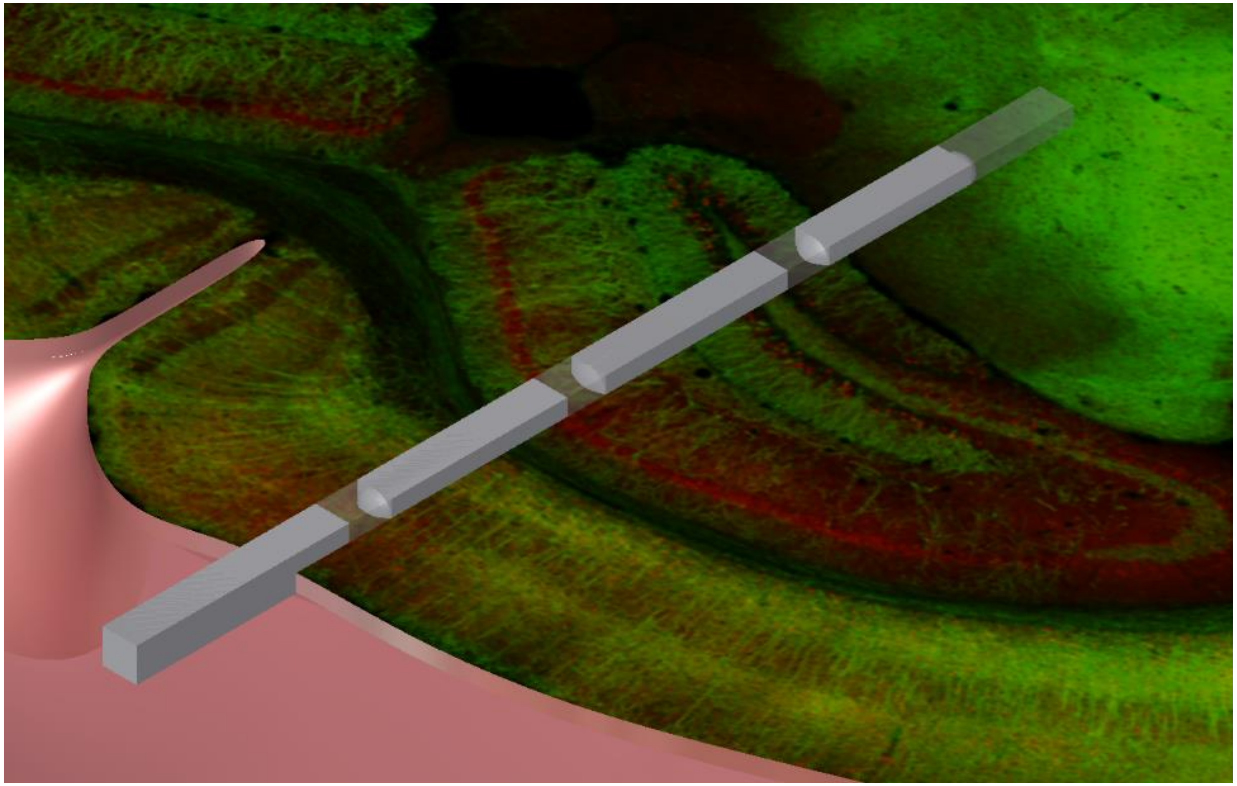
Microphotonic Technology for Inside Body Imaging



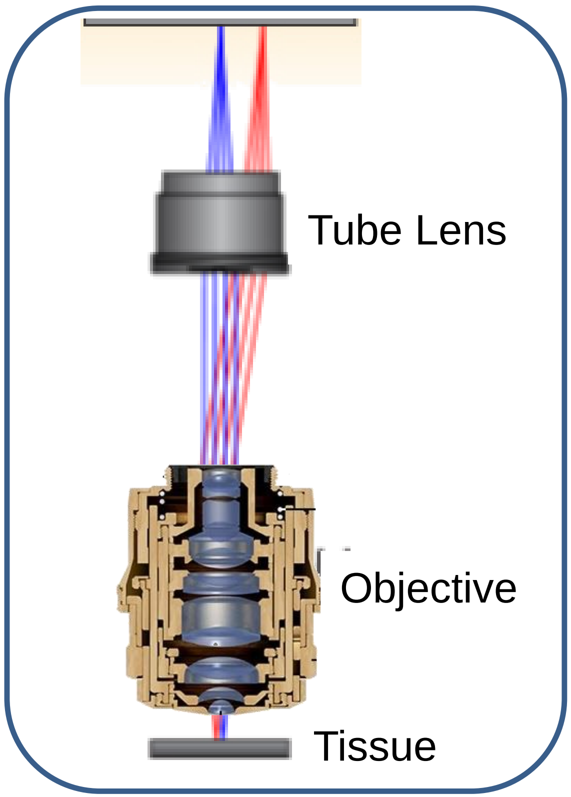
Mohammad Amin Tadayon, Michal Lipson, Kamyar Neshavdian

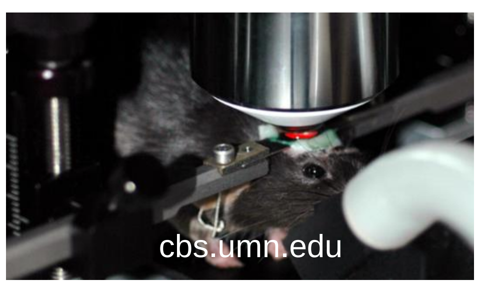
LensGuide Imaging Technology

COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK

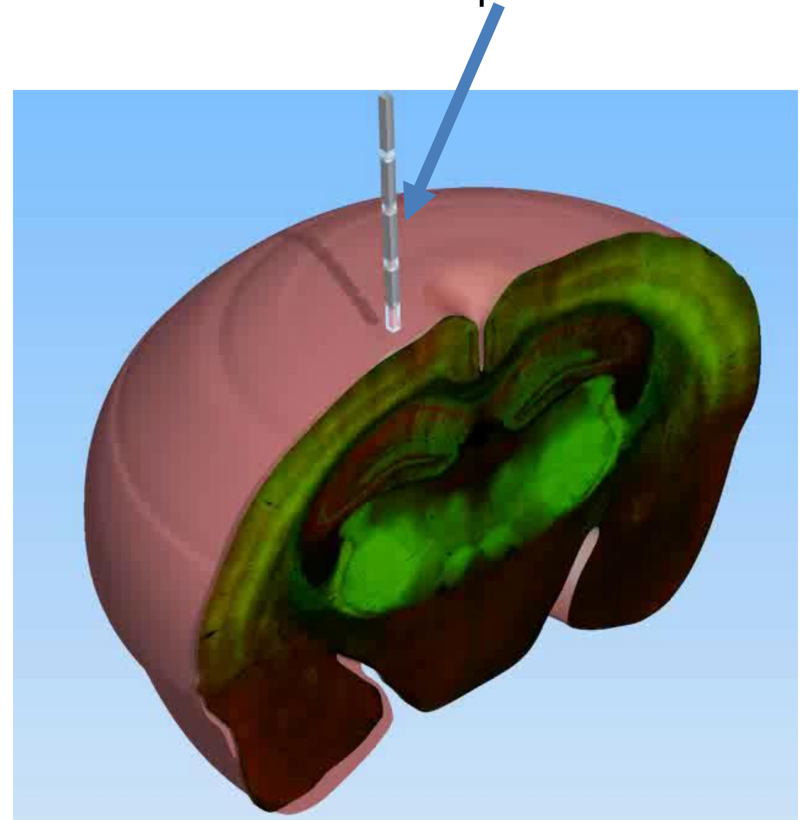
Imaging Column with Size of Less than 100 μm for Very Deep Tissue Imaging

- Miniaturizing the whole microscope system to small probe to get a great quality image at any depth





Lens-guide probe with size of less than 100 μm



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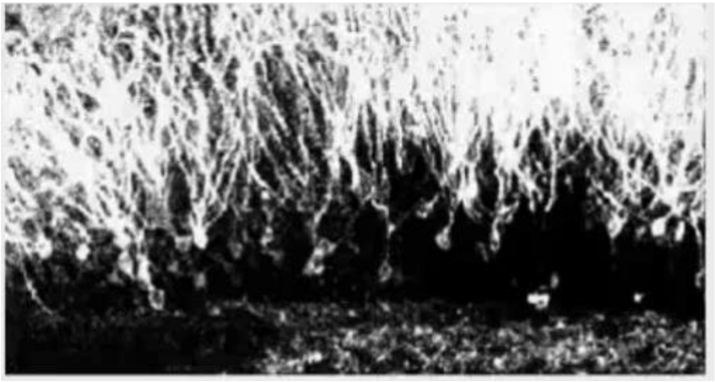
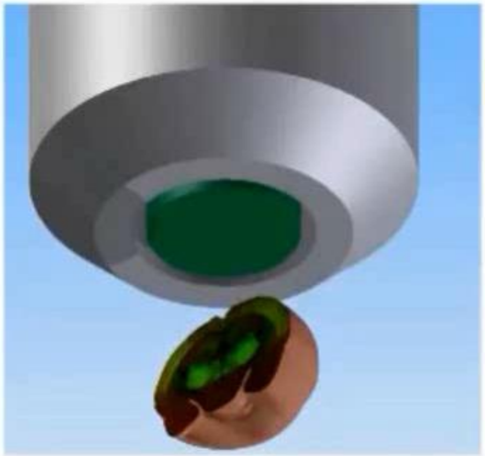
Why We Need Endoscope for Deep Tissue Imaging?

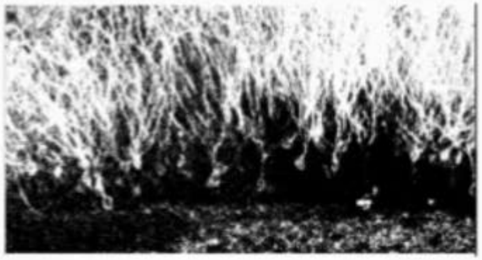
Loosing   Image Quality in Different Depth Without Endoscope



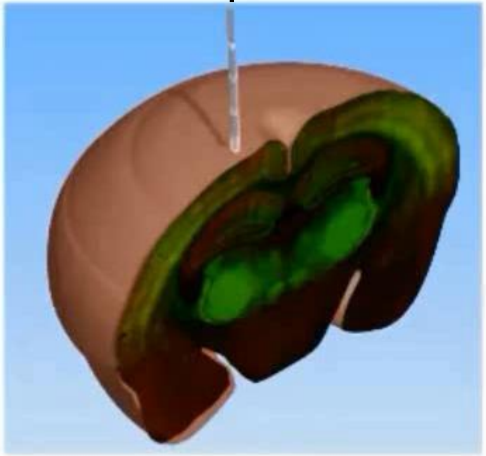
Imaging with Objective Outside of the tissue



Preserving the Image Quality in Different Depth Using Endoscope



Insertion of the Our Endoscopic Probe



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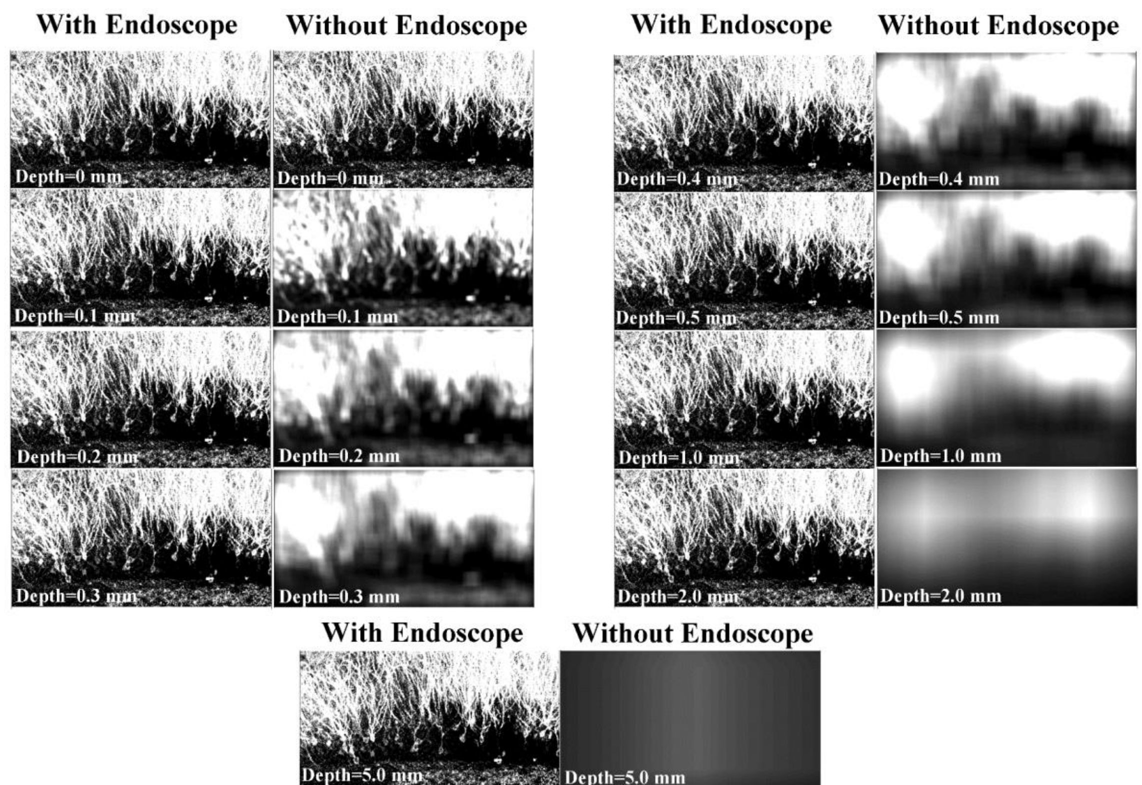
Comparing Endoscope and Regular Microscope for in Depth Imaging

- With regular microscope when we capture an image deeper in the tissue the imaging resolution degrades due to the light scattering and absorption in tissue
- Using our optical endoscope, we can avoid this problem and achieve the same image quality in any depth

Our Endoscopic Probe Resolution < 1 µm at any Depth



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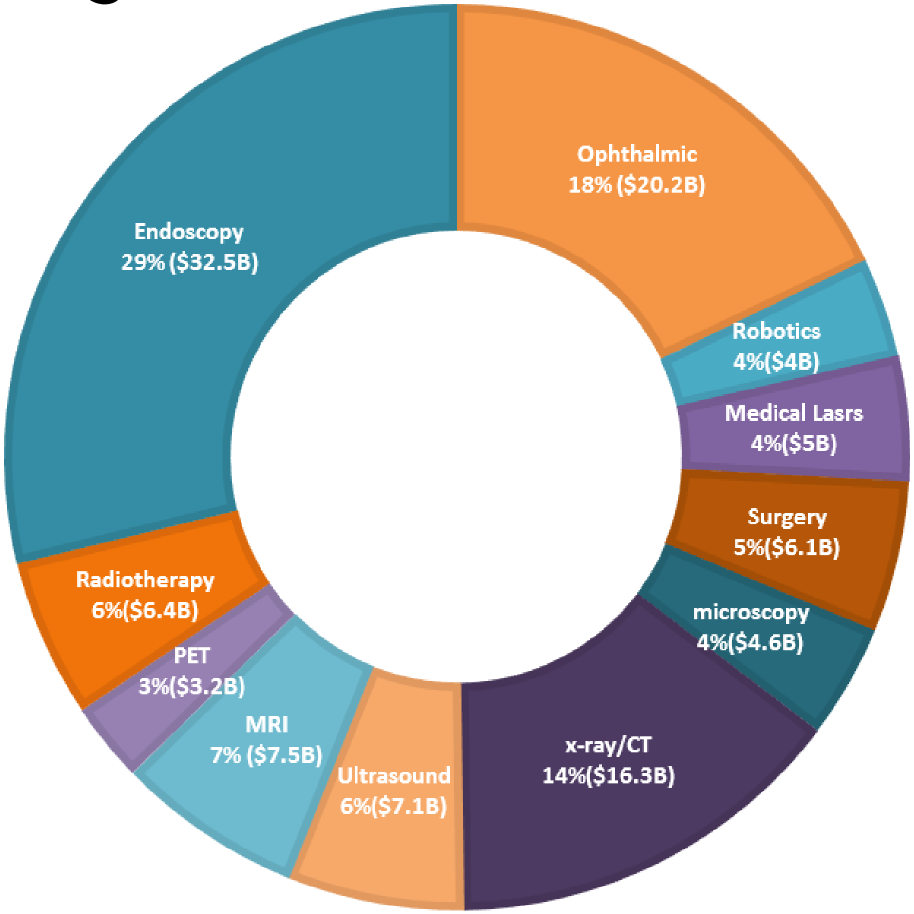
Medical Imaging Market Sections

- Endoscopy System has the Largest Market Segment in the medical imaging market.
- 4 times Larger Market than MRI or Ultrasound Imaging.



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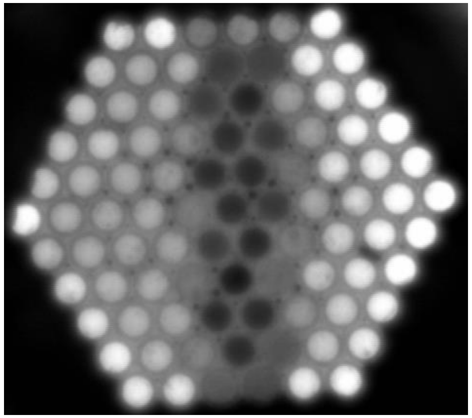
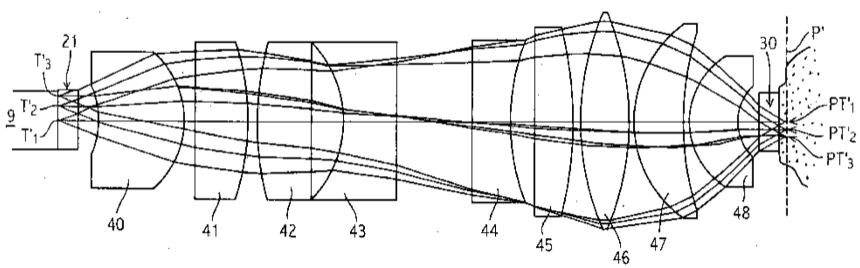
Target Market for Our Micro-Endoscope

Application	Number of Cases Per Year in US	Probe Price ($)	Market Size (Million $)/ Year
Basal Cell and Squamous Skin Cancer	5,400,000	75	405
Melanoma Cancer/Year	178,560	100	17.8
Breast Cancer/Year	252,710	200	50.5
Liver Cancer/Year	42,220	200	8.4
All type of Caners (other than Skin)/Year	1,735,350	150	260
Pharmaceutical Laboratory	Comparing with other technologies		100s
Biology and Neuroscience Laboratory	Comparing with other companies	Based on Different Configuration charges can go to $1000s	10s

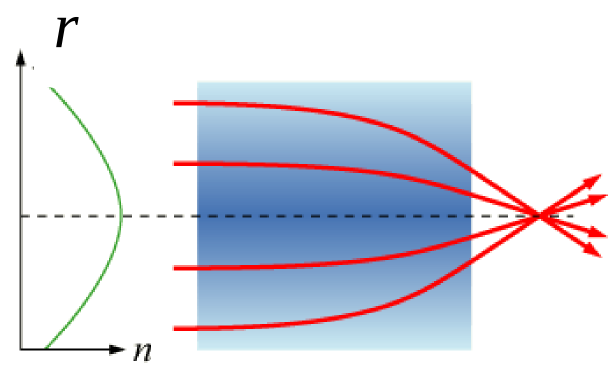
Current Technology



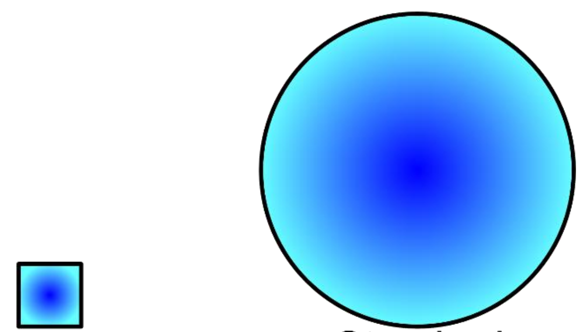
Optical Fiber Bundle
No limitation on Size,
Low Resolution (3-5 um)
Large amount of Light Loss



Miniaturized Lenses
2-4 mm Size, 1.4 um resolution
10 % Field of View



GRIN Lenses
Large Size (0.5-1 mm)
Small Field of View (~30%)
Significant Resolution Degrade
Across Field of View



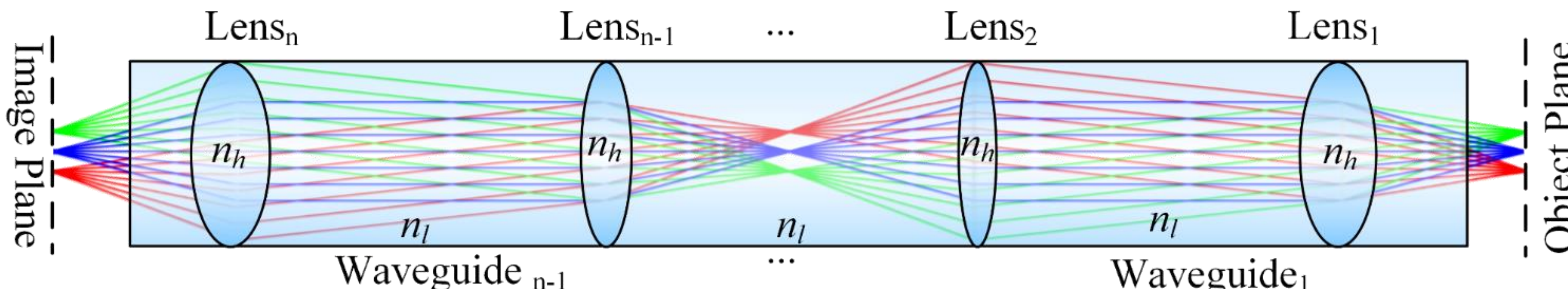
Our Lens-guide Probe
No Limitation on Size, and Resolution

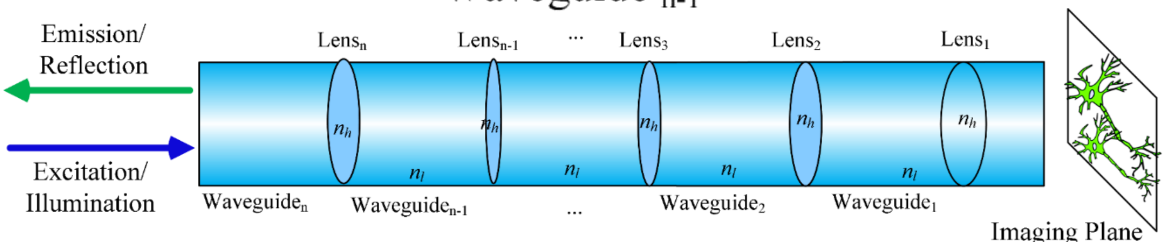
Competitors

Company	Endoscope Technology Overview	Specs and Limitations	Size / Year Estab.
Mauna Kea Tech. (France)	Using both imaging objective and optical fiber bundle for confocal microscopy. Use mostly for subcellular level imaging in the digestive tract.	Probe Size>2.4 mm→ Resolution 1.4 um Probe size~300 um → Resolution 3.3 um	100-200 employees (linkedin) / 2000
Inscopix (USA)	They use GRIN Tech GRIN lenses to do the imaging. The main innovation is in making to whole imaging system small enough which a moving animal can use it. Researcher use it more for mouse brain Study.	Probe Size→ 0.5-1 mm Resolution→ ~ 1 um. Small Field of view Significant resolution degradation across the field of view.	50-100 employees (linkedin)/ 2011
Scholley (Germany)	Mostly inside Cavities. Imaging Sensor at the tip of the Endoscope. They have also endoscope from size of 0.350 - 1mm. But all of these with the lower resolution.	Camera>1 mm; Lower resolution Micro-endoscope>0.350 lower resolution (different resolution regime). Also use it for Mechanical Inspection.	700 employees/ 1968
GRINTECH (Germany)	They sell the GRIN lenses in different configurations. They sell GRIN for endoscopy, laser diode beam shaping, sensor technology, and telecommunication	Probe Size→ 0.5-1 mm Resolution→ ~ 1 um. Small Field of view Significant resolution degradation across the field of view.	10-50 employees (linkedin)/ 1999

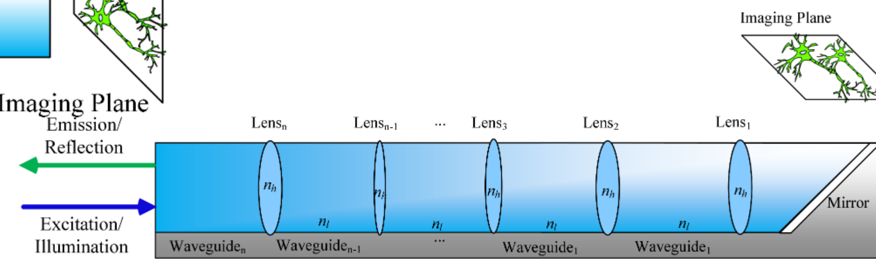
Our New Micro-photonics Endoscope Concept (Lens-guide)

- Cascade of Lenses and Waveguides
  - Minimize the Endoscope Size
  - Achieve the Highest Imaging Resolution
    - Correcting Image Aberrations and Distortions





A lot of Flexibility to Design
Different Configurations



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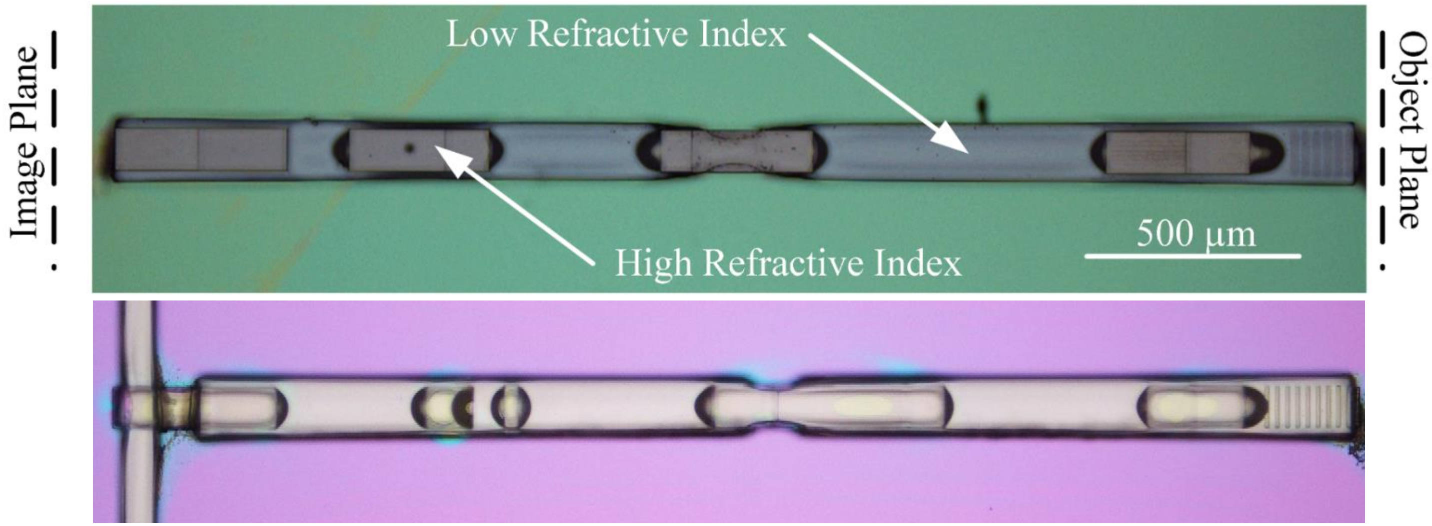
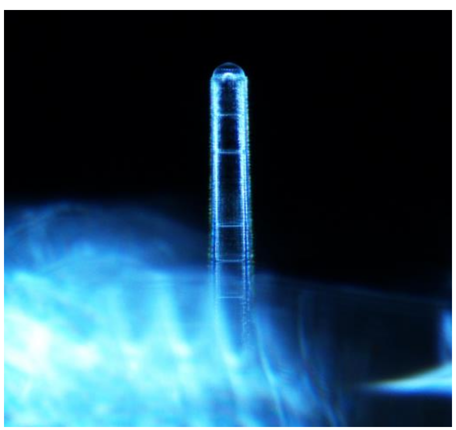
Our Fabricated Lens-guide Probe

- High Precision Fabrication Based on the Micro/Nanofabrication
  - Photolithography, 2 photon Polymerization, Micro-Molding





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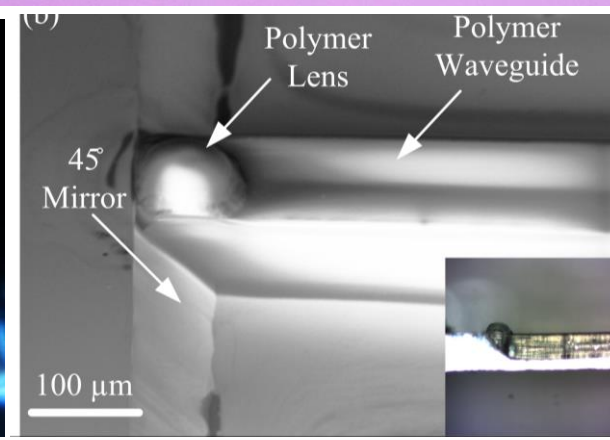
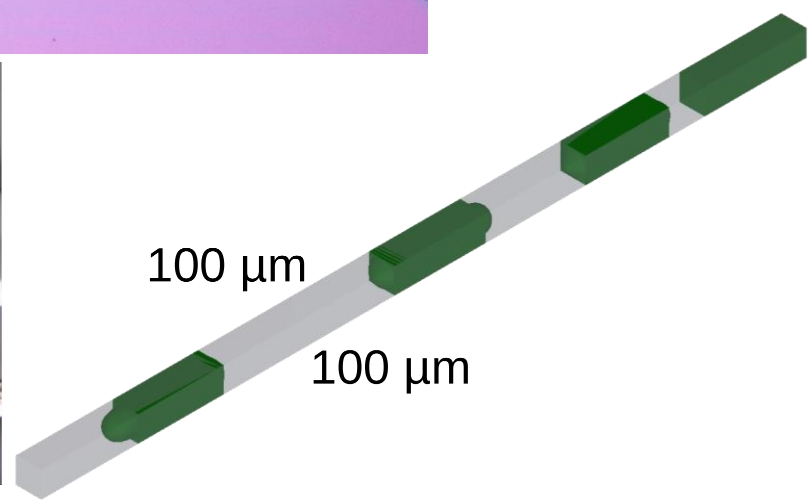
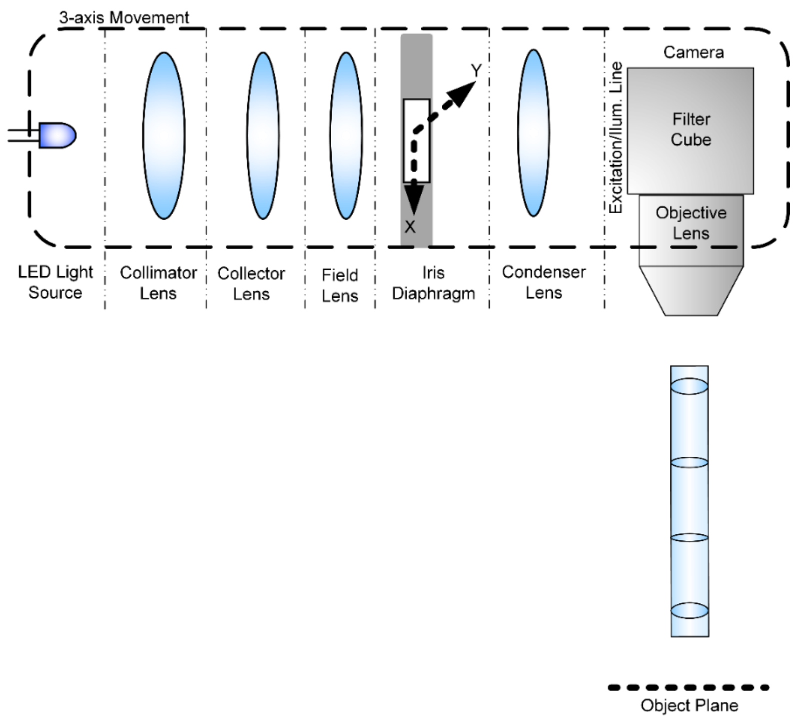




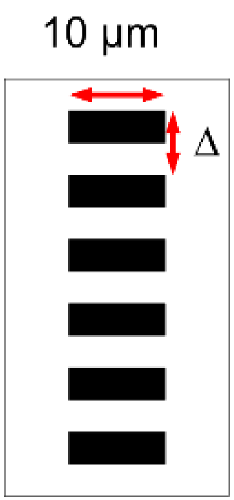
Compatibility with Variety of Imaging Systems

- The probe Can be Used with Any Optical Imaging System
  - Single/Multi Photon Imaging
  - Confocal Imaging
  - Optical Coherence Tomography



Imaging with Lens-guide

- Achieved the Resolution of 0.8 µm over the 60-100% Field of View with Minimal Distortion



Resolution Target

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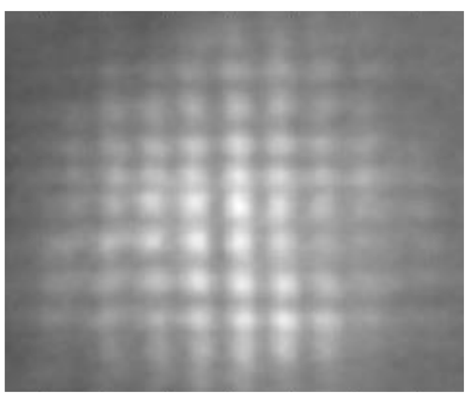


Minimal Distortion Across the Imaging Region

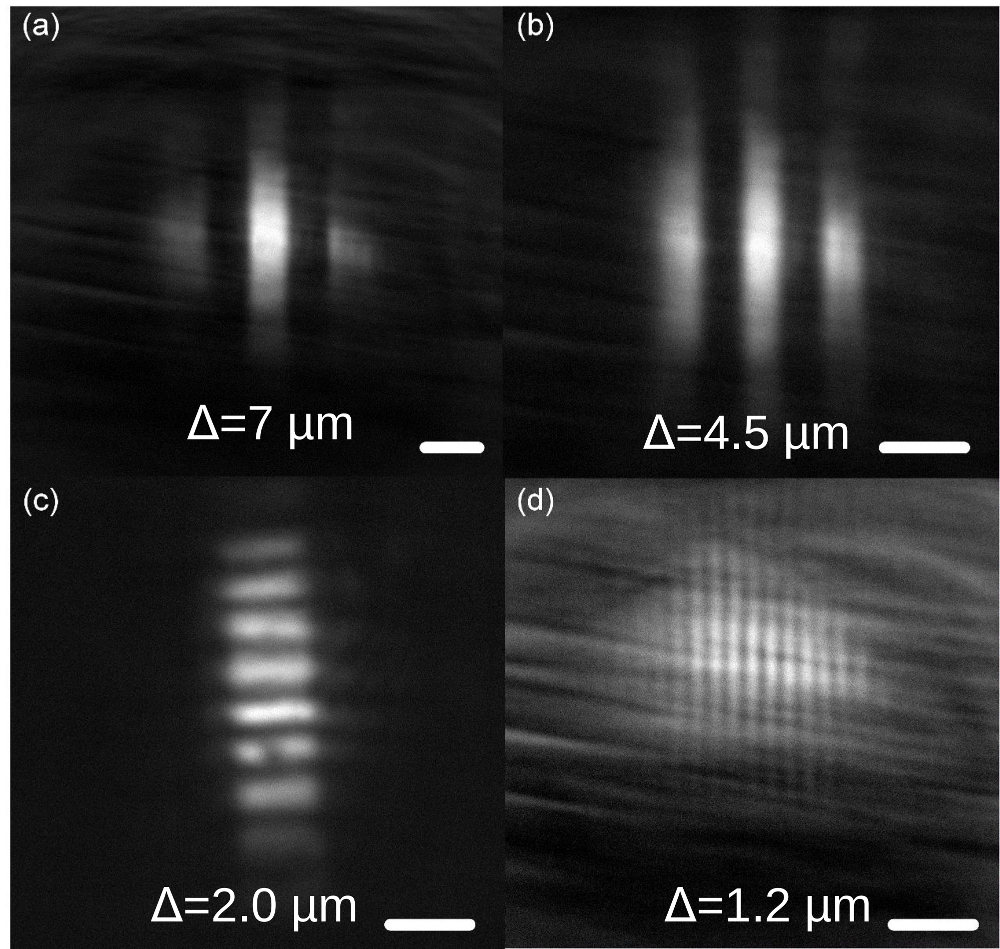
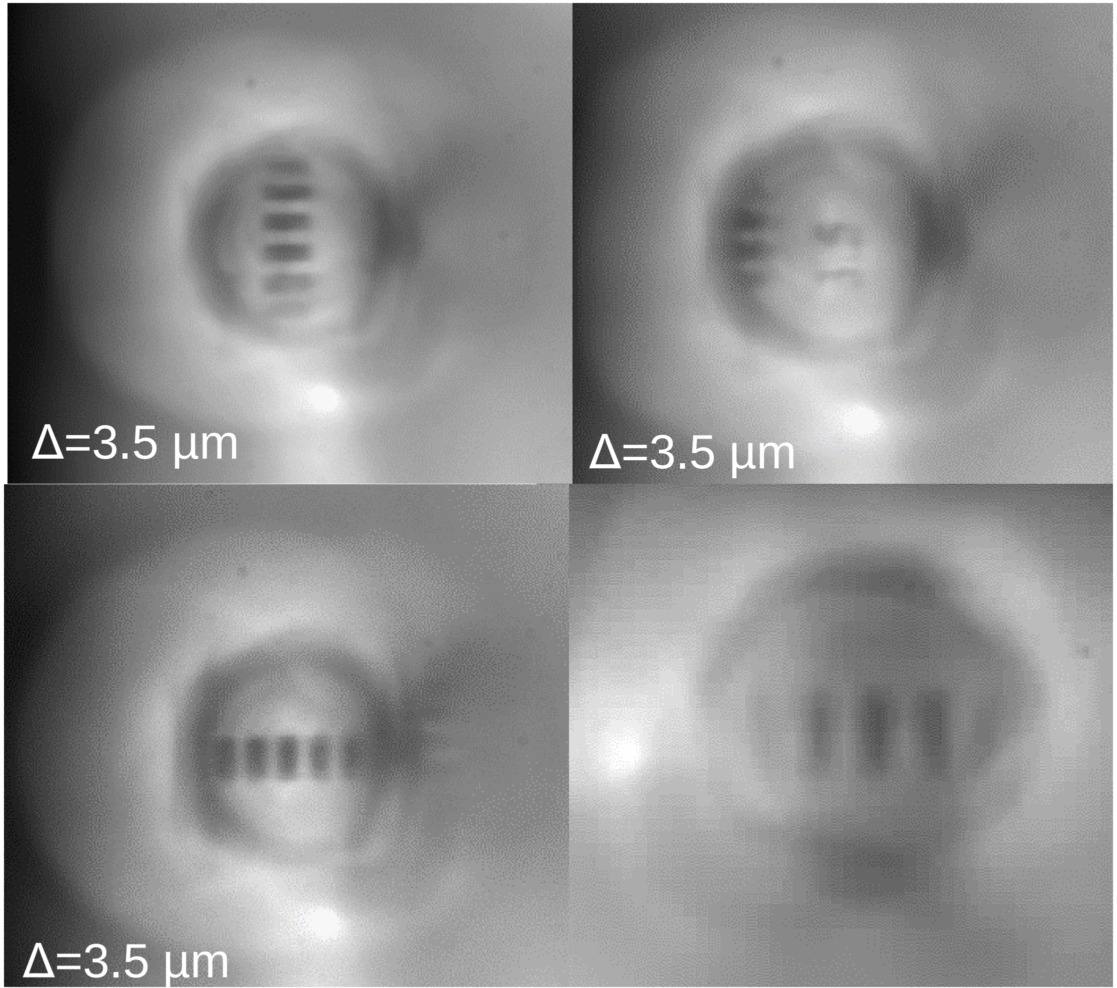


Image of the Imaging Target

- Illuminating Object from the Object Side or through the Probe



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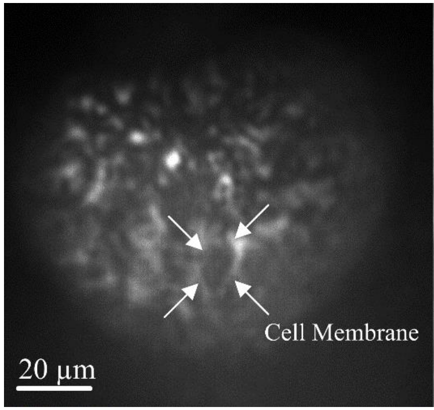
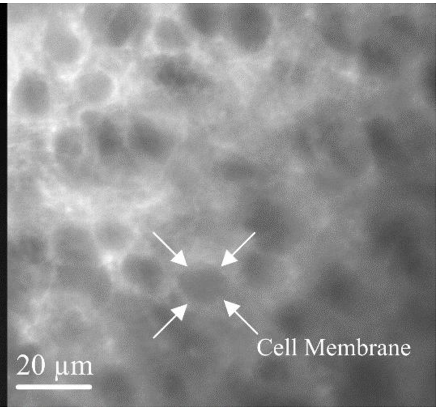
Brain Slice Image with the Probe

- Being able to resolve the cell membrane and different part of brain through our lens-guide probe
- Lens-guide has a Very High Efficiency to Image Tissue

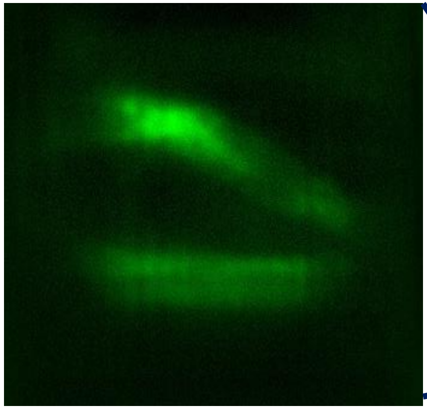
Sample Image of the Neurons with Probe



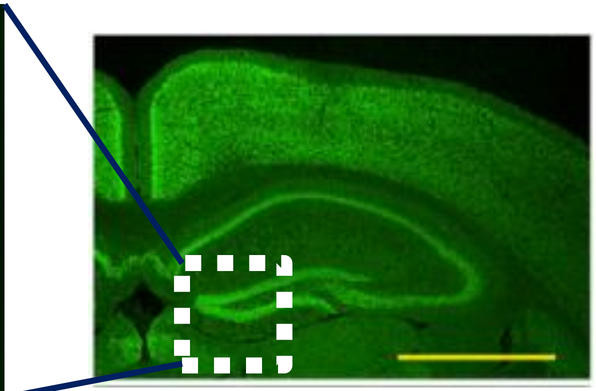
Sample Image of the Neurons with Microscope



Sample Image of the Brain Slice with the Probe



Confocal Microscopy Image of the Brain Slice



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Other Applications of the Lens-guide

- Augmented Reality
- Visual Inspection of the Mechanical Pieces
- Optical Interconnect
  - For Large Data Rate

Patents, Presentation and Publications on This Work

- **Patents:**
  - Lipson, M., Tadayon, M.A., Mohanty, A., Barbosa, F., “Integrated Micro-Lens Waveguide and Methods of Making and Using Same,” U.S. Patent No. 20,170,351,026. 7 Dec. 2017.
  - Tadayon, M.A., Lipson, M., “Microfabricated Multi-lens waveguides (lens-guide) Design, Fabrication and Application,” Patent Application.
- **Publications:**
  - Tadayon, M.A., Pavlova, I., Martyniuk, K.M., Mohanty, A., Roberts, S.P., Barbosa, F., Denny, C.A., Lipson, M. “Microphotonic Needle for Minimally Invasive Endoscopic Imaging with Sub-cellular Resolution,” Scientific Reports, Vol. 8 (2018), No. 1, 10756.
  - Tadayon, M.A., Chaitanya, S., Martyniuk, K.M., McGowan, J.C., Roberts, S.P., Denny, C.A., Lipson, M. “3D Photonic Lens-guide probe for High Resolution very Deep Tissue Optical Imaging,” Submitted.
- **Conference Presentations:**
  - Tadayon, M.A, …, Lipson, M., “Implantable lithographically defined photonic microprobe”, Photonics West. SPIE Photonics West, Jan. 29, 2018, San Francisco, CA, USA. (Oral Presentation)
  - Tadayon, M.A, ..., Lipson, M., “High resolution microphotonic needle for endocospic imaging”, Photonics West. SPIE Photonics West, Jan. 30, 2017, San Francisco, CA, USA. (Oral Presentation)
  - Tadayon, M.A., ..., & Lipson, M., “Integrated Nanophotonic Platform for High Bandwidth and High Resolution Optogenetic Excitation,” In CLEO: Applications and Technology (pp. ATu4O-4), June 7, 2016, Optical Society of America. (Invited Oral Presentation)

Key People

- Mohammad Amin Tadayon, PhD
  - Postdoctoral Fellowship at the Columbia and Cornell University, PhD University of Minnesota
  - More than 9 Years of Experience in the Area of Development of New Technology for Endoscopy Using Optics/Photonics and Micro/Nanofabrication
- Michal Lipson, PhD
  - Eugene Higgins Professor at the Columbia University, MacArthur Fellow
  - Pioneer in the Field of Silicon Photonics and Nanophotonics
  - Served as an Editorial Board, Advisory Board in Many Scientific Journals, Communities, and Organizations
  - Fellow Member of Institute of Electrical and Electronic Engineers (IEEE), and Optical Society of America (OSA)
- Kamyar Neshvadian, MSc, FRM
  - Medical Technology Entrepreneur, Team Leader, Finance and Trading Strategist
  - 15 years of Experience in Entrepreneurship, Leadership, Medical Technology Development, Capital Management, Trading and Finance.

Funding

- Use of the Fabrication Facility: $38,000/Year
- Design Software: $24,000
- Material: $15,000/Year
- Optical Set-up: $100,000
- Animal Study: $100,000/Year
- Personnel: $285,000/Year
- Total for 2 Years: $1,000,000