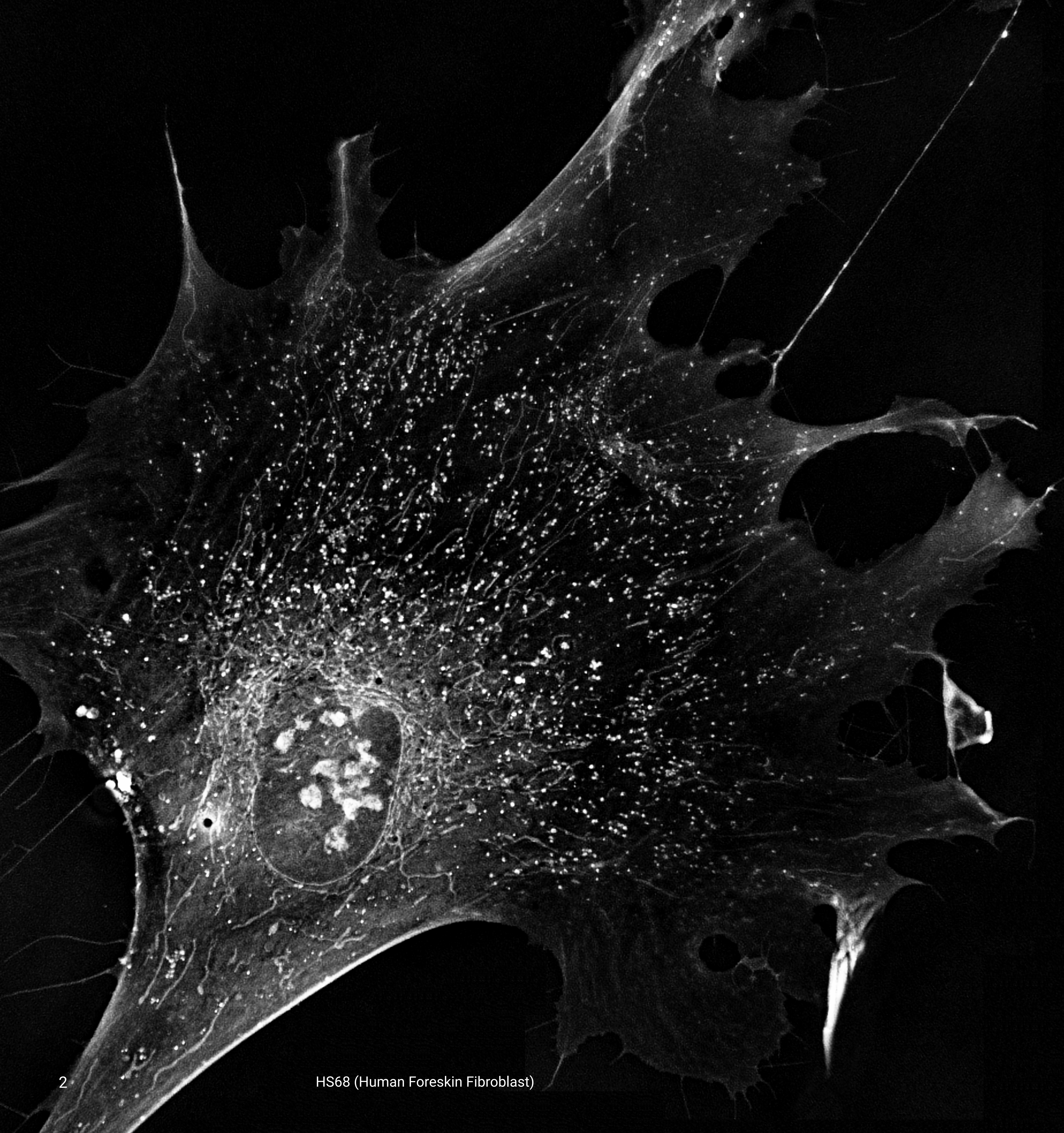
Tomocube

Holotomography:
New Insight Into Life Science



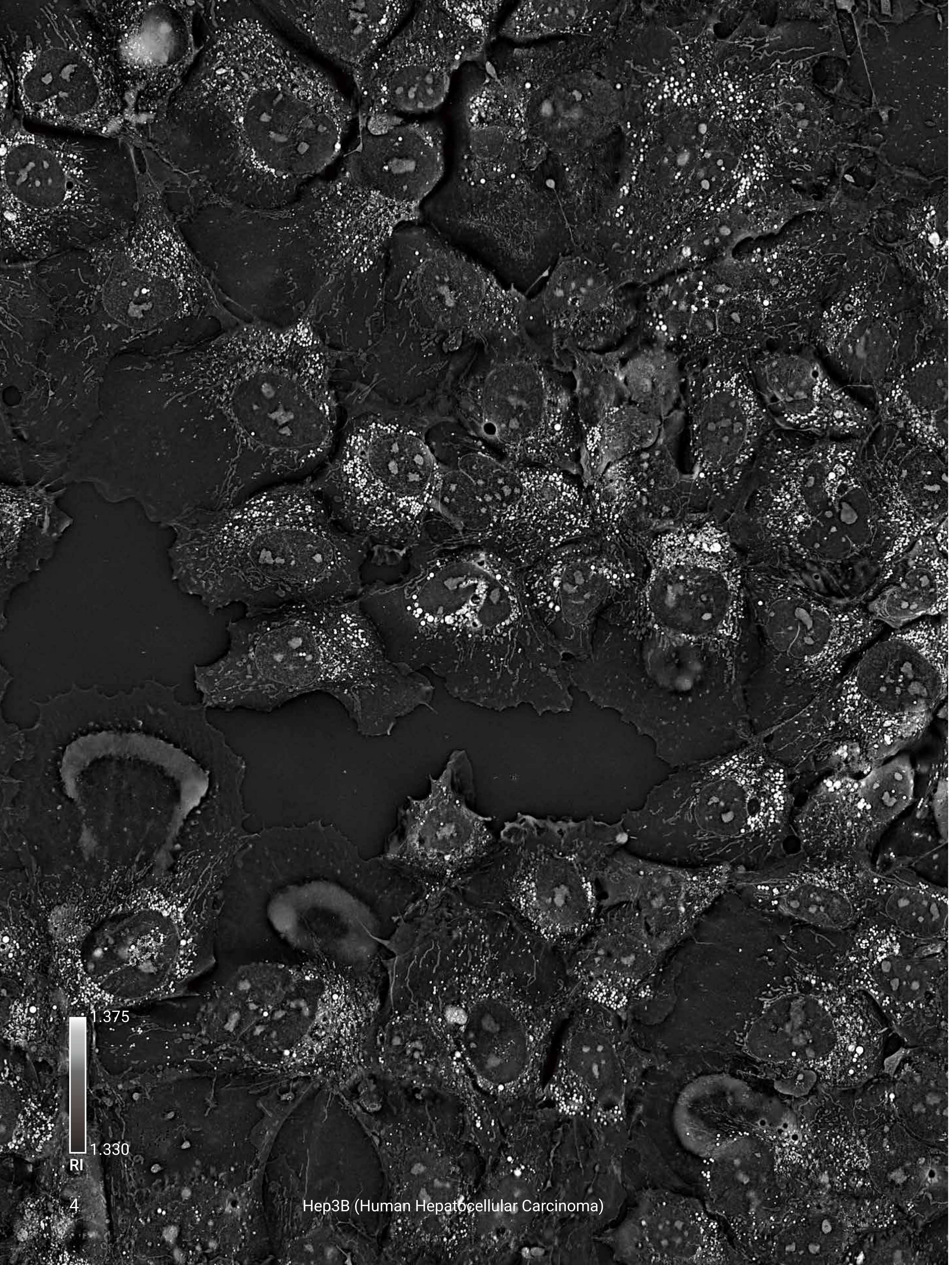
HS68 (Human Foreskin Fibroblast)

Next Generation 3D Imaging: Label-Free 3D Holotomography

Tomocube's leading-edge holotomography technology represents a groundbreaking advancement in microscopy, opening new frontiers across a wide range of research fields.

With holotomography, researchers can explore live cells in their natural state, observing real time dynamics and intricate 3D structures without the need for labeling or staining. This innovative technology is not just enhancing our understanding—it's driving new discoveries and reshaping the possibilities in biological research.

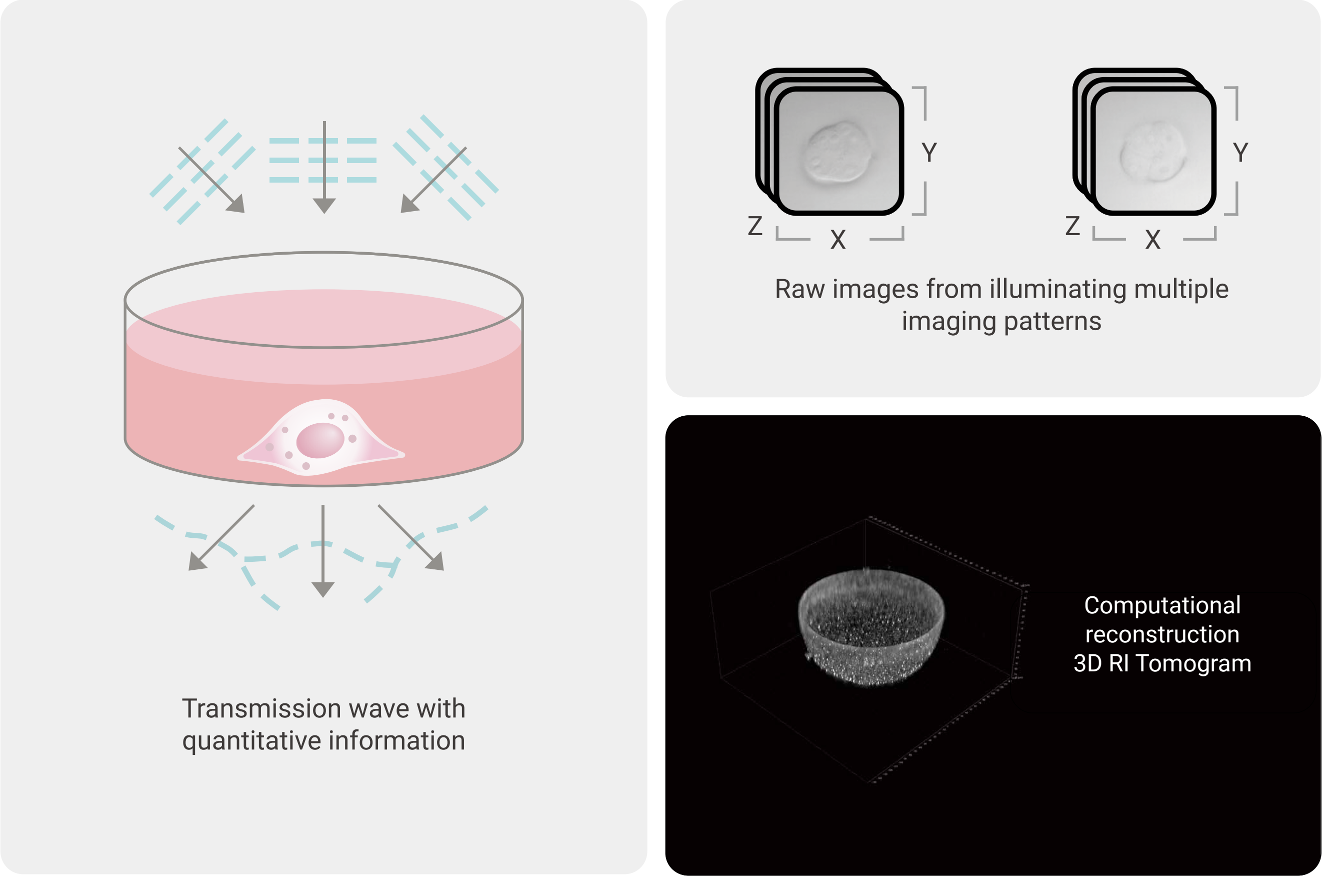
Experience the future of bioimaging. Discover new insights beyond your expectations.



Hep3B (Human Hepatocellular Carcinoma)

Holotomography captures the 3D refractive index distribution within cells.

Holotomography (HT) leverages refractive index (RI) as an intrinsic imaging contrast, transforming bioimaging with its label-free and quantitative capability. By reconstructing the 3D RI map of the sample, HT allows researchers to explore the intricate architecture of subcellular structures—such as nuclei, mitochondria, lipid droplets— in fine detail. This advanced technique supports long-term observation, without the need for potentially harmful stains or labels, a common requirement in other imaging methods. Additionally, HT can effectively integrate with fluorescence microscopy, enabling synergistic analyses that correlate fluorescence emission signals with reconstructed RI tomograms, offering both molecular and structural insights into cellular architecture.



Principle of holotomography

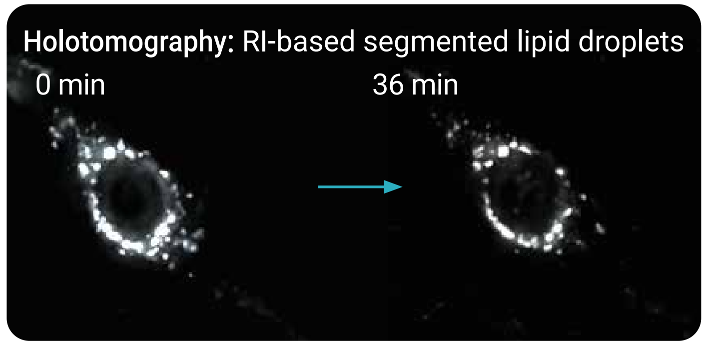
Holotomography combines the principles of holography and tomography to generate high resolution, 3D images of biological samples. When a beam of light illuminates a sample, its path scatters as it interacts with internal components of cells, which have different RI values. This scattering allows the capture of 2D images containing phase and amplitude information, which are then computationally reconstructed into detailed 3D representations. Since variations in the biomolecular concentration directly impact the overall RI of the cellular biomaterials, the reconstruction of RI tomograms by HT can retrieve important biophysical parameters such as cell volume, surface area, and protein concentration for further analysis.

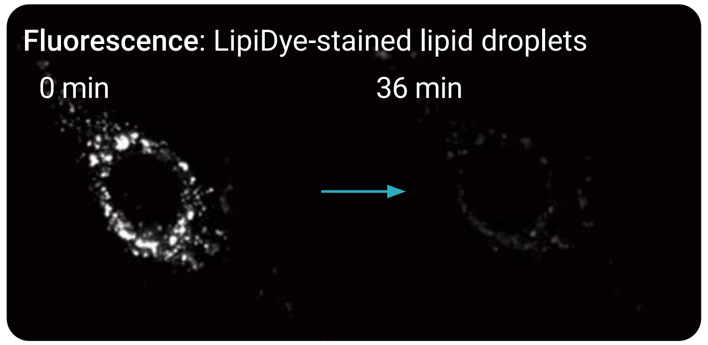
Holotomography provides key advantages that revolutionize bioimaging

High resolution imaging

- Achieve higher resolution up to 156 nm through synthetic aperture
- Distinguish diverse subcellular organelles, such as nuclei, nucleoli, mitochondria, and lipid droplets

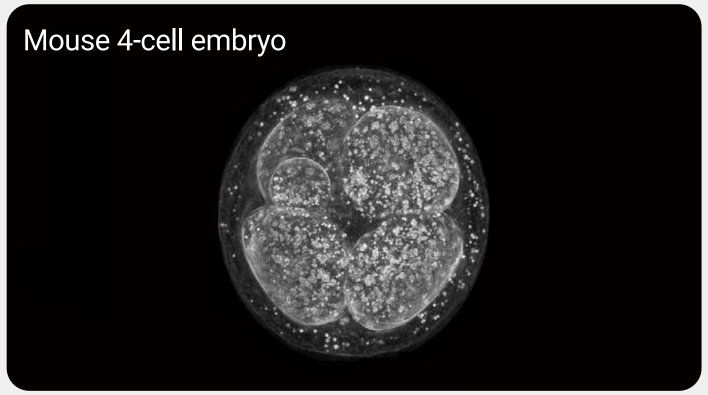
Hep3B (Human Hepatocellular Carcinoma)





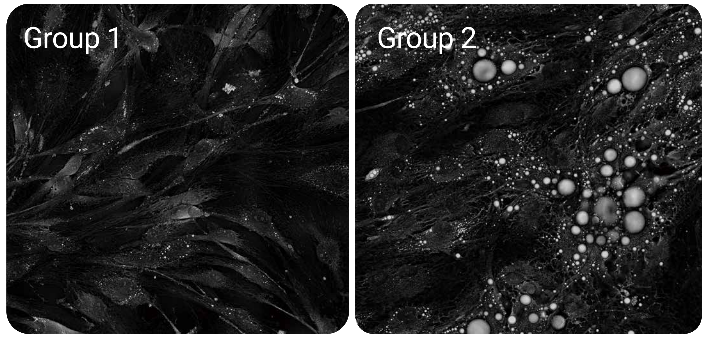
Label-free observation

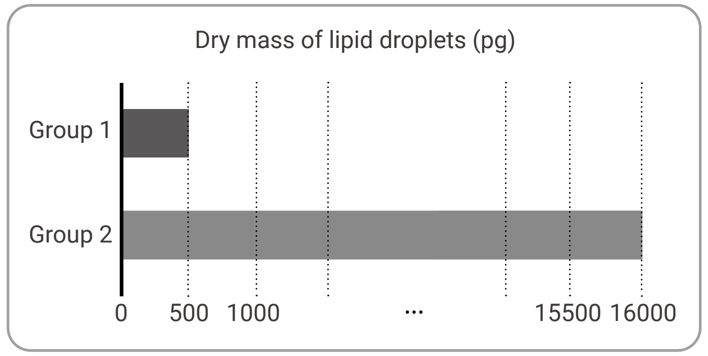
- Preserve the natural physiology of cells without the need for labeling, fixation, or sectioning.
- Minimize challenges in bioimaging such as phototoxicity and photobleaching.



3D visualization

- Utilize intracellular RI variations to clearly differentiate major subcellular structures.
- Provide detailed 3D visualization of cells and their organelles.





Quantitative analysis

- The RI value changes in direct relation to protein concentration, enabling the quantitative measurement of cellular parameters.
- Numerical variations due to imaging conditions are minimal, enabling reliable quantitative comparisons with groups.

Unveiling cellular complexity:
From individual organelles to 3D networks

Organelle

HT imaging preserves the intact morphology of live specimens, allowing for the non-invasive detection of key organelles like the nuclei, mitochondria, and lipid droplets. Label-free visualization of organelles avoids challenges in long-term observation such as photobleaching and phototoxicity. This ensures accurate and reliable analysis of organelle dynamics while preserving the natural state of the cells and their structures.

Cell

Tomocube HT offers an essential live cell imaging tool for cell biology research, providing direct, real time insights into cellular functions with remarkable clarity and precision. Holotomography's non-invasive approach allows for the study of various cellular processes, such as cell division, cell migration, cell-cell interactions, signaling pathways, and cellular responses to environmental changes, over extended periods.

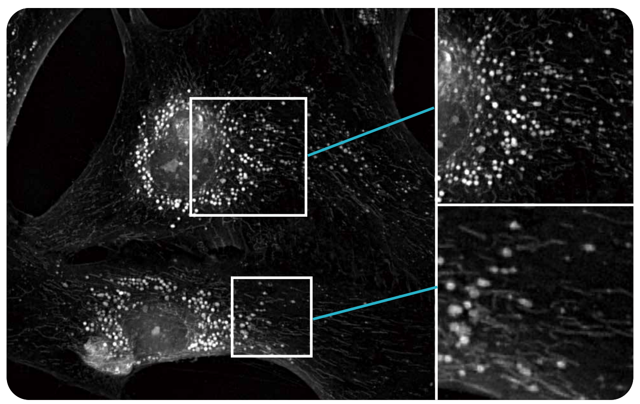
Organoid

The Tomocube 3D imaging system is well-suited for research involving 3D cell cultures such as spheroids, organoids, and organ-on-a-chip systems. It offers key advantages, including the ability to capture the complexity of 3D structures, enable non-invasive live observation of cellular dynamics within intact organoids, and provide quantitative measurement, making it ideal for high throughput applications like drug screening.

Tissue

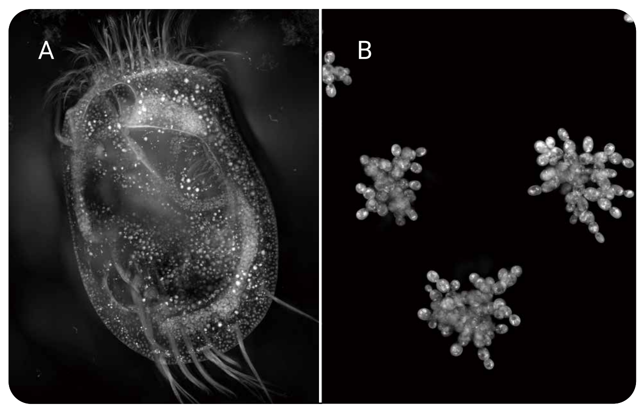
HT optimizes tissue research by providing deep structural insights from intact samples without the need for sectioning, fixation, or staining, which can compromise the morphological and physiological information. It also enables the seamless integration of these structural insights with histological data from H&E staining or immunohistochemistry, facilitating comprehensive morphological and molecular analysis.

"What we can observe?" Nanomaterial Organelles Single cell Co-culture Organoid Tissue



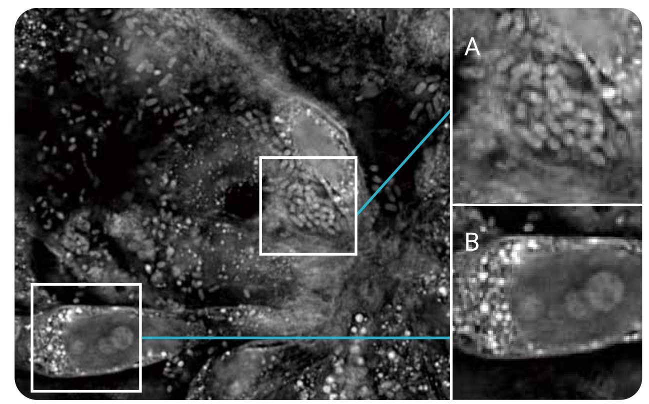
Lipid droplets & mitochondria

Mouse astrocyte
Courtesy: Dr. Jae-Hun Lee (Institute for Basic Science)



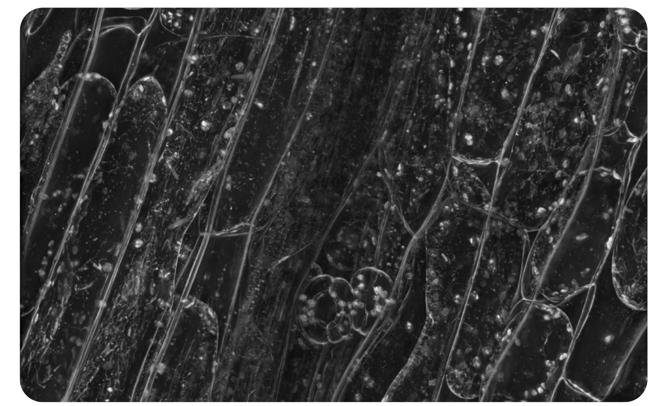
Microorganisms

(A) Euplotes (B) Snowflake yeast. Courtesy: Dr. Ben Larson (UCSF) and Prof. William Ratcliff (Georgia Tech)



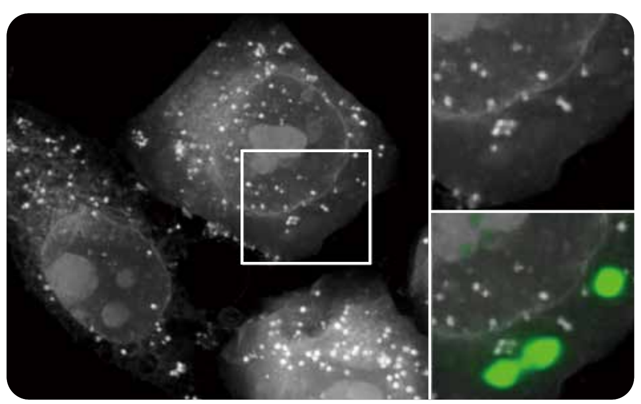
Gut organoid-microbe co-culture

(A) Bacteria living on gut chip (B) Nucleus Courtesy: Prof. CT Lim group (National University of Singapore)



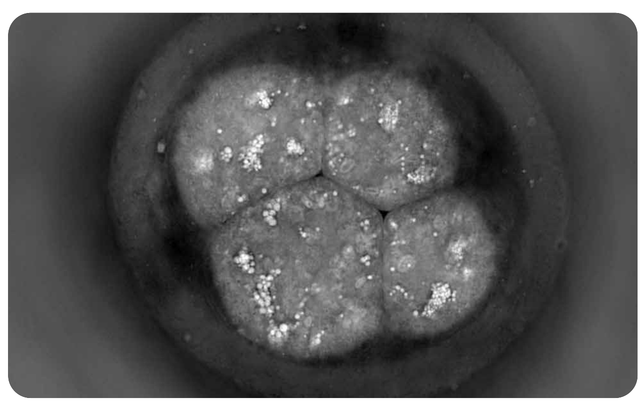
Plant

***Arabidopsis thaliana* stem tissue**
Courtesy: Dr. Haesoo Kim (Tomocube, inc.)



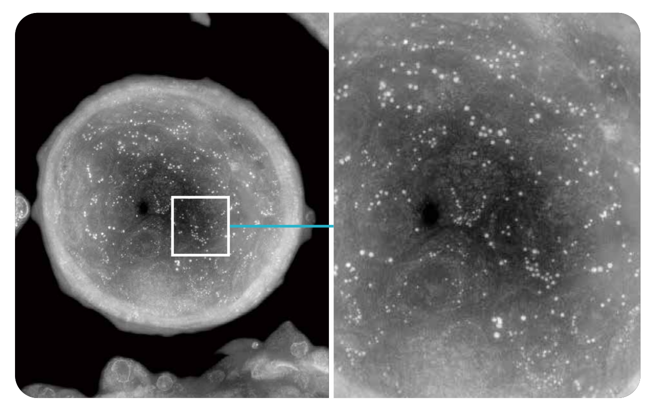
Stress granule

HeLa cells, stress granules-GFP
Courtesy: Dr. Pureum Jeon (Hannam University)



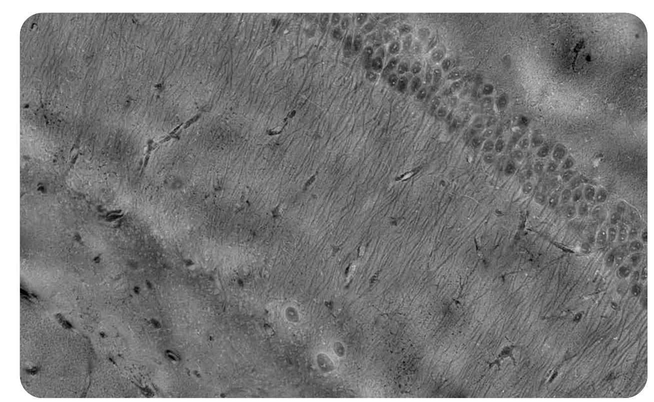
Embryo

Mouse embryo
Courtesy: Prof. Yojiro Yamanaka (McGill University)



Hepatic organoids

Patient-derived pancreatic organoid and high-RI contents (lysosome or lipid droplet) Courtesy: Prof. Hee Seung Lee (Yonsei University and Severance Hospital)



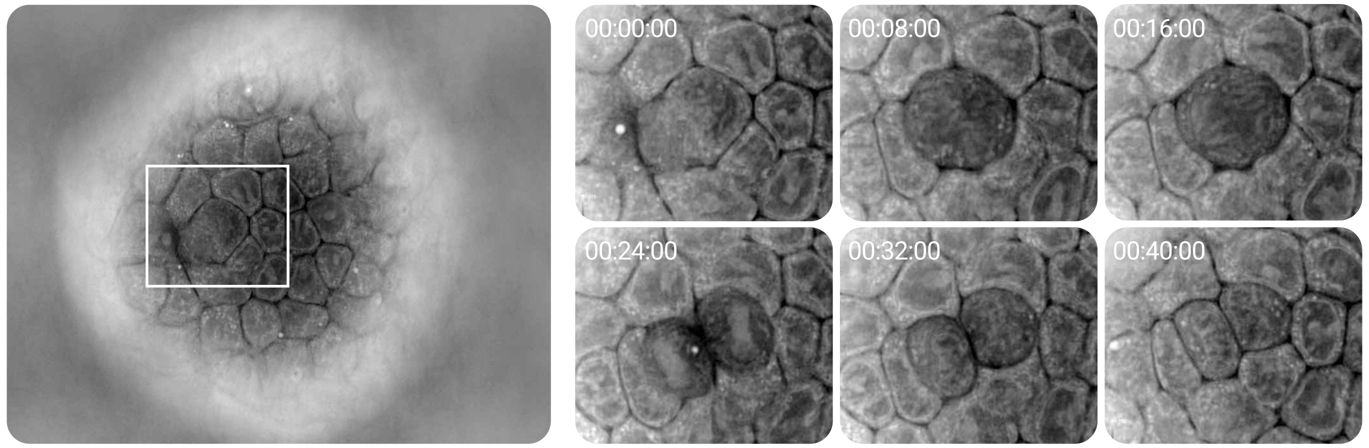
Brain tissue

Hippocampus
Courtesy: Dr. Jung Min Kyo (Korea Brain Research Institute)

Spatiotemporal tracking of cellular dynamics

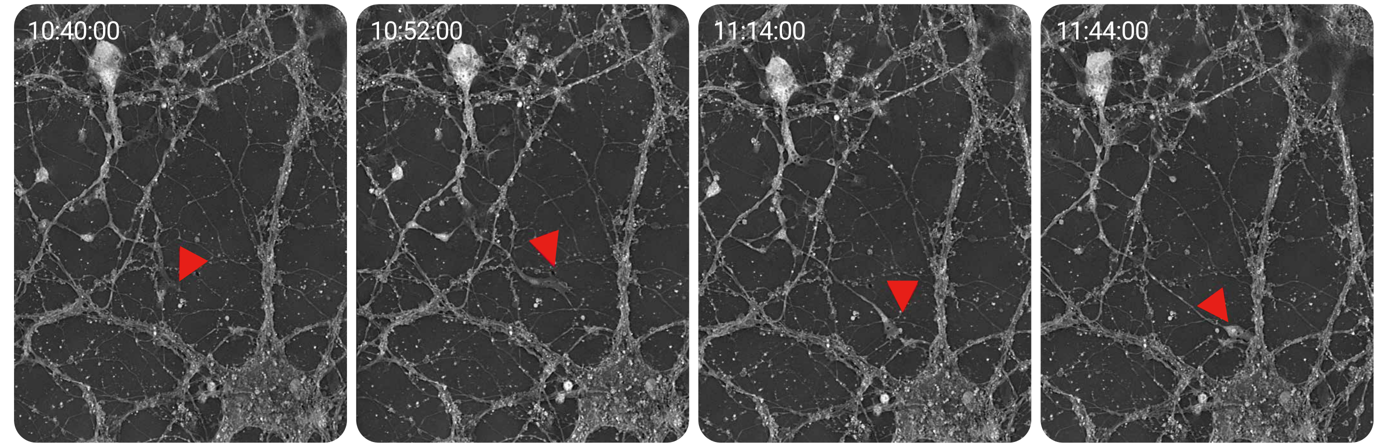
Mitosis in murine hepatic organoid

Time lapse imaging, 8-minute interval for 40 minutes



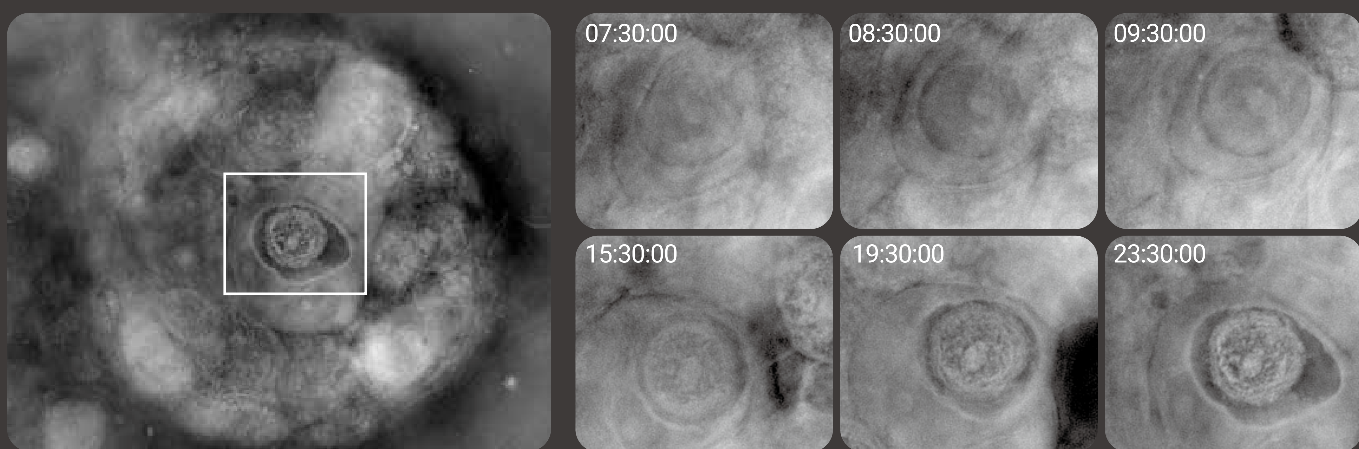
Rat primary cultured neuron

Time lapse imaging, 2-minute interval for 12 hours



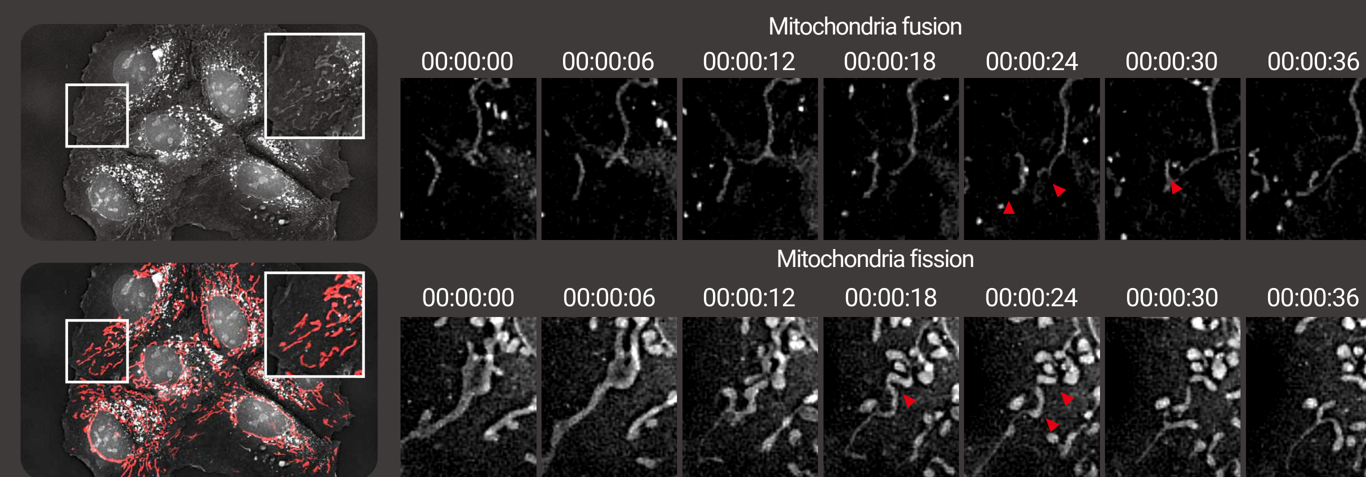
Cell-in-cell structure in human ovarian cancer organoid

Time lapse imaging, 30-minute interval for 24 hours | Courtesy: Prof. Sun-Young Kong (National Cancer Center Korea)



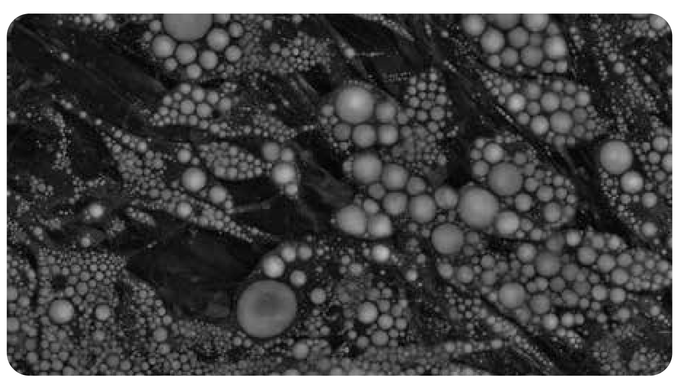
Mitochondria fusion and fission

Hep3B cells with Mito-DsRed, Time lapse imaging, 6-second interval for 2 hours



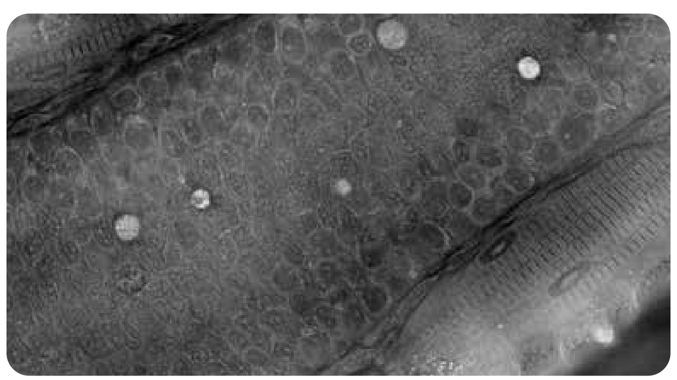
Re-differentiated human adipocyte

Courtesy: Eun Young Jeong (Chungnam National Univ. Hospital)



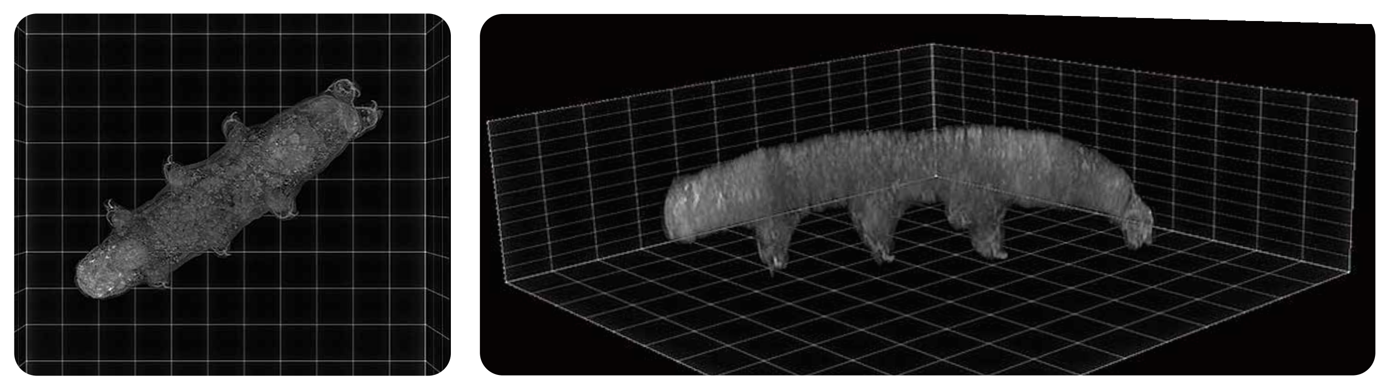
Zebrafish

Courtesy: Dr. Nicolas Dray (Institut Pasteur)



Tardigrade in live state

Courtesy: Dr. Ana Lyons (University of California, San Francisco)



HT-X1™

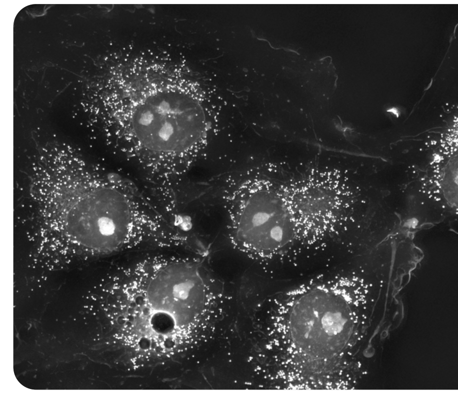
Pioneering advanced holotomography for superior imaging quality in research.

The HT-X1™ is the first model in Tomocube's second-generation HT series, meticulously engineered for advanced life science research. This innovative platform utilizes low-coherence LED light to push the boundaries of holotomography, make it possible to achieve label-free 3D live cell imaging on standard imaging plates. With its noise-free, high resolution imaging capability and unparalleled stability, the system offers researchers an unprecedented view into the dynamics of living cells.

The HT-X1™ brings new advancements by:

- Enabling high quality imaging of intact samples
- Reducing the need for system calibration and simplifying operation
- Ensuring consistent imaging quality in various environmental conditions
- Allowing flexibility with standard labware for imaging

Key features of HT-X1™

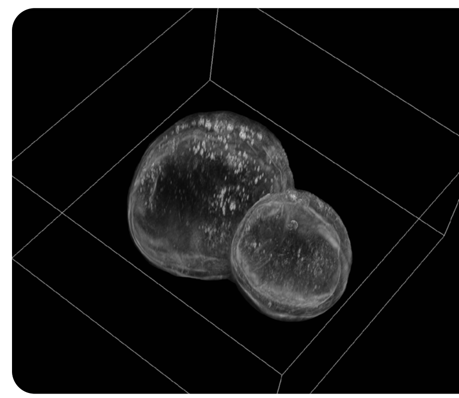


High resolution, high contrast

An LED illumination module integrated with a Digital Micro-mirror Device (DMD) achieves resolution beyond the diffraction limit, delivering higher synthetic numerical aperture and an improved signal-to-noise (SNR) ratio.

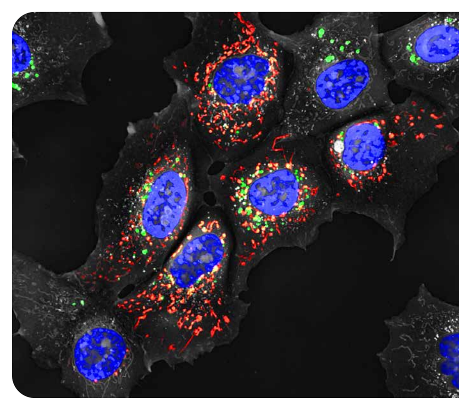
Multi-well plate compatibility

Designed to maximize user flexibility, the system employs an adaptive illumination module tailored for multi-well plates. It accommodates a wide variety of vessel types, from 35-mm dishes to 96-well plates.



140-µm depth scanning

The system is capable of imaging diverse biological specimens from bacteria to small organoids and tissue sections, with easy time lapse setup for live cell imaging and automatic stitching for wide area scans.

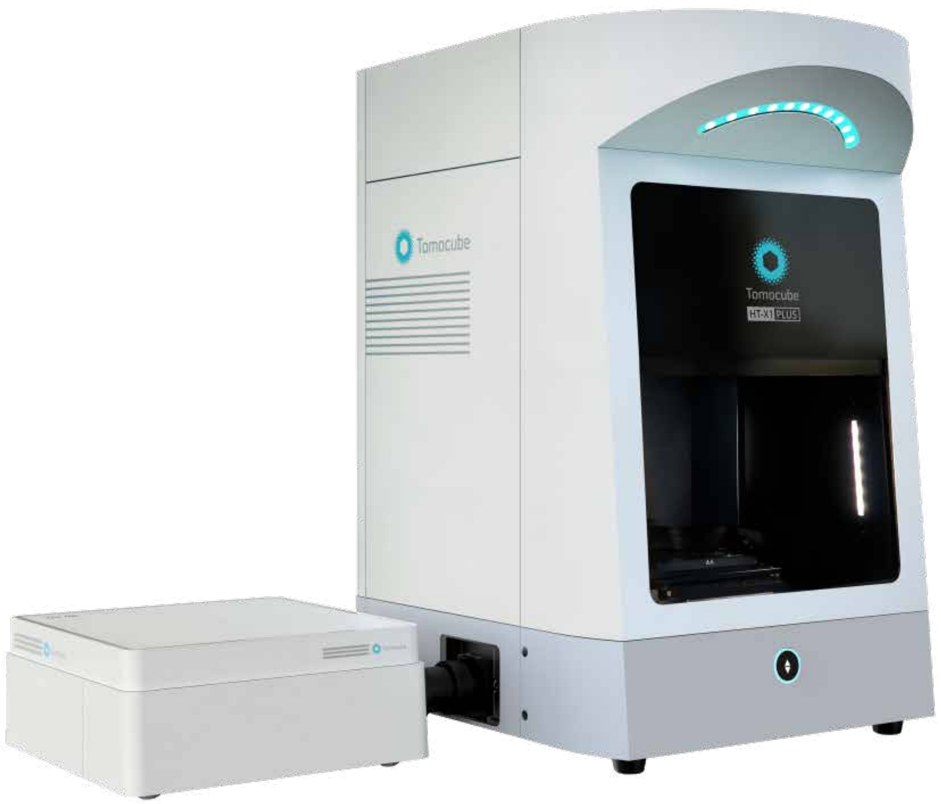


Correlative imaging with fluorescence

The combination of holotomography and fluorescence imaging enables synergistic analyses, correlating fluorescence emission signals with RI tomograms to obtain both structural and molecular insights into cells.

HT-X1™ Plus

Setting new standards in 3D imaging throughput for biomedical screening.

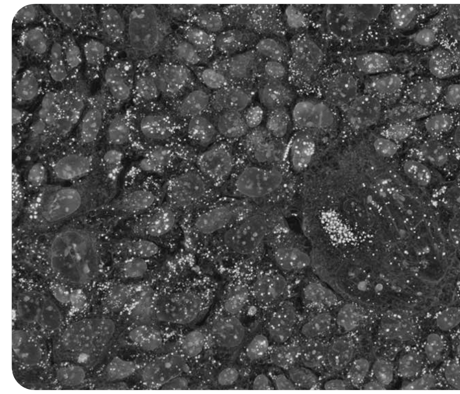


Tomocube continues to drive innovation with the HT-X1™ Plus, an advanced holotomography imaging platform built to meet the ever-growing demands of biomedical research. Building on the success of the HT-X1™, this model features significant upgrades and enhancements, delivering outstanding performance and precision across a wider range of applications. The HT-X1™ Plus system is designed to empower researchers and shape the future of biological and biomedical discovery.

With its high-end specifications, the HT-X1™ Plus is the ideal choice for researchers seeking:

- Fast, high throughput 3D image-based screening
- Clear and detailed internal analysis of intact organoids and thick tissue sections
- Enhanced sensitivity and precision in comparative analysis of fluorescence and holotomography
- Deeper insights into tissue studies with wide preview scan mode, seamlessly paired with correlative color brightfield imaging

Key features of HT-X1™ Plus

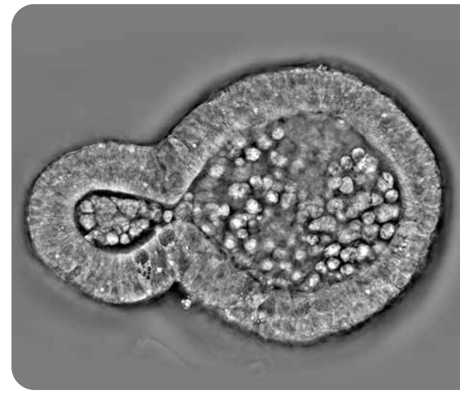


High resolution + high content screening

Expand your scanning area with a 4× larger field-of-view. Equipped with a high-performance CXP camera, the system offers rapid image acquisition, capturing a 3D image in under a second.

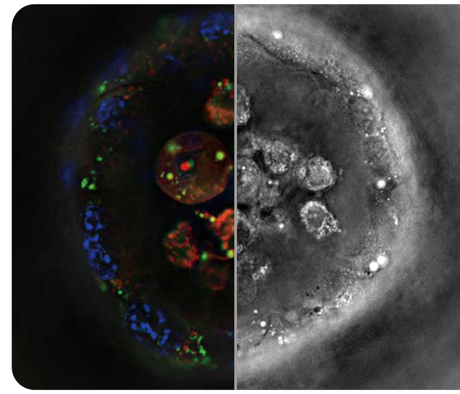
Multi-well plate + wide field scan

A dedicated low-resolution scan camera enables wide-area preview, making it easy to detect large samples, such as organoids or tissue microarrays, within a broad imaging field, ensuring efficient sample identification and analysis.



Depth scanning + multiple wavelengths

Three wavelength options let you tailor your HT imaging for optimal contrast or light penetration depth. This adaptability enables the imaging of various sample types while minimizing interference from absorption spectra.

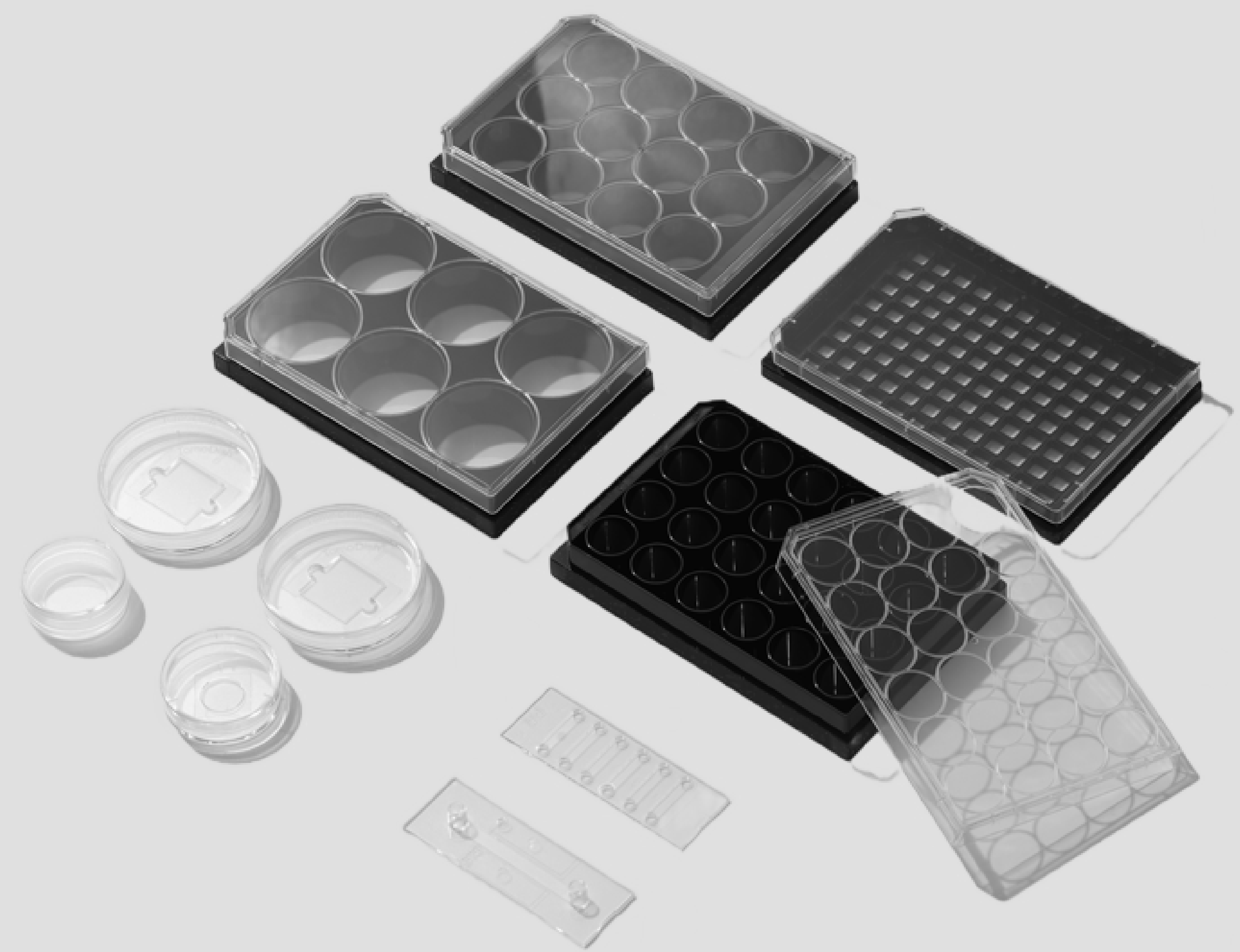


Correlative imaging + higher sensitivity

The sCMOS-equipped correlative fluorescence (FLX™) module provides high sensitivity, enabling shorter exposure times for obtaining biomolecular specificity information while significantly reducing phototoxicity.

Accessories

Optimizing high-performance holotomography imaging with flexibility.



Expand the capabilities of the HT-X1™ and HT-X1™ Plus with a range of adaptable accessories, designed to fit seamlessly into your workflow and meet the diverse demands of research.

- Optimize your holotomography imaging with a variety of cell culture dishes from 35-mm to 60-mm, as well as 6, 12, 24-well plates, and HT-Ready™ 96-well plate.
- Expand your research areas by using custom-designed vessels with #1.5H bottom thickness, such as organ-on-chips or microfluidic devices, enabling new and innovative applications.

TomoDish™

Support both adherent and suspension cells, providing optimal culture and imaging conditions for HT imaging. It is also compatible with other imaging techniques, ideal for diverse applications such as live and fixed cell imaging, long-term time lapse, immunofluorescence staining, and transfection assays.

Specifications

Diameter	50 mm
Observation area	20 × 20 mm
Glass thickness	#1.5 H (170 ± 5 μm)
Working volume	3 mL
Surface treatment	Uncoated

HT-Ready™ 96 well plate

Offer a stable cell culture environment and optimized compatibility with various imaging techniques, including HT-X1™ Holotomography, confocal, and fluorescence microscopes. Its solvent-resistant bottom coverslip ensures flatness and zero autofluorescence, providing clear imaging in high content analysis.

Specifications

Dimension	127.8 (W) × 85.5 (D) × 17.2 (H) mm
Well dimension	7.4 × 7.4 × 4.2 mm
Cell culture area	0.56 cm²
Bottom thickness	#1.5 polymer (170 μm)
Working volume	150 - 220 μL
Surface treatment	Tissue culture treated, Uncoated

Vessel holder

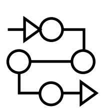
Users can select from a versatile range of vessel holders, precisely designed for specific labware. These holders offer flexibility to meet your research needs with various experimental setups, including mounting up to six dishes.

Specifications

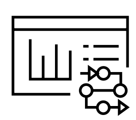
Ordering information	www.tomocube.com/products/accessories/vh

TomoAnalysis™

Workflow highlights

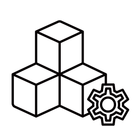


- **Pipeline wizard**: Create a customized analysis pipeline by combining modules, which are sets of processors designed for various image analyses.



- **Analysis project:** Apply pipelines to your data, obtain quantitative results, and perform batch analysis on hundreds of datasets using the same parameters.

- **Viewer**: Visualize segmented masks as high resolution 3D images, verify analysis results, and utilize image capture and time lapse recording features.



- **Data manager:** Trim specific XYZ or time dimensions, along with selected modalities and channels from your image files to enhance the usability during analyses.

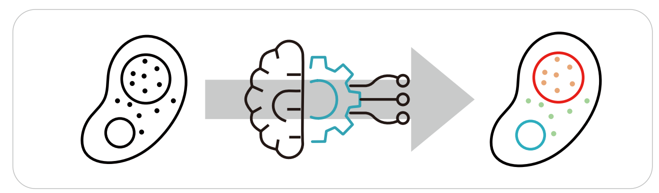
Advanced analysis and visualization software tailored for holotomography

Tomocube's TomoAnalysis™ offers advanced visualization and analysis tools for cells. Leveraging RI-based thresholding and AI-driven segmentation, the software enables precise analysis across diverse applications. TomoAnalysis™ supports flexible, customizable pipelines for comprehensive data analysis, including measurement and quantification of subcellular organelles such as lipid droplets or mitochondria. Discover how TomoAnalysis™ can accelerate your research, providing actionable insights that drive scientific innovation and discovery.

Key features of TomoAnalysis™

AI-driven structure segmentation

TomoAnalysis offers customized HT analysis by fine tuning open-source AI models.



Fine tuning StarDist, Cellpose, and ilastik for cell and subcellular structure segmentation.

Refractive index-based thresholding

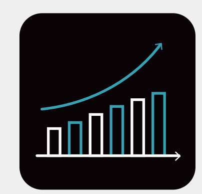
Segmenting structures of interest from the background using the RI value thresholding method.

RI-based thresholding is used for cell, lipid droplet, bacterium, and organoid segmentation.

Manual mask correction

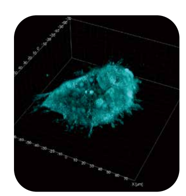
Mask Editor, equipped with drawing and label editing tools, allows users to fine tune the masks generated by their analysis pipelines.

Morphological and quantitative analysis



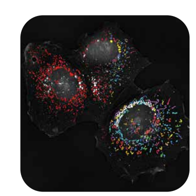
AI models and RI-based analyses provide biophysical metrics, such as volume, area, length, dry mass, and concentration, in segmented objects.

3D visualization



The immersive 3D visualization feature offers a more comprehensive structural interpretation.

Fluorescence-integrated analysis

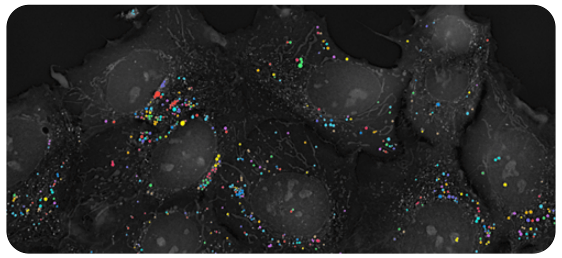


Broadens HT analysis with integrated 3D fluorescence data, enhancing its application scope.

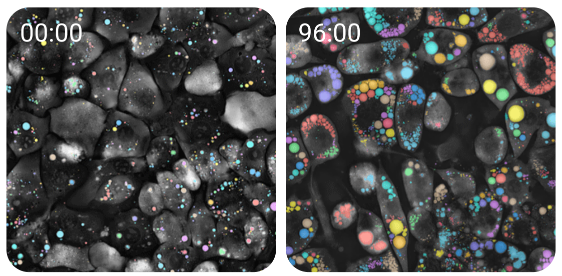
Applications

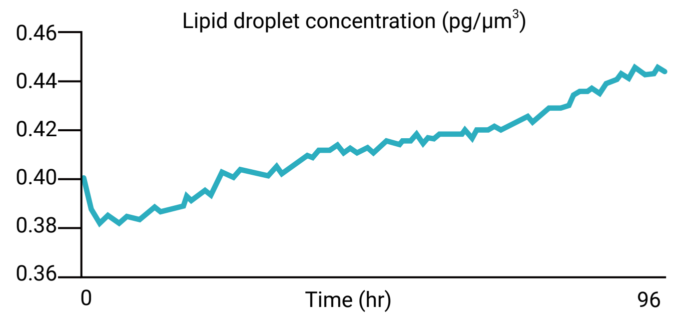
Lipid droplet quantification

- Measure changes in lipid droplet numbers over time.
- Evaluate variations in droplet volume and concentration during differentiation.



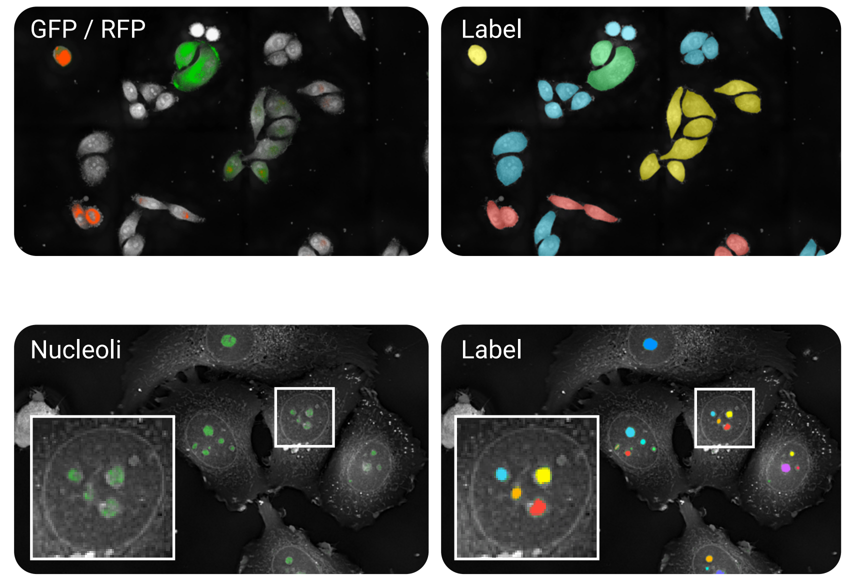
	Mean (N=845)
Refractive index	1.3686
Volume (μm^3)	0.52
Dry mass (pg)	0.1215
Concentration ($pg/\mu m^3$)	0.234

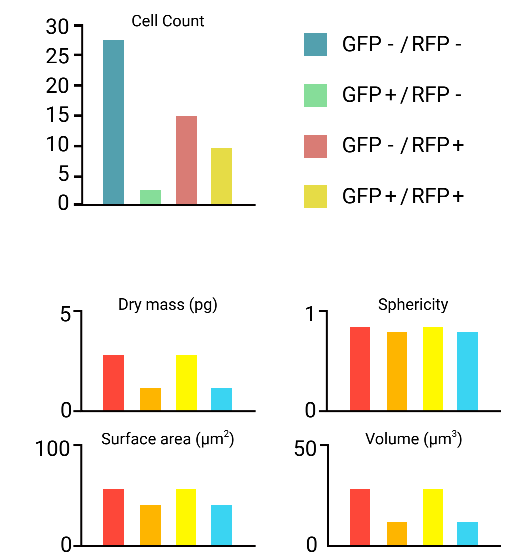




Fluorescence-assisted cell counting and quantification

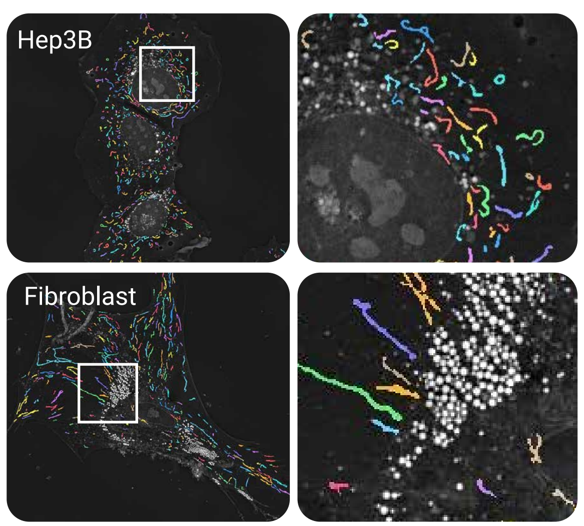
- Track changes in cell counts over time by identifying fluorescence-positive and fluorescence-negative cells.
- Label protein levels and conduct quantitative analysis of HT images using the fluorescence signals.

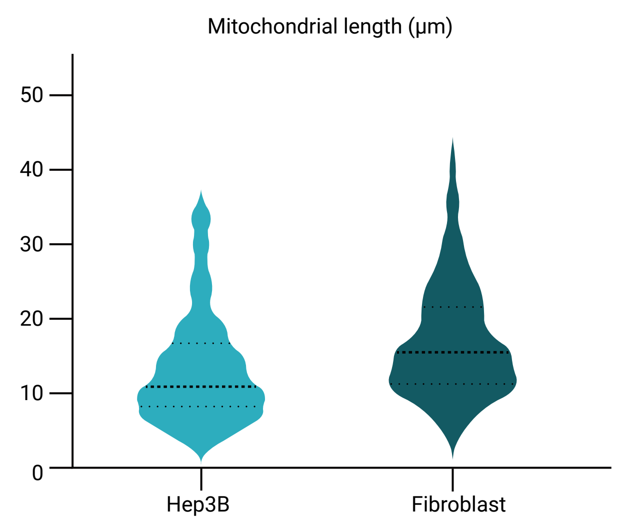




Mitochondria size analysis

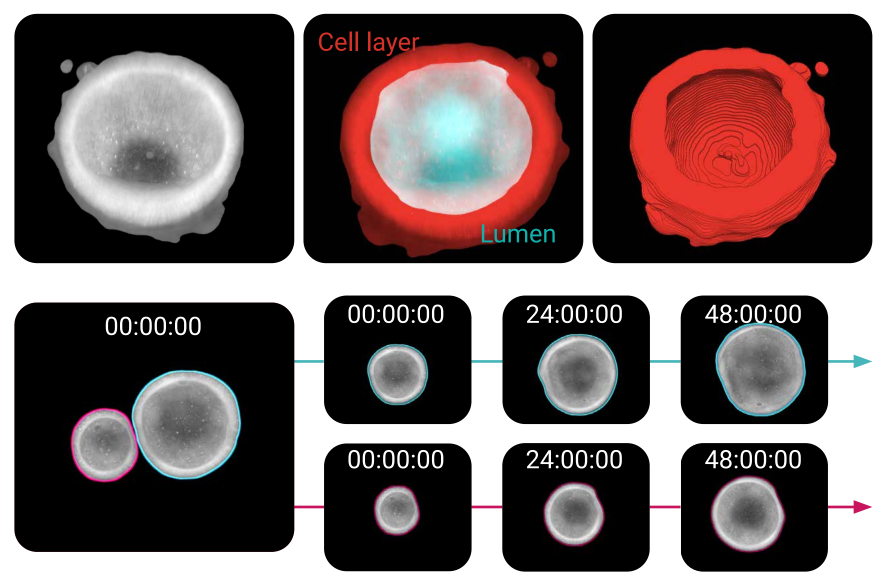
- Quantify mitochondrial length and volume using AI-based segmentation tailored to specific cell lines.
- Assess mitochondrial fission and fusion in response to drug treatments.



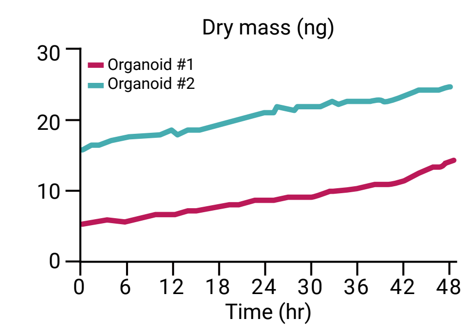


Organoid growth and morphology assessment

- Automatically segment organoids to track their growth over time.
- Quantitatively analyze the organoid lumen and cell layers to assess structural changes and cell distribution.



Mean RI	1.3418
Surface Area (mm^2)	84.8616
Volume (mm^3)	505.2924
Dry mass (ng)	16.1350
Concentration ($pg/\mu m^3$)	0.032



Specifications

HT-X1™

HT-X1™ Plus

HT-X1™ Holotomography System

Dimensions	565 (W) × 732 (D) × 921 (H) mm
Weight	90 kg
Power supply	100-240 VAC, 50/60 Hz, 5-3A
Imaging area	100 mm × 60 mm
Objective lens	40× NA 0.95 air
Objective working distance	180 μm
Condenser lens	NA 0.72
Image sensor	2.8 Megapixels CMOS
Field-of-view	218 μm × 165 μm
Auto focus	Laser-assisted active sensor
Imaging modalities	Holotomography, Brightfield (Grayscale), Fluorescence
Supported labware	Dish/Plate/Slide with #1.5 bottom thickness
Wide preview image sensor	Not available

HT-X1™ Holotomography Optics

Light source	LED
Illumination wavelength	444 nm
Axial scan range	60 - 140 μm
Lateral resolution	156 - 205 nm
Axial resolution	803 - 839 nm
Minimum acquisition speed	3.5 sec per image

Fluorescence Light Engine for HT-X1™

Light source	LEDs
Excitation filters	378/52, 474/27, 554/23, 635/18 (nm)
Emission filters	432/36, 515/30, 595/31, 698/70 (nm)
Fluorescence light source trigger	3 channels

Workstation for HT-X1™

Operating system	Windows 10 IoT
CPU	Intel Core i7 or equivalent
GPU	NVIDIA GeForce RTX 4090 or equivalent
RAM	128 GB
Screen	QHD (2560 × 1440)

Environmental Controller (HT-X1™ & HT-X1™ Plus)

Dimensions	151 (W) × 263 (D) × 196 (H) mm
Weight	3.8 kg
Power supply	100-240 VAC, 50/60 Hz
Temperature control	30 - 40°C
CO_2 range	5 - 20%
Humidity control	Heating bath humidifier

HT-X1™ Plus Holotomography System

Dimensions	565 (W) × 732 (D) × 921 (H) mm
Weight	95 kg
Power supply	100-240 VAC, 50/60 Hz, 5-3A
Imaging area	100 mm × 60 mm
Objective lens	40× NA 0.95 air
Objective working distance	180 μm
Condenser lens	NA 0.72
Image sensor	20 Megapixels CMOS, CXP-12
Field-of-view	308 μm × 308 μm
Auto focus	Laser-assisted active sensor
Imaging modalities	Holotomography, Brightfield (Color), Fluorescence
Supported labware	Dish/Plate/Slide with #1.5 bottom thickness
Wide preview image sensor	Color CMOS

HT-X1™ Plus Holotomography Optics

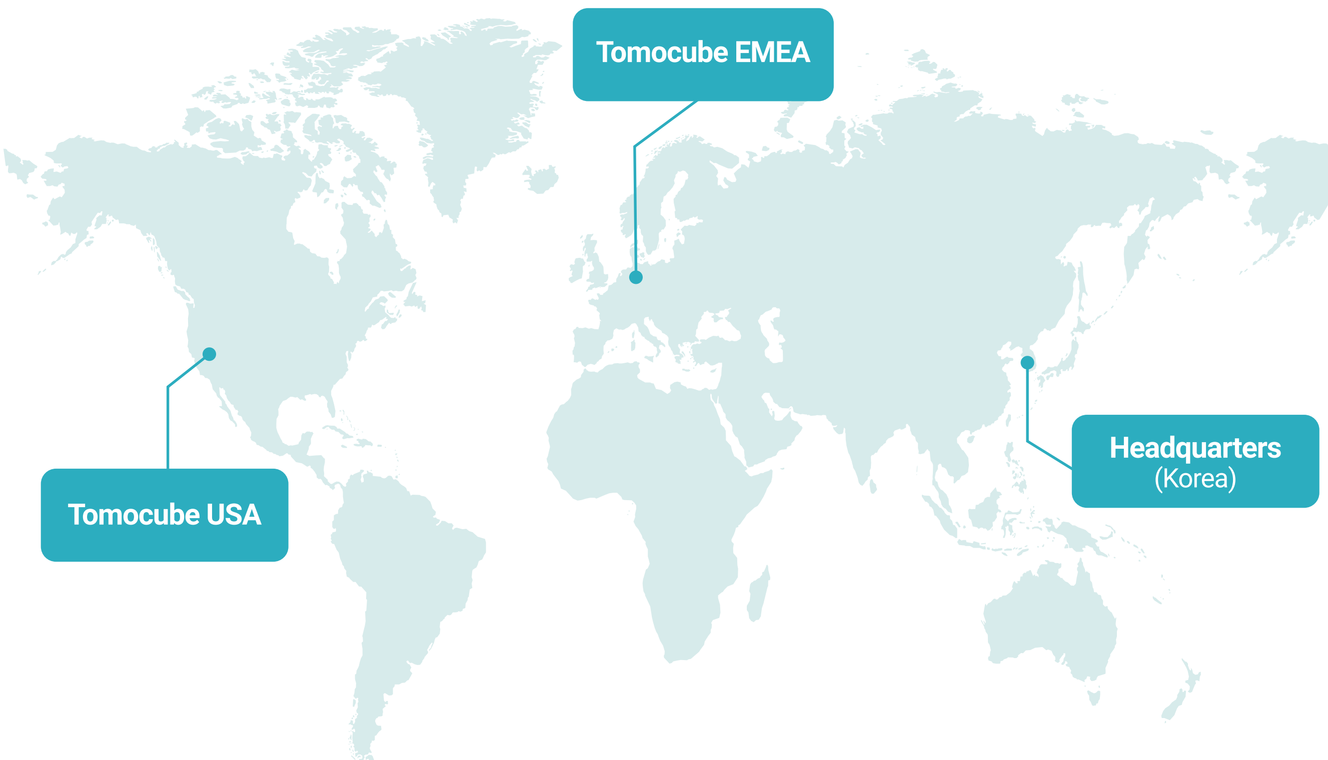
Light source	LEDs
Illumination wavelength	444, 520, 660 nm
Axial scan range	30 - 140 μm
Lateral resolution	156 - 332 nm
Axial resolution	803 - 1106 nm
Minimum acquisition speed	0.5 sec per image

Workstation for HT-X1™ Plus

Operating system	Windows 10 IoT
CPU	Intel Xeon w5-3425 or equivalent
GPU	NVIDIA GeForce 6000 Ada or equivalent
RAM	128 GB
Screen	QHD (2560 × 1440)

Fluorescence Module X for HT-X1™ Plus

Dimensions	434 (W) x 409 (D) x 174 (H) mm
Weight	25 kg
Light source	LEDs
Excitation filters	378/52, 474/27, 554/23, 635/18 (nm)
Emission filters	432/36, 515/30, 595/31, 698/70 (nm)
Filter exchange time	100 ms
Fluorescence image sensor	sCMOS
Quantum efficiency	95% (wavelength: 580 nm)
Fluorescence light source trigger	3 channels



Tomocube

Established in 2015, Tomocube is dedicated to advancing biological and medical research with its state-of-the-art optical technologies. Inspired by our philosophy, “Innovate the way we see life”, we continuously push the boundaries of 3D imaging, contributing to groundbreaking discoveries that redefine what’s possible in scientific research. Our relentless commitment to innovation not only transforms scientific methods but also enables scientists to understand the complexities of life. Through our pioneering imaging solutions, we are setting new benchmarks in scientific excellence and outcomes across the world.

Headquarters
4th Floor, 155, Sinseong-ro, Yuseong-gu, Daejeon 34109, Republic of Korea
Tel +82-42-863-1100 | info@tomocube.com | www.tomocube.com

Tomocube USA, Inc.
8880 Rio San Diego Dr, Suite #800, San Diego, CA, 92108

www.tomocube.com