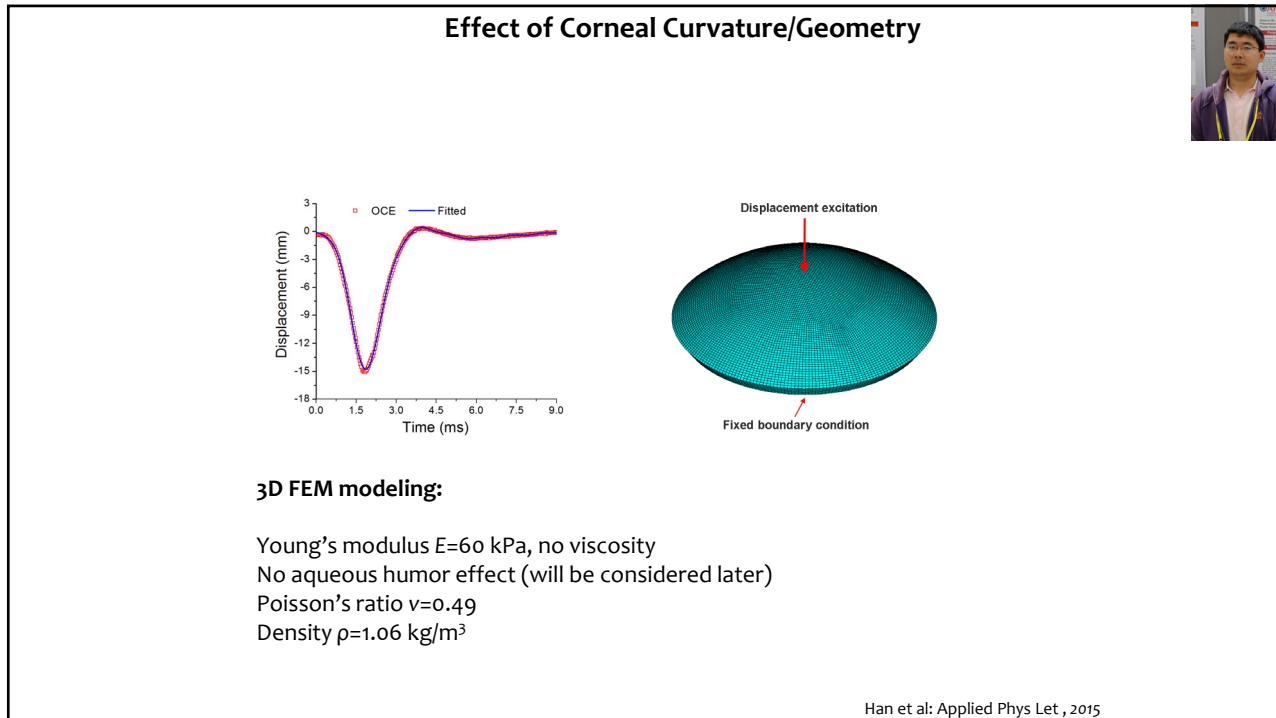
NIH	2R01EY022362 (Larin, Twa)	(2010-2020)
	1R01HD086765 (Larin, Miranda)	(2016-2020)
	1R01HL130804 (Larin, Martin)	(2016-2020)
	1R01HD095520 (Larin, Scarcelli, Finnell)	(2018-2023)
	9R01HD096335 (Larina)	(2013-2023)
	1R01EB027099 (Larina)	(2019-2022)
	1R21CA231561 (Sokolov)	(2019-2021)
	1R01HL146745 (Mayerich)	(2019-2024)

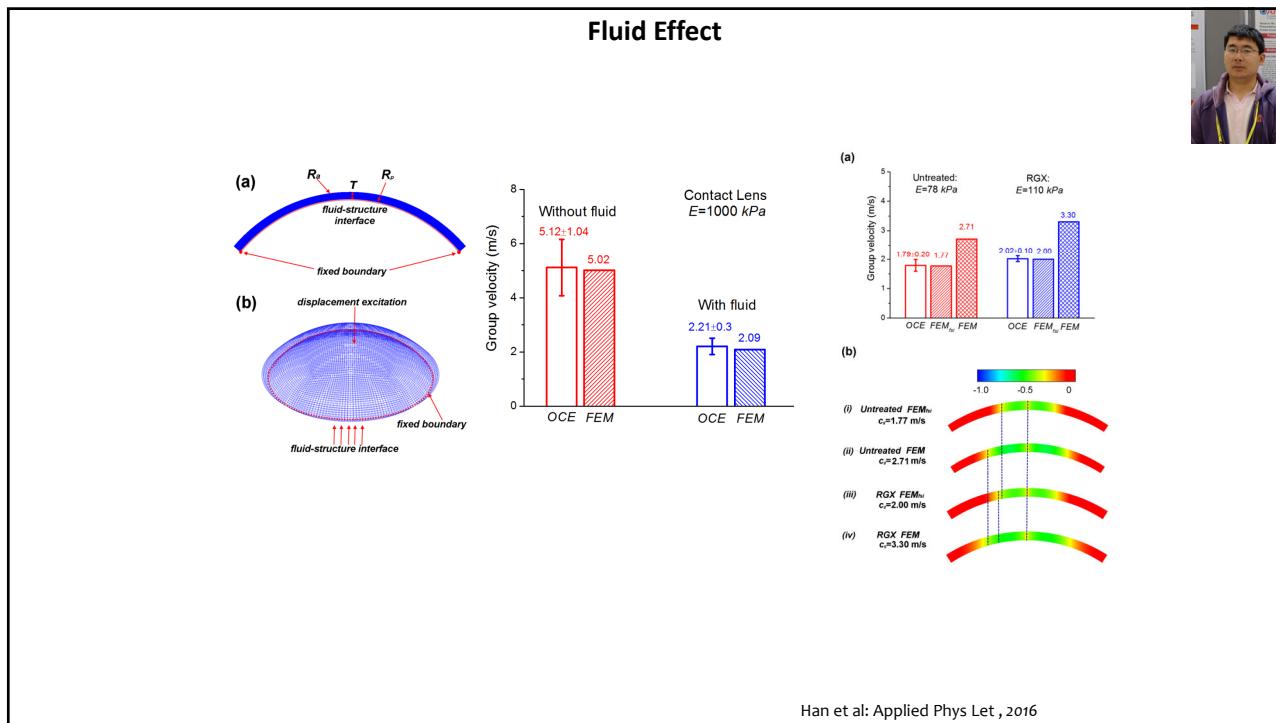
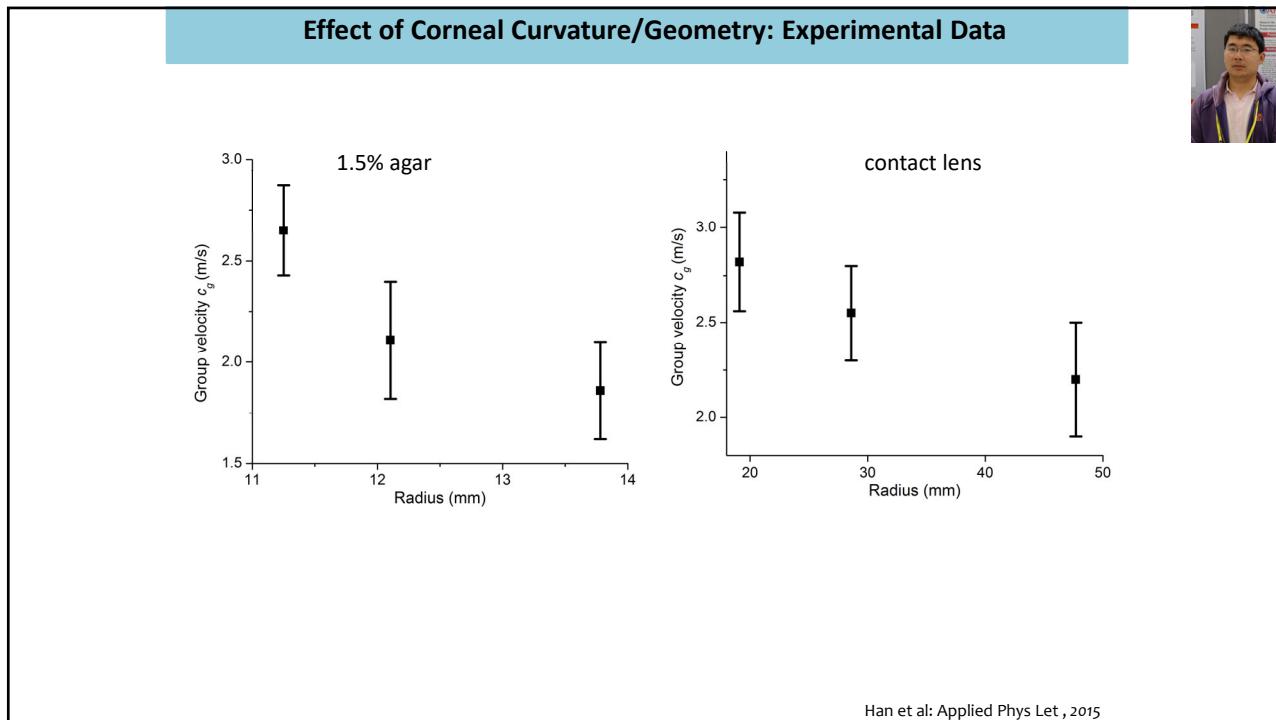
Graduate students and Postdoctoral positions are available:
Please inquire klarin@uh.edu

<http://bol.egr.uh.edu/>









Quantifying Viscoelasticity

Lamb waves: modified Rayleigh-Lamb frequency equation



Modified RLFE: $\det(M)=0$

$$M = \begin{bmatrix} (k^2 + \beta^2) \sinh(\alpha d) & 2k\beta \sinh(\beta d) & (k^2 + \beta^2) \cosh(\alpha d) & 2k\beta \cosh(\beta d) & 0 \\ 2k\alpha \cosh(\alpha d) & (k^2 + \beta^2) \cosh(\beta d) & 2k\alpha \sinh(\alpha d) & (k^2 + \beta^2) \sinh(\beta d) & 0 \\ -(k^2 + \beta^2) \sinh(\alpha d) & -2k\beta \sinh(\beta d) & (k^2 + \beta^2) \cosh(\alpha d) & 2k\beta \cosh(\beta d) & \frac{\rho_F \omega^2}{\mu_D} \\ 2k\alpha \cosh(\alpha d) & (k^2 + \beta^2) \cosh(\beta d) & -2k\alpha \sinh(\alpha d) & -(k^2 + \beta^2) \sinh(\beta d) & 0 \\ \alpha \cosh(\alpha d) & k \cosh(\beta d) & -\alpha \sinh(\alpha d) & -k \sinh(\beta d) & -\alpha_F \end{bmatrix}$$

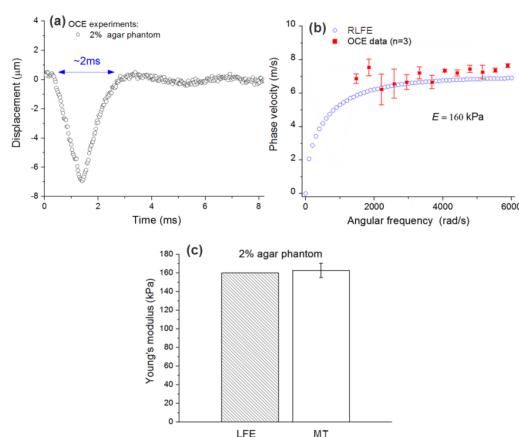
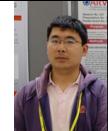
$$\begin{aligned} k^2 &= \frac{\omega^2}{c_p^2} & \alpha^2 &= k^2 - \frac{\omega^2}{c_1^2} & \beta^2 &= k^2 - \frac{\omega^2}{c_F^2} \\ \mu_D &= \mu + i\omega\eta & \alpha_F^2 &= k^2 - \frac{\omega^2}{c_F^2} & c_2 &= \sqrt{\frac{\mu_D}{\rho}} \end{aligned}$$

ω - Circular frequency
 c_p - Phase velocity
 ρ - Density
 μ - Shear elastic modulus
 η - Shear viscous modulus

c_1 - Speed of sound
 $2d$ - Thickness
 c_F - Speed of sound in fluid
 ρ_F - Density of fluid

Han et al: PMB, v. 60, 2015

Quantifying Viscoelasticity (phantoms)

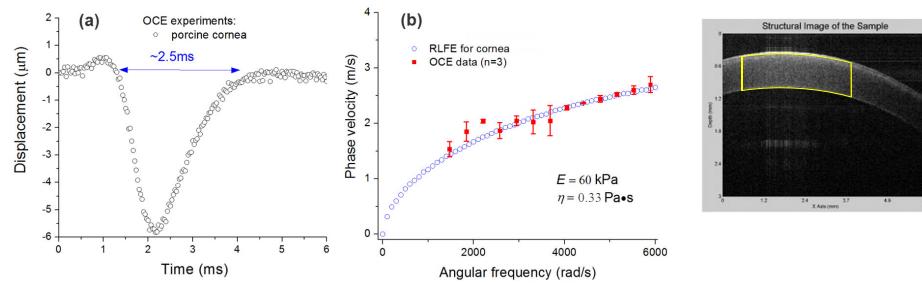
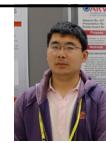


(a) Temporal displacement profile from 2% agar phantom
 (b) OCE vs RLFE for 2% agar phantom
 (c) Young's modulus of 2% agar phantom assessed by RLFE and mechanical testing (MT).

The Young's modulus of 2% phantom measured by OCE and fitted by RLFE is 160kPa, which was validated by uniaxial mechanical testing.

Han et al: PMB, v. 60, 2015

Quantifying Viscoelasticity (cornea)



For porcine cornea at IOP=20 mmHg, the Young's modulus was estimated as 60 kPa and shear viscosity as 0.33 Pa•s.

Han et al: PMB, v. 60, 2015
 Han et al: JMBBM, v. 66, 2017