

# Oral Presentations

## *Parallel 1: Brain Engineering & Neuromodulation Technologies*

### Bioinspired Nanoscale Intra and Extracellular Optoelectronic Biointerface

**Hemi Rotenberg**

*BME, Technion, Israel*

Bioelectrical signaling plays a key role in cellular communication, function, differentiation, and regeneration across diverse cellular contexts. However, the bioelectronic toolkit available for studying these phenomena does not meet the required level of complexity.

Although high-resolution biomodulation capabilities are continually improving, most available methodologies are substrate-bound and therefore cannot be applied to cells in 3D. We have recently shown that porosity-based heterojunctions offer enhanced optoelectronic performance and enable the leadless electrical modulation of hearts and nerves, but with limited spatial resolution. On the other hand, p-i-n silicon nanowires (SiNWs) can achieve intracellular sub-micron resolution, but with low optical performance.

Thus, we present porosity-based SiNWs as an optoelectronic probe with enhanced optoelectronic modulation capabilities and superior spatial resolution. This new SiNW has the potential to open the way for fundamental basic research applications in which high spatial resolution is required. We demonstrated its performance using dermal fibroblast, and its utility in myelinating cells, i.e., oligodendrocytes (OLs).

This can be used as a tool to study how electrical activity affects myelination, a process highly relevant to the progression and recovery from demyelinating diseases such as multiple sclerosis. Moreover, they can be integrated with extracellular “artificial axons” which can add the “neuronal dependent” OLs activity to investigate intra- and extracellular electrical signaling that governs myelination.

# Development of a Magneto-Conductive Implant for Neural Regeneration and Modulation in Peripheral Nerve Injuries

**Ariella Nouman, Dekel Rosenfeld**

*Bio-Medical Engineering, Tel Aviv University, Israel*

Injury to the peripheral or central nervous system often results in lasting functional deficits, as adult neurons display limited intrinsic regenerative capacity and current clinical strategies lack effective methods to restore long-range connectivity.

The formation, maturation, and long-term stability of functional neuronal networks are critically influenced by the physical and biochemical properties of their surrounding microenvironment. In this project, we aim to engineer a hybrid hydrogel scaffold that simultaneously promotes axonal growth and enhances neuronal network formation by integrating two synergistic modalities: electrical conductivity and localized neuronal stimulation with high temporal and spatial resolution.

Previous studies have demonstrated that magnetothermal stimulation can activate heat-sensitive TRPV1 ion channels, triggering calcium influx and downstream signalling cascades associated with neurite outgrowth and cytoskeletal remodelling. Building on this evidence, we hypothesized that combining magnetothermal activation with an electrically conductive matrix would create a more permissive environment for neuronal growth and communication.

This platform offers a promising route toward advanced neural scaffolds with integrated, wireless stimulation capabilities, enabling potential applications in nerve repair and regeneration, controlled neuromodulation and more.

## Breaking Barriers with Bubbles: Ultrasound Nanotechnology for Brain Therapy and Molecular Diagnostics

**Tali Ilovitsh**

*Tel Aviv University, Israel*

Focused ultrasound is emerging as a powerful noninvasive technology capable of interacting with the brain through the temporary and localized opening of the blood-brain barrier (BBB). When combined with acoustically active contrast agents, ultrasound can enable targeted delivery of therapeutics. In this talk, I will present our recent advances in ultrasound-mediated BBB opening for brain cancer applications, with a focus on the delivery of lipid nanoparticles (LNPs), the clinically established platform behind many RNA therapeutics.

By optimizing focused ultrasound and bubble-mediated BBB opening, we demonstrated targeted delivery of siRNA- and mRNA-loaded LNPs into healthy and glioblastoma-bearing mouse brains, achieving substantial increases in payload accumulation within the tumor and surrounding brain tissue. Building on this platform, we are developing next-generation nanoscale ultrasound agents designed to improve both therapeutic delivery and molecular monitoring of BBB opening. In particular, I will present our recent work using nanobubbles for enhanced BBB opening and sonobiopsy, a liquid biopsy approach in which ultrasound-mediated BBB modulation enables the release of brain-derived biomarkers into the bloodstream for noninvasive brain molecular analysis.

Together, these technologies position focused ultrasound as a programmable and noninvasive platform for overcoming biological barriers in the brain, with future potential for targeted drug delivery, molecular diagnostics, and personalized treatment of neurological diseases and brain tumors.

## Fabrication of a Magnetic Implant for Treating Nerve Injuries

**Gal Shklarski Shchori<sup>1</sup>**, Dekel Rosenfeld<sup>1,2,3</sup>

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Magnetic nanoparticles (MNPs) have emerged as a promising tool for advancing biomedical applications. They serve as magnetic transducers for activating cell signaling under external magnetic fields.

MNPs in the 20–30 nm size range efficiently dissipate heat under alternating magnetic fields (AMF), enabling magnetothermal activation of heat-sensitive receptors that regulate electrogenic cell signaling. Effective magnetothermal stimulation must maintain cell viability and optimally deliver targeted heat to the cellular microenvironment. Therefore, improved in vitro models, particularly three-dimensional (3D) cultures that better mimic the cell microenvironment, are needed to assess magnetothermal stimulation before transitioning to in-vivo demonstrations.

This study developed a tunable magnetic collagen gel to support magnetothermal stimulation while allowing control over heat dissipation and mechanical properties by adjusting MNP concentration inside the gel.

Cells embedded within the stimuli-responsive magnetic gel exhibited proliferation and cytoskeletal organization, suggesting its suitability as a biological implant. These findings advance the design of magnetothermal stimulation systems and pave new avenues for bioelectronic medicine, including the integration of magnetic implants in cell therapies.

We have preliminary results supporting the integration of neuronal cells within the collagen implant. Future applications with this magnetic implant will focus on accelerating axonal growth for regenerative approaches in peripheral nerve injuries.

# Electrotherapeutic Modulation of Cerebral Vasospasm: A Novel Approach Enabled by Neoflow Technologies

**David Skorohod**

*N/A, Israel*

Cerebral vasospasm remains a major clinical challenge following subarachnoid hemorrhage and other neurovascular injuries, often leading to delayed cerebral ischemia and long-term neurological deficits. Current therapeutic strategies, including pharmacologic vasodilators, endovascular interventions, and hemodynamic augmentation, offer limited efficacy and carry significant risks.

Neoflow Technologies introduces an emerging electrotherapy-based modality designed to minimally invasively modulate vascular tone and restore physiological perfusion through targeted electrical stimulation.

This study presents the engineering principles, preclinical evaluation, and translational potential of Neoflow's electrotherapeutic platform for vasospasm treatment. The system delivers controlled electrical fields optimized to influence smooth muscle cell polarization and calcium-dependent contractility. Computational modeling demonstrates that specific stimulation waveforms can attenuate vasoconstrictive signaling pathways while preserving endothelial integrity. In vitro experiments using isolated arterial segments show a reproducible reduction in vessel tone following stimulation, with effects comparable to standard vasodilatory agents but without pharmacologic side effects.

Preclinical in vivo testing in a vasospasm animal model indicates improved vessel diameter, enhanced regional cerebral blood flow, and favorable safety profiles. Notably, the electrotherapy approach enables localized, tunable intervention that can be applied repeatedly without cumulative toxicity.

These findings support electrotherapy as a promising alternative or adjunct to existing vasospasm treatments. By leveraging biophysical modulation rather than pharmacologic or mechanical disruption, Neoflow's technology offers a pathway toward safer, more precise management of cerebrovascular dysfunction. Ongoing work includes optimization of stimulation protocols, expanded preclinical validation, and preparation for early-phase clinical trials.

# Sleep-Guided Closed-Loop Deep Brain Stimulation for Disease-Modifying Neuromodulation in Parkinson's Disease

Samer Abboud<sup>1</sup>, George Tummer<sup>1</sup>, Hagai Bergman<sup>2</sup>, Peretz Lavie<sup>3</sup>, Zion Zibly<sup>4</sup>

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<sup>4</sup>*Yale School of Medicine, USA*

**Background/Aim:** Parkinson's disease is a progressive neurodegenerative disorder. Current deep brain stimulation (DBS) therapies provide significant symptomatic benefit, mainly for motor symptoms, but do not directly address disease progression or key non-motor manifestations such as sleep disruption and cognitive decline. Pulsetech Medical aims to develop a sleep-guided closed-loop DBS platform that leverages sleep-related brain physiology to target mechanisms associated with neurodegeneration and potentially slow disease progression.

**Method:** The proposed system combines implanted DBS hardware with sensing and adaptive stimulation capabilities. During sleep, neural signals are analyzed to identify sleep stages, abnormal brain rhythms, and disease-relevant electrophysiological patterns. Based on this real-time analysis, stimulation is delivered in a closed-loop manner to modulate targeted brain activity. The development program includes sleep-classification algorithm development, stimulation-pattern optimization, validation using available human and pre-clinical neural datasets, and planned proof-of-concept testing in relevant pre-clinical models.

**Results:** Pulsetech has established the core technological and scientific concept, assembled a multidisciplinary advisory team with expertise in DBS, sleep neuroscience, neurosurgery, and neurodegeneration, and initiated pre-clinical development activities. Initial work focuses on validating the feasibility of detecting sleep-related brain states and defining stimulation strategies intended to normalize pathological neural activity during sleep. The company is advancing toward proof-of-concept studies designed to evaluate both electrophysiological and biological outcomes.

**Conclusion:** Sleep-guided closed-loop DBS may represent a novel neuromodulation paradigm that expands DBS beyond symptomatic control toward disease-modifying intervention. If validated, Pulsetech's approach could address a major unmet need in Parkinson's disease by combining established implantable neuromodulation infrastructure with adaptive, sleep-phase-specific therapeutic stimulation.

## *Parallel 2: Bio Convergence from Lab to Market*

Medical Bioconvergence in Israel

**Shai Melcer**

*Israel Innovation Authority, Israel*

Bioconvergence is transforming health-tech through the deep integration of biology, engineering, and computation.

Israel's bioconvergence ecosystem applies technologies such as AI-driven diagnostics, bioelectronic therapies, advanced medical devices, organ- and tissue-engineering platforms, digital-biological twins, and lab-on-chip systems - to clinical challenges. The Israeli approach spans multidisciplinary research, shared infrastructure, talent development, regulatory innovation, and industry partnerships to shorten the path from discovery to bedside.

Through selected national initiatives and case studies, the talk illustrates how coordinated ecosystem design can accelerate the translation of complex bioconvergent technologies into scalable, clinically validated solutions.

# Nanopore-AI: Combining Biology, Electronics and Machine Learning to Solve Emerging Biomedical Challenges

**Amit Meller**

*Faculty of Biomedical Engineering, Technion, Israel*

Nanopores are single-molecule biosensors that exploit electrokinetic forces to capture, linearize, and detect individual biopolymers, including DNA and proteins. In this lecture, I will present our recent advances in three areas: (i) laser-based sculpturing of embedded ultrathin metal-oxide solid-state nanopores (ssNPs) in sub-3 nm membranes<sup>1</sup>; (ii) full-length protein fingerprinting based on time-resolved electrical signatures acquired during the linearized translocation of proteins through sub-5 nm ssNP<sup>2</sup>; and (iii) amplification-free classification of cell-free DNA (cfDNA) from colorectal cancer patients using 3 nm ssNPs combined with advanced machine learning (ML) model<sup>3,4</sup>.

Across these applications, time-resolved ML approaches that leverage the enhanced temporal bandwidth of the nanopore platform, together with minimal sample preparation, enable label-free classification of clinically relevant biomarkers with high sensitivity and accuracy.

The electrokinetic forces governing transport through ssNPs, including electrophoretic and electroosmotic contributions, are investigated theoretically using molecular dynamics (MD) simulations and finite-element modeling, and are further integrated with electro-optical measurements to elucidate the underlying sensing physics.

Collectively, these results establish high-bandwidth nanopore sensing, coupled with time-resolved ML, as a promising point-of-care framework for direct DNAs and proteins profiling. This approach provides a scalable route to resolve endogenous molecular heterogeneity that is inaccessible to conventional methods and highlights its potential for molecular stratification in liquid biopsy applications.

## Intraoperative Sensor and Alerting System for Phacoemulsification

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<sup>3</sup>*Electric and Electronics Engineering, Holon Institute of Engineering, Israel*

**Purpose:** To describe the development of an intraoperative sensor and alerting system for phacoemulsification.

**Methods:** A sound-insulated MEMS-based microphone connected to a touchscreen tablet-based console was designed and manufactured. Phacoemulsification was performed near it using Alcon Infinity platform and employing different power modulations and amplitudes.

**Results:** The sensor could consistently identify ultrasound signals emanating from the phaco machine and provide alerts for setting thresholds relevant to continuous phaco time, and total cumulative phaco time.

**Conclusion:** The presented sensor and alerting system can possibly increase safety of phacoemulsification and decrease postoperative corneal edema.

## Lab to Market in Bioconvergence

**Yaakov Diminsky**

*Deep Tech Venture Builder, Israel*

Bioconvergence — the integration of biology, engineering, AI and data science, advanced materials, electronics, and manufacturing — is one of Israel's designated national strategic priorities and among the most fertile grounds for the next wave of deep technology innovation. Yet despite the abundance of world-class research, the path from bioconvergence discovery to a fundable, scalable company remains poorly navigated. Bioconvergence startups face a uniquely multi-dimensional risk profile — simultaneous scientific, engineering, product, and market uncertainty — that demands a fundamentally different venture-building approach.

At the earliest stages — from idea to seed — bioconvergence ventures face a risk profile fundamentally different from conventional startups. The dominant challenge is team risk: founding teams must simultaneously master multiple scientific disciplines — biology, engineering, AI, and materials science — alongside the commercial, regulatory, and operational competencies required to build a company. This rare combination is exceptionally difficult to assemble at the pre-seed stage. Beyond team risk, ventures face two compounding structural barriers: first, scientific risk — whether the underlying biological and physical principles will actually hold at the required scale and precision; and second, engineering risk — the long development timelines and heavy CapEx burden of building stable, specialized systems long before any revenue or product-market fit is in sight. Regulatory and market risks, while real, remain secondary at this stage.

In this lecture, drawing on experience working with over 90 startups in recent years — the majority operating in complex technology domains — I will argue that the most effective way to manage the unique risks of bioconvergence ventures — and to build companies with genuine market potential — is to continuously refine the fit between three elements: a significant unmet problem, a customer who needs it solved, and the simplest possible solution that addresses it. Achieving this fit early — before significant capital is deployed — enables the critical risk reduction that the field requires. Bioconvergence startups that undergo a rigorous pre-seed de-risking process can ultimately become less risky investment propositions than conventional technology startups — precisely because the market and competitive challenges that conventional startups face late in their development are not characteristic of bioconvergence ventures.

Israel holds an exceptional bioconvergence research infrastructure. The transition from this infrastructure to potent, sustainable companies requires a shift in the way we incubate ventures — earlier, more focused, and driven by customer pain rather than technology push. This lecture offers a framework for making that shift — and for positioning Israel's bioconvergence ecosystem to convert its scientific depth into the next generation of fundable, impactful companies.

### *Parallel 3: Biomechanics and Human Performance*

#### Comparative Finite Element Evaluation of a Hybrid Total Wrist Arthroplasty Design: Biomechanical Analysis of Load Transfer and Stress Distribution

**Moshe Brand**<sup>1</sup>, Amir Arami<sup>2</sup>, Tzvi Vogel<sup>1</sup>, Yosi Hallo<sup>1</sup>, Dekel Maroz<sup>1</sup>

<sup>1</sup>*Mechanical Engineering and Mechatronics, Ariel University, Israel*

<sup>2</sup>*Department of Hand Surgery and Limb Salvage Surgery, The Chaim Sheba Medical Center, Israel*

Total wrist arthroplasty (TWA) remains a challenge in orthopedic surgery due to reported aseptic loosening rates ranging from 20% to 68%. This failure is commonly associated with non-uniform stress distribution and stress shielding at the bone-implant interface.

This study develops and validates a finite element analysis (FEA) framework to compare the biomechanical performance of three TWA systems, ReMotion, Motec, and a theoretical Hybrid implant combining ReMotion-based fixation with a dual-articulation concept, in the natural neutral wrist position. A high-fidelity 3D computational model of a human wrist was reconstructed from computed tomography (CT) scans, and physiological loading is applied to maintain neutral posture distributed among the six primary tendons.

Model validation demonstrated agreement with previously reported load transmission, with 88.5% of the load transferred through the radius. Post-implantation analysis revealed that the Motec system exhibited elevated stress levels in the carpal bones (2–12 MPa) due to its single-peg fixation. In contrast, the ReMotion and Hybrid systems share identical distal fixation, whereas the Hybrid dual-joint architecture is associated with reduced stress in the distal radius and ulna, and a more homogeneous stress distribution across the metacarpal fixation sites.

The findings indicate that implant articulation architecture influences load transfer and stress distributions in peri-prosthetic bone, with potential implications for long-term fixation stability. Future research will evaluate these findings during dynamic tasks, such as the Dart Thrower's Motion, to assess implant behavior under functional kinematics.

# From Injury to Performance: Wearable Biomechanics for Improving Human Movement

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**Background:** Orthopedic conditions such as anterior cruciate ligament reconstruction (ACLR) and lower-limb amputation are associated with persistent gait asymmetries and abnormal joint loading, increasing the risk of long-term degeneration and reduced functional performance. Despite advances in motion capture, surgery, and rehabilitation, scalable tools to understand mechanisms and guide personalized intervention remain limited, as current approaches are largely confined to expensive laboratory environments. This work aims to develop an integrated framework combining biomechanics, wearable sensing, and biomechanical modeling to (1) identify mechanistic pathways following injury and (2) modify movement through sensory-based interventions in real-world settings.

**Methods:** Across multiple studies, we assessed gait biomechanics in ACLR patients (n≈60 longitudinal cohort), below-knee amputees (n=14), and healthy controls (n=50). Data collection included 3D motion capture, force plates, wearable inertial measurement units (IMUs), and quantitative MRI (UTE-T2\*). Gait tasks included overground walking and stair negotiation. A wearable vibrotactile feedback system was developed to provide phase-specific sensory input synchronized to gait, targeting neuromechanical control and loading patterns. Biomechanical modeling approaches were used to quantify joint mechanics and interpret movement adaptations.

**Results:** ACLR cohorts demonstrated persistent gait asymmetries up to 2.5 years post-surgery, associated with altered loading patterns and structural cartilage changes. In early rehabilitation, patients exhibited significantly reduced knee flexion in the injured limb during stair ascent (p<0.01), with asymmetries persisting despite functional recovery. Additionally, wearable vibrotactile feedback (KneeMo) improved gait mechanics in amputee populations, with reduced compensatory strategies, including decreased circumduction (~17%) and improved swing-phase control.

**Conclusions:** This work establishes a continuum from mechanistic understanding to intervention. By integrating wearable biomechanics and sensory feedback, we propose a new paradigm for motion assessment and rehabilitation that enables continuous monitoring and active correction of movement in real-world environments. These approaches have the potential to improve clinical outcomes, reduce degeneration risk, and enhance human performance following injury.

## Reverse Biomimetics of Structural Mechanisms in Soft Biological Composites

**Mirit Sharabi**

*Mechanical Engineering & Mechatronics, Ariel University, Israel*

Over millions of years of evolution, biological soft fibrous tissues have developed intricate structural mechanisms that enable exceptional mechanical performance, especially in enduring large deformations. These tissues are composite materials of repeating building blocks with diverse structural motifs, including variations in fiber fraction, orientation, multi-scale hierarchy, crimping, and weak interfaces. The exceptional properties of soft tissues arise from their intricate structural complexity. While the relationship between structure and function in natural hard materials was extensively studied, soft materials have yet to receive similar attention, despite their vast prevalence in nature.

Our approach involves creating new biomimetic composite materials by combining silk and collagen fibers with hydrogels using weak and reversible interfaces. We reverse-engineered different structural motifs step-by-step to allow a toolbox that includes the isolated mechanical effect of the different motifs, such as the fiber fraction and orientation, crimping, and multi-scale hierarchy.

Moreover, we generated dedicated 3D hyperelastic and heterogeneous finite-element models to simulate the mechanical behavior of the composite laminates under physiological conditions. Our materials display hyperelastic and anisotropic behaviors, showing large deformations, including distinct regions like toe, heel, and linear regions, together with multifunctionality and morphing abilities. Furthermore, by manipulating various structural features, we've successfully customized a wide array of mechanical behaviors. Our biomimetic soft composites exhibit similar large-deformation behavior to various functional tissue structures, like intervertebral discs, knee menisci, and blood vessels.

Through reverse biomimetics applied to simpler materials, we can gain a deeper understanding of the intricate structure-function interplay in complex fibrous soft tissues. This knowledge will aid in designing next-generation materials with tailored mechanical properties, particularly for repairing soft tissues. Ultimately, we aim to create mechanically compatible materials that mimic native tissues, leading to improved applications in future soft-tissue repair and replacement.

# Unified Multimodal E-Skin: A Single-Layer Nanocomposite Platform with Synergistic Tactile, Thermal, and Magnetoreceptive Capabilities

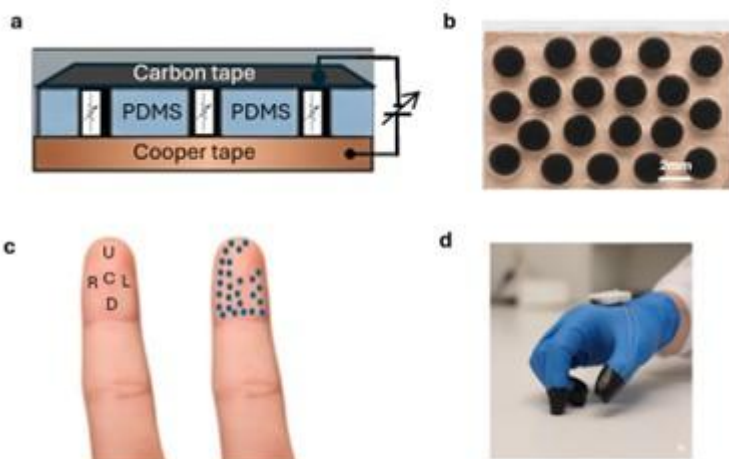
**Amos Bardea**

*Engineering, Holon Institute of Technology- HIT, Israel*

Current haptic technologies for prosthetics often rely on complex, multi-layered architectures, leading to signal interference and high costs. This proposal introduces a disruptive sensing paradigm based on a novel organomagnetic single-layer nanocomposite (PDMS/MWCNTs/NiNPs) integrated into a high-density vertical-via architecture.

Crucially, this work builds upon our preliminary research in smart organic electronic materials, specifically the development of flexible composites exhibiting robust piezoresistive and magnetoresistive properties. The core innovation lies in a discovered synergistic sensing effect: unlike traditional systems requiring discrete layers, our platform achieves simultaneous discrimination of pressure, temperature, and magnetic fields within a single active matrix.

By leveraging a parallel resistive network model, we demonstrate that localized conductive pathways act as dominant shunts, enhancing sensitivity to minute environmental changes. Key benchmarks include a high Negative Temperature Coefficient (NTC), wide-range pressure response, and a "sixth sense" via positive magnetoresistance (PMR). This eliminates complex stacking, offering a streamlined, flexible solution for "Electronic Skin." The research will transition this technology to a scalable, wearable prototype, redefining standards for human-machine interaction and smart prosthetics.



# Engineering Impact on Treatment of the Musculoskeletal System: Advances in Orthopedics and Rehabilitation

**Mark M. Levy**

*Faculty of Biomedical Engineering, Technion, Israel Institute of Technology, Israel*

**Background/Aim:** Engineering developments in Orthopedics and Rehabilitation are shown in clinical practice by improvement in diagnostics and treatment modalities.

**Method:** A review of the literature and compilation of modern technologies are included in this analysis. A multidisciplinary scope covers the influence of the digital and biological revolution, regenerative medicine, new biocompatible materials and composites, genetic and tissue engineering (GE and TE), bioprinting, personalized and/or enhanced implants, robotics in surgery and rehabilitation, implanted and external monitoring wearables sensors, AI and VR.

**Results:** Academic research with broader basic science emphasis and industrial R&D with market-oriented targets, contribute to advancement in patient care. Patent applications and market analysis of new devices and procedures, upgrade funding opportunities.

Novel techniques and biomaterials improved 3D printing capabilities, advances on bioprinting and combination with electrospinning. resulted in complex engineering tissue replacement for soft (ligaments, tendons and cartilage) and hard (bone) tissues, with improved mechanics and integration.

GE allows use of induced stem cells for TE and augmentation of allografts. Healing is enhanced by stem cells, recombinant factors, exosomes and blood factors.

Robotics coupled with navigation gives precision for spine and joint replacement surgery, for bone section and ligament balance. VR superimposes imaging to surgery fields. Robotics applications are incorporated into all layers of rehabilitation care and human work assisting devices. Gait is possible for spinal cord injury and enhanced in neurologic patients, while rehabilitation programs improved dramatically with exoskeletons, training devices, smart prosthesis, and VR.

Personalized medicine is evidenced in custom-made endoprosthesis and implants, use of sensors for implant and patient motion tracking analysis for better outcomes.

AI is becoming an effective complement to human interpretation of orthopedic imaging, improving accuracy and time; also enhances biopsy readings in musculoskeletal tumors.

**Conclusion:** Despite numerous upgrades, there's room for innovation towards improved clinical care. More interaction between industry and academy is welcomed.

# An Integrated 3D Platform for Micro- and Nanobubble Cavitation Dynamics under Low-Frequency Ultrasound

**Ilia Mezdrokhin, Tali Ilovitsh**

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**Background:** Low-frequency therapeutic ultrasound enables medical applications such as blood–brain barrier opening and targeted drug delivery by inducing controlled bubble cavitation. At low frequencies, bubble dynamics become highly nonlinear and strongly affected by surrounding biofluids and biological boundaries, producing asymmetric oscillations and inertial collapse that are not captured by conventional symmetric models.

**Aims:** This work aims to develop and experimentally validate a three-dimensional cavitation COMSOL model of free and targeted micro- and nanobubbles under low-frequency ultrasound, enabling predictive modeling of boundary-induced dynamics and supporting the development of next-generation ultrasound contrast agents.

**Methods:** A three-dimensional, time-dependent cavitation model is developed in COMSOL to simulate the nonlinear dynamics of targeted micro- and nanobubbles under low-frequency ultrasound. The framework resolves volumetric oscillations, inertial collapse, and jet formation using coupled fluid–structure interaction. A modified surface tension model is implemented to describe lipid-shell mechanics during low-frequency ultrasound-induced oscillations. Model predictions are quantitatively validated against high-speed optical imaging measurements of bubble dynamics.

**Results:** The proposed 3D COMSOL model accurately reproduces cavitation dynamics of free and targeted microbubbles ( $r_{\text{initial}} = 750 \text{ nm}$ ) under 250 kHz ultrasound sonication. For free bubbles (fig. a,b) the predicted inertial cavitation threshold of 215 kPa agrees with experiment. For targeted bubbles near a cell boundary, the model captures asymmetric expansion, collapse, and jet formation. Simulated bubble radii during initial (fig. c), expansion (fig. d), and collapse (fig. e) phases closely match high-speed camera measurements (fig. f), demonstrating strong quantitative agreement between simulations and experiments.

**Conclusions:** This work established and validated three-dimensional biomechanical COMSOL framework for modeling ultrasound-driven cavitation and resolving key fluid–structure interaction mechanisms governing asymmetric bubble dynamics. The model supports safer, more precise ultrasound-based therapies and the rational development of new ultrasound contrast agents.

Ultrafast Dynamic Contrast-Enhanced MRI with Flexible Temporal Resolution aided Deep Learning

**Eddy Solomon**

*Technion Israel Institute of Technology, Israel*

Dynamic contrast-enhanced (DCE) MRI is a powerful imaging technique for characterizing tissue perfusion and vascular properties; yet, its clinical utility is limited by a fundamental trade-off between spatial resolution, temporal resolution, and scan time. In this talk, I will introduce a novel MRI reconstruction framework for non-Cartesian radial DCE-MRI, termed Enhanced Locally Low-rank Imaging for Tissue Contrast Enhancement (ELITE).

The proposed framework combines locally low-rank (LLR) subspace modeling with deep learning to enable high spatial fidelity and ultrafast temporal imaging capabilities. ELITE was evaluated using our publicly available fastMRI breast repository designed for machine learning research, demonstrating substantial improvements in contrast-to-noise ratio (CNR) and reduced noise, while enabling flexible temporal resolution down to 1 second. Beyond breast imaging, ELITE also showed promising performance in brain and in head & neck DCE-MRI applications, highlighting its versatility across multiple anatomical regions and clinical applications.

These results suggest a pathway toward clinically practical, quantitative, and motion-robust ultrafast dynamic MRI, with strong potential for cancer imaging applications.

**Shir Gershon**<sup>1</sup>, Tal Grutman<sup>1</sup>, Tali Ilovitsh<sup>1,2</sup>

<sup>1</sup>*School of Biomedical Engineering, Tel Aviv University, Israel*

<sup>2</sup>*Sagol School of Neuroscience, Tel Aviv University, Israel*

Uncontrolled hemorrhage and thrombosis significantly contribute to mortality, requiring time-critical care. However, treatment timelines vary across patients, highlighting the need for a standardized, real-time assessment. We propose an ultrasound-based method for monitoring clotting and lysis kinetics.

We present a non-invasive speed-of-sound shift (SoS shift) method using standard B-mode images acquired with a single transducer. Our approach estimates displacements between frames with optical flow and uses them in a regularized inverse problem to reconstruct slowness-shift maps. The maps are converted to SoS shifts, which we use to quantify gelation time. The method was evaluated across varying fibrinogen and thrombin concentrations in fibrin polymerization, as well as porcine whole-blood clotting and lysis.

Our method produced spatially localized displacement and slowness-shift maps that increased over time within the sample region during clotting. Trends were consistent across inclusion locations. Increasing fibrinogen concentration (2.5-5.0 mg/ml) significantly increased SoS shifts (two-way ANOVA,  $p = 0.0267$ ), whereas higher thrombin concentration (0.3-1.0 U/ml) shortened gelation times (one-way ANOVA,  $p = 0.0491$ ). In porcine whole-blood clotting, SoS shifts were similar to fibrin polymerization, indicating comparable clotting dynamics. Finally, in porcine blood lysis experiments (tPA, 6  $\mu\text{g/ml}$ ), SoS shifts gradually reversed to baseline over time, consistent with clot dissolution kinetics. Together, these results show sensitivity to clot formation and lysis.

This work introduces a spatiotemporal ultrasound framework to monitor material formation and degradation in space and time. Demonstrated for clotting and lysis in fibrin and whole blood, it shows potential for clinical translation in hemostasis and thrombolysis monitoring and may extend to other forming and degrading biomaterials.

## Parallel 5: Optical Technologies & Therapeutic Ultrasound

### Separation and Identification of Age-Related Macular Degeneration Protein Biomarkers in Nanochannels

**Marzia Iarossi**, Noam Freundlich, Barak Marom, Rohan Lamba,  
Ivy Bhattacharya, Amit Meller  
*Biomedical Engineering, Technion, Israel*

**Background:** Age-related Macular Degeneration (AMD) represents 90% of cases of legal blindness globally, affecting the quality of life of more than 190 million people. Recently, a potential set of biomarkers, including CCI2, Rbp4, VEGF, Clusterin and Serpin, have been identified during AMD progression<sup>1</sup>. However, the identification and quantification of AMD biomarkers, is significantly hampered by the ultra-small volumes of the clinical aqueous humor and the extremely low concentrations of these biomarkers, especially at the early stage of the disease. Here, we propose a nanochannel-based device to separate and identify thousands of individual proteins, while performing single-molecule multi-color fluorescence imaging<sup>2</sup>.

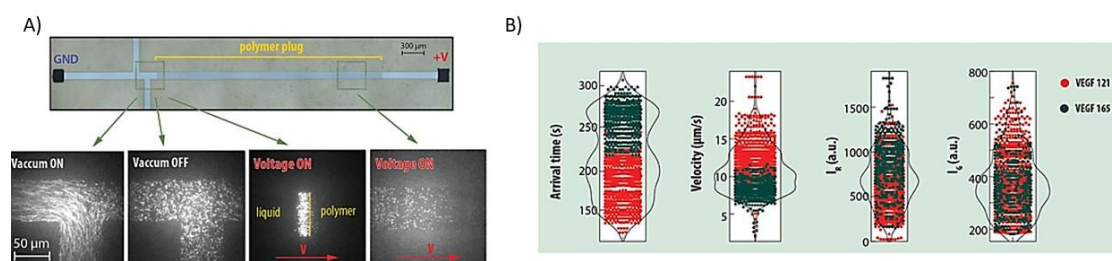
**Method:** Thin nanochannels on a silicon substrate are fabricated in-house (Figure 1A). The device is mounted on a custom-made single-molecule fluorescence imaging setup where two lasers are alternated on the chip while the fluorescence is emitted by the labelled proteins.

**Results:** Our approach enables the separation and identification of proteins by extracting information from the analysis of the trajectories, such as their arrival time, velocity and the emitted fluorescence signals, collected by imaging in two colors their motion under an applied voltage. Mixtures of two VEGF isoforms (Figure 1B), as well as CCI2 and RBP4, have been identified and quantified from the analysis of parameters extracted from their motion, namely the arrival time, the mean velocity and the red and FRET intensities by means of principal component analysis.

**Conclusion:** Our method has been successfully applied to a panel of AMD biomarkers, and it is compatible with ultra-small volumes and ultra-low concentrations required for liquid biopsy and early-detection diagnostics.

#### References

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# Symmetric Cancer Spheroid-Fibroblast 3D Organization Revealed and Characterized by PSF-Engineered High-Throughput Microscopy

**Noam Zoref**<sup>1</sup>, Maytal Avrashami<sup>1</sup>, Nadav Opatovski<sup>2</sup>, Paul Keselman<sup>3</sup>, Yosi Shamay<sup>1</sup>, Yoav Shechtman<sup>1,2,4</sup>

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High-throughput microscopy enables large-scale analysis of spheroid interactions. Integrating this technique with point-spread function (PSF) engineering, a customized optical modification of the imaging system, provides 3D imaging capabilities that enable volumetric analysis of the samples.

However, existing methods for extracting volumetric information using this approach have been demonstrated primarily on point sources or have relied on supervised training data, limiting their general applicability to complex biological samples. Here, we reveal a unique, previously unreported spheroid-fibroblast interaction pattern using high-throughput microscopy.

We further examine the interactions in 3D using a PSF-engineered high-throughput microscope, introducing unsupervised methods for 3D localization from single or dual image acquisitions. These methods enable 3D imaging with minimal phototoxicity and enhanced throughput and temporal resolution.

Our approach reveals surprising spatial cellular trajectories in which fibroblasts self-organize into discrete clusters that distribute symmetrically around the spheroid surface in characteristic "flower-like" arrangements and subsequently climb and penetrate the spheroid.

We further reveal a characteristic distance between adjacent fibroblast clusters of  $\sim 146 \mu\text{m}$  (Fig. 1). Additionally, our method enables rapid quantification and classification of drug responses that modulate these interaction patterns.

# Conformal Piezo-Phototronic Optoelectronic Device for Low-Power Wireless Biological Stimulation

**Shirley Yitzhak-David<sup>1</sup>**, Noor Abo-Ahmad<sup>2</sup>, Yonatan Calahorra<sup>2</sup>, Hemi Rotenberg<sup>1</sup>

<sup>1</sup>*Biomedical Engineering, Technion, Israel*

<sup>2</sup>*Materials Science and Engineering, Technion, Israel*

Optical energy can be used as a non-invasive tool for triggering biological responses at different scales. One of the proposed approaches for wireless conversion of optical energy to electrical energy uses optoelectronic devices.

However, efficient operation requires intimate and stable contact between the device and soft, curved biological tissues - a challenge for conventional planar systems.

Here, we introduce an optoelectronic device based on the piezo-phototronic effect to enhance light-to-electricity conversion with reduced optical power. The piezo-phototronic effect arises in semiconducting piezoelectric materials, where strain-induced polarization modulates the band structure, thus improving charge generation, separation, and recombination to reduce the applied optical power used for stimulation.

In this research we aim to fabricate Si/ZnO based thin devices that are flexible enough to conform to organs. This increases the efficiency of the device and thus reduce the optical power needed to perform stimulation in the free-standing configuration.

ZnO thin films (~100 nm) were deposited via magnetron sputtering. Structural characterization by X-ray diffraction (XRD) confirms a strong c-axis (002) orientation. Piezoelectric force microscopy (PFM) measurements yield an effective piezoelectric coefficient ( $d_{33}$ ) of 4.6 [pm/V], validating electromechanical coupling. Electrical characterization using tunneling atomic force microscopy (TUNA) demonstrates diode-like behavior of the heterojunction.

These results establish a mechanically compliant, piezo-phototronic-enabled optoelectronic interface that enhances energy conversion efficiency while reducing the optical power required for stimulation. This approach provides a promising pathway toward minimally invasive, wireless bioelectronic stimulation platforms for cardiac pacing and neuronal stimulation.

# Real-Time Localization and Control of Anti-Vascular Ultrasound in the Brain

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**Background:** Focused ultrasound (FUS) is a noninvasive therapeutic modality widely used for thermal ablation of deep brain targets. However, thermal treatments are limited to central brain regions due to skull heating and safety constraints. Anti-vascular ultrasound (AVUS) provides a non-thermal alternative by activating intravenously injected microbubbles (MBs). Under suitable FUS conditions, MBs undergo inertial cavitation, generating mechanical stresses that disrupt local vasculature and create confined lesions. We aim to develop an AVUS platform for precise, non-thermal brain lesioning with real-time monitoring and feedback control. The system will also use super-resolution ultrasound imaging to assess vascular effects in vivo.

**Methods:** A dual-mode system combining a FUS therapeutic transducer with an integrated imaging array was developed to induce MB cavitation and record acoustic emissions. In vitro phantom studies identified spectral signatures of inertial cavitation. In vivo dosing studies in mice established the FUS intensity required to trigger inertial cavitation, followed by histological evaluation of treatment outcomes.

Next, passive acoustic mapping (PAM) will spatially localize cavitation activity during ablation. A real-time feedback loop will adjust FUS amplitude in response to cavitation intensity to ensure controlled lesion formation. Ultrasound localization microscopy (ULM) will reconstruct the vascular network at super-resolution before and after treatment, enabling vivo lesion assessment without MRI.

**Results and Conclusion:** The dual-mode system enables imaging-guided FUS targeting (Figure 1b). Inertial cavitation was successfully induced in mice, with distinct spectral signatures identified (Figure 1c). ULM demonstrated MB localization in vitro (Figure 1a). Together, these components establish the foundation for controlled, non-thermal brain ablation with real-time monitoring, spatial localization, and in vivo lesion assessment.

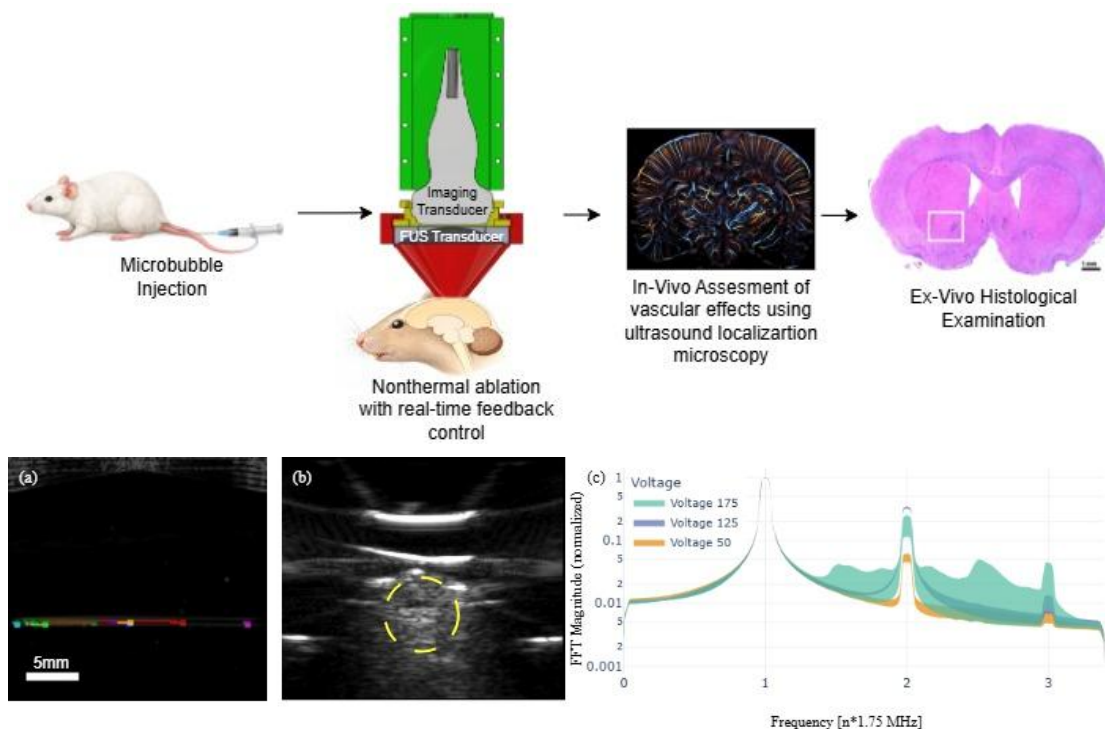


Figure 1: Preliminary results. (a) In vitro MB tracking (each color represents a detected MB). (b) In vivo ultrasound image of a brain (in yellow). (c) In vivo echo spectral signature with respect to the FUS voltage.

## Leveraging Nanobubble-Mediated Ultrasound to Improve CAR-T Efficacy in Solid Tumor Treatment

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Solid tumors remain difficult to treat due to their dense tissue and protective microenvironment, which limit therapeutic efficacy. While chimeric antigen receptor (CAR) T-cell immunotherapy has revolutionized hematological malignancy treatment, its efficacy in solid tumors is limited by physical and immunological barriers.

To address this, we propose synergistically combining CAR-T cells with nanobubble (NB)-mediated ultrasound (US) mechanotherapy to enhance therapeutic outcomes. NBs, which accumulate in tumors after systemic injection, are activated by low-frequency US to induce tumor fractionation, potentially facilitating CAR-T cell infiltration and improving efficacy against both the tumor and its microenvironment.

NBs were synthesized and activated by low-frequency US (250 kHz) to induce ablation and create cell death in vitro. Co-culture experiments revealed that NB-mediated US, when combined with CAR-T cells, significantly reduced tumor cell viability compared to either modality alone, across multiple tumor models. Next, the combination treatment was tested in vivo. Upon systemic administration and tumor accumulation, NBs were detonated, producing localized cavitation and ablation of tumor tissue while minimizing off-target effects. A few days later, CAR-T cells were systemically injected.

This combination therapy was performed in both an immunodeficient and immunocompetent model. First, in the immunodeficient model, the results demonstrated significant reduction in tumor growth in the combination group compared to either single modality alone. Next, in an immunocompetent model, flow cytometry and immunohistochemistry confirmed robust infiltration of CD45<sup>+</sup>, CD3<sup>+</sup>, CD4<sup>+</sup>, and CD8<sup>+</sup> T cells, increased macrophage activation, and greater overall immune effector recruitment to the tumor microenvironment, providing enhancement of the present immune system by the combination treatment.

Further, the combination therapy led to marked tumor regression, and prolonged survival. Overall, this research demonstrates that this method addresses major barriers to solid tumor treatment, improving physical access and immune engagement, and provides a compelling foundation for developing next-generation, clinically translatable cell-based immunotherapies.

# An Advanced Platform for Monitoring Thrombolysis in Small Vessels using Comparative Ultrasound Localization Microscopy

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**Objectives:** Microvascular obstructions play a critical role in various clinical conditions, including distal embolization after percutaneous coronary intervention, vessel injury, inflammation, and coronary microvascular disease. However, these small vessels are beyond the resolution of conventional imaging, limiting evaluation of clot dynamics and treatment response. Here, we aim to develop a non-invasive ultrasound (US) imaging and therapy framework to detect microvascular obstructions, and monitor thrombolysis in small vessels using combined US, microbubbles, and tissue plasminogen activator (tPA).

**Methods:** Fibrin and whole-blood clots were generated and embedded in US-compatible microvasculature phantoms with 0.1-1 mm channels. Microbubbles were infused to measure baseline flow using a programmable US system and ultrasound localization microscopy (ULM). Thrombolysis will be induced using tPA alone, microbubble + US, and microbubble + US + tPA. Post-treatment flow and vessel narrowing were quantified with ULM to assess pharmacological, mechanical, and synergistic effects on clot dissolution and microvascular flow recovery.

**Results:** This ULM-compatible platform specifically designed for thrombolysis experiments in small-diameter vessels, included the fabrication of complex microvascular phantoms incorporated with clots generated from porcine blood or fibrinogen and thrombin mixtures (fibrin clots), producing partial blockages that altered flow velocities (Fig. 1). ULM imaging enabled visualization and quantification of flow across multiple microvascular obstruction scenarios, with measured velocities ranging from 0.01 to 10.5 mm/s (Fig. 1B, E, G, H). Treatment with tPA at clinically relevant concentrations of 3–6  $\mu\text{g}/\text{mL}$ , reduced clot volume, increasing the available area for flow and thereby lowering the maximum velocity from 7.5 mm/sec to 3 mm/s (Fig. 1G–J).

**Conclusions:** This ULM-based framework enables quantitative evaluation of microvascular obstructions and thrombolysis while providing single-vessel insight into clot dynamics, currently unavailable with other imaging methods. Using this platform, ULM captured tPA-induced restoration of blood flow in individual small vessels, establishing a platform for therapy comparison and treatment optimization in microvascular obstruction.

Novel Cardio-Respiratory Physiological Assist Technology for Alleviating Pulmonary Congestion in Patients with Chronic Heart Failure: First-in-Human Study

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<sup>2</sup>*Biomedical Engineering, Technion-IIT, Israel*

Pulmonary congestion and the associated respiratory effort are major contributors to morbidity and frequent hospitalizations in patients with heart failure (HF). Respiratory mechanics exert opposing effects on right ventricular (RV) and left ventricular (LV) function. Specifically, negative pleural pressure enhances RV stroke volume while reducing LV stroke volume. We leverage this physiological interplay to promote pulmonary fluid clearance by increasing the likelihood that cardiac cycles coincide with phases of elevated pleural pressure.

Preclinical studies in sheep models of HF demonstrated that this approach yields significant hemodynamic improvement within minutes, supporting translation to a first-in-human study. The novel cardio-respiratory physiological assist (CRPA) technology was evaluated in HF patients with existing pacemakers. CRPA therapy was applied for 10 minutes following a 5-minute baseline period. Monitored parameters included pulmonary artery pressure (PAP), RV and LV outputs, and tidal volume.

To date, thirteen patients with severe pulmonary congestion (NT-proBNP 3,785±3,598 pg/mL) have been enrolled. CRPA had minimal effect on mean heart rate. Treatment resulted in a progressive reduction in mean PAP from 28.2±4.6 to 24.5±2.9 mmHg, accompanied by an 8.0±3.6% increase in LV output. The reduction in PAP was associated with a marked increase in tidal volume by 18.8±19.1% (from 406±91 to 524±134 mL, p=0.023), alongside a significant decrease in dyspnea score from 2.9±1.9 to 1.9±1.7 (p=0.015).

CRPA was safe, well tolerated, and imperceptible to all patients. This technology rapidly and progressively reduces PAP by favoring LV output over RV output, and is associated with significant alleviation of dyspnea and improved respiratory mechanics.

# Hemodynamic Effects of Aortic Stenosis on Coronary Flow Dynamics

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**Purpose:** Aortic stenosis (AS) commonly coexists with coronary artery disease (CAD), yet the direct hemodynamic link between valve function, coronary flow waveforms, and spatial wall shear stress (WSS) remains poorly defined. This study isolates and quantifies how AS-induced flow alterations generate atheroprone coronary environments.

**Methods:** An in vitro mock circulation loop modeled severe AS (effective orifice area 0.7 cm<sup>2</sup>) and post-transcatheter aortic valve Replacement (TAVR, Evolut R™) under 54 physiological states (heart rate 80–150 bpm; stroke volume 40–65 ml). Time-resolved coronary blood flow (CBF) measurements served as inlet boundary conditions for patient-specific computational fluid dynamics (CFD) simulations of coronary hemodynamics. Atherosclerotic risk was assessed using surface areas exposed to WSS thresholds associated with plaque initiation or vulnerability: oscillatory shear index (OSI 0.2), relative residence time (RRT 4 Pa<sup>-1</sup>), endothelial cell activation potential (ECAP 0.5 Pa<sup>-1</sup>), and time-averaged WSS (0.45 Pa or 4 Pa).

**Results:** Compared to TAVR, severe AS produced higher systolic transvalvular pressure gradients (45–70 mmHg vs. 10–25 mmHg) and lower aortic–sinus gradients, particularly at elevated heart rates (HR). Diastolic CBF was elevated at normal HR but declined with increasing HR, resulting in increased pulsatility and reduced coronary flow reserve. CFD revealed larger regions of atheroprone WSS in AS, predominantly on convex arterial curvatures, while elevated WSS localized to concave regions. TAVR reduced adverse WSS exposure by 30-50%.

**Conclusion:** AS induces hemodynamic disturbances favoring CAD progression through altered coronary flow and adverse WSS patterns. TAVR mitigates these effects, highlighting opportunities for valve design optimization to protect coronary health.

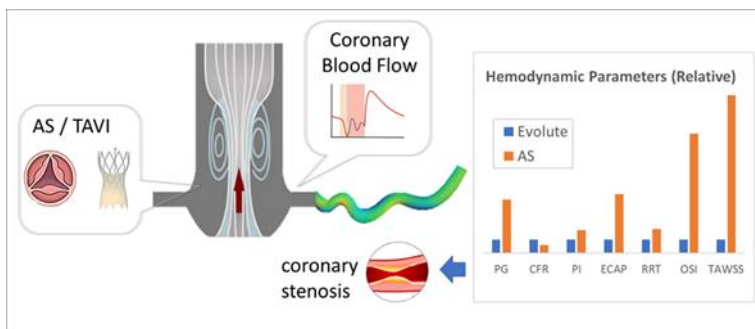


Figure 1: Overview of the research methods: the combined in-vitro and CFD approaches

Nuclear strain and fragility in beating cardiomyocytes - implications for laminopathies

**Daria Amiad Pavlov**<sup>1</sup>, Carmen Suay Corredera<sup>2</sup>, Julie Heffler<sup>3</sup>, Noam Zuela-Sopilniak<sup>3</sup>,  
Mohammad Dehghany<sup>4</sup>, Vivek Shenoy<sup>4</sup>, Jan Lammerding<sup>3</sup>, Benjamin Prosser<sup>2</sup>

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The adult cardiomyocyte continuously undergoes substantial shortening and stretch cycles. This demanding mechanical environment is supported by a complex cytoskeletal network and transmitted to the nucleus through the linker of the nucleoskeleton and cytoskeleton (LINC) complex. How the nuclei sense and respond to changes in the loading conditions to adapt cardiomyocyte function, remains unclear.

We present a new method to quantify dynamic cytoskeletal-nuclear strain transfer in adult, beating cardiomyocytes and describe the distinct effects of the LINC complex and microtubule disruption on the dynamic nuclear strain during systolic contraction, and diastolic re-lengthening.

Disrupting the LINC complex has recently emerged as a promising strategy to ameliorate *LMNA* associated cardiomyopathy. Here we utilize dynamic strain coupling and in-vivo *Lmna* cardiomyopathy mouse models, to investigate mechanisms of nuclear fragility and protection. Surprisingly, we find that the LINC complex is largely dispensable for transferring the strain of contraction into the nucleus, and that augmented nuclear strain in *Lmna* deficient myocytes is not rescued by LINC complex disruption. Instead, LINC complex disruption eliminated the cage of microtubules encircling the nucleus.

Accordingly, direct microtubules perturbation was sufficient to prevent nuclear damage and rescue cardiac function induced by lamin A/C deficiency. We further develop a computational model to define the stress fields surrounding cardiomyocyte nuclei, which demonstrates how microtubule compression exploits local vulnerabilities to damage *LMNA* deficient nuclei. This work pinpoints microtubule dependent forces transmitted through the LINC complex as a pathological driver and therapeutic target for the treatment of *LMNA* cardiomyopathy.

# Impedance Pumping in Rectangular Microchannels: A Fluid-Structure Interaction Study for Biochip Design

**Dikla Kesner**<sup>1,2</sup>, Sara Naftali<sup>2</sup>, Moshe Rosenfeld<sup>1</sup>

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<sup>2</sup>*School of Medical Engineering, Afeka Tel Aviv Academic College of Engineering, Israel*

Impedance pumps, which operate via a valveless mechanism driven by fluid–structure interaction (FSI), have attracted increasing interest due to their potential applications in biomedical and microfluidic systems. This study investigates the physical mechanisms governing net flow generation in a three-dimensional (3D) rectangular impedance pump, with emphasis on wave dynamics, resonance behavior, and nonlinear flow effects in geometries relevant to lab-on-chip devices. Fully coupled numerical simulations were used to examine the influence of actuation and flow parameters on pumping performance.

A 3D FSI model was developed for a rigid rectangular channel incorporating a compliant latex membrane segment subjected to periodic localized pinching. Transient incompressible Navier–Stokes equations were fully coupled with nonlinear membrane mechanics. A systematic parametric study was performed, varying pinching frequency, amplitude, location, Reynolds number, and the number and phase synchronization of multiple pinchers.

The results demonstrate a strong dependence of net flow rate (NFR) on membrane wave patterns. High NFRs were typically associated with standing waves formations near resonant conditions, yielding NFR values of up to approximately 2.45 ml/min for a single pincher operating at 100 Pa. In contrast, propagating wave regimes produced significantly lower NFR values, often below 0.5 ml/min. Notably, substantial net flow was also observed under specific non-resonant conditions, indicating that resonance is not a strict requirement for effective impedance pumping. Increasing the Reynolds number enhanced NFR by up to a factor of three, highlighting the critical role of nonlinear inertial effects. In multi-pincher configurations, synchronized actuation with an appropriate phase difference increased NFR to approximately 2.65 ml/min, even at reduced pinching amplitude.

These findings provide new quantitative insight into the interplay between wave dynamics, resonance, and nonlinear flow mechanisms, and offer practical design guidelines for efficient valveless pumping in microfluidic and biomedical flow systems.

## Sex-Specific Differences in Sinoatrial Node Function Are Driven by Mitochondrial Ca<sup>2+</sup> Influx

**Rami Eid**<sup>1</sup>, Héctor H. valdivia<sup>2</sup>, Carmen Valdivia<sup>2</sup>, Yael Yaniv<sup>1</sup>

<sup>1</sup>*Faculty of Biomedical Engineering, Technion-IIT, Israel,* <sup>2</sup>*Cardiovascular Research Center, Department of Medicine, University of Wisconsin, USA*

Sex differences in the prevalence of cardiovascular disease are well established; however, sex-dependent differences in therapeutic responses and the cellular mechanisms governing heart rate regulation remain incompletely understood.

The sinoatrial node (SAN), the heart's primary pacemaker, generates rhythmic activity through the coordinated interaction of membrane ion channels and intracellular Ca<sup>2+</sup> cycling, conceptualized as the coupled-clock system. This system is tightly regulated by cAMP/PKA signaling and mitochondrial energetics. Importantly, Ca<sup>2+</sup> and cAMP/PKA signaling reciprocally regulate mitochondrial function, including mitochondrial Ca<sup>2+</sup> uptake via the mitochondrial Ca<sup>2+</sup> uniporter (MCU), thereby linking bioenergetics to SAN activity.

We hypothesized that sex-dependent differences in SAN responsiveness to pharmacological modulation of the cAMP/PKA pathway arise from differential mitochondrial Ca<sup>2+</sup> handling. Using isolated SAN tissue from adult male and female mice, we combined high-resolution Ca<sup>2+</sup> imaging, real-time FRET-based measurements of PKA activity, and quantitative proteomics. Basal beat interval (BI) and BI variability were similar between sexes.

However, pharmacological BI shortening induced by phosphodiesterase inhibition or direct PKA activation was significantly greater in males than in females. These functional differences were accompanied by higher maximal PKA activation in males, whereas PKA inhibition produced comparable effects in both sexes.

Proteomic analysis revealed no sex-dependent differences in membrane ion channels or sarcoplasmic reticulum Ca<sup>2+</sup>-handling proteins. In contrast, mitochondrial proteins exhibited marked sexual dimorphism, including higher MCU expression in males. Functional inhibition of MCU abolished sex differences in drug-induced BI shortening and selectively reduced the magnitude of BI acceleration in males, indicating a critical role for MCU in mediating sex-specific pacemaker regulation.

Together, these findings identify mitochondrial Ca<sup>2+</sup> signaling as a key determinant of sex-dependent SAN responsiveness to cAMP/PKA pathway modulation. Higher MCU expression, and thus enhanced mitochondrial Ca<sup>2+</sup> uptake, in males likely augments energetic support for pacemaker acceleration, whereas reduced mitochondrial Ca<sup>2+</sup> influx in females constrains this response.

# Cardiovascular Bioconvergence: First-in-Class Light-Induced Cardioversion Platform Integrating Gene Therapy and Flexible Micro-LED Bioelectronics for Atrial Fibrillation

**Yaki Eidelstein**, Lior Gepstein, Yehuda Wexler, Nitai Hanani  
*OptoRhythm LTD, Israel*

**Background/Aim:** Atrial fibrillation (AF) affects millions of patients and remains inadequately controlled in persistent disease, where ablation efficacy declines and electrical cardioversion is painful and often non-durable. OptoRhythm, a bioconvergence startup supported by the Israel Innovation Authority and NGT VC, is advancing a first-in-class therapeutic platform that integrates cardiac gene therapy with implantable optical bioelectronics to enable painless, repeatable cardioversion. The program is currently in large-animal proof-of-concept (POC) studies, with a defined and executable pathway toward first-in-human application.

**Method:** The platform combines localized atrial AAV-mediated delivery of light-sensitive ion channels with a flexible micro-LED array designed for epicardial illumination and closed-loop operation. The development program follows a rapid, milestone-driven translational pathway from small-animal validation to large-animal functional studies and clinical readiness. In pigs, we established targeted atrial gene painting for localized transduction and developed a procedural framework for acute optical electrophysiology experiments. Current POC studies are designed to demonstrate light-based control of atrial electrical activity (pacing and defibrillation) in a large-animal model.

**Results:** Small-animal in vivo studies established optogenetic control of atrial rhythm. In pigs, atrial gene painting achieved robust epicardial transgene expression at 3 weeks, confirming the feasibility of targeted gene delivery in a large heart. Ongoing large-animal POC experiments are designed to deliver the first demonstration of optogenetic pacing and atrial fibrillation cardioversion in a porcine model, representing a critical inflection point for clinical translation.

**Conclusion:** This work represents a transition from academic optogenetics to a clinically oriented cardiovascular bioconvergence platform. By integrating gene therapy and flexible micro-LED medical devices into a unified system, OptoRhythm is advancing a non-destructive alternative to shock-based and ablative AF therapies. The current large-animal POC stage, combined with a clear regulatory and clinical pathway, positions this technology for rapid progression toward first-in-human studies and establishes a new modality for cardiac rhythm control.

*Parallel 8: Tissue Engineering & Regenerative Medicine*

Advanced Tools to Study Human Physiology

**Ben M. Maoz**

*Tel Aviv University, Israel*

Neurological conditions affect over 40% of the global population, yet a clinically validated method to deliver drugs to the brain does not exist.

The blood-brain barrier (BBB) prevents therapeutic levels of drugs from entering the brain, and there is a lack of alternative biological pathways. As a result, over 98% of drugs for central nervous system (CNS) diseases are ineffective, causing poor outcomes and disease progression.

One of the main challenges are the lack of human-relevant models, as between 60-90% of the drugs that successfully pass animal trials fail in human clinical trials. In this talk, I will present and review, the state of the art tools that are available for studying human physiology, emphasizing the brain and the BBB.

# Enhancing Structural and Vascular Stability in Engineered Cardiac Tissues through Material and Cellular Strategies

**Shira Landau-Levi<sup>1,2</sup>, Milica Radisic<sup>2</sup>**

<sup>1</sup>*Faculty of Biomedical Engineering, Technion, Israel*

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A key limitation in cardiac tissue engineering is the lack of structural stability and long-term vascularization in engineered constructs. Most hydrogel-based systems suffer from cellular compaction and poor mechanical resilience, while vascular networks often fail to remain perfusable and functional over extended culture. Addressing these challenges is essential to enable applications in regenerative medicine, disease modeling, and drug testing.

In two independent but complementary studies, we explored distinct strategies to overcome these barriers. In the first study, we developed a composite bioink composed of elastomeric POMaC microparticles embedded in biologically derived hydrogels (GelMA, fibrin, alginate). This granular formulation preserved the cell-compatible properties of the base hydrogel while enhancing elasticity, compressive strength, and shape fidelity. Using extrusion and stereolithographic printing, we generated complex, cell-laden 3D constructs that resisted compaction and deformation during *in vitro* culture and after implantation. These constructs supported the formation of cardiac and vascular tissues with improved mechanical integrity and host integration.

In the second study, we investigated the role of primitive yolk sac-like macrophages derived from human pluripotent stem cells in promoting vascular stability within heart-on-a-chip systems. Using a quad-culture of endothelial cells, stromal cells, cardiomyocytes, and primitive macrophages, we observed enhanced vessel patency, perfusability, and cardiomyocyte function over two weeks *in vitro*. Transcriptomic analysis revealed upregulation of angiogenic and cardioprotective signaling pathways, including IGFBP7 and HGF, and suggested that both paracrine signaling and direct macrophage-endothelial interactions contributed to vascular maturation and tissue homeostasis.

These studies demonstrate two effective and modular strategies, one materials-based and one cell-based, for addressing the dual challenge of mechanical and vascular stability in engineered cardiac tissues. Each approach independently advances the development of more robust and physiologically relevant human cardiac models.

## Micro and Nano- Structuring of Hydroxyapatite-MMT Loaded Hydrogels for Bone Regeneration Applications

**Tom Hanoon Kogan**<sup>1</sup>, Inbar Eshkol-Yogev<sup>1,2</sup>, Inbar Levi<sup>1</sup>, Meital Zilberman<sup>1,3</sup>

<sup>1</sup>*School of Biomedical Engineering, Tel Aviv University, Israel*

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*College London, United Kingdom, <sup>3</sup>Dept. of Materials Science and Engineering, Tel Aviv University, Israel*

Bone regeneration focuses on creating functional tissue to repair bone defects. Creating a biodegradable scaffold hydrogel that combines a hemostatic agent with bioactive ceramics can afford the biological and mechanical benefits of both components.

In the present study, we developed an injectable gelatin-alginate dual composite hydrogel, i.e. loaded with two functional fillers, hydroxyapatite (HA) and the hemostatic agent montmorillonite (MMT). HA (Microparticles and nanoparticles) was incorporated at concentrations of 10-30 mg/mL, with and without MMT at 20 mg/mL.

The effects of functional fillers and their concentration on the microstructure and resulting physical and mechanical properties were studied, and a qualitative model summarizing these effects was developed. All formulations exhibited clinically appropriate gelation times (5-29 seconds). n-HA significantly prolonged gelation time, reaching  $29 \pm 3$  s at 30 mg/mL, while MMT reduced gelation time at all concentrations. The tensile strength of the unloaded hydrogel reached 20 kPa and increased to 57 kPa with 30 mg/mL of n-HA.

The tensile strength even increased further with the addition of MMT (77 kPa). The results indicate that the combination of HA and MMT produced dual micro-composite hydrogels with moderate reinforcement, whereas the combination of n-HA and MMT generated dual nano-micro composites with synergistic effects. The latter exhibited the highest strength and sealing ability, while maintaining clinically relevant gelation times and controlled swelling behavior.

In conclusion, the combination of MMT with n-HA or HA enables the creation of functional hydrogels with controlled properties, tailored to specific applications in bone regeneration.

# Regenerative Potential of Mesenchymal Stem Cell-Derived Extracellular Vesicles Loaded with PTEN siRNA for Facial Nerve Injury

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<sup>1</sup>Faculty of Biomedical Engineering, Technion, Israel

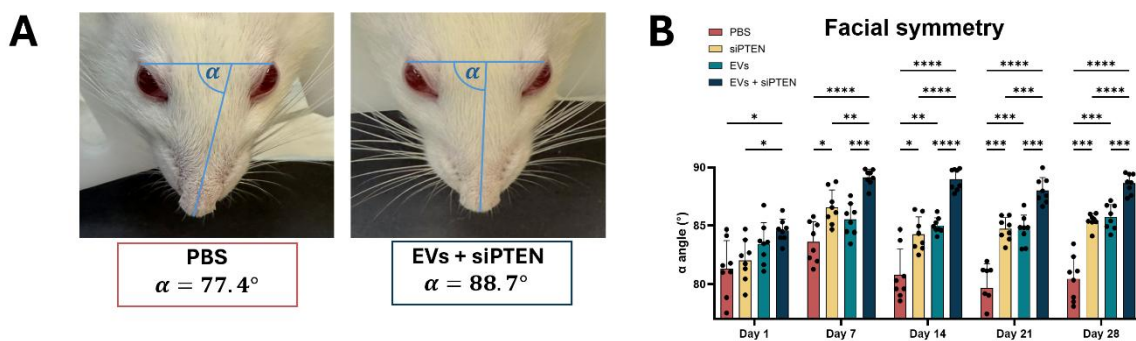
<sup>2</sup>NurExone Biologic Ltd, Israel

Facial nerve injuries are a significant cause of peripheral nerve damage, affecting millions worldwide and impairing both physical and psychological well-being. Current treatments often fail to achieve full functional recovery, requiring innovative regenerative strategies. Mesenchymal stem cell (MSC)-derived extracellular vesicles (EVs) demonstrate therapeutic potential by supporting Schwann cell function, promoting angiogenesis, and reducing inflammation. Downregulating phosphatase and tensin homolog (PTEN) can enhance nerve regeneration, and MSC-derived EVs provide an effective bioinspired nanocarrier system for targeted delivery of PTEN-silencing siRNA (siPTEN).

Human bm-MSC-derived EVs were isolated by differential centrifugation and loaded with glucose-conjugated siPTEN to promote nerve regeneration. To determine the optimal administration route, we conducted an *in vivo* biodistribution study in a rat model of facial nerve injury. Labeled EVs were delivered via intravenous, intranasal, or intralesional (IL) routes, with distribution tracked using IVIS imaging.

IL administration resulted in the most targeted delivery, with significantly higher DiR signal in the injured nerve. The MSC-EV-siPTEN group showed the greatest improvements in facial symmetry and eyelid closure. Notably, symmetry improved within one day post-injury, suggesting a neuroprotective effect. By day 28, CMAP analysis confirmed the highest functional recovery. Gene expression analysis demonstrated increased activation of pathways associated with nerve growth and Schwann cell activity. Histological evaluation revealed improved tissue organization and nerve fiber regeneration in the MSC-EV-siPTEN group, whereas PBS-treated nerves showed poor structural repair. Overall, the treatment promoted coordinated and mature regeneration.

These findings support bm-MSC-derived nanoscale EVs loaded with siPTEN as a promising, minimally invasive therapy for facial nerve injuries.



## MSC-EV-siPTEN promotes functional recovery following facial nerve injury (FNI).

(A) Representative images of facial symmetry at day 28 post-FNI, showing the  $\alpha$  angle used to quantify symmetry. (B) Quantification of facial symmetry ( $\alpha$  angle) over time across treatment groups.

# Hybrid Bioprinting of Vascularized Bone Tissue Using a Thermosensitive, Mechanically Robust Bioink

**Majd Machour**, Roy Meretzki, Yuval Moshe Haizler, Margarita Shuhmaher,

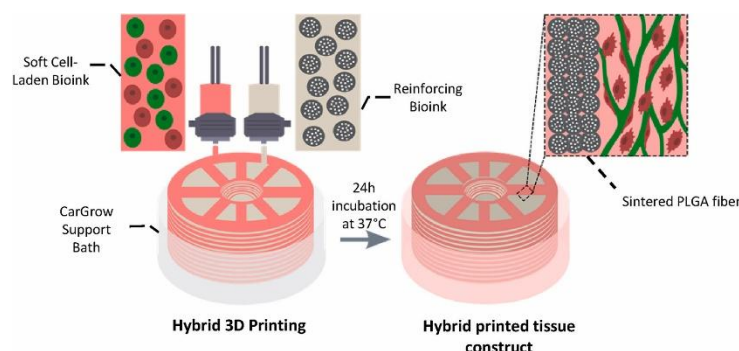
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**Background/Aim:** 3D bioprinting is an emerging tissue engineering technique advantageous for fabricating intricate structures; however, creating functional, implantable tissues remains challenging. Commonly utilized hydrogel bioinks offer desirable printability and a cell-friendly environment but often lack the mechanical robustness necessary for post-printing maturation, handling, and implantation. These limitations are particularly critical for bone tissue, where treating bone loss from trauma or infection poses a significant clinical challenge and surgical interventions frequently lead to complications. Thus, a strategy to enhance the mechanical integrity of bio printed constructs while maintaining cellular compatibility is needed. The aim of this study is to present a novel hybrid bioprinting approach to create mechanically robust, vascularized bone tissue.

**Method:** A reinforcing bioink was developed using a blend of poly(lactic-co-glycolic) acid (PLGA), hydroxyapatite (HA), and polyethylene glycol (PEG) microparticles. This blend is thermosensitive due to a reduced glass transition temperature ( $\sim 36^\circ\text{C}$ ), enabling sintering under physiological conditions. This reinforcing bioink was co-printed with a cell-laden, extracellular matrix (ECM)-based hydrogel. The microparticles were allowed to sinter at  $37^\circ\text{C}$  to form a porous, stiff scaffold. To evaluate efficacy, the constructs were assessed *in vitro* for cellular behavior and implanted *in vivo* into a rat femoral defect model to compare bone regeneration against acellular controls.

**Results:** The hybrid bio printed constructs demonstrated high cell viability, successful vascular network formation, and robust osteogenic differentiation. Following *in vivo* implantation in the rat femoral defect model, the cell-laden hybrid scaffolds revealed superior bone regeneration compared to the acellular controls.

**Conclusion:** This study highlights the strong potential of hybrid bioprinting for creating bone tissues that exhibit both high cell viability and enhanced mechanical properties, effectively overcoming existing barriers to their handling and clinical implantation.



*Parallel 9: Nanotechnology & Microfluidic*

Magnetic Nanocomposites for Controlling Cell Signaling

**Dekel Rosenfeld**

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Israel*

Cell signaling can be mediated by heat generated from magnetic nanoparticles (MNPs) that dissipate heat efficiently when exposed to alternating magnetic fields (AMFs).

Our lab develops novel approaches for remote AMF-based activation of deep organs via implantable, biocompatible magnetic polymeric hydrogels with controlled magnetic and mechanical properties, tailored to different organ tissues. The AMF-driven activation targets heat-sensitive ion channels, such as the transient receptor potential vanilloid 1 (TRPV1), with a temperature threshold above 42 Celsius.

The magnetic hydrogels achieve wireless, on-demand control of cell signaling. This control is crucial for cell excitability, making our work highly relevant to the fields of neuroscience, tissue engineering, and drug delivery.

# AI in Cancer Nanomedicine: From Text Mining to Meta-Synergy and Automated Discovery

**Yosi Shamay**

*Faculty of Biomedical Engineering, Technion-IIT, Israel*

The field of drug delivery, particularly the area of cancer nanomedicine, is undergoing a significant transformation driven by the convergence of artificial intelligence (AI) and wet lab automation. In my talk, I will present transformative approaches my laboratory has developed to master the complexities in the field and solve hard biomedical problems.

First, I will describe how we leverage text mining and computational approaches to construct dynamic knowledge bases that enable hypothesis generation for cell-specific drug delivery. By systematically mining biomedical literature, we can uncover hidden relationships between drugs, targets, and disease mechanisms that would otherwise remain obscured in the vast scientific literature.

Second, I will describe our concept of meta-synergy framework we introduced to optimize and classify multi-drug combinations across multiple dimensions including chemical loading, pharmacodynamics, and pharmacokinetics. This approach moves beyond simple two-drug synergy to explore the "synergy of synergies," combining chemical, pharmacological, and biological cooperation to achieve therapeutic effects that are greater than the sum of their parts. Third, I will describe how we utilize automation and advanced screening methodologies, particularly aggregation-induced emission (AIE), to accelerate nanoparticle discovery and characterization.

These high-throughput approaches enable us to navigate the vast design space of nanomedicine formulations more efficiently. I will argue that rather than avoiding or simplifying complexity, we should use AI to embrace it as an opportunity.

By developing sophisticated tools and frameworks to work within this complexity, we can manifest new therapeutic possibilities and pave the way for more effective, precise, and adaptive cancer treatment strategies.

## Ultrasound Mediated Polymerization for Cell Delivery, Drug Delivery, and 3D Printing

**Lior Debbi**, Majd Machour, Daniel Dahis, Hagit Shoyhat,  
Margarita Shuhmaher, Ruth Potter, Yael Dinkovich, Idit Goldfracht,  
Itiel Dennis, Tom Blechman, Theodor Fuchs, Haim Azhari, Shulamit  
Levenberg  
*Faculty of Biomedical Engineering, Technion-Israel Institute of  
Technology, Israel*

Safe and accurate in situ delivery of biocompatible materials is a fundamental requirement for many biomedical applications. These include sustained and local drug release, the implantation of acellular biocompatible scaffolds for supporting the regeneration of major tissue loss, and the transplantation of cells and engineered tissues for functional restoration of damaged tissues or organs.

The common practice today includes highly invasive operations with major risks of surgical complications including adjacent tissue damage, infections, and long healing period of the patient. In addition, the ability to deliver drugs locally with high precision for sustained and prolonged release remains challenging without a stable and defined matrix.

In this work, we present a novel non-invasive delivery method for scaffolds, cells, and drug delivery deep into the body to target inner organs and tissues with high spatial control. Our technology is based on acoustic-sensitive materials which are polymerized by ultrasound induction through an external transducer in a rapid and local fashion without using additional photo initiators or precursors.

We demonstrated the applicability of this technology for viable and functional cell delivery, for drug delivery with sustained release profiles, and for 3D printing. Moreover, the mechanical properties of the delivered scaffold can be tuned to the desired target tissue as well as controlling the drug release profile.

This promising technology may shift the paradigm for local and non-invasive material delivery approach in many clinical applications as well as a new printing method - "acousto-printing" for 3D printing and in-situ bioprinting.

# Coupling Electrokinetic Bioparticle Focusing in Continuous Microfluidics with Electrowetting-on-Dielectric Droplet-Based Extraction

Amir Hillman<sup>1</sup>, Sinwook Park<sup>1</sup>, Gilad Yossifon<sup>1,2</sup>

<sup>1</sup>*School of Mechanical Engineering, Tel Aviv University, Israel*

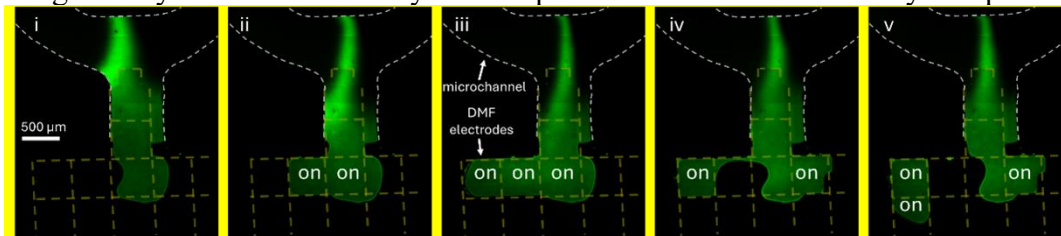
<sup>2</sup>*School of Biomedical Engineering, Tel Aviv University, Israel*

**Background/Aim:** Ion concentration polarization (ICP), generated near ion-exchange membranes under an applied electric field, enables continuous electrokinetic focusing of dilute analytes such as bioparticles. Although ICP-based preconcentration enhances bioanalytical sensitivity, maintaining the concentrated plug requires sustained flow and voltage, which complicates the extraction of discrete, concentrated samples for downstream analysis. This study aims to develop a hybrid microfluidic platform that couples continuous ICP-based preconcentration with electrowetting-on-dielectric (EWOD) digital microfluidics (DMF) to enable efficient droplet-based extraction of concentrated biomolecules.

**Methods:** We designed a hybrid system that interfaces a continuous-flow microchannel with a DMF electrode array via a stagnant fluid region. ICP is induced using ion-permselective membranes to generate depletion and enrichment zones, enabling electrokinetic focusing of biomolecules. The concentrated species are subsequently transferred into individually addressable droplets on the DMF platform while preserving their concentrated state. Experimental observations were supported by numerical simulations and analytical modeling.

**Results:** The proposed configuration successfully enabled the transfer of ICP-preconcentrated biomolecules into discrete droplets without disrupting the concentrated state. The hybrid architecture overcame limitations of existing continuous–discrete integration strategies that rely on oil phases or fixed geometries. Experimental results showed qualitative agreement with both simulations and theoretical analysis, validating the underlying transport mechanisms.

**Conclusion:** This work demonstrates a viable strategy for coupling continuous electrokinetic focusing with droplet-based digital microfluidics. The presented platform facilitates efficient isolation of preconcentrated samples and provides a foundation for integrated hybrid microfluidic systems capable of downstream bioanalytical processing.



# Engineering a Mechanoresponsive DNA Origami Capsule for Drug Delivery to Narrowed Arteries

**Hadas Omer**, Yuval Garini<sup>1</sup>, Nethanel Korin<sup>1</sup>, Ariel Kaplan<sup>1</sup>  
*Technion, Israel*

Atherothrombosis is one of the leading causes of death and disability worldwide, as it can lead to severe complications such as stroke, pulmonary embolism, and heart attack<sup>1</sup>. Despite advances in cardiovascular medicine, acute thrombotic events remain a major cause of morbidity and mortality under the current standard of care<sup>2-3</sup>.

To address these challenges, we present a novel mechano-responsive capsule-like nanostructure made of DNA. DNA origami allows one to construct nm-size structures from pure DNA and by targeted drug release, it provides thrombosis treatment in narrowed blood vessels.

Each structure consists of a hollow box enclosed by two rectangular lids, linked to the box via DNA strands functioning as a spring. The spring is designed alongside polymer physics principles, enabling to control the capsule opening only at the narrow artery. This targeted mechanism ensures that the drug, such as tPA, is released only at the site of vascular obstruction, enhancing therapeutic efficacy.

The small size of the capsule cannot be observed by optical microscopy, and we mainly use atomic force microscopy (AFM) and Cryo-TEM for structural characterization. We also use optical tweezers to study the mechanical properties of the DNA spring. Analysis of the AFM and Cryo-TEM images fully confirms the design of the structures. This method can be adapted for various applications beyond thrombosis, offering a versatile platform for targeted drug delivery in vascular disorders.

# Low-Frequency Ultrasound-Enhanced Microdroplet Cavitation for Active Scaffold Modulation in Tissue Engineering

**Hen Shenhav**, Tiran Bercovici, Tali Ilovitsh  
*Biomedical Engineering, Tel Aviv University, Israel*

The development of porous scaffolds with tunable mechanical and structural properties is crucial for tissue engineering. Scaffold porosity supports 3D cell nutrition, migration, and proliferation but can compromise mechanical stability. Contamination and infection also risk implant rejection and regenerated-tissue dysfunction. This study introduces drug-loaded microdroplets that, when activated by low-frequency ultrasound, enable on-demand antibiotic release, controlled pore formation, and stiffness modulation, providing a remotely tunable, multifunctional strategy for enhancing scaffold performance and tissue regeneration.

Advanced lipid-shell microdroplets containing antibiotics and Perfluorohexane in their core were fabricated using microfluidic chips and incorporated into collagen hydrogels. Exposure to a 1D rotating ultrasound imaging transducer induced droplet vaporization, followed by low frequency insonation at 200 kHz to enhance microbubble expansion and collapse. This process enabled antibiotic release, micropore formation, and modulation of rheological properties. Porosity and mechanics were assessed via histology, microscopy, and rheometry, while antibacterial efficacy and fibroblast proliferation were evaluated.

Blank microdroplets (1.1  $\mu\text{m}$ ) were incorporated into collagen hydrogels to study ultrasound-induced mechanical and structural modulation. A 1D rotating imaging ultrasound transducer (MI 1.84) vaporized droplets into microbubbles, yielding 13.72 dB contrast enhancement. Subsequent low frequency insonation at 200 kHz induced microbubble collapse, contrast reduction, and pore formation. Scanning electron microscopy revealed pores of  $39.42 \pm 10.28 \mu\text{m}$ , consistent with Marmottant model predictions of 56  $\mu\text{m}$ . Rheology showed increased scaffold elasticity and deformation resistance after ultrasound treatment. Antibiotic-loaded microdroplets were then embedded in the scaffolds, enabling ultrasound-triggered antibacterial activity, while cell studies demonstrated 30% higher cell growth compared with controls.

In this study, drug-loaded microdroplets were designed to solubilize antibiotics within their core and incorporated into collagen scaffolds. Ultrasound activation induced pore formation, mechanical enhancement, and on-demand antibacterial activity while promoting fibroblast growth, reducing contamination risks and implant rejection, and enabling tunable, multifunctional platforms for tissue regeneration

Biomechanical Characterization of Arteries Using a Novel Pressure–Pressure Loop Approach

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**Background:** Vascular elasticity and lumen narrowing play a critical role in cardiovascular hemodynamics, pulse pressure transmission, and tissue perfusion. Alterations in arterial mechanical properties due to ageing, disease, or implantation of artificial blood vessels significantly affect pressure wave dynamics. While existing clinical indices focus primarily on flow or pressure gradients, there remains a need for functional, pressure-based approaches that can characterize biophysical vessel properties without reliance on direct flow measurements.

**Objectives:** The goal of this study was to develop a pressure-based method for functional biophysical characterization of blood vessels, with particular emphasis on vascular elasticity and viscoelastic energy dissipation, using pressure-only measurements.

**Methods:** An in vitro closed-loop experimental system was constructed using seven flexible tubes, including silicone, latex, and clinically used artificial blood vessels. Pulsatile flow of a blood-mimicking glycerol–water solution was generated, and intraluminal pressure waves were acquired using two high-fidelity Millar pressure sensors positioned along the tube. Controlled stenosis levels (0%, 50%, and 90%) were applied. Pressure–pressure loops were constructed from paired pressure signals, and loop morphology and slope were analyzed. Uniaxial tensile testing provided independent Young’s modulus measurements.

**Results:** Different morphologies of pressure–pressure loops were observed across the tube materials. Silicone tubes exhibited broad hysteresis loops; latex tubes showed phase transitions along the loop; and artificial blood vessels exhibited nearly linear loops. The loop morphology was largely preserved across levels of stenosis, while the pressure amplitude increased with stenosis severity.

**Conclusion:** Pressure–pressure loop analysis provides a novel, pressure-only framework for functional characterization of vascular mechanical behavior. By integrating elastic stiffness and viscoelastic energy dissipation, this approach offers mechanobiological insight with potential applications in vascular assessment and artificial blood vessel design.

## Toward Physiological Performance: Reinforced Polymeric Valves with Embedded Fiber Architecture

**Omer Tal**, Yevgeniy Kreinin, Dmitry Korneyev, Netanel Korin  
*Biomedical engineering, Technion - Israel Institute of Technology, Israel*

**Background:** Valvular heart disease affects ~2.5% of the population, rising to 13.3% in those over 75. Mechanical valves are durable but require lifelong anticoagulation, whereas bioprosthetic valves provide better hemodynamics but degenerate over time. Polymeric valves are a promising alternative but remain limited by fatigue, thrombosis, and calcification. Here, we present a biomimetic approach using embedded three-dimensional fiber architectures inspired by native collagen organization to improve durability while preserving function.

**Methods:** A polymeric aortic valve with embedded fibers was developed in four configurations: biomimetic, horizontal, ply-based, and unreinforced. Valves were fabricated using multi-material 3D printing and heat-assisted compression within a polycarbonate urethane matrix (PCU). Two leaflet thicknesses, 0.3 mm and 0.2 mm, with corresponding fiber diameters, were investigated. In vitro hydrodynamic testing was performed for the 0.3 mm valves under near-physiological conditions (6 L/min), assessing geometric orifice area and leakage. Finite element simulations evaluated leaflet kinematics and stress distributions, were compared with the 0.3 mm in vitro results, and were extended to the 0.2 mm design.

**Results:** For the 0.3 mm valves, in vitro and in silico results showed good agreement. The biomimetic design reduced peak stresses and decreased belly-region stresses by ~50–60% compared with the unreinforced valve, with a modest ~10% reduction in geometric orifice area. In silico analysis of the 0.2 mm configuration indicated improved performance, with stress reduction maintained and valve opening better preserved, approaching clinically relevant ranges. Horizontal and ply configurations showed inferior performance.

**Conclusions:** Biomimetic embedded fiber reinforcement improves durability-related mechanical performance while preserving valve function. Reducing leaflet thickness further improved the balance between stress reduction and functional performance, supporting this approach as a promising direction for next-generation polymeric heart valves.

# Interfacial Fluid Confinement-Based Intravascular Device for Targeted Brain Aneurysm Therapy

**Tirosh Mekler**<sup>1</sup>, Dmitry Korneyev<sup>1</sup>, Maria Khoury<sup>1</sup>, Mark Epshtein<sup>2</sup>,  
Yevgeniy Kreinin<sup>1</sup>, Josué Sznitman<sup>1</sup>, Netanel Korin<sup>1</sup>

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Israel*

<sup>2</sup>*Medical School, University of Massachusetts, USA*

**Introduction:** Current localized intravascular therapies rely on solid implants or direct injections, which risk off-target dispersion and complications. Therefore, strategies that precisely confine injectable therapeutics are needed. Here, we present a fluid-based localization approach that exploits immiscible fluid interactions to enable confined treatment of brain aneurysms (Khoury et al., 2024) and we explore an intravascular device that supports this procedure while maintaining physiological arterial flow.

**Methods:** Computational simulations and in vitro experiments using reconstructed brain aneurysm models were conducted to study isolation using two immiscible phases (IMPs; air and a fluorocarbon oil (FC-40) phase). Subsequently, selective therapeutic delivery was evaluated in patient-specific models. To advance this concept toward clinical application, a hollow intravascular device was engineered to enable treatment while preserving arterial flow. The fabricated device using SLA-based 3D printing, incorporates two separate tubes for injection and withdrawal, with enlarged diameters at both ends to minimize gaps and maintain the IMP.

**Results:** Computational and experimental results showed that an IMP can be positioned at the aneurysm neck to achieve effective sealing and isolation. Localized treatment was demonstrated in endothelialized patient-specific models, as well as embolization via delivery of fibrinogen and thrombin, forming a fibrin hydrogel. However, this method requires temporary cessation of arterial flow. Therefore, A hollow device enabling to perform the procedure while maintaining parent artery flow was therefore explored. While rigid devices allow limited flow (150 ml/min) require a flexible design to minimize gaps between the device and the artery.

**Conclusion:** Immiscible-phase-based fluid confinement provides a minimally invasive, non-mechanical strategy for aneurysm isolation and localized therapy. The development of hollow intravascular devices may enable such treatments while ensuring that physiological arterial flow is maintained during the procedure. This platform may offer precise control over localized treatment at vascular disease sites.

# CereNex Medical: A Versatile Intracascular System for enhanced Cerebral Aneurysm Treatment

**Reuven Filman**  
*Cerenex Medical, Israel*

**Background:** CereNex Medical is startup company established in 2025, developing multi-layer intracascular device for the treatment of challenging cerebral aneurysms.

Endovascular treatment of brain aneurysm continues to face challenges in achieving durable occlusion, addressing complex morphologies, and reducing procedural complexity. This presentation introduces a novel, under development, medical device aimed at improving treatment outcome.

**Technology:** The device consists of a Nitinol braid designed to redirect flow away from the aneurysm and enable effective aneurysm sac filling. Its Self-Expanded superstructure with multi-layer nitinol mesh generates higher flow disruption inside the aneurysm. Its unique geometry provides strong wall apposition and neck sealing. The design provides user experience similar to conventional coil deployment, facilitating ease of use.

Compared to existing technologies the device is designed to improve aneurysm packing efficiency, simplified procedure workflow with potential benefits in enhancing recovery and reducing recurrence risk.

**Results:** Bench testing in anatomical silicon models demonstrated effective flow disruption improved aneurysm filling characteristics. Preliminary usability assessment indicated an intuitive deployment process. In vivo proof of concept evaluation demonstrated the feasibility to achieving immediate aneurysm occlusion.

**Conclusion:** This presentation will introduce the device concept, its differentiation from current endovascular solutions and initial test results supporting the design rationale. The technology represents a promising approach toward improving versatility, usability and treatment outcomes in cerebral aneurysm treatment.

## Acunex Vascular Systems: A Catheter-Delivered Continuous Suturing System for Durable EVAR Graft Fixation

**Yathreb Asaad-Helou<sup>1</sup>, Areen Shtewe<sup>1</sup>**  
*Acunex Vascular Systems, Israel*

Every year, 200,000 patients die from abdominal aortic aneurysm. Endovascular Aneurysm Repair (EVAR) transformed how we treat this disease, but it left one critical problem unsolved: Up to 40% of patients develop Type I endoleaks and 30% suffer graft migration, both stemming from poor fixation: current available fixation methods including hooks, barbs, and staples grip at scattered points and leave the circumference unprotected.

Patients return for reinterventions costing up to \$50,000 each, with overall post-procedural expenditure rising by 50%. Decades of iteration on the same discrete-fixation concept have yielded diminishing returns. What the field needs is not a better anchor; it needs a different principle entirely.

The global EVAR market stands at \$3.5 billion, growing at 8% annually toward \$5 billion by 2030, driven by over 200,000 procedures per year. The opportunity is not a niche; it is the entire market, because every single one of those procedures carries this unresolved fixation problem.

Acunex is pursuing what no minimally invasive device has achieved: replicating the durable fixation of open surgical repair through a catheter-based approach. In open surgery, the graft is directly sutured to the aorta, effectively forming a single unified structure. Acunex delivers this endovascularly through a one-directional needle that penetrates both the EVAR graft and the aortic wall, sewing them together continuously and circumferentially.

Acunex has moved from principle to proof. A 21-gauge needle prototype was validated in vitro, demonstrating one-directional graft penetration with anchors maintaining firm fixation against detachment, the first physical evidence that continuous endovascular suturing is mechanically achievable. A provisional patent application has been filed to protect the core technology. This progress builds on iterative CAD development, formal feasibility validation with a leading medical device engineering firm, and clinical input from five vascular surgeons across Israel and Canada who confirmed no adequate solution exists.

## ViaOne - Safe Access to the Pericardial Space Utilizing a Blunt Tip Concealed Needle Mechanism

**Ziv Menshes, Or Hazan**  
*Cardiovia, Israel*

**Background/Aim:** Safe, reproducible access to the pericardial space remains a barrier to broader adoption of epicardial therapies (mapping, ablation, device implantation, and targeted biologic delivery). ViaOne (CardioVia) was developed to reduce the risk of cardiac puncture and procedural variability associated with sharp-needle techniques and to enable controlled, scalable epicardial access. The aim is to validate a system that shortens the learning curve, improves safety, and supports commercialization and wider clinical adoption.

**Method:** ViaOne is a concealed, blunt-tip mechanical retraction and suction-based epicardial access platform with an integrated tissue-grip mechanism and pressure-confirmation sensor. Development included iterative bench engineering for manufacturability, preclinical validation in animal models, and first-in-human feasibility studies focused on procedural success, safety endpoints, and usability across operator experience levels. Parallel activities comprised regulatory readiness, IP protection, and establishment of clinical training and proctoring programs. Commercial planning prioritized initial user centers, distributor partnerships, and logistics (3PL) to support rollout.

**Results:** Preclinical and early clinical experience demonstrated consistent pericardial access with atraumatic tissue engagement and reliable placement confirmation via pressure sensing. Compared with traditional sharp-needle approaches, ViaOne reduced instances of inadvertent myocardial puncture in tested models and facilitated controlled entry in operators with varied experience. Device design features supported reproducible workflows and integration into electrophysiology lab procedures. Organizational outcomes include completed regulatory milestones toward market entry - FDA clearance obtained, secured intellectual property, established training curricula, and confirmed partnerships to enable staged commercialization and evidence generation at initial user centers.

**Conclusion:** ViaOne offers a mechanically distinct approach that enhances the safety and predictability of epicardial access, potentially expanding the eligible patient population and accelerating adoption of epicardial therapies. Ongoing and planned clinical evaluations, combined with targeted commercialization and training strategies, aim to validate clinical benefit, support reimbursement pathways, and drive broader integration across electrophysiology and adjacent cardiac specialties.

*Parallel 12: Artificial Intelligence & Deep Learning Applications*

The Deep Learning Revolution in Single-Molecule Localization Microscopy

**Yoav Shechtman**

*Technion Israel Institute of Technology, Israel*

Single-molecule localization microscopy has fundamentally transformed biological research by providing nanoscale insights into cellular structures, bypassing the classical optical diffraction limit. However, the technique has traditionally faced significant computational challenges, particularly when resolving dense emitter populations, achieving high-speed 3D imaging, or capturing rapid spatiotemporal dynamics.

In this talk, I will describe how our group has integrated deep neural networks with optical point-spread-function (PSF) engineering to overcome these limitations.

While classical algorithms that rely on explicit model fitting, deep learning models can be trained on large-scale physics-based simulations to enable fast, parameter-free reconstruction of super-resolution data. Key advancements include: dense emitter localization in 2D and in 3D, joint optimization of the optical system with the decoding algorithms for volumetric and multispectral imaging, and spatio-temporal super-resolution.

I will also discuss the democratization of these methods, both in hardware, via simple fabrication of diffractive optics, and in software.

Molecular MRI Meets Physics-Guided Deep Learning: From Neurodegeneration  
Biomarkers to Cancer Treatment Response

**Or Perlman**

*Biomedical Engineering, Tel Aviv University, Israel*

Changes in molecular tissue properties, such as intracellular pH and protein/metabolite concentrations, are known to underlie a variety of neurological diseases and precede anatomical or structural changes.

While non-invasive imaging of these processes is key for early diagnosis, current clinical in-vivo molecular imaging techniques are often slow, nonspecific, or require radioactive or metal-based contrast agents.

This talk will present several AI-based strategies for molecular MRI, offering substantial acceleration, biophysical parameter extraction, and uncertainty quantification. Potential applications spanning cancer treatment monitoring and neurodegeneration characterization will be discussed.

## Label-Free AI-Aided Imaging Flow Cytometry of Cancer Cells

**Natan T. Shaked**

*School of Biomedical Engineering, Tel Aviv University, Israel*

I will present our latest advances in label-free imaging flow cytometry for detecting cancer cells in liquid biopsies, such as blood and urine. Our approach integrates a microfluidic chip with a motion-sensitive event-based camera, an interferometric phase microscopy module using a conventional frame-based camera, and a real-time deep-learning classifier that operates directly on raw interferograms during cell flow.

The event-based camera captures activity from flowing cells at an effective rate corresponding to thousands of frames per second and triggers the significantly slower interferometric camera only when a rare cancer cell requiring more sensitive analysis is detected. This selective triggering is enabled through real-time analysis of a single raw interferogram, substantially reducing the overall data volume.

The raw interferometric data are then processed by a deep neural network for rare-cell classification. We demonstrate the system's capability to detect and grade rare cancer cells in blood samples: the event-based camera rapidly distinguishes common white blood cells from rare cancer cells, while the interferometric module classifies the cancer cells as primary or metastatic. This framework serves as a human model for the detection and grading of circulating tumor cells in liquid biopsies.

# Artificial Intelligence as an Infrastructure Component of Modern Cardiology: An Overview of Promising Solutions and Clinical Effectiveness

**Igor Grinshteyn**

*Clinical Research Center "Point of Care Clinic", Slovenia*

**Background:** Artificial intelligence (AI) technologies are increasingly used in cardiology practice. The consistent and safe introduction of AI into cardiology requires continuous systematization and analysis of the effectiveness of existing solutions for the timely correction of possible risks.

**Objective:** To analyze the effectiveness and possible limitations of the use of Russian and foreign AI solutions in cardiology. **Material and methods.** An analysis of literature for the period from 2020 to 2026 was conducted in the PubMed, Cochrane Library, and eLibrary.ru databases.

**Results:** AI-based technologies improve the accuracy of various diagnostic methods, including computed tomography, magnetic resonance imaging, echocardiography, and electrocardiography. The introduction of clinical decision support systems improves the differential diagnosis of diseases and increases doctors' adherence to clinical guidelines. The introduction of telemonitoring tools into practice with the aim of improving the control of chronic diseases is extremely promising.

**Conclusions:** Artificial intelligence has enormous potential to transform medical care for cardiovascular diseases. However, at the current stage, large-scale randomized studies, external validation of models, development of standards for the application of AI technologies, and assessment of their effectiveness are necessary for the safe and effective introduction of AI into cardiology. **Keywords:** artificial intelligence, clinical decision support systems, cardiovascular diseases, machine learning, deep learning, cardiovascular imaging, risk stratification

**Ofri Goldenberg**

*Biomedical Engineering, Technion, Israel*

Localization microscopy has overcome the diffraction limit, i.e. the conventional resolution limit of a microscope, enabling nanoscale biological imaging by precisely determining the positions of individual emitters such as single fluorescent molecules.

However, the performance of deep learning methods, commonly applied to these tasks, depends significantly on the quality of training data, typically generated through simulation. Creating simulations that perfectly replicate experimental conditions remains challenging, resulting in a persistent simulation-to-experiment gap.

To bridge this gap, we propose a physics-informed generative model leveraging self-supervised learning directly on experimental data. Our model extends the Deep Latent Particles (DLP) framework by incorporating a physical model of the Point Spread Function (PSF; the image of a single point source in the microscope) into the decoder, enabling it to disentangle learned realistic environments from emitters. Trained directly on unlabeled experimental images, our model intrinsically captures realistic background, noise patterns, and emitter characteristics. The decoder thus acts as a high-fidelity generator, producing fully labeled, realistic training images with known emitter locations.

Using these generated datasets significantly improves the performance of supervised localization networks, particularly in challenging scenarios such as complex backgrounds and low signal-to-noise ratios. We demonstrate our approach on a variety of experimentally measured microscopy data, including super-resolution imaging in 2D and 3D and particle tracking in live cells, showing substantial improvements in localization precision and emitter detection.

The code will be made publicly available.

# X-ray2CTPA: Leveraging Diffusion Models to Enhance Pulmonary Embolism Classification

**Noa Cahan**<sup>1</sup>, Eyal Klang<sup>2</sup>, Galit Aviram<sup>3</sup>, Yiftach Barash<sup>4</sup>, Eli Konen<sup>4</sup>, Raja Giryes<sup>1</sup>, Hayit Greenspan<sup>1,5</sup>

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Chest X-rays (CXR) are widely used in clinical workflows due to their accessibility and low radiation burden, yet their limited contrast resolution and two-dimensional nature restrict diagnostic accuracy compared with computed tomography (CT), particularly contrast-enhanced CT pulmonary angiography (CTPA).

In this work, we investigate cross-modal translation from a 2D CXR input to a synthesized 3D CTPA representation using a diffusion-based generative framework. The proposed approach learns from paired CXR-CTPA data and operates in latent space to model the structural and semantic relationship between modalities, enabling generation of anatomically consistent volumetric scans conditioned on a single radiograph.

We train a conditional diffusion model that integrates radiographic encoding with volumetric reconstruction, allowing synthesis of pseudo-CTPA volumes that preserve cross-slice coherence and clinically relevant anatomical structure. Generated scans are evaluated using quantitative metrics, including structural similarity and perceptual measures, and are incorporated into a downstream classification pipeline for pulmonary embolism (PE) detection. Results demonstrate that classifiers trained using synthesized CTPA volumes significantly outperform CXR-only baselines, improving AUC from 0.69 to 0.80 and approaching performance obtained using real CTPA scans. Expert reader studies further suggest that the generated volumes provide diagnostically meaningful cues that enhance PE identification compared to interpretation of CXRs alone.

Beyond PE classification, the framework highlights a generalizable paradigm for cross-modality translation, enabling high-resolution volumetric information to be inferred from low-cost imaging inputs. By augmenting radiographic data with pathology-like three-dimensional representations, this approach has the potential to reduce unnecessary CT utilization, lower radiation exposure, and support more accessible AI-driven decision making in emergency and resource-limited clinical settings.

An Augmented Reality Tool for Obstacle Avoidance Rehabilitation Paradigms

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Many balance, stroke and walking rehabilitation paradigms include walking around obstacles. Such tasks are inherently cumbersome as they require physically re-positioning obstacles and limit us to certain types (e.g. light enough to move). Recently virtual-reality solutions have been suggested to mitigate these issues, but their adoption has been limited by safety issues, and their disconnect from the real world and between patient and practitioner. We suggest that using augmented reality and performing the tasks in the real world offers advantages of both approaches.

We developed an augmented-reality tool which places augmented obstacles in a corridor, tested its usability (n=7), and then tested whether users (n=31) treated augmented obstacles as real obstacles. In the usability test Participants experienced the tool and walked down corridors with real and virtual objects, with our main measures being adverse effects, comfort and correct system functionality. In the basic science experiment the participants walked down corridors with real and virtual objects, critically they were instructed simply to reach the other end and not instructed regarding obstacles, with our main measures being kept distance from each obstacle and subjective reports.

We successfully implemented the tool. Usability testing was successful with no adverse effects reported. Obstacle testing revealed that most participants (89%) did not treat the virtual and real obstacles differently, though a small subgroup treated virtual objects as less of an obstacle. This was reflected also in their subjective reports.

Our tool is successfully implemented and offers a practical solution for rehabilitation paradigms involving obstacle avoidance readily deployable in any corridor. It is currently being tested with clinical populations. Our basic science finding on how users treat augmented obstacles has general implications for the design of augmented-reality tools for rehabilitation.

## Lessons Learned: Telemedicine & Remote Care Technologies

**Rachel Sarafraz**

*Sheba Tel Hashomer Medical Center, Israel*

This presentation will be given from the perspective of the hospital innovation director leading the development, adoption, and implementation of remote care technologies within Sheba Beyond. Sheba Beyond is Sheba Medical Center's virtual hospital, offering a variety of hospitalization and ambulatory remote services. Technologies and digitalization are an important part of the strategic shift from synchronous tele-medicine toward asynchronous models of remote care.

We will begin with a practical overview of telemedicine and Hospital-at-Home technologies currently used in real clinical operations, including remote monitoring platforms and AI-supported workflows.

Rather than focusing only on the promise of digital health, the presentation will then explore the operational realities of scaling remote care inside public healthcare. We'll discuss usability challenges for both patients and clinicians, interoperability between systems, technological burden on staff, dependence on additional hardware, implementation barriers, and the economic difficulty of establishing and sustaining innovative services over time.

We'll conclude with lessons learned from implementing remote care and supporting technologies.

## Speculate Gynecology

**Or Weis Ginsburg**<sup>1,2</sup>, Gili Gipsz<sup>1</sup>, Anastasia Nepomnyashchaya<sup>1</sup>

<sup>1</sup>*Speculate Gynecology, Israel*

<sup>2</sup>*Technion - Israel Institute of Technology, Israel*

Speculate Gynecology is building the future of gynecological exams through a scalable, data-driven medtech platform. The current main examination tool - the vaginal speculum - has remained largely unchanged since the Roman era nearly 2,000 years ago. Speculate Gynecology's patent-pending solution introduces a new approach that combines a self-use, disposable, anatomically adapted device with optical imaging, real-time guided positioning, AI decision support software, and long-term follow-up capabilities.

Designed to address key barriers to routine pelvic care, including pain, discomfort, stigma, and limited access, the platform aims to create a more accessible, patient-centered, and technology-enabled exam experience. This approach aims to improve adherence to gynecological care, support earlier detection, and reshape diagnostics and monitoring. Speculate Gynecology is currently advancing its MVP, actively seeking investment, and has recently received support from the Israel Innovation Authority, in addition to winning several competitions and participating in leading startup programs.

We were invited to participate by Prof. Amir Landsberg, President of ISMBE, who reached out to us knowing or from her time in the Technion's dual-degree program in Medicine and Biomedical Engineering. As he suggested, we would be pleased to contribute either as speakers or as panel participants to discuss the dual-degree track. We would also be glad to present Speculate Gynecology in the startup section through a booth or poster, and to take part in the startup pitch competition.

GerdCare Medical: Israel-Based Digital Therapeutics Innovator Delivering eGERD,  
a First-in-Class Wearable, Drug-Free GERD Therapy Restoring EGJ Barrier  
Function and Tackling the Disease at Its Root

**David Hanuka**, Ram Dickman  
*Gastroenterology, Rabin Medical Center, Israel*

With over 1 billion people suffering from GERD, and nearly 40% unresponsive to conventional drug therapies, GerdCare is tackling a long-overlooked and rapidly growing global health challenge. Current treatments, including PPIs and surgery, either mask symptoms without addressing the underlying cause or expose patients to significant risks and complications.

GerdCare has developed the world's first wearable, drug-free, non-invasive GERD treatment designed to restore the functionality of the gastroesophageal (EGJ) barrier, targeting the root cause rather than just its symptoms. Our integrated system combines a smart wearable delivering targeted electrical stimulation, a proprietary mobile app for personalized treatment tracking, and a secure clinician dashboard that enables remote monitoring and data-driven care.

In a pilot clinical study published in *Neurogastroenterology & Motility* and presented at DDW 2025, our solution demonstrated meaningful clinical impact, including significant reductions in esophageal Acid Exposure Time and marked improvements in heartburn, regurgitation, and other GERD-related symptoms, with an excellent safety profile. Patients experienced substantial normalization of esophageal acidity within just 3–4 days, a 75% reduction in regurgitation versus 17% with PPIs, and consistently strong safety outcomes across both PoC and pilot studies.

A pivotal, FDA-approved clinical study is currently underway to further validate these results.

The commercial potential is substantial: a 6.3B+ dollar global GERD therapeutics market growing at 3.6% annually, and an estimated 23 million PPI non-responders in the US and EU alone who are left today without an effective solution. GerdCare's razor-and-blade business model, driven by recurring consumables revenue, supports attractive long-term economics. Market launch is planned for 2028, with projected sales exceeding 315M dollars by Year 5 and gross margins above 85%.

## *Parallel 15: Biomedical Robotics Surgical Procedure*

Bowel incision closure with a semi-automated Robot-assisted laser tissue soldering system

Shani Arusi<sup>1†</sup>, Max Platkov<sup>2†</sup>, Barak Rosenberg<sup>1</sup>, Svetlana Basov<sup>3</sup>, Ido Ashbell<sup>4</sup>, Tom Polovin<sup>4</sup>, Yoel Chocron<sup>5</sup>, Abraham Katzir<sup>6</sup>, Ilana Nisky<sup>1</sup>, **Uri Netz**<sup>4,5,\*</sup>

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<sup>5</sup> *Department of Surgery A, Soroka University Medical Center, Beer-Sheva, Israel*

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<sup>†</sup>*Equal Contribution*

Traditional methods for closing gastrointestinal (GI) surgery incisions, like suturing and stapling, present significant challenges, including potentially life-threatening leaks. These techniques, especially in robot-assisted minimally invasive surgery (RAMIS), require advanced manual skills.

While their repetitive and time-consuming nature makes them suitable candidates for automation, the automation process is complicated by the need for extensive contact with the tissue. Addressing this, we demonstrate a semi-autonomous contactless surgical procedure using our novel Robot-assisted Laser Tissue Soldering (RLTS) system on a live porcine bowel.

Towards this *in-vivo* demonstration, we optimized soldering protocols and system parameters in *ex-vivo* experiments on porcine bowels and a porcine cadaver. To assess the RLTS system performance, we compared the pressure at which the anastomosis leaked between our robotic soldering and manual suturing. With the best setup, we advanced to an *in-vivo* Heineke Mikulicz closure on small bowel incision in live pigs and evaluated their healing for two weeks.

The five pigs that successfully completed the procedure, survived without leaks and histology indicated mucosal regeneration and fibrous tissue adhesion. This marks the first *in-vivo* semi-automated contactless incision closure, paving the way for automating GI surgery incision closure which has the potential to become an alternative to traditional methods.

Crossevia Medical is Revolutionizing Cath Lab Interventions with Advanced Access  
Devices and Enabling Endovascular AI Robotic Navigation

**Tamir Nahmias**

*BD, Crossevia Medical, Israel*

**Conventional Guidewire Limitations:** Traditional guidewires depend on torque transmission for vessel navigation, but distal extensions cause friction and stress, eroding control and leading to complications like vessel damage, extended times, and failures. Premium wires are costly yet underperform in tough cases.

**Our Breakthrough: Isolated Tip Torque (ITT) Technology:** Crossevia's ITT system isolates 360° rotation and deflection to the tip, bypassing full-wire torque. AI robotics deliver real-time control for agile distal navigation, minimizing friction and enabling seamless crossings of calcifications, bifurcations, or aneurysms. It integrates with cath labs, using AI for predictive guidance.

**Flagship Product & Pipeline:** Our 0.014" neurovascular guidewire, for stroke and aneurysm treatments, eyes FDA 510(k) clearance in 2026. Pipeline includes structural heart tools like TAVR/mitral repairs, with AI enhancements like haptic feedback and ML optimization to reduce variability.

## LapBox: Setting a New Safety Standard in Minimally Invasive and Robotic Surgery

**Stav Tori**

Ark Surgical, Israel

Minimally invasive and robotic surgery continue to expand rapidly worldwide, particularly in gynecologic procedures such as hysterectomy and myomectomy. While these approaches offer significant benefits to patients—including faster recovery, reduced pain, and shorter hospital stays—tissue extraction during laparoscopic surgery remains a critical safety challenge. The potential spread of malignant or contaminated tissue during specimen removal has raised concerns among regulators, surgeons, and healthcare systems.

Ark Surgical developed LapBox, an FDA-cleared tissue containment system designed to address this safety gap. LapBox introduces a patented dual-wall “bag-in-bag” architecture that creates a sealed containment chamber during tissue extraction, helping prevent tissue spillage during both manual and power morcellation. The system is designed to provide reliable containment while maintaining ease of use within standard laparoscopic workflows.

Technology responds to a growing demand for improved surgical safety as minimally invasive and robotic procedures continue to increase globally. Hospitals and surgeons are seeking solutions that protect patients while also reducing clinical and legal risks associated with tissue dissemination during surgery.

LapBox is currently being used in U.S. hospitals and has demonstrated strong interest from surgeons seeking safer and more reliable containment solutions for tissue removal. By establishing a new safety standard for tissue extraction in minimally invasive surgery, Ark Surgical aims to support better patient outcomes while helping healthcare systems strengthen risk management and surgical best practices.

As robotic surgery adoption continues to accelerate worldwide, technologies that enhance safety without compromising surgical efficiency are becoming increasingly important. LapBox represents a step toward advancing surgical safety and supporting the next generation of minimally invasive and robotic procedures.

## Preclinical Evaluation of the MicroSteer FALCON System for Device-Assisted Endoscopic Submucosal Dissection in a Porcine Gastrointestinal Model

Sergei Vosko<sup>1</sup>, Eyal Ben-Esti<sup>2</sup>, Ahmad Hassan<sup>2</sup>, Ariel A. Benson<sup>3</sup>

<sup>1</sup>*GI Endoscopy, Hadassah Medical Center, Israel*

<sup>2</sup>*Microsteer Ltd., Israel*

<sup>3</sup>*GI Endoscopy, Shaare Zedek Medical Center, Israel*

**Background:** En bloc resection of complex gastrointestinal lesions adoption is limited by steep learning curves, operator dependency, long procedure times, and risk of perforation. We evaluated a novel single-use endoscope-mounted add-on device that decouples knife steering from endoscope manipulation via a joystick-controlled interface in a preclinical in vivo porcine model, comparing its safety, performance, and tissue effects with the current standard-of-care (SOC).

**Methods:** A controlled preclinical study was performed using four live porcine subjects (Landrace, 70-90 kg). A total of 16 simulated lesions (20-50 mm) were marked and dissected across gastric (n=11) and colonic (n=5) sites: 10 using the FALCON™ System (MicroSteer Ltd.) and 6 with SOC technique. Primary endpoints included device-related adverse events (perforation, muscle injury, bleeding) and en bloc resection rate. Secondary endpoints included dissection rate, procedure time, histopathological tissue response, and structured operator usability assessment using NASA Task Load Index. Histological analysis was performed by a blinded GLP-certified laboratory.

**Results:** Both FALCON System and SOC achieved 100% en bloc resection. No FALCON device-related perforations occurred; one perforation in the SOC group was managed with clips. Mean dissection rate was 46.5 mm<sup>2</sup>/min for FALCON versus 24.4 mm<sup>2</sup>/min for SOC. Histopathological evaluation at 48-96 hours demonstrated equivalent tissue healing between the groups, with no evidence of excessive necrosis, transmural inflammation, or device-related pathological findings. Usability scores indicated reduced physical and mental demand, improved knife stability, and enhanced procedural control with FALCON.

**Conclusion:** MicroSteer's FALCON demonstrated a favorable safety profile and superior procedural efficiency compared with SOC in a porcine model. The near-doubling of dissection rate, absence of device-related adverse events, equivalent tissue healing and favorable usability score support the device's potential to lower the technical barrier to ESD, enabling broader adoption of en bloc resection for complex GI lesions. These preclinical findings warrant further evaluation in human clinical trials.

Engineering Nanoscale Hierarchy for Tailored Biomaterial Design

**Zohar Arnon**<sup>1,2</sup>

<sup>1</sup>*Incoming Assistant Professor, Biotechnology Engineering, Ben Gurion University of the Negev, Israel,* <sup>2</sup>*Chemical Engineering, Columbia University, USA*

Sequence-specific biopolymers such as DNA and peptides provide complementary routes to structural precision and functional complexity in materials science. DNA nanotechnology enables programmable control over nanoscale geometry, valence, and assembly pathways, while peptides and proteins offer diverse chemical functionality and emergent material properties. The central question guiding my research is: how can we harness the architectural precision of DNA origami to organize functional biomolecules across length scales and engineer materials with tailored properties?

I will present some of the work done in my postdoc, showcasing how DNA origami assemblies can serve as a platform for nanoscale structural control. Polyhedral DNA origami frames behave as patchy particles, where short single-stranded DNA “sticky ends” mediate directional interactions and drive crystallization into ordered superlattices. By introducing a linker-mediated assembly strategy using complementary double-stranded DNA linkers, we achieved tunable coordination without redesigning the origami frame itself. Modulating linker length induces reversible phase transitions between simple cubic, body-centered cubic, and face-centered cubic lattices, enabling independent control of crystal symmetry and lattice parameters. These results establish a versatile route to programmable three-dimensional architectures spanning the nanoscale to the microscale.

Building on this structural foundation, I will outline a vision for my new lab at Ben-Gurion University integrating peptides and proteins into DNA-engineered frameworks. By positioning functional biomolecules at precise nanoscale coordinates and controlling their spatial density and orientation within larger assemblies, we can decouple structure from function and systematically study how organization governs collective behavior.

This strategy enables the rational design of biomaterials with programmable biological, chemical, and mechanical properties, and opens new avenues for engineering hierarchical materials that operate across scales with unprecedented precision.

# Tailoring the Structure and Antibacterial Properties of Self-Assembled Fmoc-Phenylalanine Nanostructures through Positional Fluorination

Moran Aviv<sup>1,2,3,4</sup>, Noam Rattner<sup>2,3,4</sup>, Dana Cohen-Gerassi<sup>2,3,4,5</sup>,  
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<sup>5</sup>*Materials Science and Engineering, Iby and Aladar Fleischman Faculty of Engineering, Tel Aviv University, Israel*

**Background:** Antimicrobial resistance poses a major global challenge, motivating the development of antibacterial strategies based on functional materials rather than conventional drugs. Inspired by antimicrobial peptides, fluorenylmethoxycarbonyl-phenylalanine (Fmoc-Phe) derivatives can self-assemble into nanostructured hydrogels with inherent antibacterial activity. This study investigates how fluorination number and position modulate their structure–function relationships.

**Method:** A series of mono-, di-, and fully fluorinated Fmoc-Phe analogues was synthesized and characterized using microscopic, spectroscopic, rheological, and X-ray diffraction techniques, complemented by molecular-dynamics simulations and real-time microfluidic monitoring. Antibacterial activity was evaluated against *Streptococcus mutans*, alongside biofilm inhibition and cytocompatibility assays.

**Results:** Fluorination patterns strongly influenced self-assembly, nanofibril morphology, and mechanical properties. Fmoc-3,5-F-Phe formed the stiffest hydrogels, whereas fully fluorinated Fmoc-F<sub>5</sub>-Phe produced weaker, unstable gels. Real-time microfluidic monitoring, X-ray diffraction, and molecular-dynamics simulations confirm hierarchical assembly pathways and more compact aggregation for Fmoc-3,5-F-Phe. Despite structural differences, all hydrogels showed potent antibacterial activity, with several derivatives fully inhibiting bacterial growth at 0.1 mg mL<sup>-1</sup> via membrane disruption and reactive oxygen species (ROS) generation. Biofilm formation was significantly reduced, while materials remained cytocompatible with mammalian cells.

**Conclusion:** These findings establish fluorination patterning as a key design parameter for antibacterial supramolecular hydrogels, supporting their potential in infection-resistant biomedical applications.

## Novel Antibiotic-Eluting Gelatin-Alginate Soft Tissue Adhesives for Various Wound Closing Applications

**Adaya Shefy-Peleg, Meital Zilberman**  
*Biomedical Engineering, Tel Aviv University, Israel*

Antibiotic-loaded bio adhesives have recently gained attention to prevent and treat infections at wound sites while simultaneously closing the tissue.

These materials can reduce the risk of postoperative infections and eliminate the need for systemic antibiotic therapy. Therefore, interest in tissue adhesives as an alternative to conventional wound closure methods has increased in recent decades due to their numerous advantages, including less discomfort, reduced tissue trauma, and lower cost. In the current study, we developed soft tissue adhesives based on gelatin and alginate, crosslinked by carbodiimide.

The antibiotic drug ceftazidime was incorporated for prevention of infection. The effect of the adhesive components on the bonding strength and swelling ratio was evaluated, as well as ceftazidime release profile and biocompatibility tests on fibroblast cells.

The results showed that the bonding strength of the bio adhesives increased with the increase in their component concentrations and the incorporation of drug (antibiotic) molecules decreases the bonding strength and increases the water uptake, probably due to a decrease in the crosslinking density.

Overall, the high bonding strength and good biocompatibility turns these new bio adhesives into a promising alternative for use in wound closing applications.

## Dissolving Microneedles for Systemic and Brain Delivery of Melatonin

Hadar Nimni<sup>1</sup>, Vladisla Nesterenko<sup>2</sup>, Nadeen Bader<sup>1</sup>, Yara Sheeni<sup>2</sup>,  
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Medicine, Hebrew University of Jerusalem, Israel*

Oral melatonin is widely used for the management of insomnia and circadian rhythm disorders; however, its clinical efficacy is limited by poor aqueous solubility, extensive first-pass metabolism, and short systemic half-life. Dissolving microneedles (MNs) offer a minimally invasive strategy to overcome these limitations by enabling rapid and efficient transdermal drug delivery while bypassing the gastrointestinal tract. In this study, dissolving MN arrays composed of hydroxypropyl methylcellulose (HPMC) and polyvinylpyrrolidone (PVP) were fabricated using a vacuum-assisted micromolding technique and evaluated as a transdermal delivery system for melatonin.

Among the tested formulations, MNs containing 10% (w/v) HPMC and 10% (w/v) PVP exhibited favorable mechanical strength and insertion capability. Melatonin was successfully incorporated into the microneedle shafts, achieving a drug loading of  $1.83 \pm 0.05$  mg/MN patch. Fourier-transform infrared spectroscopy and differential scanning calorimetry confirmed molecular dispersion of melatonin within the polymeric matrix, stabilized by intermolecular interactions. In vitro release studies demonstrated rapid dissolution, with approximately 87% of melatonin released within 60 min, while ex vivo porcine skin experiments showed complete microneedle dissolution within 3 min.

In vivo pharmacokinetic evaluation in mice revealed rapid systemic absorption following MN application, accompanied by a prolonged elimination of half-life. Importantly, melatonin was detected in brain tissue, reaching a maximum concentration of  $6.08 \pm 3.65$  ng/g and exhibiting extended residence time, indicating effective central nervous system exposure.

Overall, these findings demonstrate that dissolving HPMC–PVP microneedles represent a promising transdermal platform for melatonin delivery, with potential to improve bioavailability, accelerate onset of action, and enhance therapeutic performance in sleep-related disorders.

## Transmuting Long-Acting Injectables Platforms

**Peter Siman**<sup>1</sup>, Arnon Aharon<sup>1</sup>, Christine Warwar-Damouni<sup>1</sup>, Narmeen  
Matta<sup>1</sup>,  
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Ein Kerem, The Hebrew University of Jerusalem, Israel*

Long-acting injectable (LAI) therapeutics are increasingly recognized as an important modality for improving treatment adherence, pharmacokinetic stability, and patient convenience across multiple therapeutic areas including oncology, metabolic disease, and biologics. However, many currently available technologies rely on solvent-based formulations, complex preparation steps, or are limited in drug compatibility and loading capacity. To address these limitations, IntraGel Therapeutics has developed SRGel, a solvent-free, lipophilic depot platform designed to enable ultra-concentrated, ready-to-use long-acting injectable formulations compatible with small molecules, peptides, and biologics.

Following injection, SRGel forms a surface-eroding depot that enables controlled drug release ranging from days to months while maintaining small injection volumes and compatibility with standard clinical administration routes including subcutaneous, intramuscular, and intratumoral delivery. The platform supports high drug loading exceeding 400 mg/mL and allows the formulation of ready-to-use products without the need for reconstitution or organic solvents.

Clinical validation of the platform is demonstrated through TumoCure, a cisplatin-SRGel intratumoral formulation currently evaluated in a Phase 1b study in patients with locally advanced head and neck squamous cell carcinoma who are ineligible for systemic cisplatin therapy. Early clinical observations indicate favorable safety and tolerability, sustained local drug exposure for approximately two months, and encouraging therapeutic responses including substantial tumor shrinkage in treated patients.

Beyond oncology, the SRGel platform is being applied to multiple pipeline programs including long-acting GLP-1 analog formulations for metabolic diseases, peptide therapeutics, and biologics such as monoclonal antibodies and antibody-drug conjugates. In parallel, IntraGel has secured investment and a strategic collaboration as part of its Series A financing to advance the Phase 2 clinical development of TumoCure while expanding metabolic pipeline programs and monoclonal antibody delivery applications.

Together, these results highlight SRGel as a versatile next-generation platform for ultra-concentrated long-acting injectable therapeutics with the potential to transform drug delivery across multiple therapeutic modalities and disease indications.

## A Novel Device to Enhance the Hemostatic Efficacy of Plasma in Hemorrhagic Events

**Ze'ev Dvashi**<sup>1</sup>, Adam Lee Goldstein,<sup>2</sup> Mordechai Shimonov<sup>3</sup>,  
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Pavel Svoboda<sup>8</sup>, Ondrej Urban<sup>9</sup>, Nir Wasserberg<sup>10</sup>, Vered Yahalom<sup>10</sup>,  
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Republic, Czech Republic*, <sup>10</sup>*Surgery, Hematology and Blood Bank,  
Beilinson medical Center (Rabin), Israel*, <sup>11</sup>*the Division of Laboratories  
and Department of Clinical Biochemistry at Hadassah University  
Hospital in Jerusalem., Hadassah Medical Center, Israel*

**Introduction:** Upper gastrointestinal bleeding (UGIB) is one of the most common acute care emergencies and is associated with significant morbidity and mortality. Plasma transfusion is commonly used to reduce bleeding; however, it may introduce fibrinolytic factors that impair clot stability and contribute to continued bleeding. ClearPlasma is a single-use device designed to process donor plasma prior to transfusion by selectively removing plasminogen, thereby generating plasminogen-depleted plasma (PDP). By reducing fibrinolytic activity, PDP is expected to enhance clot stability, reduce bleeding, and potentially decrease the need for additional blood products. In this study, we evaluated the safety and efficacy of ClearPlasma in patients presenting with acute UGIB requiring plasma transfusion.

**Methods:** An international, multicenter, randomized, double-blind controlled trial was conducted to evaluate the safety and efficacy of PDP transfusion in patients with acute UGIB. Patients receiving PDP were compared with a matched cohort transfused with standard fresh frozen plasma (FFP).

**Results:** Two deaths occurred in the standard FFP group during the 30-day follow-up compared with none in the PDP group. No adverse events were reported during transfusion in the PDP group, whereas two adverse events occurred in the FFP group. Within the first 8 hours, the PDP group demonstrated a smaller increase in D-dimer levels ( $p=0.04$ ), suggesting reduced systemic fibrinolysis. Trends toward shorter time from intervention to discharge (4.7 vs. 6 days,  $p=0.21$ ) and shorter overall hospitalization (5.2 vs. 6.4 days,  $p=0.22$ ) were observed. No platelet transfusions were required in the PDP group compared with 7.7% in the FFP group ( $p=0.032$ ). No major adverse events or transfusion-related serious adverse events were observed in the ClearPlasma group.

**Conclusion:** ClearPlasma was safe and associated with reduced systemic fibrinolytic activity, as reflected by lower D-dimer levels, and a lower mortality rate. The absence of platelet transfusions in the PDP group and trends toward shorter hospitalization suggest potential clinical and resource utilization benefits.

# Poster Presentations

Analysis of High-Resolution X-Ray Images for Hgb (Hemoglobin) Level Detection

**Omri Adler**<sup>1</sup>, John Kennedy<sup>1</sup>, Zohar Keidar<sup>1</sup>, Eyal Bercovich<sup>2</sup>

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<sup>2</sup>*Radiology, Rambam Health Care Campus, Haifa, Israel., Israel*

**Background/Aim:** Chest X-ray images are often available due to routine checks, and have an immediate visual output, while blood samples might take a while to get results. A suggested theory was that there might be an expression of Hemoglobin levels in the chest X-ray images due to slight changes in the absorption (image intensity), and that correlation between fine details within the X-ray images and the Hemoglobin levels within the blood was analyzed.

**Method:** The images went through a deep learning analysis. This analysis starts by drawing the data by batches and reshaping the image into a predefined standard size, then dividing the high-resolution images into small tiles and applying a normalization of the values within the tiles. The next step is to get each tile into 2 consecutive pairs of convolution layer and pooling layer, followed by a fully connected layer. Then the tiles are stacked through an attention layer which weighs the tiles by correlation to prediction and sums them into one weighted features tile. and a final classification decision.

**Results:** A few trials were running on a dataset of 1,500 x-ray images, including different number of epochs (20, 30, 40, 50), and different number of learning rates (0.001, 1e-4, 1e-5, decreasing). The best classification was found while using 40 epochs (50 epochs simply did not improve the results) and using the "decreasing" learning rate with an initial value of 0.001 and reduction pace of 0.5 multiplication every 5 epochs (every 2 epochs and every 7 epochs options were also tested, but without improvement), and it seems to produce an Accuracy of  $218/294=74.15\%$ , Sensitivity of  $179/204=87.75\%$ , Specificity of  $39/90=43.33\%$ , PPV of  $179/230=77.83\%$ , and NPV of  $39/64=60.94\%$ .

**Conclusion:** It seems like there might be a correlation between Hgb levels and chest x-ray images, and further investigation is needed.

## Light- and Ultrasound-Induced Antibacterial Properties of *Pistacia lentiscus* and *Laurus nobilis* Leaf Extracts

**Tigabu Haddis Ale<sup>1</sup>**, Faina Nakonechny<sup>1</sup>, Marina Nisnevitch<sup>1</sup>  
*Department of Chemical Engineering, Ariel University, Israel*

The rapid emergence of antibiotic-resistant bacteria poses a major global health challenge, underscoring the urgent need for alternative antimicrobial strategies. Plant-derived bioactive compounds activated by photodynamic and sonodynamic processes represent promising approaches for bacterial inactivation.

This study evaluated the antibacterial activity of *Pistacia lentiscus* (*Pistacia*) and *Laurus nobilis* (*Laurus*) leaf extracts under light and ultrasonic activation against *Staphylococcus aureus*, methicillin-resistant *S. aureus* (MRSA), and *Escherichia coli*. Crude extracts and their fractions obtained using RP-18 cartridges were investigated to separate highly active components. Under photodynamic activation, *Pistacia* and *Laurus* extracts showed strong antibacterial activity against *S. aureus*, causing significant inhibition after 10 min of light exposure.

Both extracts also demonstrated time-dependent inactivation of MRSA under light irradiation, leading to complete bacterial inhibition after 40 min. In contrast, treatments performed in the dark showed no antibacterial effects, confirming an illumination-dependent mechanism. Under sonication, *Pistacia* extract effectively eradicated *E. coli* after 60 min of ultrasonic treatment, whereas *Laurus* extract showed no significant activity. Fractionation of extracts further enhanced antibacterial performance, as several fractions from both extracts completely inhibited *S. aureus* after only 1 min of light exposure, and one *Pistacia* fraction eradicated *S. aureus* after 3 min of sonication. However, under sonication, none of the *Laurus* fractions achieved complete inhibition of *S. aureus*.

These findings suggest that *Pistacia* and *Laurus* extracts contain photoactive and sonoactive compounds with potential as natural sensitizers for photodynamic and sonodynamic antimicrobial strategies against antibiotic-sensitive and resistant pathogens.

## An Implantable Nitinol-Based Micro-Actuated Drug Delivery Device

Israel Alexandron<sup>1</sup>, Alaa Dar Diab<sup>1</sup>, Tony Jurban<sup>1</sup>, Gal deBotton<sup>1,2</sup>

<sup>1</sup>*Biomedical Engineering, Ben Gurion University of the Negev, Israel*

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**Background/Aim:** Implantable drug delivery systems capable of localized, on-demand dosing are highly desirable for chemotherapy and pain management, as they reduce systemic exposure and associated side effects. However, compact, biocompatible, and MRI-compatible actuation mechanisms remain a key engineering challenge. This work investigates the feasibility of using a Shape Memory Alloy (Nitinol) actuator to drive an implantable micro-syringe for targeted drug administration.

**Method:** A proof-of-concept pumping module was designed, fabricated, and experimentally evaluated. A Nitinol coil spring is mechanically coupled with a bias spring and connected to a syringe plunger. Joule heating induces spring contraction to draw fluid from a subcutaneous reservoir through a one-way inlet valve, while passive cooling to body temperature restores the spring and expels the fluid through an outlet valve, enabling controlled unidirectional delivery. The actuator, syringe, and valves are integrated into a compact cylindrical assembly.

**Results:** The prototype demonstrated thermally driven actuation and pumping. The suction and injection pressures achieved during experiments were equivalent to approximately 25 mmHg, confirming physiologically relevant driving pressures. Each actuation stroke displaced approximately 160  $\mu$ L of fluid, a volume suitable for localized drug delivery and implantable infusion systems. The dimensions of the prototype are 12x12x30 mm<sup>3</sup>. Further miniaturization is feasible.

**Conclusion:** These results demonstrate the practicality of a compact Nitinol-driven actuator for implantable drug delivery. The proposed approach offers a lightweight, scalable, and MRI-compatible solution that may enable long-term localized therapy with reduced clinical burden. Future work will integrate a drug reservoir, power source, and closed-loop control toward a fully implantable system.

## An Active Nitinol-Based Orthosis to Facilitate Mobility in Patients with Drop Foot

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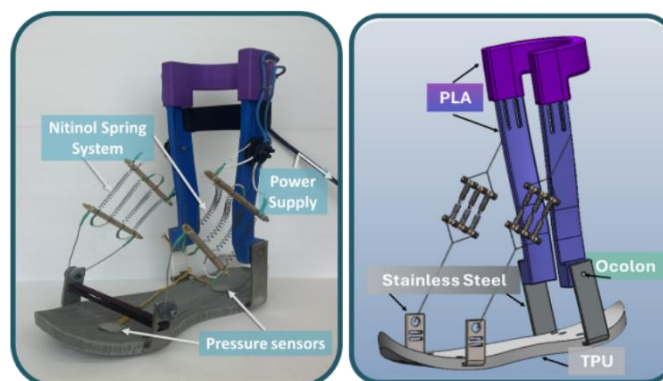
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**Background/Aim:** Drop foot is a neuromuscular impairment characterized by insufficient ankle dorsiflexion during gait, leading to reduced mobility, compensatory walking patterns, and increased risk of falls. Conventional ankle-foot orthoses (AFOs) provide passive support but do not adapt dynamically to the gait cycle. The aim of this study was to develop and preliminarily evaluate an active Nitinol-based AFO designed to provide gait-synchronized dorsiflexion assistance.

**Method:** An active orthotic prototype was developed using electrically heated Nitinol springs as thermally driven actuators exploiting the shape memory effect. A lightweight mechanical structure was fabricated using additive manufacturing. Plantar pressure sensors embedded in the insole were employed for ground-contact phase detection, and a LabVIEW-based control system was used to coordinate sensing and actuation. Mechanical, electrical, and thermomechanical characterization tests were conducted to evaluate actuator force output, contraction behavior, and energy requirements. System-level evaluation was performed under controlled wearable testing conditions.

**Results:** Prototype testing demonstrated Nitinol-spring actuation capable of producing assistance toward ankle dorsiflexion. Limitations were identified in pressure-sensor-based synchronization with the gait cycle and in actuator cooling rate following activation, which currently prevent continuous multi-step walking trials. Consequently, the evaluation focused on controlled assistance during a single step and on defined portions of the gait cycle. Electrical activation of the Nitinol spring resulted in significant spring contraction and a corresponding change in ankle angle during controlled single-step assistance.

**Conclusion:** The results demonstrate the preliminary feasibility of active dorsiflexion assistance using Nitinol-based actuation within an orthotic prototype, while highlighting key challenges that must be addressed for fully dynamic operation. Future work will integrate plantar pressure sensing with inertial measurement units to improve gait-phase identification and synchronization and will explore multi-spring actuation architectures to mitigate cooling limitations. These developments are expected to enable continuous cyclic operation and advance the system toward a wearable, clinically relevant solution.



# Long-Term Learning Analysis Via Image Processing and Kinematic Analysis in Knot-Tying Task

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**Background:** Robot-assisted minimally invasive surgery (RAMIS) has become a surgical cornerstone, yet objective skill evaluation remains challenging. Knot-tying is sensitive to errors, but current performance assessment relies heavily on subjective expert observation or kinematic analysis limited to robotic end-effectors. A critical gap remains: the literature lacks a mathematically grounded framework to characterize the full spatiotemporal behavior of the suture thread. This research develops a robust mathematical framework for thread motion during knot-tying using the da Vinci Research Kit, deriving objective metrics for performance classification and error prediction.

**Methods:** We leveraged the BGU-SKILLS dataset with an integrated computer vision-kinematic modeling framework we developed. Spatial data extraction is grounded in a marker less point estimation paradigm, utilizing DeepLabCut to track high-dimensional thread deformations. Rather than relying on basic curve-fitting, we model the underlying physical motion and behavior of the thread by segmenting the knot-tying operation and applying flexible basis function families. This alignment transforms raw trajectories into robust mathematical signatures representing the underlying logic of the surgeon's gestures.

**Results:** The framework provides a precise, parametric model for thread kinematics. Simulations demonstrate that these mathematical signatures and their derived metrics effectively differentiate between successful and unsuccessful knot-tying attempts. We successfully mapped specific surgical gestures to their mathematical counterparts, with statistical analysis, including t-tests and ANOVA, confirming the model's ability to track fine contours and classify performance quality accurately.

**Conclusion:** We provided a precise framework for spatial thread characterization that correlates with task success. Future work will focus on scaling the analysis across the full BGU-SKILLS dataset to further reinforce the framework. Additionally, we aim to validate these metrics for real-time error prediction and to provide surgeon feedback and training dedicated to improving their surgical skills.

## Engineering a 3D-Bioprinted Model for In Vitro Cancer Research

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Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest forms of cancer, known for its aggressive nature, poor prognosis, and significant resistance to conventional therapies.

PDAC is characterized by a dense desmoplastic stroma and a highly complex tumor microenvironment (TME) with low vascularization that further complicate treatment efforts. A key element in the PDAC TME are the cancer-associated fibroblasts (CAFs), which promote ECM remodeling, support tumor growth, and contribute to the hypovascular nature of tumor. Traditional 2D cell culture models lack the ability to mimic the intricate architecture and cellular interactions found in vivo.

Existing animal models are expensive, time-consuming, raise ethical challenges and poorly replicate human carcinogenesis, often leading to limited translation of findings to human trials. To bridge this gap, we developed a 3D-bioprinted tumor model incorporating patient-derived PDAC organoids, CAFs, and vascular elements to better mimic the complexity of the PDAC TME. The bioprinted constructs successfully recapitulate key in vivo features. Conditions with CAFs led to increased cellularity, extracellular matrix (ECM) remodeling, disrupted vascular organization, and organoid invasion into surrounding stroma.

Notably, immunofluorescence staining revealed E-CAD<sup>+</sup>/CD31<sup>+</sup> co-expression within organoids, suggesting tumor cell plasticity and potential endothelial-like trans-differentiation. In contrast, non-CAF conditions exhibited organized vasculature and well-contained, developed organoids without signs of plasticity. These findings demonstrate the model's capacity to mimic hallmark PDAC characteristics - hypo vascularity, invasion, and heterogeneity, providing a powerful platform for studying cancer progression and therapy response.

## Expanding VR Exposure Therapy for PTSD to Civilian Scenarios

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**Background:** Post Traumatic Stress Disorder (PTSD) is a severe psychological condition which some patients develop after traumatic experiences. One treatment line for PTSD is prolonged exposure, in which patients relive events together with their therapist. Virtual reality (VR) offers great promise for this goal as it provides immersive environments with ecological validity, personalization, and precise tracking capabilities. BraveMind is a Virtual Reality Exposure Therapy (VRET) system designed specifically for PTSD in US army veterans. It enables patients to confront trauma-relevant environments in a controlled and therapist-guided setting. However, its adoption is limited given its focus on the military scenarios in which the trauma occurred and the lack of scenarios with civilian contexts and stressors which contain the everyday PTSD triggers.

**Method:** We seek to address this gap by developing civilian VR scenarios, integrating psychological trigger mechanisms and real-world environments as a basis for testing its generalization beyond military contexts. Specifically, to test this approach we will create the Beer Sheva Central Bus Station, a large civilian center with widespread familiarity and with many potential triggers.

**Results:** We have created the functional prototype scene and successfully tested its usability. This scenario features modular, interactive triggers that allow clinicians to simulate real-world stressors in a controlled urban hub.

**Conclusion:** This project demonstrates the feasibility of adapting military-grade VRET systems for civilian use. By integrating generative 3D tools and modular triggers to quickly create more such environments, the framework provides a scalable solution for treating a broader range of PTSD cases and triggers. Future work will focus on full-scale feasibility evaluations with clinicians to validate the system's effectiveness in real-world therapeutic settings.

# Mechanical Ventilation Induced Increase in Intrapulmonary Postcapillary Resistance Play Key Role in Diminishing Left Ventricle Filling and Cardiac Output

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**Introduction:** Mechanical ventilation (MV) can decrease cardiac output (CO). This decrease in CO is commonly attributed to the well-known effect of MV on the right ventricular (RV) preload and afterload.

**Hypothesis:** MV directly reduces LV filling and CO by decreasing the intrapulmonary vascular transmural pressures, which increases the vascular resistance. The phenomenon is critical in the postcapillary vessels with the lower intravascular pressure, where it can lead to postcapillary collapse.

**Methods:** The hypothesis was validated in healthy sheep (N=6) under regular pressure-controlled ventilation (PEEP:  $2.4 \pm 0.89$  cmH<sub>2</sub>O, driving pressure:  $12.4 \pm 0.89$  cmH<sub>2</sub>O; inspiration/expiratory ratio 1:2). The effects of MV on pulmonary hemodynamics and cardiac functions were measured by simultaneous recording of both right and left pressure-volume loops, utilizing two impedance catheters (CD-Leycom) within both ventricles.

**Results:** During inspiration the RV systolic pressure increased despite the prominent inspiratory decrease in RV end-diastolic volume (EDV) and stroke volume (SV). While the RV systolic pressure increased, there was significant decreases in the LV end-diastolic volume and SV ( $-5.57 \pm 6.16$  [ml],  $-15.98 \pm 19.16$  [%]), measured at the time of peak inspiratory LV systolic pressure relative to the end-expiratory values. Interestingly, in most cases, a progressive decrease in LV filling followed by a progressive decrease in LV-SV was observed immediately from the beginning of inspiration. This decrease in LV filling despite the increase in RV systolic pressure could be explained by an increase in pulmonary vascular resistance to flow. The immediate decline in LV filling could not be attributed to the effects of MV on RV function, which should appear with some delay. The immediate decrease in LV filling strongly supports the immediate development of intrapulmonary postcapillary high resistance to flow, which in turn could have a significant impact in determining CO.

**Conclusions:** MV can decrease the CO and aggravate pulmonary edema by increasing the postcapillary resistance which directly diminishes LV filling. This mechanism is critical in optimizing MV and oxygen delivery to improve ventilated patients' mortality rate.

# From High Flow to Healthy Perfusion: A Turbulent Flow Simulation of Arteriovenous Fistula Steal Syndrome Treatments

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**Background:** Arteriovenous fistulas (AVFs) are the preferred vascular access for hemodialysis, yet they present significant hemodynamic challenges, particularly when complicated by high-flow conditions and dialysis-associated steal syndrome. These complications lead to severe imbalances, resulting in ischemia, stenosis, and vascular remodeling. Surgical interventions, such as revision using distal inflow (RUDI) and banding, aim to manage these challenges, but their influence on post-operative flow dynamics remains complex. This study aims to evaluate the hemodynamic efficacy of RUDI and banding treatments in pathological high-flow AVF models using computational fluid dynamics (CFD).

**Method:** Three-dimensional AVF geometries were modeled, including a high-flow baseline (inlet flow rate of ~4 L/min) alongside four distinct configurations for each treatment technique. Transient CFD simulations were performed under physiological pulsatile flow conditions. Unlike previous studies that relied on laminar flow assumptions, this research utilizes an advanced turbulence-transition model to accurately capture the transitional flow regimes, turbulent jets, and shear layers inherent in high-flow pathologies. Key hemodynamic metrics, including wall shear stress (WSS), velocity, vorticity, and mass flow rate, were quantified.

**Results:** The native pathological model exhibited elevated WSS and disturbed flow patterns. Post-treatment simulations revealed substantial variability: while RUDI technique successfully redirected blood flow and reduced venous mass flow, it introduced undesirable high WSS levels at the artery bifurcation and graft-artery interface. Conversely, banding technique struggled to consistently achieve a desired balance between flow reduction and adequate arterial perfusion, with tighter bands increasing WSS in the distal artery.

**Conclusion:** These findings emphasize that while surgical treatments can restore more physiological flow, accurately resolving turbulence is critical for identifying potential new complication sites. Ultimately, this study underscores the value of advanced computational modeling as a clinical decision-support tool for preoperative planning and risk mitigation in complex AVF repairs.

## Bowel incision closure with a semi-automated Robot-assisted laser tissue soldering system

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Traditional methods for closing gastrointestinal (GI) surgery incisions, like suturing and stapling, present significant challenges, including potentially life-threatening leaks.

These techniques, especially in robot-assisted minimally invasive surgery (RAMIS), require advanced manual skills. While their repetitive and time-consuming nature makes them suitable candidates for automation, the automation process is complicated by the need for extensive contact with the tissue. Addressing this, we demonstrate a semi-autonomous contactless surgical procedure using our novel Robot-assisted Laser Tissue Soldering (RLTS) system on a live porcine bowel.

Towards this *in-vivo* demonstration, we optimized soldering protocols and system parameters in *ex-vivo* experiments on porcine bowels and a porcine cadaver. To assess the RLTS system performance, we compared the pressure at which the anastomosis leaked between our robotic soldering and manual suturing. With the best setup, we advanced to an *in-vivo* Heineke Mikulicz closure on small bowel incision in live pigs and evaluated their healing for two weeks.

The five pigs that successfully completed the procedure, survived without leaks and histology indicated mucosal regeneration and fibrous tissue adhesion. This marks the first *in-vivo* semi-automated contactless incision closure, paving the way for automating GI surgery incision closure which has the potential to become an alternative to traditional methods.

# Multimodal Haptic Interfaces for Upper-Limb Prosthetics: Integrating Force and Thermal Feedback

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**Background:** Upper-limb amputees rely heavily on visual monitoring due to the loss of natural somatosensation. While modern prostheses offer advanced mechanical function, the lack of tactile feedback hinders intuitive grip regulation, increases cognitive load, and contributes to device abandonment. Restoring closed-loop interaction through artificial feedback is essential for functional recovery. Force feedback is critical for grasp stability, while thermal cues provide relevant information regarding material properties and environmental safety. This study investigates how concurrent, non-invasive force and thermal feedback influence task performance and sensory integration in prosthetic-oriented haptic interfaces.

**Method:** A multimodal haptic system was developed comprising a sensorized gripper and a wearable feedback armband. The gripper utilized force-sensitive resistors and thermistors to capture interaction data in real-time. These signals were translated into proportional mechanical pressure via a servo-actuated contracting band (force) and localized heating/cooling via Peltier elements (thermal) delivered to the user's upper arm. Twenty-four participants performed grasp-and-lift tasks with objects of varying weights under two conditions: thermal-only and combined force-thermal feedback. Performance metrics included absolute grip force error, force variability, temperature recognition accuracy, and task completion time.

**Results:** The addition of force feedback improved grip regulation, reducing absolute force error and inter-participant variability compared to the thermal-only condition. This effect was particularly pronounced for heavier objects. Temperature recognition accuracy remained high (95%) and was not affected by the concurrent force modality. A minor but consistent increase in task completion time was observed during combined feedback, suggesting a modest cognitive demand for integrating multiple sensory streams.

**Conclusion:** These findings demonstrate that non-invasive multimodal feedback enhances prosthetic grip control while preserving thermal perception. This practical, low-cost approach to sensory restoration could improve usability and embodiment in future prosthetic interfaces by enabling more intuitive, closed-loop manipulation without requiring invasive surgical procedures.

# Illuminating the Underlying Mechanism of Intracellular Optoelectronic Modulation Using Silicon Nanowires

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Menahem Y. Rotenberg<sup>1,2</sup>

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Strategies to electrically stimulate cells with sub-cellular resolution while minimizing invasiveness have the potential to revolutionize bioelectronic research, particularly in systems where traditional electrodes or genetic tools are limited. Optoelectronics, particularly silicon nanowires (SiNWs), offer a promising approach due to their biocompatibility, spontaneous internalization into a wide range of cell types, and photoelectrochemical properties that allow localized modulation of intracellular environments. SiNW-based probes are increasingly studied, yet the mechanisms by which they trigger intracellular calcium transients remain unclear.

In this study, we mechanistically investigated intracellular calcium fluxes. SiNWs spontaneously internalized into fibroblasts were optically stimulated while calcium responses were recorded via live-cell imaging. Depleting intracellular calcium stores demonstrated that responses originate from internal organelles rather than plasma membrane permeabilization or extracellular influx.

To decouple photothermal and photoelectrochemical effects, we used intrinsic, photoanodic (n-i-p), and photocathodic (p-i-n) SiNWs, enabling comparison of how distinct SiNW configurations influence intracellular signaling. Both photoanodic and photocathodic interfaces generated stronger calcium responses than intrinsic SiNWs, which produce photothermal effects, confirming the dominant role of photoelectrochemical activity in driving intracellular calcium dynamics.

Reactive oxygen species (ROS) dominated the photoanodic effect, providing a strategy to tune oxidative stress and insights into Faradaic contributions. In contrast, the photocathodic response modulated calcium via voltage-gated and calcium-sensitive organelle channels, evidenced by pharmacological inhibition of key organelles and signaling pathways, demonstrating a distinct, ROS-independent mechanism. These complementary pathways highlight that different SiNW doping schemes can be selected depending on whether ROS-associated signaling or minimally oxidative modulation is desired.

This work provides mechanistic insights into SiNW-mediated intracellular modulation, guiding development of leadless optoelectronic systems for precise, cell-specific interrogation in 3D constructs. By separating photothermal, photoanodic, and photocathodic effects, these findings lay the foundation for safe, efficient, and spatially precise intracellular bioelectric modulation and support integration of SiNWs into bioelectronic and biomedical applications.

# Mechanical Properties and Stress Shielding Analysis of Ti-6Al-4V TPMS Lattice made via SLM for Hip Implant Application

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This research examines how lattice structures can enhance the desired properties of Ti-6Al-4V hip implants (femoral stems) manufactured by SLM. Titanium-based materials are widely used in medical applications due to their high mechanical and corrosion resistance properties. Ti-6Al-4V is applicable for hip implants because of its low Young's modulus, good tensile and fatigue strength, and biological compatibility.

Lattice structures determine the mechanical and biological properties (osteointegration rate) of titanium made implants. They are generally categorized into strut-based and surface-based families. Strut-based lattices consist of repeating unit cells formed by intersecting beams, called struts, which often exhibit stress concentration at the connection points (nodes), which is undesirable. In contrast, surface-based lattices are composed of repeating unit cells derived from triply periodic minimal surfaces (TPMS), featuring smooth and continuous surfaces that reduce stress concentration and improve strength.

For this reason, the Gyroid TPMS lattice was chosen. Its advantages include a high surface area to volume ratio, easier adjustment of geometric parameters, and a continuous structure that allows improved fluid flow without enclosed voids. The TPMS Gyroids with 4 variations of geometrical parameters (cell size and sheet thickness) were additively manufactured by SLM machine from Ti-6Al-4V plasma atomized powder.

Compression testing was performed to determine the effective compressive modulus of the gyroid lattices, which serves as an initial indicator of stiffness matching with bone and the potential for reducing stress shielding.

## A Feedback Scaffold for Predictive Control in de novo Motor Learning

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Skilled motor behavior relies on both corrective feedback and predictive feed forward control, yet how their contributions evolve with practice remains unclear, partly because most paradigms study learning within a single day using discrete movements, rather than tracking the continuous dynamics of control as skill develops across multiple days.

In this work, we studied de novo motor skill acquisition using a novel continuous mirror-reversal visuomotor tracking task practiced over five days, allowing dissociation of control mechanisms through frequency-based analysis. We observed a robust temporal separation between learning processes: early learning was dominated by rapid online feedback corrections expressed primarily at low movement frequencies, whereas predictive feed forward control emerged gradually with extended practice and became essential for successful performance at higher frequencies where sensory feedback is intrinsically delayed and ineffective.

Cursor-jump perturbations showed that feedback responses adapted early, whereas changes in initial movement direction of point-to-point reaching evolved slowly, mirroring the time course of high-frequency improvements. These results provide direct quantitative evidence for a dynamic transition from feedback-dominated to feedforward-dominated control during skill learning. A recurrent neural network model in which an adaptive feedback controller (cerebellar-like) supplies a teaching signal to a predictive policy (cortical-like) reproduced the key behavioral signatures.

Together, our findings establish a behavioral dissociation between feedback and feedforward learning in a continuous task and provide a computationally grounded perspective consistent with the observed learning dynamics.

# Acceleration of Molecular Cardiac MRI using a Physics-Aware Vision Transformer

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**Background:** Chemical exchange saturation transfer (CEST) MRI provides non-invasive detection of biomarkers for myocardial creatine concentration, intracellular protein levels, and tissue fibrosis.

These molecular properties offer important insights into pathologies like heart failure with preserved ejection fraction (HFpEF), a pathology that remains clinically challenging to identify and is associated with increasing mortality rates.

However, the long scan times associated with traditional cardiac CEST MRI hinder its routine use in the clinic. This work aims to substantially reduce scan time by developing a vision-transformer-based deep-learning framework for image reconstruction.

**Methods:** A physics-aware vision transformer framework was developed (Fig. 1) to receive both under sampled radial k-space trajectories and acquisition-parameter information as input. The transformer was trained to reconstruct high-SNR, high-quality images that reflect an oversampled target (1000 spokes, 3.33x beyond Nyquist). Heart and liver molecular MRI datasets were acquired from 142 mice using a 7T Bruker MRI system. The radial trajectories were under sampled to 192 spokes and reconstructed using the BART NUFFT toolbox. Data augmentation (rotations and flips) was performed, and the loss was defined as a combination of SSIM and L1.

**Results:** Validation on an unseen dataset (2,542 images from 14 mice) achieved a normalized root-mean-squared error (NRMSE) of  $3.3 \pm 1.08$  [%], a structural similarity index (SSIM) of  $0.85 \pm 0.02$ , and a peak signal-to-noise ratio (PSNR) of  $30.26 \pm 2.5$  dB (Fig. 2a). In all cases, the improvements were statistically significant ( $p < 0.001$ , Fig. 2b) compared to the NUFFT-reconstruction and represented an acceleration of 36% compared to Nyquist (and 80% compared to the oversampled target).

**Conclusion:** A transformer-based framework for accelerating cardiac MRI scans was developed and validated on extensive mouse data. The successful reconstruction of both liver and cardiac anatomy and molecular information highlights the model's generalization capabilities, suggesting its potential for diverse clinical applications.

# Anatomical Token Uncertainty for Transformer-Guided Active MRI Acquisition

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Compressed Sensing MRI (CS-MRI) accelerates scans by reconstructing images from under-sampled k-space data, posing two challenges: where to sample and how to reconstruct. Adaptive CS-MRI addresses these by dynamically selecting measurements tailored to patient-specific anatomy.

In this work, we propose a novel active sampling framework that utilizes a pretrained anatomical tokenizer and a Transformer-based reconstruction model. By operating in a quantized latent space, our model constrains reconstructions to anatomically plausible features, providing a robust priority even at high acceleration factors.

We introduce and compare three distinct active sampling policies: (1) Latent Entropy Selection (LES), a zero-shot approach that identifies k-space lines by projecting patch-wise token entropy into the k-space domain; (2) Gradient-based Entropy Optimization (GEO), which identifies regions of maximum uncertainty reduction via the k-space gradient of a total latent entropy loss; and (3) Cross-Attention Token Selection (CATS), an architecture that utilizes learned k-space tokens to query image patches for latent refinement.

We evaluate our framework on the fast MRI Knee and Brain datasets at 4x, 8x, and 16x acceleration. Our results demonstrate that our active policies outperform state-of-the-art baselines in perceptual metrics (LPIPS, DISTS) and feature-based distances (SSFD).

# Development of Sports Protectors Based on 3D-Printed Anisotropic Lattices

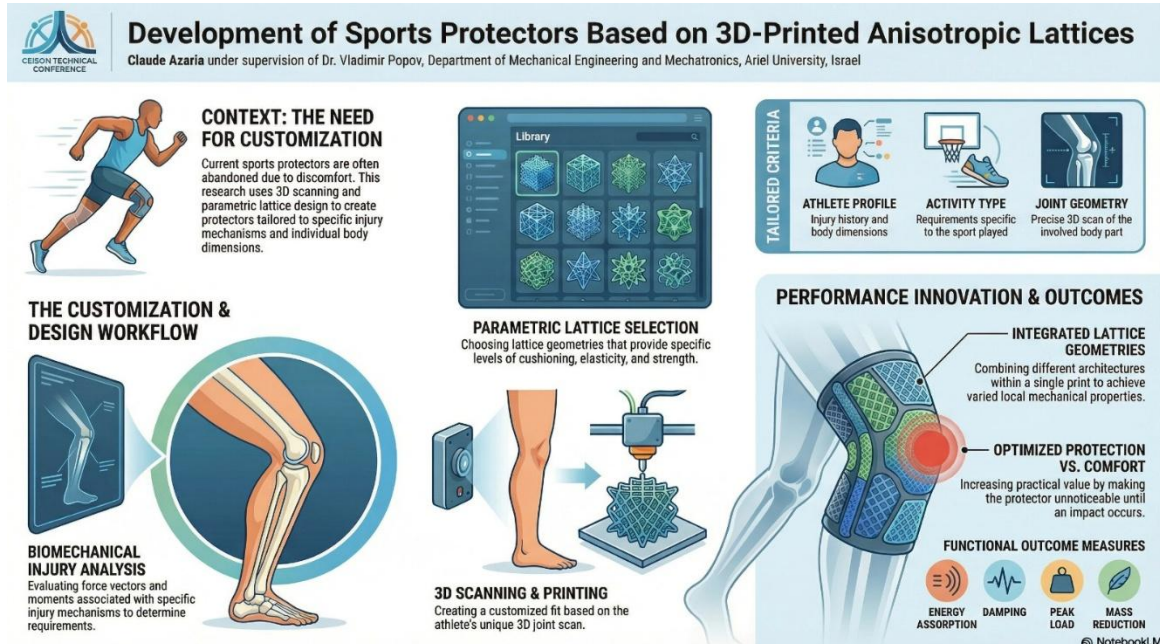
Claude Azaria, Vladimir Popov

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The quality of sports protective gear is primarily defined by the balance between protective performance and comfort. Many athletes currently avoid wearing necessary gear due to discomfort, highlighting a need for protectors that remain unobtrusive during normal activity but provide high efficacy during extreme sport activities.

This research proposes a novel approach to developing customized sports protectors by leveraging 3D scanning and additive manufacturing to match an athlete's specific body dimensions, injury profile, and sport-specific requirements. The central objective is the development of a family of anisotropic lattice structures with diverse cushioning, flexibility, and strength properties. The primary innovation of this work is the integration of multiple lattice geometries within a single 3D-printed component. This allows for the achievement of a broad spectrum of local mechanical properties, such as energy absorption, stiffness and damping, tailored to the specific functional needs of different regions of the protector.

By using parametric design models, these architectures can be precisely adapted to withstand the specific mechanical loads, vectors, and moments acting on a joint during physical activity or injury-related events. Using the knee joint as a primary example, this methodology demonstrates how customized 3D-printed designs can transition from injury analysis to high-performance mechanical solutions that prioritize both safety and user fit. This generic and adaptable framework offers a significant advancement in the production of personalized, high-performance protective equipment for various sports and joints.



Similarly Fluent? Similarity Analysis in Children with Epilepsy and Children with Dyslexia in Relation to Reading Fluency: An fMRI Study

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Reading fluency relies on Audiovisual integration (AVI) – the synchronization of visual and auditory systems to link letters with sounds, as well as on executive functions regulating this process. We investigated whether the shared dysfluency in children with Rolandic epilepsy (RE) and children with dyslexia, who exhibit reading difficulties (RD), stems from similar neural mechanisms compared to typically developing (TD) children. Functional magnetic resonance imaging (fMRI) data were collected from 103 7-14-year-old children (mean age: 10.52, SD: 1.96) while they performed a lexical decision task and during a resting-state scan. Functional connectivity between sensory networks (AV) and four cognitive control networks (i.e. cingulo-opercular (CO) network involved in task maintenance, the frontoparietal (FP) network involved in adaptive control, and the dorsal and ventral attention networks). Group comparisons were conducted using a Representational Similarity Analysis (RSA).

Results indicated the greatest scores in reading fluency in the TD group, followed by the RD group and then RE. Neurobiologically, in the lexical decision task, TD children showed the strongest internal connectivity within the CO network compared to the other two groups. The RD group showed greater functional connectivity between the auditory and FP networks than the RE and TD groups. The RE group showed reduced functional connectivity within the CO network compared with the TD group but did not exhibit the elevated auditory-FP connectivity observed in the RD group. At rest, the RD group showed stronger functional connectivity within the dorsal attention network than the RE group.

Results suggest that RD relies on compensatory auditory-FP connectivity, whereas RE is characterized by reduced CO integrity without such compensation. This indicates that similar reading dysfluency in these groups stems from distinct neural mechanisms, requiring targeted interventions.

# Quantitative AI-Boosted Molecular Magnetic Resonance Fingerprinting of Lipids and Macromolecules in Multiple Sclerosis in Vivo

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**Introduction:** Multiple sclerosis (MS) is characterized by immune-mediated demyelination and neurodegeneration. While conventional MRI offers lesion detection, it lacks specificity for the underlying biochemical changes. Molecular MRI techniques, such as saturation transfer, may offer an alternative by detecting the signals associated with the semisolid macromolecule magnetization transfer (MT) effect (which reflects myelin integrity) and the relayed nuclear Overhauser effect (rNOE) signals at -3.5 ppm and -1.6 ppm from water, which inform on aliphatic protons and mobile macromolecules, respectively. However, simultaneous quantification of these overlapping exchanging pools is a long-standing challenge. Here, we developed an AI-boosted molecular MR fingerprinting (MRF) approach for the rapid quantification of these molecular phenomena and validated it in a cuprizone mouse model.

**Methods:** Demyelination was induced in C57BL/6J male mice (n=12) via a 7-week cuprizone diet, followed by a 5-week recovery. Longitudinal 7T MRI was performed at baseline and at weeks 4, 7, and 12. Three sequential magnetic resonance fingerprinting (MRF) protocols were acquired in under 6 minutes to encode the semi-solid MT and rNOE (at -3.5 and -1.6 ppm) information into unique signal trajectories. A deep neural network was trained using 20 million synthetic signals to quantify the proton volume fraction (f) and exchange rate (k) of each compound pool.

**Results:** In the corpus callosum, the proton volume fraction of the semi-solid MT (fss) and the rNOE pools was significantly decreased during the treatment phase (Fig. 1). Following treatment cessation, fss showed a significant recovery trend, while both rNOE pools displayed a clear visual trend toward recovery. Crucially, while conventional T1 and T2 values showed significant elevation only at peak demyelination, all MRF-derived proton volume fractions detected the pathology as early as week 4, demonstrating superior sensitivity to early-stage damage.

**Conclusion:** We developed a rapid, AI-boosted molecular MRI framework capable of isolating and quantifying specific MS-related biomarkers in vivo. This method offers higher specificity and sensitivity compared to conventional MRI, enabling earlier intervention and monitoring.

# Predictive Sensor Fusion Architecture for CPG-Driven Lower-Limb Exoskeleton Gait Control

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**Background:** Lower-limb exoskeletons are vital for mobility assistance. Traditional control architecture often utilizes Electromyography (EMG) as a direct proportional input to actuators, an approach that frequently results in arbitrary, rigid kinematics and high susceptibility to muscle fatigue. Meanwhile, Electroencephalography (EEG) studies in this domain frequently focus on post-hoc, offline action classification rather than real-time application. Achieving intuitive control requires predicting user intent prior to movement execution and translating it into an adaptable kinematic response.

**Method:** This study proposes a novel control architecture shifting from traditional direct-input EMG to a predictive sensor fusion approach. We focus on the Pre-Motor Cortex to decode and predict movement intent via EEG just before actual execution. Concurrent EMG signals are integrated – not as direct continuous actuator inputs – but to refine intent classification and ensure precise temporal synchronization. Upon accurate intent validation, a biomimetic Central Pattern Generator (CPG) network governs the gait. To validate this framework, a custom 6-DoF motorized exoskeleton platform was developed, designed with consideration for the anatomical structure of the leg and mass distribution along the limb. The research is currently in its initial experimental phase, establishing a protocol to evaluate the system on healthy subjects during baseline walking tasks.

**Results:** As the study is currently in its preliminary experimental stages, quantitative data is still being collected. However, it is anticipated that extracting predictive cues from the Pre-Motor Cortex, synergized with the temporal precision of EMG, will bridge the gap toward real-time intent classification compared to conventional post-hoc methods. Furthermore, decoupling EMG from direct motor control and utilizing CPG-based trajectory generation is expected to produce an adaptive, compliant gait rather than a rigid mechanical response, maintaining essential actuator backdrivability.

**Conclusion:** By prioritizing the prediction of cortical intent via EEG and synergizing it with EMG for precise classification and execution timing, this CPG-driven architecture represents a highly promising framework. It provides a robust foundation for developing responsive, real-time, and adaptive assistive robotic systems.

## Digital Implementation of a Scalable Virtual-Cell Framework

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Biological systems exhibit nonlinear, stochastic, and highly parallel dynamics that challenge conventional experimental and computational approaches. Understanding how molecular interactions determine cellular behavior is central to biomedical engineering, particularly in areas such as drug-response modeling, synthetic gene circuits, and systems-level disease analysis.

Although virtual-cell models provide a powerful framework for investigating intracellular mechanisms, large-scale simulations remain computationally demanding and difficult to scale efficiently using traditional software-based platforms. This project proposes the development of fully digital virtual-cell architecture designed to enable scalable and hardware-efficient modeling of cellular dynamics.

The proposed framework relies on a discrete-time representation of essential cellular mechanisms, including transcription, molecular production, degradation, and threshold-based activation, implemented through hardware-description-based state-update models. Deterministic reaction kinetics are translated into structured logic equations, while stochastic behavior is incorporated through digitally generated random processes to emulate biologically relevant variability, including Poisson-like reaction events. The architecture is modular by design, allowing replication of virtual-cell units to support large-scale parallel simulations while maintaining resource efficiency.

The project is currently in the architectural design and validation phase, with ongoing work focused on integrating stochastic modules, optimizing hardware utilization, and evaluating scalability through simulation-based analysis. By translating cellular dynamics into a structured hardware-oriented framework, this approach seeks to bridge systems biology and digital design, providing a foundation for efficient large-scale biological simulations and future bio-digital platforms.

# Targeted Therapeutic Release via Ultrasound Nanodroplets for Tumor Therapy

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**Background:** Solid tumors present significant treatment challenges due to dense structures and immunosuppressive microenvironment, which limit effective drug and gene delivery. To address this, we present a non-viral, non-invasive, ultrasound-responsive nanodroplet platform designed for targeted delivery and mechanical tumor disruption. We generate stable nanodroplets.

**Method:** Lipid-based nanodroplets (NDs) with a perfluorohexane core, either blank or loaded with fluorescent-molecules or 5-fluorouracil (5-FU) chemotherapy, were synthesized using microfluidics. Characterization included size-distribution, morphology, stability, acoustic vaporization thresholds, and controlled drug release tests. In vitro and in vivo studies in a breast cancer mouse model assessed cavitation dynamics, NDs biodistribution, mechanotherapy effects, tumor growth inhibition, and increased survival time.

**Results:** NDs exhibited long-term stability (1 month) and in vivo stability for at least 24 h, maintaining a monodisperse size 10 dB contrast enhancement at 25-42°C and up to MI 1.9, and 5-FU-loaded NDs achieved a ~3-fold increase in drug release. 5-FU-loaded NDs facilitated controlled drug release, reducing cell viability to 7% compared to controls, while in vivo, fluorescent NDs extravasated into tumors and penetrated tumor cells. At 24 h, tumor fluorescence was ~3-fold higher than controls, whereas liver signal returned to baseline. Ultrasound treatment with 5-FU NDs significantly inhibited tumor growth and prolonged survival (~74% increase vs untreated, ~70% vs 5-FU NDs alone, and ~40% vs ultrasound with blank NDs).

**Conclusion:** This work integrates microfluidic production of NDs, core-loading of 5-FU and fluorescent molecules, and dual-transducer ultrasound into a single theranostic platform. The system enables targeted drug release and imaging, demonstrating strong efficacy against breast cancer with potential for broader solid tumor applications.

## 3D Bioprinting of Elastic Macro-Vessel Networks within Multi-Layered Tissue Flaps

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The fabrication of large, implantable tissue flaps relies on the spatial complexity and physiological relevance of engineered macro-vessels. While current designs and methods utilize a single vessel, extending vascular coverage to support larger tissue volumes remains a key objective.

Hierarchical vascular structures have been incorporated into engineered tissues to address this, and aligning the macro-vessels mechanical behavior with native arteries and veins remains a priority. This will help to optimize flaps function under physiological flow and ensure long-term stability. Specifically, native vascular mechanics rely on the synergistic contribution of extracellular matrix components, particularly elastic elements.

Reproducing this synergy presents a significant opportunity to enhance current bioink formulations. We aim to develop elastic macro-vessel networks integrated within multi-layered tissue flaps to enable immediate perfusion, physiological compliance, and scalability toward larger tissue constructs. To achieve this goal, we combine extrusion-based 3D bioprinting with injection molding to create geometrically complex, perfusable vascular architectures. This hybrid approach facilitates the integration of elastic biomaterials to match native vessel mechanics. As a step toward upscaling, we fabricated a U-shaped tissue flap model containing a centrally embedded PLLA-PLGA macro-vessel, designed to function as an arterio-venous shunt.

Extrusion-based 3D bioprinting was utilized to construct the surrounding multi-layered tissue, incorporating spatially organized skeletal muscle, smooth muscle, endothelial cells, and pericytes. In vivo testing in ovine models validated this construct as a proof-of-concept for flap upscaling and arterio-venous integration. In parallel, to enable greater geometrical complexity, we developed an injection molding strategy using sacrificial inserts.

This technique successfully produced hollow, multi-generational macro-vessel networks, including complex 3D bifurcations, using both polymers and hydrogels. Collectively, these approaches define a scalable framework for engineering perfusable, mechanically relevant vascularized tissue flaps.

## Leadless Optoelectronic Artificial Axons for Studying Activity-Dependent Myelination

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Activity-dependent myelination plays a crucial role in shaping neural circuit function. However, current *in vitro* models rely on biological axons that are heterogeneous and difficult to control.

While existing artificial axon (AA) systems successfully replicate axonal geometry, they lack electrical activity—an essential physiological signal known to influence oligodendrocyte (OL) differentiation and myelin formation. We aimed to develop an optoelectronic active silicon-based AA platform that decouples geometry and excitability from biological variability, providing a stable and tunable model for studying activity-dependent myelination.

Two- and three-dimensional silicon “axons” with micron-scale diameters were microfabricated using standard cleanroom processes on SOI wafers. The devices were integrated with LED-based optical stimulation to induce localized photo-generated extracellular currents. Patch-clamp recordings were used to quantify photocurrent amplitude and temporal dynamics under patterned illumination mimicking physiological firing regimes. Primary rat oligodendrocyte lineage cells were cultured on active and non-active structures, and cell survival, process extension, and myelin-related marker expression were assessed by immunofluorescence analysis.

Silicon AAs generated robust and reproducible photocurrents in the picoampere range under optical stimulation. OL lineage cells demonstrated stable attachment and process extension on both 2D and 3D configurations. Preliminary comparisons between stimulated and non-stimulated axons indicate activity-dependent modulation of myelin-associated marker expression.

This hybrid bioelectronic platform overcomes the limitations of geometry-only artificial axon models by introducing controlled electrical functionality. It enables systematic investigation of how axonal activity, geometry, and material properties regulate myelination and remyelination, and provides a scalable framework for mechanistic studies and future drug-screening applications.

# A Data-Driven Approach for SFA Restenosis Prediction: Integrating Patient-Specific CFD and Machine Learning

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Despite advances in endovascular treatments, stenosis of the superficial femoral artery (SFA) remains a major cause of critical limb ischemia. While stenting is a primary intervention, approximately 30% of patients develop restenosis within the first year—often without clinical symptoms. Stent edge restenosis (SER) is a common complication in this process, driven by complex mechanical forces and flow disturbances. This study aims to predict SER by analyzing the interplay between arterial geometry and local hemodynamics in the proximal stent-edge region.

Patient-specific 3D models were reconstructed from CT scans of patients who developed restenosis within one-year post-stenting and a control group who did not. Computational fluid dynamics (CFD) simulations were performed to quantify local hemodynamic parameters.

Results indicate significant group-level differences in hemodynamic conditions. Specifically, patients developing restenosis exhibited elevated Wall Shear Stress (WSS), Oscillatory Shear Index (OSI), and Relative Residence Time (RRT) at the proximal stent edge post-intervention. Arterial geometric features, such as curvature and tortuosity, demonstrated high inter-patient variability and strong associations with these hemodynamic disturbances.

Statistical and machine learning analyses revealed distinct patterns. Principal Component Analysis (PCA) showed that geometric and hemodynamic features account for 71.9% of the total variance. Linear Discriminant Analysis (LDA) indicated a separation trend driven by a combination of RRT, OSI, and curvature metrics. Notably, a Decision Tree classifier achieved complete separation between the restenosis and non-restenosis groups based solely on OSI and RRT thresholds.

These findings suggest that while arterial geometry predisposes the vessel to disturbed flow, local hemodynamic markers (OSI, RRT) are potent predictors of SER. Integrating these parameters provides a robust framework for identifying patients at high risk of restenosis, potentially guiding patient-specific surveillance and treatment strategies.

# Daily Living Gait Measures Derive from Wrist Accelerometers and a Deep Learning Pipeline are Associated with Postmortem Brain Pathologies

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**Background:** Wrist-worn accelerometers enable continuous gait monitoring during daily living, capturing mobility patterns that brief supervised assessments may miss. While physical activity measures from these devices reflect overall movement levels, detailed gait-specific metrics may provide unique insights into underlying brain pathology.

**Objective:** To determine whether daily-living gait metrics from wrist accelerometry are associated with postmortem pathologies, even after adjusting for demographics, clinical gait speed, and general physical activity measures.

**Methods:** We analyzed data from older adults in the Rush Memory and Aging Project who had wrist accelerometry (10 days) and postmortem neuropathological evaluation (N=236). Daily living gait features (walking volume, speed, cadence, stride length, regularity) were extracted using ElderNet, our recently developed self-supervised deep-learning foundation model for daily-living gait analysis. ElderNet leverages self-supervised pretraining on UK Biobank wrist accelerometry (N=100,000) and was fine-tuned on Rush Memory and Aging Project data (N=820) to optimize performance for older adults and individuals with impaired gait. We performed hierarchical regression, sequentially adding: (1) demographics (age, sex, education), (2) clinical gait speed from 8-foot walk, (3) physical activity metrics, and (4) daily living gait features (3 principal components). Eleven neuropathologies were examined, including Alzheimer's disease, Parkinson's disease and vascular pathologies.

**Results:** Daily-living gait metrics explained substantial additional variance beyond the base model (demographics + clinical speed + physical activity) for all pathologies examined (Figure 1). The mean added  $R^2$  was 15.3%, ranging from 4.3% (hippocampal sclerosis) to 37.3% (tangle density). Notable increments were observed for Lewy body pathology (+23.1%), arteriolosclerosis (+21.3%), cerebral amyloid angiopathy (+20.0%), and cerebral atherosclerosis (+16.8%).

**Conclusions:** Daily-living gait metrics from wrist accelerometry provide unique information about brain pathology that is not captured by demographics, brief supervised gait assessment, or general physical activity measures. These findings support the value of continuous, free-living gait monitoring for understanding the neural substrates of mobility decline in aging.

## AI-Driven Patient Phenotyping for ICU Nutrition

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**Background/Aim:** Critically ill patients exhibit marked heterogeneity in nutritional risk and gastrointestinal tolerance, making decisions regarding supplemental parenteral nutrition (SPN) challenging and often reliant on clinical judgment. This study aims to develop an AI-based phenotyping framework that identifies clinically meaningful ICU subgroups associated with SPN-related outcomes, supporting future data-driven decision support in critical care nutrition.

**Method:** We analyzed adult SPN-treated ICU patients from Beilinson Hospital (2011-2018), excluding ICU stays  $\leq 7$  days and records with missing key nutrition variables. After preprocessing (standardization, skewness transformation, and correlation-based feature selection), we clustered patients using K-prototypes, selecting the final model by Elbow/Silhouette metrics and clinical interpretability. ICU mortality, 90-day mortality, and length of stay were used for post hoc validation.

**Results:** The cohort included 273 patients; K-prototypes identified three phenotypes ( $n = 90/104/79$ ). SPN timing differed across clusters ( $p = 0.001$ ), driven by Cluster 0 having the highest rate of Late SPN (47.78%) and being significantly different from both Clusters 1 and 2 after adjustment. Mortality differed by phenotype (ICU  $p = 0.010$ ; 90-day  $p = 0.001$ ), with the lowest rates in Cluster 0 (ICU 21.11%, 90-day 27.78%). Clinically, Cluster 0 was younger with lower kidney disease prevalence, whereas Clusters 1-2 were older and higher-risk, including an obese subgroup with high kidney disease (Cluster 1) and an underweight subgroup with higher GI burden and sepsis (Cluster 2).

**Conclusion:** Three clinically interpretable phenotypes among SPN-treated ICU patients differed significantly in SPN timing and mortality risk, highlighting heterogeneity within this population. The phenotype-specific patterns in SPN initiation - driven by a Late-enriched cluster contrasted with Early-enriched higher-risk profiles - support future phenotype-guided stratification to inform more personalized SPN-related decision support in critical care.

# Ophthalmology Foundation Models for Clinically Significant Age Macular Degeneration Detection

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Self-supervised learning (SSL) has enabled Vision Transformers (ViTs) to learn robust representations from large-scale natural image datasets, enhancing their generalization across domains. In retinal imaging, foundation models pretrained on either natural or ophthalmic data have shown promise, but the benefits of in-domain pretraining remain uncertain.

To investigate this, we benchmark six SSL-pretrained ViTs on seven digital fundus image (DFI) datasets totaling 70,000 expert-annotated images for the task of moderate-to-late age-related macular degeneration (AMD) identification. Our results show that iBOT pretrained on natural images, achieves the highest out-of-distribution generalization, with AUROCs of 0.80-0.97, outperforming domain-specific models, which achieved AUROCs of 0.78-0.96 and a baseline ViT-L with no pretraining, which achieved AUROC of 0.68-0.91. These findings highlight the value of foundation models in improving AMD identification and challenge the assumption that in-domain pretraining is necessary.

Furthermore, we release BRAMD, an open-access dataset (n=587) of DFIs with AMD labels from Brazil.

# Novel Edible Bioinks for Cultivated Meat: Evaluating Feasibility and Effects on Intestinal Epithelium

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The increasing demand for sustainable and ethical protein alternatives has accelerated the development of cultivated meat technologies, with bioprinting emerging as a key approach for structuring edible tissues. Plant-derived, food-grade bioinks have been explored to support cell attachment and tissue formation; however, challenges remain in achieving scalable, high-throughput fabrication while maintaining structural precision and food safety requirements. At the same time, the design of bioinks suitable for food applications remains challenging, as many high-performance formulations developed for bioprinting in biomedical contexts rely on non-food-grade components that may raise regulatory and safety concerns when considered for edible use.

This project aims to evaluate the feasibility and safety of novel protein-based bioinks designed for cultivated meat. The bioinks were optimized for bioprinting and used to fabricate mini-steak-shaped constructs containing bovine satellite cells. The constructs were cultured, and the bioinks were evaluated for their suitability to support cell growth and differentiation.

To assess the potential health impacts of consuming such bioinks, a three-dimensional human intestinal organoid-based platform was developed. This platform preserves multicellular architecture and functional differentiation, making it an advanced model for studying bioink uptake and epithelial responses. Using this novel model, we investigate the uptake of the bioinks and assess their effects on epithelial health, including barrier integrity, viability, and functional cellular responses.

Overall, this study bridges advanced bioprinting and food safety evaluation to address a critical knowledge gap in the scalability and safety of cultivated meat technologies. By focusing on food-grade bioinks and a physiologically relevant intestine model, this work provides essential insights into the biological responses to edible biomaterials. Together, these findings support the development of scalable bioprinting approaches for cultivated meat production.

## Guiding Epidural Needle Insertion Training with Task-Specific Metrics and Motor Control Principles

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Epidural administration involves injecting anesthetics into the epidural space (ES) using an epidural (Tuohy) needle and a ‘loss of resistance’ (LOR) syringe to sense tissue stiffness. Complications, such as accidental dural punctures and failed epidurals, often arise from inexperience. Robotic simulation provides a safe training alternative for novices, enabling extensive practice and objective skill assessment through kinematic data.

Towards this goal, we developed a simulation-based training protocol using a haptic bimanual simulator we previously designed, incorporating task-related variability and proficiency-based progression (PBP) feedback. Reanalyzing data from anesthesiologists that were collected in a previous experiment, we identified successful strategies: increased number of probing movements with the LOR syringe, especially in the three layers preceding the ES, and reduced needle velocity near the ES, which were used as performance metrics. In our second experiment, forty healthcare students were divided into four training groups to assess the effects of variability and PBP feedback on skill acquisition.

No difference in success rates highlighted the importance of alternative metrics for evaluating performance. PBP feedback improved probing strategies, whereas variability did not. Since neither proficiency-based progression (PBP) nor motor variability led to meaningful improvements in velocity control, we are currently evaluating alternative instructional strategies. In addition to a control group, we tested three instruction conditions, all incorporating depth markers on the epidural needle. These markers enhance realism and may support implicit integration of spatial and temporal cues relevant for velocity estimation.

The conditions include: (i) depth markers only; and two velocity-feedback conditions providing information relative to a target velocity range: (ii) post-task knowledge of results, and (iii) a real-time binary indicator. We compare performance across the four groups, as well as generalization and robustness under multitasking disruptions, to determine which approach most effectively supports acquisition of this critical skill.

# Parallel and Targeted Cell Electroporation via Optoelectronically Controlled Janus Micromotors

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**Background:** Self-propelling Janus micromotors have emerged as powerful tools for single-cell manipulation, acting as mobile “floating microelectrodes” that generate strong localized electric-field gradients under external electrical excitation. These localized fields enable site-specific dielectrophoretic trapping and electroporation. However, most conventional electric-field-based platforms rely on globally applied fields, which lack spatial selectivity and restrict independent control over multiple micromotors and their interactions with individual target cells. The aim of this study is to develop a platform that enables parallel, programmable, and highly localized electroporation of selected cells using electrically actuated Janus micromotors.

**Method:** We present an optoelectronic actuation platform in which dynamically projected light patterns onto a photoconductive substrate generate reconfigurable virtual electrodes under an applied AC voltage. These light-defined electrodes produce spatially confined electric fields that allow independent and parallel guidance of multiple Janus micromotors along prescribed trajectories. During navigation, illumination intensity is precisely controlled to maintain cells under minimal or near-zero background electric-field exposure. Once micromotors reach selected target cells, the projected light patterns are dynamically modulated to enable controlled micromotor–cell contact. Localized electroporation is then triggered using short-duration continuous or pulsed AC excitation.

**Results:** Upon contact, the Metallo dielectric asymmetry of the Janus micromotors produces strong local electric-field intensification at the particle–cell interface, resulting in electroporation confined to a small region of the cell membrane. This localized interaction enables selective electroporation of targeted cells while leaving neighboring, non-contacted cells unaffected, thereby reducing nonspecific membrane damage and preserving cell viability. Parallel operation of multiple optoelectronic ally controlled micromotors significantly enhances electroporation throughput without requiring mechanical positioning or alternative steering mechanisms.

**Conclusion:** This optoelectronic Janus micromotor platform provides a versatile and scalable strategy for enhanced-throughput, cell-specific electroporation. The approach offers precise spatial control and high selectivity, enabling targeted intracellular delivery, gene transfection, and studies of cell–particle interactions.

## Compact 3D Imaging Flow Cytometry for Volumetric Analysis of Nanoparticle Uptake

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Flow Cytometry (FC) is a common research tool in biology for cell sorting and measuring cell properties but lacks direct morphological information. Imaging flow cytometry (IFC) addresses this limitation by integrating optical imaging with conventional FC, enabling structural characterization of cells at high throughput.

However, many existing IFC systems are complex, bulky, and require trained personnel, limiting their accessibility. Here we present a simple, tabletop, portable, cost-effective, easy to use IFC system with volumetric analysis. The optical system is mainly 3D printed and includes a few additional optical components. A custom-designed illumination system is implemented to allow multimodal imaging of the flowing sample, including bright-field, dark-field, and fluorescence imaging.

Flow is achieved using custom capillary-driven microfluidic chips, eliminating the need for external pumping systems. Volumetric information is recovered through two complementary optical strategies. First, a controlled tilt of the microfluidic channel relative to the imaging plane effectively generates a focal stack during cell flow, enabling volumetric reconstruction. Second, point-spread function (PSF) engineering is performed, by means of an optical element added to the imaging system, which shapes the wavefront of the incident light. The addition of this phase mask allows for encoding the z position in the images.

We are testing the platform on volumetric analysis of nanoparticle uptake in cells, where the combination of the defocus-based focal stack and PSF engineering-based depth encoding should enable differentiation between nanoparticle internalization and membrane-bound particles during flow. This work demonstrates an accessible IFC architecture that enables cost-effective volumetric cytometry, expanding the availability of 3D cell imaging beyond specialized research facilities.

# Vascular Inflammatory Signaling at the Blood–Brain Barrier: A Model for Hypertensive Neurovascular Injury

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Hypertension is a major contributor to cerebrovascular disease and cognitive decline and is strongly associated with chronic injury to the cerebral microvasculature and blood–brain barrier (BBB). While elevated blood pressure drives mechanical stress on vascular endothelium, accumulating evidence suggests that persistent low-grade inflammation plays a key role in promoting endothelial dysfunction, BBB disruption, and subsequent neurovascular injury. However, the mechanistic links connecting peripheral inflammatory activation, endothelial remodeling, and barrier breakdown remain poorly defined.

The present study investigates the bone marrow–brain axis in hypertension with an emphasis on vascular inflammatory signaling and its impact on BBB integrity. We employ *in vitro* BBB models to delineate how hypertensive stimuli influence endothelial activation, tight-junction organization, and overall barrier stability. These models allow controlled examination of molecular and functional markers relevant to vascular inflammation and permeability, thereby providing insights into the cellular mechanisms underlying BBB dysfunction in hypertensive conditions.

Preliminary findings from these *in vitro* experiments suggest that hypertensive stress induces endothelial activation characterized by altered expression of key adhesion and junctional molecules and by impaired barrier function. Such responses may mirror early events *in vivo* that precede neurovascular inflammation and damage. Importantly, these observations support the concept that vascular inflammatory signaling contributes directly to BBB vulnerability in hypertension rather than being a secondary consequence of systemic changes.

Future work builds on this foundation by focusing on specific mediators, including vascular cell adhesion molecule-1 (VCAM-1), which may serve as a molecular link between bone marrow–derived inflammatory activation and cerebral endothelial dysfunction. By integrating these insights across *in vitro* and *in vivo* systems, this project ultimately seeks to define new therapeutic targets to preserve BBB integrity and mitigate neurovascular injury associated with hypertension.

## Development of a Novel Sensor-Integrated Eight-Plate for Adolescent Limb Deformity Correction

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**Background:** Angular deformities of the lower extremities (coronal plane), such as genu valgum and genu varum, are commonly treated using guided growth techniques. While tension band plating using the traditional 8-plate effectively corrects these deformities with success rates exceeding 85%, continuous tracking of the biomechanical changes remains a significant clinical challenge. Current follow-up protocols rely almost exclusively on periodic radiographic imaging (X-rays), which expose pediatric patients to ionizing radiation and fails to provide continuous biomechanical data throughout the longitudinal growth process. Furthermore, existing measurement systems lack the necessary spatial resolution for in-vivo applications. This study aims to develop and validate a "Smart 8-Plate" system capable of continuously monitoring mechanical strains and tracking the degree of angular limb correction and growth plate kinetics during the guided growth process.

**Method:** To achieve this, a standard orthopedic 8-plate was custom-engineered to incorporate miniature sensing elements for strain measurement. To capture and process this biomechanical data, a custom wireless data acquisition architecture was designed. This sensory framework is integrated with a telemetry module that enables continuous, location-independent data streaming to a cloud-based platform, allowing for remote, real-time monitoring of the implant's status.

**Results:** Preliminary results demonstrate the system's core functionality, specifically its ability to reliably acquire and wirelessly transmit mechanical load data to the cloud. These initial findings validate the general feasibility of the proposed approach, while comprehensive trials to establish a precise correlation between mechanical strain and structural correction are planned for future research phases.

**Conclusion:** The developed Smart 8-Plate architecture establishes a robust framework for the continuous tracking of biomechanical development. By transitioning from periodic radiographic snapshots to continuous data acquisition, this technology offers an innovative monitoring alternative with significant potential for personalized orthopedic care.

# Multiparameter Uncertainty Mapping in Quantitative Molecular MRI by a Physics-Structured Variational Autoencoder (PS-VAE)

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**Introduction:** Quantitative molecular MRI aims to characterize molecular tissue properties through biophysical modeling of saturation-transfer spin dynamics. This enables the non-invasive objective mapping of proton exchange rates and compound volume fractions - promising indicators of cancer treatment response. As the inverse problem of parameter quantification is ill-posed and computationally intensive, various neural network (NN) approaches have recently been used for acceleration. However, NNs often prioritize smoothness over data consistency, making uncertainty quantification (UQ) essential for reproducibility and trust towards clinical translation.

**Methods:** Quantitative molecular MRI scans were acquired in phantoms, pediatric tumor-bearing mice (n=7), healthy human volunteers (n=7), and a subject with glioblastoma, using adapted magnetic resonance fingerprinting (MRF). The MRF pattern-matching was extended into a rigorous Bayesian framework that replaces point estimates with full posterior probability distributions. As the brute-force approach fails to scale, a novel NN training architecture that combines a variational autoencoder with biophysical modeling was designed (Fig.1) to rapidly approximate the posterior distribution and derive multivariate confidence regions (CRs) and univariate confidence intervals (CIs).

**Results:** On a standard GPU, the NN processed a high-resolution 3D volume (105 voxels) in 1sec. The NN-based CRs/CIs were in good agreement with the reference method (intersecting in 95% of voxels) and captured parameter correlations under the posterior, reflecting the underlying physics of proton exchange models. Applications include qualitative/visual (Fig. 2a-d, 3) and quantitative (Fig. 2e-h) UQ-informed assessment of the discriminative power of univariate/multi-parameter biomarkers, and scan time reduction - via real-time tracking of progressive uncertainty decrease and convergence and early stopping (Fig. 4).

**Conclusions:** The proposed framework transforms NN usage in quantitative MRI from a “black-box” liability into a trustworthy asset by providing uncertainty quantification alongside rapid inference. PS-VAE can empower probabilistic quantification in any imaging modality by using the appropriate forward model in the decoder.

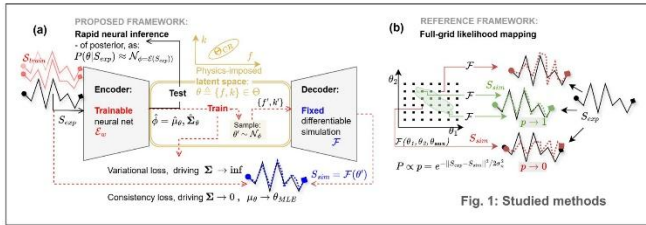


Fig. 1: Studied methods

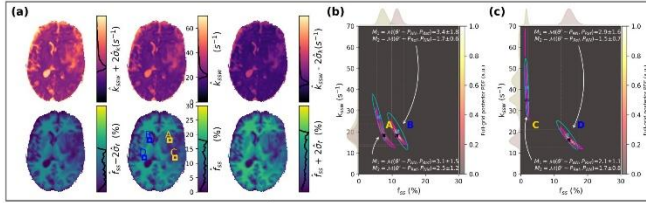


Fig. 3: Validation in a subject with brain tumor at 3T

Fig. 4: Confidence Region shrinking dynamics to inform adaptive acquisition

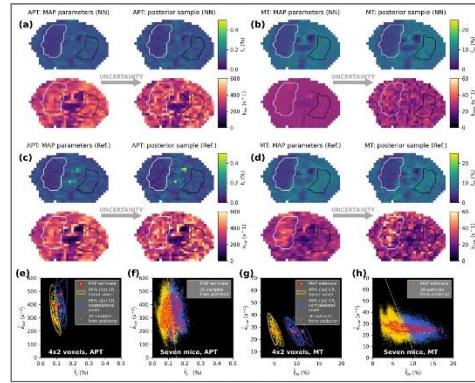
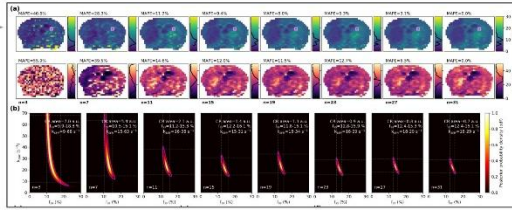


Fig. 2: Validation in rodent tumor models, Semisolid/Amide Proton Transfer at 7T. (a-d) Visualizing uncertainty as generation of observation-consistent noising of quantitative maps; enables UQ-aware evaluation of biomarker potential of individual tissue parameters. (e-h) Demonstrating sampling from posterior concept (e, f) and using it for data augmentation towards UQ-aware learning of multi-parametric quantitative imaging biomarkers (mpQIBs).

## 3D Printed Vascularized Tissue Flaps Enabling Direct Anastomosis for Reconstructive Clinical Applications

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<sup>1</sup>*Biomedical Engineering, Technion, Israel*

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3D bioprinting of soft tissue is an emerging approach for treating extensive tissue loss resulting from trauma or surgical resection. In this work, we apply multimodal bioprinting strategies to fabricate large-scale, clinically relevant soft tissue flaps while preserving structural fidelity and high cellular viability.

For successful implantation and translation, rapid nutrient delivery, efficient cellular waste removal, and prevention of tissue swelling are critical for post-implantation survival. To address these challenges, we fabricated vascularized soft tissue flaps incorporating printed inlet and outlet vessels forming a pre-designed arteriovenous shunt, interconnected with a bio printed microvascular network and an integrated lymphatic network.

This hierarchical architecture enables direct anastomosis to the host circulatory system while supporting perfusion and interstitial fluid drainage in an *in vivo* model. The engineered flaps were evaluated in both small and large animal models, demonstrating scalability, functional integration, and translational potential toward clinical applicability.

# Numerical Analysis of the Hemodynamics and Performance of Miniature Ventricular Assist Devices

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<sup>2</sup>*Mechanical Engineer, Tel Aviv University, Israel*

**Introduction:** The use of percutaneous left ventricular assist devices (p-LVADs) has surged in acute heart failure treatment. Although the improvement of those devices provided, there is still high mortality and a wide burden of disease, mostly due to related thrombosis, and hemolysis. p-LVADs designs with reduced blood trauma are likely to improve clinical outcomes and expand p-LVAD therapy to patients with less severe heart failure. This study used numerical methods to explore two p-LVAD configurations: a magnetic levitation-driven floating impeller and a motor-driven suction pump. Computational fluid dynamics assessed the impact of hub geometry on parameters of hemodynamics, pump performance, and blood damage. Those parameters were examined in their correlation with flow patterns, based on non-dimensional numbers.

**Methods:** Four impellers (5-6mm in diameter) underwent analysis across various pressure head and angular velocity conditions using the Reynolds-Averaged Navier-Stokes model with the SST turbulent model. The simulations assumed steady-state flow within a rotating frame, and it has been confirmed that it approximates well the average flow of the transient case.

The risks for platelets activation and hemolysis were estimated for each case using four different estimation methods: Eulerian turbulence-based hemolysis indices (HI1 and HI2) and Lagrangian median stress accumulation (SA) for platelet activation and exposure time above 425 Pa (tATA) for hemolysis.

**Results:** Results highlighted the profound effect of hub shape on flow patterns, performance, and blood damage risk. Converging hub impellers promoted recirculation and extended residence time, while impellers with an expanding hub had higher wall shear stress with less flow separation and regions of reversed flow. A strong correlation emerged between angular velocity and hemolysis risk across all models.

This study illuminates the pivotal role of hub configuration and angular velocity in p-LVAD performance and blood damage risk. In addition, correlations were found between non-dimensional numbers and the risk for blood damage and performances. Lastly, integrating Eulerian and Lagrangian frameworks is essential for comprehensive blood damage assessment. These findings have far-reaching implications for future p-LVAD designs, promising more effective treatment options.

## Targeting Ubiquitin Signaling: A Novel Cyclic Peptide Therapy for Multiple Myeloma

**Dima Ghannam Shahbari**

*Oncology Drug Development, UB Therapeutics, Israel*

**Background / Aim:** Multiple myeloma remains an incurable hematologic malignancy despite significant therapeutic advances, including proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, and cellular therapies. However, resistance to existing therapies and disease relapse remain major clinical challenges. The ubiquitin-proteasome system plays a central role in protein homeostasis and tumor cell survival. UB Therapeutics is developing a novel cyclic peptide designed to selectively target ubiquitin signaling pathways involved in protein degradation. The aim of this study was to evaluate the preclinical efficacy, safety, and translational potential of UB4A-GRR as a therapeutic candidate for multiple myeloma.

**Method:** UB4A-GRR is a rationally designed synthetic cyclic peptide engineered to selectively bind K48-linked ubiquitin chains, key regulatory signals directing proteins to proteasomal degradation. Preclinical evaluation included biochemical binding assays, cellular studies in multiple myeloma models, and in vivo efficacy studies in xenograft mouse models following subcutaneous administration. Non-clinical safety assessment included preliminary toxicology and pharmacokinetic characterization. Translational pharmacokinetic and pharmacodynamic (PK/PD) modeling was used to integrate exposure and efficacy data and guide prediction of human dosing for first-in-human clinical studies.

**Results:** UB4A-GRR demonstrated significant tumor growth inhibition in multiple myeloma xenograft models. Pharmacokinetic analyses confirmed systemic exposure following subcutaneous administration, while preliminary toxicology studies supported tolerability within the evaluated exposure range. Translational PK/PD modeling predicted clinically feasible dosing regimens capable of achieving exposure levels associated with anti-tumor activity observed in preclinical studies.

**Conclusion:** These findings support ubiquitin signaling as a promising therapeutic target in oncology. UB Therapeutics is advancing UB4A-GRR toward a Phase I clinical study in patients with relapsed or refractory multiple myeloma.

## Mechano-Profiling and Modulation of Red Blood Cell-Based Shear-Responsive Carriers

Anat Glozman, Danielle Nemcovsky, Netanel Korin

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**Introduction:** Red blood cells (RBCs) offer a unique nano-engineering platform for drug delivery due to their long circulation lifetime and exceptional deformability. The potential for controlled release from these unique carriers could enable localized therapy, such as treating post-aneurysm vasoconstriction, while minimizing systemic side effects. Our study evaluates the feasibility of shear-responsive RBCs as drug carriers, specifically, how modulation of membrane mechanics influences carrier stability, transport, and drug retention under physiologically relevant flow conditions.

**Methods/Materials:** RBCs were loaded with Dextran-FITC via hypotonic dialysis and compared to native cells. Mechanical properties were modulated using membrane crosslinking (glutaraldehyde or transglutaminase), thermal treatment, and lipid enrichment (cholesterol) to adjust stiffness and release behavior. Static mechanical responses were characterized by using deformation assays in aqueous liquid crystal environments, quantifying elongation and deformation indices. To evaluate shear-responsive delivery, we employed in vitro vasoconstriction models replicating the elevated shear conditions of cerebral vasospasm. In parallel, dynamic transport and deformability were assessed in a pulmonary capillary-mimicking microfluidic platform.

**Results:** Preliminary findings indicate that hypotonic-dialysis-loaded RBC carriers retain mechanical and functional properties comparable to native cells. In the pulmonary capillary model, the carriers underwent substantial deformation and successfully passed through constrictions without measurable cargo leakage. In vasoconstriction models, they remained stable under physiological flow, with cargo release localized to regions of elevated shear. Mechanical tuning influences release behavior under constricted conditions and cell's stability.

**Conclusions:** Studying and tuning the mechanical properties of RBCs based carriers may be valuable to improve their function as a versatile and controllable platform for flow-responsive targeted drug delivery.

**Acknowledgements:** This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation programme (grant agreement n°101002057)

# A Novel Active Transparent Model for In-Vitro PIV Investigation of Left Ventricular Hemodynamics

**Itamar Goshen, Idit Avrahami, Oren Salimi**

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Accurate characterization of the complex three-dimensional flow field within the left ventricle (LV) is essential for understanding ventricular hemodynamics and its relationship to cardiac function and pathology. Optical flow measurement techniques, such as Particle Image Velocimetry (PIV) and Particle Tracking Velocimetry (PTV), are widely used for two- and three-dimensional flow evaluation. These methods require a transparent model of the LV lumen to enable optical access.

To date, most transparent LV models have relied on simplified kinematic assumptions, typically reproducing ventricular motion through passive radial expansion and contraction driven by pressure differences between the internal working fluid and an external fluid surrounding the model. While such approaches enable basic flow visualization, they do not accurately represent the true myocardial motion, limiting the fidelity of the extracted flow fields.

In this study, we present the development of a novel active transparent LV model that combines passive deformation with externally controlled actuation. The model incorporates dedicated actuators that impose prescribed wall motion, enabling more realistic reproduction of ventricular kinematics beyond simple pressure-driven behavior. This approach allows independent control of wall motion and intraventricular pressure conditions.

The proposed active transparent LV model enables high-resolution measurement of the three-dimensional intraventricular flow field using advanced optical techniques such as PTV and 3D PIV, while simultaneously accounting for physiologically relevant myocardial motion. This methodology provides a new experimental platform for studying LV hemodynamics under more realistic conditions and may improve the understanding of flow-wall interactions in both healthy and pathological ventricles.

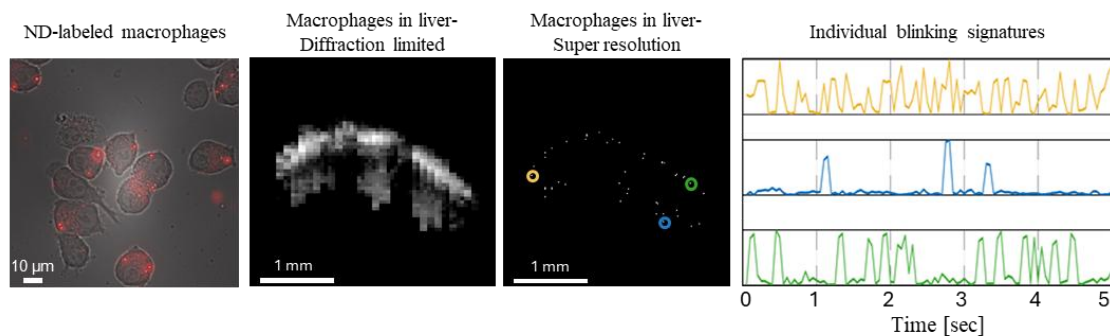
# Super-Resolution Intracellular Ultrasound Imaging using Blinking Nanodroplets

Saar Gotshal, Tiran Bercovici, Tali Ilovitsh

*School of Biomedical Engineering, Tel Aviv University, Israel*

Real-time intracellular imaging within deep organs remains a significant challenge in biomedical engineering. While ultrasound offers excellent penetration depth for non-invasive body imaging, it typically lacks the spatial resolution required to visualize individual cells. Macrophages are critical targets for cellular ultrasound imaging, as they play a key role in immune response. Tracking them non-invasively offers vital insights for cell-based therapies. To enable ultrasound-based cell tracking, we leveraged macrophages' natural endocytic activity to label them with phase-shifting nanodroplets, a new class of acoustic contrast agents that undergo reversible phase transitions between liquid and gas states under ultrasound exposure. These transitions generate stochastic acoustic blinking, creating temporal sparsity that distinguishes labelled cells from static tissue. This allows for the isolation of individual point spread functions (PSF) and precise localization of the cells.

We fabricated  $\sim 170$  nm nanodroplets using microfluidics and confirmed macrophage uptake by microscopy. Following systemic injection of labeled macrophages into mice, we performed ultrasound experiments using a programmable system and a high-frequency probe (18 MHz) on internal organs and phantoms. Acquiring data at 20 Hz, thousands of blinking events were captured. The signal processing pipeline involved frame-to-frame differentiation to separate blinking NDs from static tissue, followed by the identification of NDs based on spatial peak intensities and individual temporal signatures. Finally, localization of temporally isolated PSFs was performed using 2D elliptical Gaussian fitting. Localization summation created a super-resolution image of macrophage distributions in the liver. Our method achieved an 8.2-fold improvement in spatial resolution. This work establishes functional ultrasound imaging at the cellular level in deep tissue, fundamentally extending the capabilities of ultrasound toward intracellular-scale imaging and offering powerful new insights for cell-based therapies.



# Leveraging Symmetrical Flow Matching for Source-Free Domain Adaptation in Medical Image Segmentation

**Tal Grossman**, Noa Cahan, Hayit Greenspan  
*Tel Aviv University, Israel*

Domain shift across imaging modalities and acquisition sites remains a significant barrier to the clinical deployment of segmentation models. Source-free unsupervised domain adaptation (SFUDA) provides a practical solution by adapting a pretrained model to an unlabeled target domain without requiring access to sensitive source data. We introduce a novel SFUDA framework built on *\emph{Symmetrical Flow Matching}* (SymmFlow), a generative formulation that unifies semantic segmentation and conditional image synthesis within a single model.

By modeling forward and reverse transformations jointly, SymmFlow enforces bi-directional consistency and preserves essential structural properties across domains. Our pipeline leverages this symmetry to generate reliable pseudo-labels and corresponding source-like synthetic images from unlabeled target data, creating a generative replay buffer that anchors source knowledge during adaptation. We then perform generative self-training by fine-tuning on a joint set of real target images and synthetic source-like images, improving robustness to target appearance while maintaining stable and anatomically plausible predictions.

We evaluate our method on diverse benchmarks, including abdominal multi-organ and heart segmentation, covering cross-modality (from MRI to CT and vice versa) domain shifts, and multi-site prostate segmentation involving protocol and site variations.

Results demonstrate that our approach achieves high performance over extensive datasets, yielding superior results compared to state-of-the-art SFUDA methods and even outperforming conventional UDA approaches.

# CERNAL: A Transcriptome-Driven Compiler for RNA-Based Cellular Logic Circuits

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**Background:** The ability to regulate gene expression based on specific conditions, such as tissue types or disease states, is essential for advancing biosensing, cancer therapy, and agriculture. However, no generic, model-based approach currently exists to automate this process. Traditional regulation via condition-specific promoters lacks versatility and predictive modelling. Despite the availability of high-resolution RNA sequencing data, there is a lack of a general framework to translate these transcriptomic signatures into programmable cellular responses. We aim to bridge this gap by developing CERNAL, a computational compiler for RNA-based logic circuits.

**Method:** CERNAL is designed as a computational platform that automates the translation of transcriptomic data into genetic circuits. The system identifies differential gene expression signatures and maps them to logic gates composed of programmable RNA elements, such as toehold switches and CRISPR guide RNAs. The compiler will generate optimized circuit architectures tailored to specific cellular environments by selecting the most robust regulatory components.

**Results:** We will demonstrate the platform's versatility through two proof-of-concept applications. First, we aim to design a highly specific PFAS biosensor for *E. coli* for environmental monitoring. Second, we will develop a transcriptome-responsive therapeutic strategy for endometriosis, where circuits are intended to trigger a localized response only in the presence of disease-specific markers. We expect the platform to yield circuit designs characterized by high dynamic range and minimal crosstalk, providing a roadmap for future in vivo implementation.

**Conclusion:** CERNAL provides a scalable, data-driven approach to cellular programming. By streamlining the transition from transcriptomic data to functional RNA logic, this platform is expected to facilitate the rapid design of precision diagnostics and smart therapeutics across various organisms and disease models.

# Experimental Quantification of Three-Dimensional, Time-Resolved Fluid–Structure Interaction in a Left-Ventricular Phantom

**Omer Hadar**<sup>1</sup>, Boaz Meivar<sup>2</sup>, Shai Avidan<sup>2</sup>, Alex Liberzon<sup>1</sup>

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<sup>2</sup>*School of Electrical and Computer Engineering, Tel Aviv University, Israel*

Intraventricular transport and wall-shear-related flow phenomena are governed by the coupled interaction between ventricular wall motion and fluid dynamics, yet these relationships remain difficult to resolve in a time-resolved and spatially consistent manner.

This study aims to establish an experimentally validated framework for quantifying fully coupled left-ventricular fluid-structure interaction and extracting spatially organized hemodynamic descriptors from direct measurements.

We conducted an in vitro experiment using a compliant silicone left-ventricular phantom integrated into a physiological mock circulatory loop. Time-resolved three-dimensional particle tracking velocimetry provided Lagrangian measurements of intraventricular flow, while simultaneous optical tracking and time-resolved segmentation of surface markers enabled reconstruction of dynamic ventricular wall kinematics. A dedicated calibration, synchronization, and co-registration workflow unified flow and deformation within a common three-dimensional reference frame across repeated cardiac cycles.

This physically coupled dataset enabled direct, cycle-resolved estimation of wall-adjacent velocity gradients and transport-based descriptors without reliance on numerical flow reconstruction or prescribed boundary conditions. Spatially resolved distributions of time-averaged wall shear stress, oscillatory shear index, and residence-time-related metrics were computed and regionally organized throughout the ventricular cavity.

The framework produces reproducible, spatially structured hemodynamic fields linked to regional wall-motion patterns. The results reveal a correlation between time-averaged wall shear stress and ventricular wall acceleration, compare Eulerian shear-based residence-time proxies with direct particle trajectories, and demonstrate robust flow-organization trends across different heart rate conditions.

## Leadless Biomechanical Innovative Technologies for Cardiac Repair

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<sup>1</sup>*Department of Biomedical Engineering, Technion-Israel Institute of Technology, Israel*

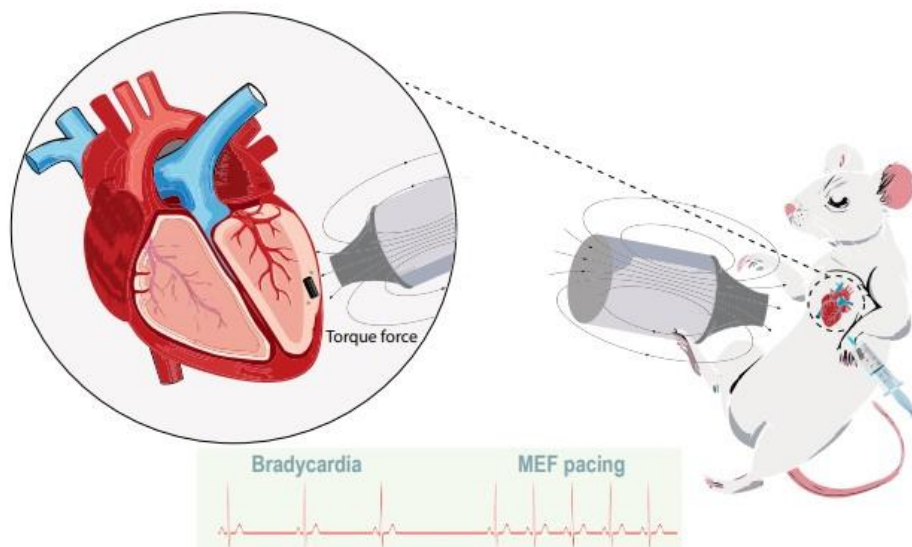
<sup>2</sup>*Russell Berrie Nanotechnology Institute, Technion-Israel Institute of Technology, Israel*

Conventional electroceutical devices for cardiac pacing rely on wired leads and bulky implants that may cause chronic complications, including tissue erosion, limited battery longevity, and size constraints that hinder translation to small animal models and future miniaturized therapies.

In this work, we present a leadless biomechanical strategy for cardiac stimulation based on magneto-mechanical actuation and mechano-electrical feedback (MEF). Soft ferromagnetic structures, like iron rods and superparamagnetic iron oxide (SPIO) tablets, are used to convert external magnetic fields into localized mechanical strain within cardiac tissue. Electromagnet design and field distribution were optimized through COMSOL Multiphysics simulations, enabling controlled torque generation and angle-dependent stress profiles.

Ex vivo validation was performed using Langendorff-perfused rat hearts, demonstrating successful magnetic capture and pacing under non-uniform magnetic fields. Comparative studies between iron rods and SPIO tablets revealed differences in stimulation endurance and strength–duration characteristics.

Confocal imaging with propidium iodide staining indicated that magneto-mechanical pacing can induce functional activation while maintaining acceptable levels of tissue viability. The results highlight the potential of magnetically driven anisotropic structures to achieve minimally invasive, wireless cardiac modulation. This platform provides a scalable framework for future studies and the development of next-generation leadless bioelectronic therapies that integrate biomechanics, materials engineering, and electrophysiology.



## Visualizing Vascular Bone Marrow Niche Alterations in Diabetes

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**Introduction:** Diabetes mellitus is characterized by chronic hyperglycemia that leads to systemic vascular complications. Hyperglycemia impairs endothelial function and promotes vascular inflammation, resulting in leukocytosis, altered hematopoiesis, and cardiovascular complications. Bone marrow endothelial cells play a pivotal role in regulating myeloid progenitor cells and leukocyte trafficking. However, the effects of diabetes on the structure and function of bone marrow vasculature remain poorly understood. To address this, we employed a multiscale imaging approach integrating intravital microscopy, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), and multispectral optoacoustic tomography (MSOT) to investigate diabetes-induced vascular changes in the bone marrow.

**Methods:** Diabetes were induced in C57BL/6J mice using streptozotocin (STZ). Flow cytometry and histology characterized bone marrow myeloid progenitors, blood leukocytes and bone marrow endothelial cell populations, as well as hypoxia. Intravital microscopy was used to visualize vascular density, permeability and sprouting angiogenesis in the calvarial marrow. DCE-MRI quantified vascular density and permeability in the femoral marrow, while MSOT assessed hemoglobin oxygenation in the calvarial marrow. **Results:** Hyperglycemia led to increased myelopoiesis, evidenced elevated leukocytosis driving diabetic inflammation. Flow cytometry and histology showed heightened endothelial cell numbers, while intravital microscopy revealed increased vascular density, permeability and sprouting angiogenesis in diabetic bone marrow. DCE-MRI confirmed heightened vascular density and leakiness, while MSOT demonstrated reduced hemoglobin oxygenation and hypoxia in the diabetic marrow, indicating a hypoxic environment in which HSPCs thrive. This hypoxia likely triggers angiogenesis, contributing to enhanced vascular remodeling, elevated leukocytosis and inflammatory hematopoiesis in diabetes. **Conclusion:** This study demonstrates that diabetes induces profound vascular remodeling and hypoxia in the bone marrow, reshaping the hematopoietic niche and driving myelopoiesis and leukocytosis. By validating DCE-MRI and MSOT as non-invasive translational tools, coupled with intravital microscopy, we provide a comprehensive framework for exploring novel therapeutic strategies that target bone marrow vasculature to mitigate inflammation-driven outcomes in diabetes.

# Advanced Signal Processing and Multi-Criteria Ranking Framework for Cuffless Systolic Blood Pressure Estimation Based on Photoplethysmography (PPG) Signal Analysis

**Ami Hauptman**<sup>1</sup>, Yirmi Hauptman<sup>2</sup>, Adi Rachel Diamant<sup>2</sup>, Rotem Rabin<sup>2</sup>,  
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**Background:** Hypertension is a leading risk factor for cardiovascular morbidity and mortality. Conventional cuff-based measurements require active patient involvement and are unsuitable for continuous monitoring. Photoplethysmography (PPG)-based estimation of systolic blood pressure (SBP) has gained significant attention; however, major challenges remain in extracting robust morphological features and in selecting clinically reliable machine learning (ML) models.

**Objective:** To develop a non-invasive SBP estimation framework based on advanced PPG signal processing and machine learning, and to introduce a multi-metric ranking mechanism for optimal and safety-oriented model selection.

**Methods:** Data were collected from 31 healthy volunteers (ages 20-70) under four controlled physiological conditions using a fingertip PPG sensor sampled at 2,000 Hz (ethics approved). The signal processing pipeline included powerline noise removal, bias removal, normalization, smoothing, and automated quality assessment. Morphological features were extracted from the PPG signal and normalized relative to heart rate. Feature selection methods were used to obtain the optimal feature set.

Three nonlinear ML models, XGBoost, Random Forest, and Gaussian Process Regression, were evaluated across several hyperparameter configurations. Performance was assessed using MAE, RMSE, clinical accuracy ( $\pm 10$  mmHg). Two novel ranking strategies were developed: (1) an Average-Ranking score integrating multiple metrics, and (2) a Distribution & Safety Score that penalizes SBP underestimation to prioritize clinical safety.

**Results:** XGBoost demonstrated superior performance. Three leading configurations achieved the most accurate results, offering different tradeoffs between lowest prediction error, stability and clinical safety.

**Conclusion and Significance:** This study presents an integrated signal processing and ML ranking framework for cuffless SBP estimation. The proposed safety-oriented evaluation approach enables reliable model selection tailored to diverse clinical needs and supports future integration into wearable cardiovascular monitoring systems.

# Multi-Contrast Generation and Quantitative MRI using a Transformer-Based Framework with RF Excitation Embeddings

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<sup>4</sup>*Department of Artificial Intelligence in Biomedical Engineering, Friedrich-Alexander Universität Erlangen-Nürnberg, Germany*

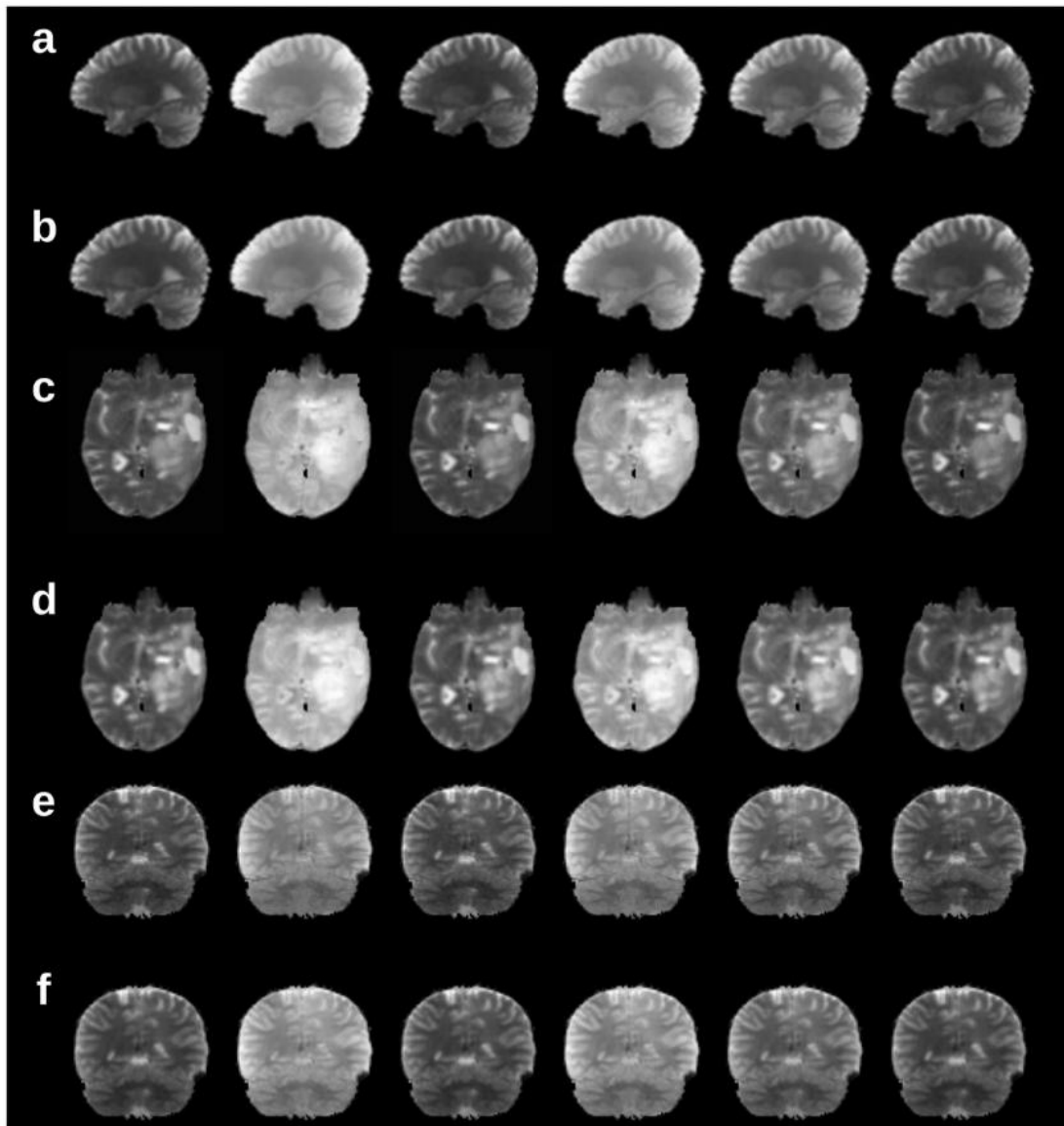
<sup>5</sup>*Sagol School of Neuroscience, Tel Aviv University, Israel*

**Background:** Magnetic Resonance Imaging (MRI) is a powerful diagnostic tool [1], yet its potential for comprehensive quantitative imaging is limited by lengthy multi-sequence acquisitions [2],[3]. While MR fingerprinting [4] and deep learning-based reconstruction [5] have accelerated quantitative imaging, accurately modeling complex molecular environments remains challenging [6]. Here, we developed a transformer-based MRI framework (TBMF) for generating diverse contrasts and quantitative parameter maps from a single, ultra-short scan (less than 30 seconds).

**Method:** A two-step deep learning pipeline was designed. First, a transformer-based core module was developed to predict the next six contrasted-weighted images in a sequence. By processing a rapid 28.2 s calibration scan alongside radiofrequency (RF) excitation embeddings (saturation pulse frequency offset and power), this module learns to predict the tissue responses to unseen excitations. Second, we implemented a quantification model that leverages these learned biophysical features to simultaneously generate six fully quantitative parameter maps (fss, kssw, B0, B1, T1, T2) from the same input, effectively translating the learned dynamics into tissue properties. The framework was trained using over 3 million image pairs from 9 healthy subjects and validated on 7 unseen subjects including a patient with glioblastoma across two imaging sites using different scanner models.

**Results:** The TBMF achieved a scan time acceleration of 94% compared to state-of-the-art multi-sequence protocols (28.2 seconds vs. 8.5 minutes). The framework successfully reconstructed high-fidelity quantitative parameter and field maps. AI-generated images demonstrated high structural similarity (SSIM 0.96) and low error rates (NRMSE 4%) compared to ground truth.

**Conclusion:** We developed and validated a biophysical-model-free framework for multi-contrast generation and quantitative MRI, unbiased by pre-existing parameter assumptions. The system rapidly generates multi-contrast chemical exchange saturation transfer (CEST) and semisolid magnetization transfer (MT) images alongside water relaxation and field maps. This ultra-fast approach may facilitate the efforts to accelerate clinical MRI workflows.



# Brightfield Snapshot 3D Microscopy: Towards In-Vivo Imaging

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**Background:** Three-dimensional (3D) microscopy is essential for resolving complex biological structures, yet conventional microscopes inherently acquire two-dimensional (2D) projections. In brightfield microscopy, 3D imaging is commonly achieved by axial scanning, which limits acquisition speed and may introduce motion artifacts in-vivo. Snapshot alternatives avoid scanning but suffer from resolution tradeoffs and reduced field-of-view or sensitivity. This work aims to enable snapshot 3D imaging in brightfield microscopy, by jointly encoding depth information through optical point-spread-function (PSF) engineering, traditionally used in fluorescence microscopy, and decoding it using computational reconstruction. The focus is on capillary-like structures in biological environments.

**Method:** We formulate a Fourier imaging model for partially coherent brightfield microscopy under Köhler illumination to guide PSF engineering. A novel PSF, termed Tripod, is designed to enhance depth encoding for elongated structures. The optical system is implemented experimentally by adapting the illumination and introducing a phase mask in the Fourier plane. To reconstruct volumetric information from a single 2D image, we develop a computational framework that combines a modified Richardson-Lucy deconvolution with neural fields, adapted from prior work in fluorescence microscopy.

**Results:** Simulations demonstrate that volumetric 3D structure can be reconstructed from a single 2D image using the proposed Tripod PSF. Experimental measurements show that the engineered PSF encodes depth-dependent features in a single snapshot under partially coherent illumination, validating the proposed depth-encoding optical design. Together, these results highlight the feasibility of snapshot volumetric imaging in brightfield microscopy.

**Conclusion:** This work demonstrates an optical-computational framework for in-vivo snapshot 3D imaging in brightfield microscopy, enabling rapid acquisition without axial scanning. PSF engineering, traditionally explored in fluorescence microscopy, is extended here to partially coherent brightfield imaging. Combined with computational reconstruction, this framework enables depth encoding and volumetric reconstruction from a single image.

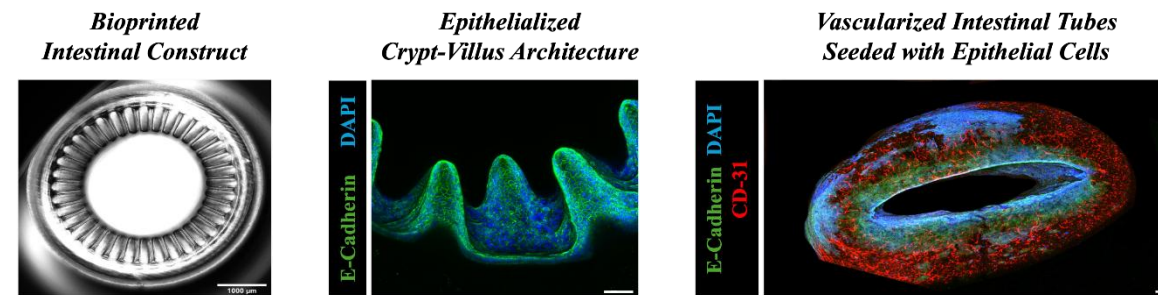
# A 3D Bioprinted Vascularized, Perfusable Intestinal Model for Drug Evaluation and Disease Modeling

**Adina Israel Fried**, Adi Amrusi, Maya Yaakov, Shaked Roi, Hagit Shoyhet, Shulamit Levenberg  
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**Introduction:** Human-relevant in vitro models for drug absorption are needed to overcome limitations of animal studies and current platforms. Conventional 2D monolayers lack physiological polarity and mechanical cues, while organoids offer limited luminal access. Organ-on-a-chip systems enable perfusion but often rely on simplified epithelial organization. We developed a vascularized, bioprinted 3D intestinal model for disease modeling and real-time drug absorption, hypothesizing that integrating native-like cellular complexity, geometry, and flow would better recapitulate intestinal function.

**Materials and Methods:** Constructs were fabricated by digital light processing (DLP) using an rhCollMA bioink. Printing fidelity and architectural optimization were first validated with acellular bioink, then reprinted with endothelial cells and human pericytes. After 5 days of static culture, Caco-2 or organoid-derived intestinal epithelial cells were seeded into the lumen and maintained under dynamic flow for 96 h. Permeability was evaluated using 3 kDa Cascade Blue and 65 kDa fluorescein dextrans with confocal imaging every 10 min for 1 h. Fixed samples were stained for CD31 and epithelial junction markers.

**Results and Discussion:** Tubular constructs replicating crypt-villus architecture were successfully printed and supported formation of a continuous epithelial lining. Porogen-supplemented bioink containing endothelial and supportive cells promoted formation of vascularized submucosa with self-assembled capillary-like networks. Dynamic culture enhanced epithelial maturation, tight junction organization, and barrier integrity. Permeability assays demonstrated size-dependent transport, with restricted passage of 65 kDa tracers compared with 3 kDa molecules.



**Conclusions:** This human-relevant gut model enables disease modeling, drug discovery, and nutrition research while reducing reliance on animal models. Integration of human epithelial and vascular components within a physiologically relevant architecture allows for more predictive assessment of absorption, metabolism, and toxicity. Initial studies demonstrate feasibility for testing small-molecules and peptide therapeutics and for inducing IBD-like inflammation, underscoring the model's translational potential.

## Exploring Genome Organization at the Nanometric Scale in the Cell Nucleus

**Rand Kamal**

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Chromatin in the nucleus is highly organized, but the mechanisms maintaining this structure are unclear. Lamin A is crucial for nuclear organization, and its depletion disrupts chromatin dynamics and chromosome territories, although its exact role in processes such as transcription and the formation of topologically associated domains is not fully understood.

This research investigates the relationship between lamin A, RNA polymerase II, histones, and genome organization using super-resolution microscopy. By overcoming the diffraction limit of conventional light microscopy, this approach enables imaging at 20 nm resolution and detailed analysis of nuclear proteins using specialized fluorescent probes.

We use stochastic optical reconstruction microscopy (STORM), which relies on synthetic dyes that stochastically switch between fluorescent and dark states, allowing precise localization of individual molecules beyond the diffraction limit. Sequential image acquisition and point spread function analysis provide insights into protein spatial organization within the nucleus. Lamin A, RNA polymerase II, and histone H3 are fluorescently labeled to examine their spatial relationships, revealing how lamin A regulates genome organization and transcription, interacts with other nuclear components, and how disease-associated lamin A mutations disrupt these processes, contributing to the molecular basis of laminopathies and potentially guiding future therapeutic strategies.

# Ultrasonic Speed-of-Sound Shift Imaging for Microbubble-Mediated Therapeutic Applications

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*Biomedical Engineering, Tel-Aviv University, Israel*

In the past decade, quantitative ultrasound modalities in the field of speed-of-sound imaging (SoSI) have emerged, leveraging spatial variations in sound speed as diagnostic biomarkers for tissue characterization.

Here, we present the first proof-of-concept SoSI approach tailored to microbubbles (MBs), widely used as ultrasound contrast agents and increasingly as mediators for therapy (e.g., drug delivery, blood-brain barrier opening, sonothrombolysis). Our aim is to estimate MB-induced speed-of-sound (SoS) shifts as a quantitative indicator of MB concentration and localization, supporting improved therapy guidance and monitoring. We propose a SoSI pipeline to estimate MB-related SoS shifts from ultrasound image sequences. First, Farnebäck optical flow is applied to compute pixel displacements associated with changes in MB concentration. Second, a Tikhonov-regularized pseudo-inverse formulation is used to recover SoS shifts from the displacement field.

The method was evaluated in tissue-mimicking phantoms and in breast cancer mouse models. Phantom experiments covered MB concentrations from 0 to  $5 \times 10^6$  MB/mL, using three transmit voltages (15, 25, 40 V) and two inclusion diameters (6 and 8 mm). In vivo experiments were performed in six tumors, imaged longitudinally following a systemic injection of  $5 \times 10^8$  MBs.

In phantoms, MB inclusions were detected with moderate-to-high sensitivity across voltages. Pearson correlations between average SoS shift and mean B-mode intensity within the MB region of interest ranged from -0.34 to -0.83, consistent with an inverse relationship. Two-way ANOVA indicated significant dependence of maximum and average SoS shifts on both voltage and concentration ( $p \ll 0.001$ ). In vivo, maximum estimated SoS shifts ranged from -15 to -95 m/sec, and MB inflow and clearance dynamics in the tumor were observed over time post-injection.

These results provide initial evidence that MB presence can be quantified via SoS shifts in tissue, enabling estimation of MB concentration and localization. This capability may enhance MB-mediated therapy by improving image guidance, treatment monitoring, and delivery assessment.

## Exploring Distance: Dependent Mechanical Communication During Sprouting Angiogenesis

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Sprouting angiogenesis is a fundamental process in vascular development and homeostasis, essential for establishing the hierarchical networks required for nutrient and gas exchange. While biochemical regulators and fluid-induced shear stress have been extensively characterized, the mechanical interactions between endothelial cells and the 3D extracellular matrix (ECM) remain poorly understood. Specifically, the fibrous nature of the ECM exhibits hyper-elastic properties that significantly influence mechanical signal transduction and cellular communication.

This study utilizes an in-vitro model featuring two blood vessels embedded in a hydrogel to investigate the mechanical sensing distance between neighboring vessels. We examine how varying distances between vessels influence sprout length, angle, and directionality, testing the hypothesis that matrix-mediated mechanical cues guide sprouts toward adjacent vessels. Furthermore, we analyze the rearrangement and behavior of hydrogel fibers to characterize the specific strain fields generated by cells during the sprouting process.

This research provides a deeper understanding of the biomechanical dialogues governing vascular patterning, offering insights into the rational design of engineered tissues. By optimizing network organization and improving graft integration, this work supports the development of more functional and stable hierarchical vasculatures in regenerative medicine.

# Corticomotoneuron Suppression and Facilitation Map onto Null and Potent Population Dynamics during Dexterous Movements

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Dexterous movements, especially of the fingers, are a primate hallmark, enabled by the motor cortex's ability to sculpt precise patterns of muscle activation and suppression. However, population-level descriptions of dexterous finger control remain incomplete, often failing to specify how individual corticomotoneurons (CM) M1 output neurons with monosynaptic connections to spinal motoneurons-act on their target muscles. We address this by linking the muscle-specific functional role of single CM cells to population potent and null dynamics during execution of individuated finger movements.

Two rhesus monkeys performed individuated digit movements (5 digits, 2 directions) while we recorded CM single-unit activity (n=298), forearm EMG (n=29), and full finger kinematics. Spike-triggered averaging classified CM neurons by their effect on muscle activity: post-spike facilitation (PSF) or post-spike suppression (PSS). For each movement, muscles were labeled as agonists, antagonists, or stabilizers.

At the single-cell level, many PSS neurons in antagonist muscles were active in the premovement period, well before PSF neurons in agonist muscles and observable EMG. To identify population dimensions driving or not driving muscle output, we mapped neural activity to EMG output to define potent and null subspaces. This neural-to-EMG mapping showed very strong alignment. Computing a potency and nullity index for each neuron revealed three dissociations: (1) During premovement, CM neurons producing PSS in antagonist muscles expressed significantly larger nullity than PSF neurons, reflecting preparatory control reshaping neural states without producing EMG. (2) CM neurons producing PSF in agonist muscles showed greater potency than nullity both before and during movement, aligning with movement-generating output. (3) Flexion and extension occupied distinct low-dimensional trajectories with clear digit-specific separation, emerging during premovement and peaking during execution.

These results provide a mechanistic link between single CM cell functionality and population dynamics geometry: suppression organizes premovement states within null dimensions, whereas facilitation engages potent dimensions together to drive dexterous movement.

# Toward Patient-Specific Optimization of Systemic-to-Pulmonary Shunts in Single-Ventricle Physiology

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<sup>2</sup>*Schneider Children's Hospital, Israel*

**Background:** Single-ventricle (SV) physiology with ductal-dependent pulmonary circulation requires staged palliation, typically starting with a systemic-to-pulmonary shunt. Balancing pulmonary and systemic blood flow is crucial: excessive pulmonary flow compromises systemic perfusion, while insufficient flow leads to hypoxemia and early reintervention. Proper shunt placement also fosters adequate pulmonary artery growth for subsequent surgeries. However, such decisions rely on clinical experience and 2D echocardiography. This work aims to automate the execution of computational fluid dynamics simulations to enable patient-specific comparison of shunt type, size, and placement.

**Methods:** Pre-intervention patient angiograms are segmented to reconstruct fluid domain geometry, followed by a virtual shunt placement, mesh generation, and hemodynamic simulation. A physiological inlet flowrate is prescribed at the ascending aorta, while all outlets are coupled to a 1D electrical analogy (Windkessel) models by a user-defined function. A set of identical resistance and capacitance parameter values is assumed for the three aortic arch branches, another set for both pulmonary arteries, and a third set for the descending aorta, totaling in nine independent parameters. Parameter calibration is performed using built-in capabilities in Ansys Fluent. Parameters are optimized through automated simulations to achieve physiological flowrate reaching the pulmonary arteries. Once The calibration is complete, the simulation process will be automated using Python and Scheme scripts.

**Results:** Currently, the patient-specific modeling and simulation pipeline has been established, including geometry reconstruction, mesh generation, and implementation of Windkessel boundary conditions. Work is ongoing to complete parameter calibration and automate the meshing and simulation processes.

**Conclusions:** This work aims to develop a patient-specific computational framework for evaluating surgical options in single-ventricle physiology. Once completed, the proposed approach will allow automated comparison of shunt type, size, and placement, with the goal of supporting clinical decision-making through quantitative hemodynamic assessment. Future work will focus on full pipeline automation and validation against clinical data.

## Three-Dimensional Magneto Responsive Scaffolds for Remote Cellular Stimulation

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Remote magnetic stimulation offers a unique opportunity to modulate cellular signaling without electrodes, optical means, or direct contact. When exposed to alternating magnetic fields (AMF), magnetic nanoparticles (MNPs) generate localized heat capable of engaging temperature-sensitive signaling, including heat-sensitive ion channels.

Despite this promise, most existing magnetothermal systems rely on single MNP injections, which disperse rapidly in biological environments, reducing their effectiveness and lacking the properties required for stable, reproducible, and spatially confined activation. Moreover, delivering MNPs to soft and gentle tissues is challenging as it can involve penetration into the tissue.

To address these limitations, we introduce a strategy for creating three-dimensional magneto-responsive hydrogels with inherent adhesive properties and heat-dissipating capabilities under AMF stimulation. This platform combines the biocompatibility and structural stability of the hydrogel with the functional responsiveness of embedded MNPs, forming cohesive constructs that maintain nanoparticle distribution within a controllable microenvironment

We examined how interactions between the hydrogel and MNPs influence gelation, network architecture, mechanical properties, and heat dissipation under AMF exposure. In addition, we verify the biocompatibility and viability of primary neuronal culture grown within the three-dimensional magnetic system. This project opens new avenues for precise magnetothermal stimulation in deep organs.

# Cryoablation Temperature Monitoring with Dense Ultrasonic Slowness Shift Imaging

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<sup>1</sup>*School of Biomedical Engineering, Tel Aviv University, Israel*  
<sup>2</sup>*The Sagol School of Neuroscience, Tel Aviv University, Israel*

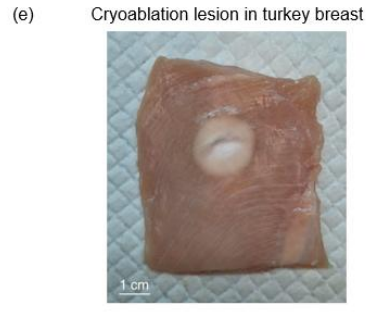
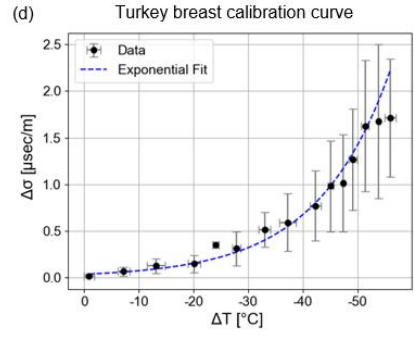
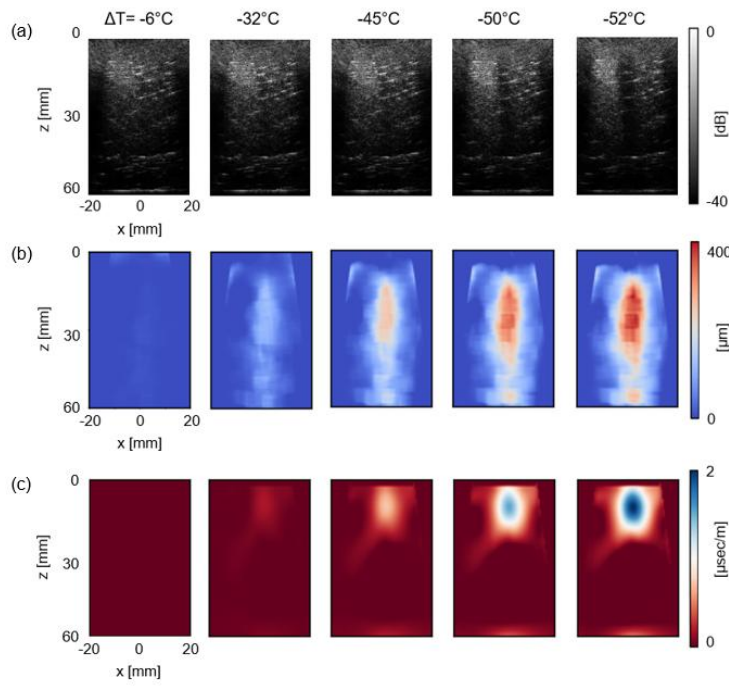
**Background:** Cryoablation is a minimally invasive technique for tumour destruction using extreme cooling, where achieving lethal temperatures while avoiding collateral damage requires accurate temperature monitoring. While effective, current temperature monitoring techniques rely on invasive thermometry, which carries risks of infection and additional tissue damage, or costly imaging modalities, limiting spatial coverage and clinical practicality. This work aims to develop a non-invasive, ultrasound (US) based method for real-time, spatially resolved temperature monitoring during cryoablation using a single transducer.

**Methods:** US RF data were acquired using a linear array transducer during cryoablation and reconstructed into B-mode images via Hilbert-based envelope detection. Dense optical flow was applied to consecutive B-mode frames to estimate temperature-induced pixel displacements. These displacement fields were incorporated into an inverse problem framework to estimate spatial slowness (inverse speed-of-sound) deviations, which were correlated with temperature changes. Experiments were conducted in agar phantoms and ex-vivo turkey breast samples, with thermocouple measurements serving as a reference.

**Results:** The proposed method was validated on tissue-mimicking agar phantoms and ex-vivo turkey breast samples undergoing cryoablation with a custom-built liquid nitrogen cryoprobe. Invasive thermometry served as the reference standard. Results showed a strong correlation between temperature drop,  $\Delta T$ , and speed-of-sound shifts, with measurable changes tracked from 11°C to -30°C in agar and from 15.7°C to -30°C in turkey breast. In the phantom, the dependence was linear with a relation of  $-20.70 \text{ ns}\cdot\text{m}^{-1}\text{C}^{-1}$ , while in turkey breast it presented an exponential relationship of  $34.04 \times \exp(0.075(-\Delta T)) \text{ ns}\cdot\text{m}^{-1}\text{C}^{-1}$ . The algorithm detected sub-degree temperature variations and accurately tracked cooling down to  $-39.4 \pm 5.6^\circ\text{C}$ .

**Conclusion:** This study demonstrates the feasibility of a single-transducer, US-based approach for non-invasive, spatial temperature monitoring during cryoablation. The results show the tissue-dependent nature of the temperature-slowness relationship and the need for calibration across tissue types, supporting the potential of this method for real-

time guidance of cryoablation therapies.



## Medical Device Lifecycle and Regulatory Compliance Diagram

**Shay Leventhal Gabay<sup>1</sup>**  
*RA360 Consulting, Israel*

In today's medical device environment, speed to market and regulatory compliance are no longer competing objectives. When regulatory strategy is integrated early and aligned with the business plan, compliance becomes a driver of innovation, quality, and commercial success rather than a source of delay.

This presentation emphasizes the importance of embedding regulatory strategy from the earliest stages of product conception, in parallel with technical development and commercial planning. Using U.S. FDA requirements and the EU Medical Device Regulation (Regulation (EU) 2017/745) as reference frameworks, regulatory science is presented as a risk-based, lifecycle-oriented discipline that directly influences development pathways, evidence generation, and market access decisions. Early clarity on regulatory classification and applicable controls is essential to avoiding late-stage redesign, unplanned clinical demands, and delays to commercialization.

Effective Regulatory Affairs leadership must combine three key domains: regulatory frameworks, the specific medical device technology, and associated medical and biological claims supporting the intended use. When these elements are aligned, regulatory strategy becomes a translational tool that connects engineering innovation with clinical and commercial realities.

The presentation will highlight how early adoption of a risk-based approach, including the application of ISO 14971 and alignment with quality system principles such as ISO 13485, supports informed decision-making throughout the device lifecycle. Through real-world examples, the session will demonstrate how lifecycle integration, cross-functional collaboration, and strategic Regulatory Affairs decisions enable earlier market access, stronger regulatory submissions, and more predictable development timelines.

Importantly, a well-defined regulatory strategy also plays a critical role in building trust—with investors, partners, regulators, and clinicians. Clear regulatory assumptions, risk transparency, and credible compliance planning strengthen investor confidence and support sustainable growth.

By integrating regulatory strategy, risk management, and business planning from the outset, medical device innovators can reduce uncertainty and ensure that compliance fuels excellence rather than delays innovation.

## Cellulose Fibers Enhance the Function of Hemostatic Composite Medical Sealants

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Dual-composite hydrogels represent a promising class of biomaterials whose performance can be tailored through the incorporation of functional fillers. By modifying the hydrogel's composition, these fillers influence its mechanical integrity, physical behavior, and ultimately its suitability for specific biomedical applications.

This study investigates a gelatin–alginate hydrogel cross-linked with carbodiimide and reinforced with two functional fillers—kaolin, a hemostatic agent, and cellulose fibers—to enhance mechanical strength and hemostatic performance for use as a medical sealant. The effect of the formulation parameters on the mechanical and physical properties was studied, as well as the biocompatibility and microstructure. The dual micro-composite structure exhibited uniform filler dispersion and strong interfacial adhesion, resulting in significant enhancements in sealing ability (247%), tensile strength (400%), and Young's modulus (437%) compared to the unfilled hydrogel. Cytotoxicity tests confirmed high cell viability for all formulations.

A comparative mathematical analysis was conducted to evaluate the combined influence of kaolin and cellulose fibers on the hydrogel's mechanical and physical performance. The relative results of each formulation were calculated with respect to the unfilled base hydrogel, and the averaged results were visualized in scatter plots. The analysis revealed a monotonic increase in mechanical performance with higher filler concentrations, demonstrating a synergistic effect at elevated fiber contents, where kaolin further enhanced strength. In contrast, improvements in physical properties—such as viscosity, gelation time, and swelling degree—were mainly attributed to fiber incorporation, while kaolin showed minimal impact.

Overall, the developed dual micro-composite hydrogels demonstrate strong potential as biocompatible, high-performance medical sealants, particularly when rapid and effective sealing is required. Understanding the relationship between formulation composition and material properties enables precise optimization for various clinical applications.

Selective Targeting of Non-Small Cell Lung Cancer in Three-Dimensional Models by Non-Thermal Millimeter-Wave Irradiation. Liberman-Aronov S.

**Stella Liberman-Aronov**, Helena Tuchinsky, Boris Litvak, Vladimir Freydin, Yosef Pinhasi, Asher Yahalom, Dhaval Patel  
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**Background:** Non-small cell lung cancer (NSCLC) represents approximately 85% of lung cancer cases and remains a leading cause of cancer-related mortality worldwide. Although systemic therapies have improved outcomes, treatment resistance and dose-limiting toxicities restrict their long-term efficacy. There is a critical need for innovative, non-invasive therapeutic strategies with improved selectivity. Millimeter-wave (MMW) radiation (30–300 GHz) is a non-ionizing electromagnetic modality with emerging biomedical applications, yet its therapeutic potential in solid tumors remains insufficiently explored.

**Methods:** Human NSCLC cell lines (NCI-H1299 and A549) and non-malignant lung fibroblasts were cultured as three-dimensional (3D) spheroids and micro-droplet assemblies to better mimic tumor architecture. Cells were exposed to frequency-swept MMW irradiation (90–96 GHz) using calibrated pyramidal horn and waveguide antennas under tightly controlled, non-thermal conditions. Exposure durations of 10, 30, and 60 minutes were applied. Cellular responses were evaluated 48 hours post-irradiation using XTT metabolic assays and flow cytometric analysis of apoptosis and necrosis. Long-term proliferative capacity was assessed using colony formation assays over 10–12 days.

**Results:** MMW irradiation induced a significant, exposure-dependent reduction in NSCLC cell viability. Metabolic activity decreased to approximately 85%, 62%, and 38% following 10, 30, and 60 minutes of irradiation, respectively, compared with sham controls. In contrast, non-malignant fibroblasts maintained high viability, demonstrating tumor-selective sensitivity. Flow cytometry revealed increased apoptotic fractions with minimal necrosis, and clonogenic assays confirmed sustained suppression of proliferative capacity.

**Conclusion:** Low-power, non-thermal MMW irradiation selectively inhibits survival and proliferation of NSCLC cells in physiologically relevant 3D tumor models. These findings support further mechanistic investigation and translational development of MMW-based non-invasive therapeutic strategies for solid tumors.

## Biomechanics Modeling of Traumatic Spinal Cord Injury Due to Ischemia

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**Background/Aim:** Traumatic spinal cord injury (SCI) involves primary neural damage and secondary damage triggered by vascular compromise, which may involve vascular compression that can lead to ischemia. The contribution of vascular compression to eventual neurological deficit remains poorly understood. This study aims to develop computational multi-physics models coupling organ-scale biomechanics with hemodynamic and oxygen transport to investigate secondary ischemic injury.

**Method:** The main focus of this study is on the hemodynamic-oxygen diffusion modelling that will ultimately be incorporated into a 3D mechanical SCI model of a human spine. First, to understand the connection between vessel geometry and flow resistance, computational fluid dynamics analyses were created to evaluate five buckled tube configurations representing compressed vessels. To understand the physics of oxygen diffusion and mass transfer, a Krogh-type cylinder model was also implemented. This baseline oxygen transport model utilizes a thermal analogy, defining metabolic oxygen consumption as a sink term via Michaelis-Menten kinetics. The next steps of this ongoing work will combine flow and oxygen diffusion into unified framework to investigate the transport in microvasculature deformed by traumatic injury.

**Results:** The buckled vessel simulations demonstrated that transitioning from an elliptical to an hourglass cross-sectional profile caused an exponential increase in flow resistance. Flow separation and vortex formation were observed downstream of maximum tapering in extreme narrowing, significantly influencing local hemodynamic. The resistance to oxygen transport is also expected to be significantly altered.

**Conclusion:** Multiphasic coupling of biomechanics, mass transfer, and oxygen diffusion provides vital insights into secondary SCI mechanisms. The coupling with the distinct SCI patterns (burst fracture, dislocation, and distraction) is expected to affect the oxygen distribution, which can help identify risks of ischemia.

## Virtual Reality Systems for Treating PTSD: Israeli-Tailored Prolonged Exposure and Place Attachment Therapy

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The war which broke out on October 7th has caused widespread psychological trauma among soldiers and civilians, leading many of them to develop conditions such as post-traumatic stress disorder (PTSD).

While traditional therapies offer some relief, the global mental health crisis, limited access to care, technical limits, and lack of personalization hinder effective treatment. Furthermore, existing treatments simply do not help all patients. Virtual Reality (VR) is emerging as a promising tool to address these challenges. Chief among the approaches to utilizing VR for prolonged exposure therapy is project Bravemind, which was developed in the US for veterans of the Iraq and Afghanistan wars and has shown impressive clinical results.

We will discuss how we are adapting this tool and expanding its capabilities to align with the specific needs of soldiers and civilians affected by the Israeli Palestinian conflict. This includes new tailored scenarios and events that match local conditions, geography and culture guided by a focus group of seasoned Israeli therapists.

Additionally, we are developing a novel VR tool called re-PAVeR that focuses on Place Attachment theory and bereavement processing, facilitating emotional processing by reconstructing damaged emotionally critical scenes such as a damaged Mamad and dynamically interacting with them in real-time. Ultimately, our research seeks to contribute to the development of accessible and effective mental health interventions, particularly for individuals who have experienced trauma and loss.

# Effects of Arterial Wall Roughness and Mechanical Stiffness on Hemodynamics in 3D-Printed Vessel Models

**Shai Maman**<sup>1</sup>, Moshe Halak<sup>2</sup>, Idit Avrahami<sup>3</sup>, Moran Aviv<sup>4</sup>, Zehava Blechman<sup>1</sup>

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<sup>3</sup>*Department of Mechanical Engineering and Mechatronics, Ariel University, Israel,*

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**Background:** Arterial stiffness governs pressure-wave propagation and cardiovascular risk. Pulse transit time (PTT) and pulse wave velocity (PWV) quantify arterial mechanics. While bulk stiffness effects are established, the contribution of intraluminal wall roughness and its interaction with fluid properties remain unclear.

**Objective:** To examine how arterial wall roughness and mechanical stiffness influence pressure-wave propagation in 3D-printed vessel models.

**Methods:** Elastic vessel models were fabricated using PolyJet™ 3D printing (Elastico™ photopolymer) with controlled stiffness and intraluminal textures. Mechanical validation included Shore-A calibration, Micro-CT–based inflation, and uniaxial tensile testing, confirming graded stiffness levels within clinically relevant ranges. Surface morphology was assessed by profilometry and Micro-CT. Hemodynamics were evaluated in a closed-loop pulsatile system in which fluid viscosity was systematically varied. Pressure waveforms were recorded using dual high-fidelity pressure sensors (Millar Instruments Inc.) at 10 kHz. PTT and PWV were computed using a dedicated pressure signal-processing algorithm developed and implemented in MATLAB software (MathWorks Inc., USA).

**Results:** Mechanical testing confirmed graded stiffness behavior within clinically relevant ranges. Inflation yielded physiologically consistent compliance trends, whereas tensile testing revealed anisotropy and stiffness overestimation related to additive manufacturing. Surface analysis demonstrated submicron roughness in smooth-walled models and measurable deviations from nominal geometry in dense roughness configurations. Increasing fluid viscosity prolonged PTT and reduced PWV in smooth-walled models. High-density wall roughness further modulated pressure-wave propagation, indicating interaction between stiffness, surface geometry, and fluid properties.

**Conclusions:** Arterial wall roughness and mechanical stiffness jointly modulate hemodynamic wave propagation beyond bulk elasticity alone. The multidimensional experimental framework developed in this study enables controlled dissociation and quantification of structural contributions (arterial stiffness and surface morphology) as well as fluid-dynamic effects (related to viscosity) through dedicated pressure wave analysis. The current approach provides a powerful biophysical characterization platform for assessing arterial compliance and guiding the design of biomimetic vascular systems.

# Biomimetic Silk-Reinforced IPN Hydrogel Composite Tubular Constructs for Coronary Artery Replacement: Mechanical Performance

**Dekel Maroz, Yana Portnov, Mirit Sharabi**

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Coronary artery disease (CAD) remains the leading global cause of death, with over 450,000 coronary artery bypass graft (CABG) surgeries performed annually in the U.S. alone. Current graft options for small-diameter arteries face critical limitations, including compliance mismatch and poor long-term durability. This work presents a novel silk-reinforced interpenetrating polymer network (IPN) hydrogel composite designed to replicate key structural and mechanical features of native coronary arteries.

The composite combines a crosslinked alginate–polyacrylamide hydrogel matrix, mimicking elastin and proteoglycans, with silk fibers oriented longitudinally and cross-plied to emulate collagen. Tubular grafts were fabricated by wrapping and crosslinking fiber-reinforced hydrogel sheets. Mechanical testing included uniaxial tension, cyclic loading, compliance measurement, and hydrostatic burst pressure testing, benchmarked against native porcine arteries.

Results show the composite achieves tensile strengths of 6.77–8.13 MPa and strain-to-failure near 47–48%, with toughness exceeding 5.8 MJ/m<sup>3</sup>. The material demonstrated low hysteresis under cyclic loading and maintained structural integrity in tear resistance tests. These properties closely align with the mechanical behavior of native vessels.

This biomimetic design highlights the importance of structure-function replication in vascular graft development. By integrating soft, extensible IPNs with collagen-like reinforcement, the composite achieves mechanical compatibility with native arteries and shows strong potential for use in small-diameter coronary grafts.

Soft Tissue Hybrid Bioprinting for Tissue Engineering using a PLGA-Particle  
Reinforcement Bioink

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Three-dimensional bioprinting has emerged as a significant technology in tissue engineering, enabling the fabrication of complex, patient-specific constructs with high precision. This approach typically utilizes soft, cell-laden hydrogels that mimic the native extracellular matrix, providing a supportive environment for cellular growth and differentiation.

However, a critical and persistent challenge in soft tissue bioprinting is the significant structural contraction and deformation of these constructs over time. This phenomenon, driven by the contractile forces exerted by the embedded cells, compromises the intended architecture, mechanical integrity, and overall functionality of the engineered tissue, representing a major challenge in the field.

This research presents a novel hybrid bioprinting approach that incorporates a stiff, thermosensitive reinforcement network within the soft tissue matrix to reduce deformation. Our goal is to create large, mechanically stable constructions that resist contraction while still supporting cellular proliferation and maturation. We developed a reinforcement bioink composed of biocompatible Poly(lactic-co-glycolic acid) (PLGA) and PEG microparticles engineered to sinter at physiological temperature. This bioink was co-printed with soft, cell-laden hydrogels (Collagen Methacrylate and Fibrin) to form hybrid constructs. We evaluated the system with various cell types, including myoblasts and fibroblasts.

Characterization of the constructs included SEM imaging, rheology, immunofluorescence, and time-lapse analysis of construct contraction. In skeletal muscle models, the hybrid reinforced constructs significantly mitigated cell-induced shrinkage, retaining approximately 76% of their original surface area after 5 days, compared to 35% retention in non-reinforced controls. Biologically, the reinforcement actively enhanced tissue maturation; reinforced constructs exhibited significantly higher expression of the myogenic marker desmin and superior myotube alignment compared to controls.

This research demonstrates a hybrid bioprinting platform that effectively combines structural stability with biological compliance. By preventing hydrogel contraction and promoting tissue maturation, this approach enables the bio fabrication of large-scale, dimensionally accurate soft tissues for regenerative medicine.

# Quantitative Monitoring of Immunotherapy Treatment Response in Pediatric Tumors Using Molecular CEST MRI

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**Introduction:** Brain tumors remain the leading cause of cancer-related mortality in children. CAR T cells recently sparked hope as a potential therapeutic avenue. However, subject-specific optimization necessitates noninvasive monitoring of treatment response. As conventional MRI primarily detects late structural changes in tumor volume, it cannot reliably distinguish treatment response from progression. Chemical exchange saturation transfer (CEST) MRI is an emerging imaging technique capable of providing molecular tissue biomarkers that precede anatomical changes. Here, we developed a physics-driven AI CEST framework to derive quantitative biomarkers for early detection and assessment of immunotherapy response in a pediatric tumor mouse model.

**Methods:** CEST MRI data were acquired longitudinally in immunotherapy treated tumor-bearing mice (n=29, 48% control). Each scan took 4 minutes. Quantitative biomarker maps for intracellular pH, mobile protein and semisolid macromolecules concentration were extracted using mathematical tissue models and a self-supervised variational autoencoder (inference time= 3 minutes).

**Results and Discussion:** The resulting biomarkers were compared to survival rates, conventional tumor volume estimates and immunohistochemistry (IHC). All CEST-derived parameter maps yielded a clear delineation of the tumor regions and demonstrated statistically significant separation from healthy tissue (p<0.01). A decreased amide proton volume fraction was observed in the tumor, consistent with the substantial edema shown in the anatomical images. A statistically significant decrease in the amide proton exchange rate was observed in the tumor by week 2 in the treated mice, yet not in the control mice (p ≤ 0.0001), in agreement with the necrosis observed by IHC. Amide proton exchange rates were also correlated with survival rates.

**Conclusion:** A rapid and quantitative molecular MRI method was developed, capable of detecting the tissue cell death associated with immunotherapy treatment response.

# Fiber-Reinforced Interfaces Enhance Mechanical Integrity in Biomimetic Intervertebral Discs

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The exceptional biomechanical performance of the intervertebral disc (IVD) arises from its complex hierarchical structure, where interlamellar and radial fiber networks play critical roles in load transfer and mechanical resilience. However, the precise contribution of these fiber networks remains incompletely understood.

Here, we present a biomimetic strategy that replicates these native interfaces using silk-based sutures to fabricate annulus fibrosus–nucleus pulposus (AF–NP) constructs. Mechanical testing revealed that suture-reinforced laminates exhibited superior shear strength ( $0.87 \pm 0.06$  MPa) and markedly reduced tensile modulus variability (from 43% to 4%), reflecting enhanced interlamellar cohesion.

Radial fibers further improved compressive performance by limiting radial expansion and maintaining internal pressure. Finite element (FE) modeling confirmed that these fibers redistributed stresses at the AF–NP interface, reduced peak matrix strains, and promoted broader circumferential fiber activation under physiological loading.

Collectively, our results highlight the critical role of fibrous interfaces in IVD mechanics and demonstrate that their replication within simplified biomimetic constructs enhance mechanical integration and load distribution. This framework offers valuable design principles for next-generation IVD repair and replacement strategies and informs broader approaches to soft tissue engineering.

## Synthetic Modular Contact-Dependent Microbe-to-Mammalian Communication

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Currently, synthetic biology most often incorporates genetic circuits that take effect within a single cell – the cell detects changes in the internal composition and generates an output.

In recent years a few genetic circuits started involving communication between cells. However, these genetic circuits either involve direct communication between two cells of the same type (e.g. mammalian cells with mammalian cells, bacteria with bacteria) or indirect communication between two different types of cells (e.g. bacteria releasing immune modulators to diffuse and be picked up by immune cells, mammalian cells releasing bacterial quorum-sensing molecules to the environment to modulate bacterial growth).

Here, we present a system allowing direct protein-protein communication between bacteria and mammalian cells. Unlike indirect forms of communication, direct communication in the form of protein-protein interaction requires the physical presence of both the sender and the receiver of the signal. This flexible well-regulated platform based on efficient prokaryote-eukaryote interaction provides a new toolbox to program host cells interacting with their environments.

## Seaweed-derived Cellulose Scaffolds: A Novel Platform for Mammalian Cell Cultures with 3D Infiltration and Proliferation

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The extracellular matrix (ECM) provides essential structural and biochemical support for cell growth, attachment, and proliferation, which greatly impact cell fate. This study investigates the use of seaweed cellulose (SC) scaffolds derived from green macroalgae as innovative biomaterials for mammalian cell culture and evaluated as alternative ECM candidates.

SC scaffolds were fabricated using an optimized decellularization process that preserved their distinct porous (*Ulva*) architectures. The SC scaffolds were evaluated for their toxicity, biocompatibility, and ability to support 3D cell infiltration and proliferation. Several mammalian cell lines—NIH3T3 fibroblasts, C2C12 myoblasts, and NIH3T3-L1 preadipocytes—were cultured on the SC scaffolds. Each of the three cell types was cultured individually on the scaffold and subsequently co-cultured to generate a tissue-like construct.

Fluorescence microscopy, confocal laser scanning microscopy, environmental scanning electron microscopy (ESEM), and an image-processing algorithm were employed to evaluate cell attachment, morphology, infiltration, and scaffold structure. The results demonstrated successful cell adhesion, growth, and infiltration throughout the scaffold depth, with variations in nanostructure and pore size influencing cellular behavior.

These findings highlight the potential of seaweed-derived cellulose scaffolds as biocompatible and sustainable alternatives for tissue engineering applications. Further research is warranted to address natural variability in seaweed composition and optimize long-term scaffold performance.

Overall, this work presents a promising step toward the development of marine-based biomaterials for regenerative medicine.

## Biomechanics Modeling of Traumatic Spinal Cord Injury Due to Hemorrhage

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**Background/Aim:** Traumatic spinal cord injury (SCI) affects approximately 180,000 individuals worldwide annually, often leading to permanent neurological dysfunction. While initial mechanical trauma causes immediate damage, secondary injury processes, specifically vascular disruption leading to hemorrhage, may aggravate long-term neurodegeneration. However, the relative contribution of mechanical versus vascular factors to neurological deficits is yet to be fully understood. This research aims to develop and apply computational multiphysics models to identify and quantify the risk of hemorrhage across various SCI scenarios.

**Method:** Numerical simulations were performed using Simulia Abaqus to model the thoracic human spine. The model incorporated detailed anatomy, including white/gray matter, pia mater, dural and epidural sac, and employed smoothed particle hydrodynamics (SPH) for the cerebrospinal fluid (CSF). Three injury patterns are being simulated: burst fracture, dislocation, and distraction. Hemorrhage risk will be evaluated by monitoring stress and strain levels, with vascular rupture predicted when thresholds are exceeded. A rat cervical spine model was also developed to validate the model against experimental data.

**Results:** In the rat model, the strain patterns showed high correlation with experimental results across two distinct injury mechanisms: contusion and dislocation. For the human model, simulations were performed in different velocities and displacements to observe the distribution of maximum principal strain across the cord. The ongoing work includes implementing a burst fracture injury scenario and integrating hemorrhage detection capabilities. After modeling the other injury patterns, it will be possible to compare them and analyze how each scenario affects the hemorrhage risk.

**Conclusion:** By correlating mechanical loads with vascular rupture risk, these models provide a tool to map high-risk hemorrhage regions onto spinal anatomy. Validating these predictions against experimental data will improve the understanding of secondary injury mechanisms, potentially informing clinical assessments of injury severity and progression.

# Benchmarking AI Against Expert Ophthalmologists for Clinical Detection of Referable Eye Diseases

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**Introduction:** The past few years have witnessed a rapid proliferation of AI systems for the automated interpretation of digital fundus images (DFIs). However, their comparative performance against human expert interpretation remains insufficiently characterized. The aim of this study was to compare the diagnostic performance of an AI system, Lirot.ai, with that of board-certified ophthalmologists in detecting referable eye diseases from single, color non-mydratric DFIs.

**Methods:** This study evaluated the detection of three vision threatening ophthalmic diseases: (1) referable diabetic retinopathy (rDR), (2) referable age-related macular degeneration (rAMD), and (3) glaucomatous optic neuropathy (GON). Primary endpoints included the sensitivity and specificity for detection of each referable eye disease by Lirot.ai versus human readers. Secondary endpoints include inter-reader agreement ( $\kappa$ ), human-hours required to annotate, and subset analysis of detection performance on images marked ungradable by human readers.

**Results:** A total of 10 ophthalmologists were recruited for the study: 80% of whom were specialists and 80% of whom had  $\geq 6$  years of clinical experience. Fleiss'  $k$  among readers was 0.401 for GON detection, 0.663 for rAMD detection, and 0.719 for rDR detection. Lirot.ai's sensitivities across GON, rAMD, and rDR detection were the maximum among readers while maintaining specificities within the observed range of reader performance. Lirot.ai detected GON with an AUROC of 0.860 (sensitivity and specificity of 88.2% and 74.3%, respectively), rAMD with an AUROC of 0.923 (sensitivity and specificity of 92.9% and 89.6%, respectively), and rDR with an AUROC of 0.954 (sensitivity and specificity of 91.7% and 94.0%, respectively) where sensitivities and specificities maximize Youden's Index. Lirot.ai met or exceeded readers' disease detection across GON, rDR, and rAMD as evident by readers' sensitivity-specificity performance along or below the ROC curve.

**Conclusion:** Lirot.ai demonstrated expert-level performance across all referable eye diseases and even surpassed human readers in GON detection, demonstrating the potential of AI to provide consistent, high-quality interpretation of fundus images. These results highlight how AI systems can enhance clinical decision-making and expand access to eye care by supporting large-scale, efficient screening pathways.

# A Microfluidic Nanoliter-Well Platform for Direct-from-Sample Rapid Phenotypic Antimicrobial Susceptibility Testing

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**Background:** The escalating global threat of Antimicrobial Resistance (AMR) demands diagnostic tools that are faster and more sensitive than traditional bulk-culture methods. Current gold-standard techniques often require 24–72 hours for pathogen isolation and susceptibility profiling, leading to the prolonged use of suboptimal broad-spectrum antibiotics. To address this, we develop a microfluidic platform designed to provide rapid phenotypic antimicrobial susceptibility testing (AST) results directly from complex clinical samples by leveraging nanoliter-scale cellular partitioning.

**Methods:** The technology utilizes a microfluidic architecture to discretize liquid samples into thousands of isolated nanoliter wells. This confinement is engineered to accelerate the detection of metabolic signals by concentrating bacterial activity within a minute volume, improving the existing lengthy pre-enrichment. An automated high-throughput reader monitors growth dynamics in real-time. We are currently integrating Machine Learning (ML) algorithms to automate bacterial identification and enable the resolution of polymicrobial infections. The system's robustness is being evaluated using clinical matrices, including blood and urine, to assess performance across varying pathogen loads and sample compositions.

**Results:** Preliminary testing demonstrates that the platform can enable transfer to AST from a whole blood sample within 6 hours, which is significantly faster than standard methods. Experiments with contrived polymicrobial mixtures demonstrate that partitioning individual cells within the micro-well array allows for the de-convolution of complex polymicrobial samples and the identification of hetero-resistant phenotypes, sub-populations which are typically masked in bulk culture. The integrated microfluidic metering has shown high precision in handling the dynamic range of clinical samples, ensuring consistent loading across the array.

**Conclusion:** This microfluidic-ML hybrid approach aims to bring novel engineering approaches to the clinical microbiology lab. By delivering rapid, actionable phenotypic guidance directly from samples, the platform provides a scalable solution to optimize antibiotic stewardship and improve patient outcomes in the face of rising antimicrobial resistance.

## Enhancing Drug Permeability into Solid Tumors Via Opto-Electronic Silicon Nanowires Mediated Electroporation

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**Objective:** Many solid tumors are harder to treat due to physical barriers that often limit therapeutic agent distribution and efficacy. Several external stimuli methods, such as ultrasound, ionizing radiation, and photothermal stimulation, are being tested to improve drug delivery into solid tumors. Electroporation (EP) uses electric pulses to permeabilize cell membranes to insert macromolecules such as oligonucleotides and proteins in in-vitro cell cultures. Currently, EP is applied invasively, requiring electrodes to be placed in direct contact with the cells to deliver the electrical pulses. In this study, we evaluate optoelectronic silicon nanowires (SiNWs) which are semiconducting nanomaterials capable of light-triggered electrical stimulation, as a tool to remotely induce membrane poration as a minimal-invasive strategy to enhance permeability in 2D and 3D cancer models.

**Methods:** 2D and 3D in vitro models of Head and Neck Squamous Cell Carcinoma cultures (Cal33) were used to test SiNWs photoelectrical effects. Uptake of SiNWs was visualized via bright-field, light-sheet fluorescence, and confocal microscopy, followed by 3D reconstruction in Imaris. Samples were optically stimulated using LED pulses by using Incucyte microscope and a tailor-made LED system. Viability was assessed with the CellTiter-Glo assay, and membrane permeability was tested by propidium iodide penetration assays.

**Results:** Confocal and light sheet microscopy confirmed SiNW internalization in both 2D cells and 3D spheroids. Post-stimulation cell viability showed high safety profile and optically stimulated spheroids exhibited an increase in non-permeable propidium iodide uptake compared to unstimulated controls.

**Conclusion:** Preliminary results show that optoelectronic stimulation using SiNW enhances spheroids' permeability. In future work, we plan to optimize the method to achieve better poration results and to enhance the permeability of different macromolecules, drugs, and nanoparticles for cancer treatment.

## Combining Supramolecular and Covalent Chemistry to form versatile Reinforced Fibrillar Network Hydrogels from Fibrin and Methacrylated Fibrinogen

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Fibrin hydrogels provide a highly supportive environment for three-dimensional cell growth and morphogenesis but are limited by insufficient stability to maintain their shape and mechanical integrity.

We developed a fibrin hydrogel reinforced with photopolymerized methacrylated fibrinogen (FibMA) to overcome this limitation. Hydrogels were formed through thrombin activation of fibrinogen to initiate the supramolecular assembly of fibrin (i.e., fibrillogenesis), followed by light-activated covalent crosslinking of the FibMA (i.e., photopolymerization). The unique interaction between the supramolecular chemistry and covalent chemistry, in tandem, resulted in a reinforced fibrillar network (RFN) structure which contributed to exceptional mechanical properties of these interpenetrating polymer network (IPN) hydrogels.

Precise control over the final Fibrin-FibMA IPN hydrogel (i.e., FibMAtrx) modulus was achieved simply by delaying the initiation of the photochemistry, thereby increasing the thrombin reaction time (TRT). We observed an increase in modulus following covalent crosslinking of the FibMAtrx by more than one order of magnitude, depending on the TRT and the extent of the supramolecular reaction between fibrin and FibMA. Cell growth experiments with fibroblasts within the FibMAtrx IPN showed high viability and extensive morphogenesis, with quantitative cell spreading influenced more by the FibMA content than by the modulus of the hydrogel. Cell-mediated hydrogel shrinkage following one week (i.e., compaction) was limited, likely due to the FibMA reinforcement of the fibrin, whereas in comparison, fibrin single network hydrogels (SNH) compacted to a fraction of their original size.

Our study demonstrates the potential of developing proteinaceous reinforced fibrillar network hydrogels from fibrinogen and FibMA that support cellular growth, enable tunable mechanical properties, and maintain shape integrity by mitigating the rapid shrinkage associated with cell growth in fibrillar protein hydrogels.

“Programmable Hybrid Systems for Targeted Cancer Therapy: Integrating Engineered Bacteria and Mammalian Cells”

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Synthetic biology is revolutionizing cancer therapeutics through the engineering of gene circuits, which has shown remarkable success in cancer treatment. However, the treatment of solid tumors remains limited by systemic toxicity and poor spatial precision.

Engineered bacteria have been shown to possess an innate capacity to colonize the immunosuppressive tumor microenvironment (TME), yet they lack the intrinsic potency required for complete tumor regression. Chimeric Antigen Receptor (CAR) T-cell therapies, meanwhile, provide highly potent cytotoxic activity but also remain limited by off-tumor toxicities. To address these limitations, we developed a programmable hybrid platform that integrates engineered bacteria and mammalian immune cells to achieve tumor-restricted therapeutic activation.

The platform includes two modules: (1) a bacteria–CAR-T system in which tumor-homing bacteria present an activation cue that conditionally induces CAR expression in SynNotch-engineered T cells only at the tumor site; and (2) a bacterial–mammalian communication module in which lentivirally programmed tumor cells express a SynNotch receptor that detects engineered bacteria, triggering localized expression of cytotoxic factors within the TME. By requiring both tumor-specific signaling and physical cell-cell interaction, this dual-verification architecture functions as a biological "AND-gate," strictly confining cytotoxic activity to the TME.

Furthermore, a quorum-sensing-based "CLOCK" system was incorporated into program bacterial self-lysis, ensuring post-delivery biosafety. This modular strategy establishes a high-precision framework for immunotherapy, significantly enhancing the safety and efficacy of solid tumor treatments.

## Early Detection of CAR-T-Associated Neurotoxicity via Cytokine Monitoring in Serum

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Immune effector cell-associated neurotoxicity syndrome (ICANS) is a common and life-threatening complication of chimeric antigen receptor (CAR) T-cell therapy. Clinical management currently relies on neurological assessment after symptom onset, limiting opportunities for early intervention.

Cytokines such as interleukin-6 (IL-6) are key mediators of the inflammatory cascade underlying ICANS pathogenesis, but prospective clinical evidence for their predictive value is limited. In a prospective cohort of 40 CAR-T patients (270 longitudinal serum samples), we performed daily IL-6 monitoring using a simple in-house microfluidic bead immunoassay and evaluated its temporal association with ICANS development.

IL-6 levels were significantly elevated one day prior to ICANS onset. In generalized estimating equation models, a 3.4-fold rise in IL-6 concentration was associated with a 74% increase in the odds of developing ICANS the following day, independent of other clinical variables. These findings provide prospective evidence that short-term IL-6 dynamics can serve as an early-warning biomarker for CAR-T-associated neurotoxicity.

Motivated by the need for practical, frequent cytokine surveillance, we subsequently developed a compact, pump-free optofluidic microfluidic platform for rapid, random-access biomarker quantification. The system integrates passive capillary-driven flow with bead-based sandwich immunoassays and automated fluorescence imaging, enabling quantitative cytokine measurement from small sample volumes without external pumps or centralized instrumentation.

Designed for on-demand, single-sample operation, the platform demonstrates the feasibility of translating longitudinal cytokine monitoring into a simplified point-of-care format. Together, our clinical findings establish IL-6 as a prospective predictor of next-day ICANS, and our engineering approach provides a pathway toward accessible, near-patient cytokine monitoring for safer CAR-T therapy management.

# Selective Anti-Cancer Influence of Millimeter-Wave Irradiation on Solid Tumor Viability and Division

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**Background:** Millimeter-wave (MMW) irradiation represents a promising non-invasive, non-thermal modality for cancer treatment. However, the influence of uniform electromagnetic parameters on genetically distinct solid tumors remains insufficiently characterized.

**Methodology:** Lung (NSCLC), breast, and melanoma cancer cell lines, together with corresponding non-cancerous controls, were exposed to 90-96 GHz MMW irradiation generated by a frequency-sweeping synthesizer and delivered via a calibrated pyramidal horn antenna with a power density of 5 mW/cm<sup>2</sup>. Irradiation was applied at constant, non-thermal power density with controlled exposure durations. Experiments were performed on 2.5×10<sup>4</sup> cells in 20 μL droplets to ensure consistent field distribution. Acute cytotoxicity (day 2) was evaluated using a % cell proliferation assay, chronic effects (day 10) by colony formation assay, and apoptosis by flow cytometry.

**Results:** Under identical electromagnetic conditions, MMW irradiation induced significant time-dependent cytotoxicity in cancer cells with minimal effects in normal counterparts. Lung cancers showed genotype-dependent sensitivity, with p53-deficient H1299 more affected than KRAS mutant A549 under 60 min exposure. Breast cancer responses were subtype-specific: MCF7 exhibited greater sensitivity at shorter exposure, whereas MDA MB 231 required longer duration for maximal apoptosis. Melanoma exhibited the strongest response, with A375 and A2058 reaching 95–97% apoptosis versus ≤8% in BJ fibroblasts. Although all tumor types showed a response, the duration of exposure needed to achieve significant cytotoxic effects varied among different genotypes. Chronic assays showed greater suppression, confirming cumulative non-thermal effects.

**Conclusion:** Non-thermal 90–96 GHz MMW irradiation induces selective, genotype-dependent anticancer effects across solid tumor models. Tumor-specific biological properties—not field intensity—determine cytotoxic sensitivity, identifying exposure duration as the key biological tuning parameter. These findings support the development of precision, tumor-type-specific irradiation protocols and highlight MMW irradiation as a promising, non-invasive therapeutic strategy.

## Design of Bioactive Titanium Porous Structures via Binder Jetting, Partial Sintering and Surface Modification

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Additive manufacturing offers unprecedented control over the microstructure and porosity of biomaterial scaffolds.

Here we present a strategy for producing bioactive, porous Ti-6Al-4V structures using binder jetting (BJ), controlled partial sintering, and subsequent oxidizing surface modification. Near-spherical, plasma-atomized Ti-6Al-4V powder was printed on an ExOne M-Flex machine using a water-based binder to fabricate 10 mm cubic specimens. The green parts were cured at 200 °C for 4 h and then sintered at 900 °C for 4 h in an argon/oxygen mixture (99.9%/0.1%) to promote interparticle necking and the formation of a TiO<sub>2</sub> oxide layer while preserving high levels of open porosity. Bulk density and microstructural analysis confirmed a relative density of ~0.25–0.30 with neck formation between the original powder particles.

Uniaxial compression testing demonstrated that the partially sintered specimens exhibited a typical cellular solids response, with an average peak compressive stress of  $18.4 \pm 0.3$  MPa, sufficient to maintain structural integrity during handling and subsequent processing.

To enhance bioactivity and corrosion resistance, porous samples with a thin surface oxide layer were dip-coated, forming a surface layer enriched in calcium and phosphorus compounds. Scanning electron microscopy and energy-dispersive X-ray spectroscopy demonstrated that sintering in an argon-oxygen mixture yields a conformal nanoporous TiO<sub>2</sub> matrix coating without compromising the sample's mechanical strength. Calcium and phosphorus precursors are then applied to the matrix coating as a base, forming an amorphous hydroxyapatite structure.

The combined BJ sintering-dip coating method provides a flexible, scalable approach for targeted modification of the mechanical properties and surface chemical composition of titanium implants. By adjusting sintering temperature and duration, pore geometry and mechanical strength can be independently modified, while the dip-coating method provides a bioactive surface suitable for osseointegration. Thus, this method enables the creation of customized, load-bearing titanium scaffolds for orthopedic applications.

## Fiber-Oriented Composite Design for Biomimetic Aortic Valves

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Heart valve pathologies affect millions worldwide each year. Bioprosthetic and mechanical valves remain the standard of care for surgical replacement, yet both options have persistent limitations, including finite durability, anticoagulation, and impaired hemodynamics. Prior studies have advanced tissue-engineered heart valves through structural and material strategies to improve functional performance. Here, we investigated how fiber architecture influences mechanical behavior and dynamic valve function.

Two fiber-oriented laminates were engineered with circumferentially aligned primary fibers; one design incorporated an additional radial ply. Mechanical properties were quantified by uniaxial tensile testing along circumferential and radial axes across predefined leaflet regions and benchmarked against reported native leaflet properties. Additional testing included damage tolerance behavior and hysteresis under 1000-cycle loading. Tissue-engineered valves preserving each laminate architecture were then fabricated and tested in a pulsatile heart-pump system to quantify geometric opening area and observe diastolic pressure.

Both laminate designs demonstrated anisotropic, nonlinearly elastic behavior. The radially reinforced architecture more closely reproduced native-like mechanics in both axes, whereas the circumferential-only design primarily matched native behavior along the circumferential axis. In pulsatile testing, valves incorporating the radial architecture achieved a larger opening area and improved diastolic pressure holding, consistent with enhanced coaptation.

In conclusion, biomimetic leaflet behavior is most effectively achieved when circumferential and radial architectures are combined. Radial reinforcement alongside circumferential alignment improved mechanical behavior and functional performance under pulsatile flow, underscoring fiber architecture as a primary design lever for advancing durable, hemodynamically competent engineered aortic valves.

# Predicting Arteriovenous Fistula Failure: An Iterative CFD Framework for Intimal Hyperplasia Progression

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**Background:** Hemodialysis is the primary treatment for over two million end-stage renal disease patients globally. Arteriovenous fistula (AVF) remains the "gold standard" for vascular access, yet 20-60% fail within the first year due to hemodynamic disturbances triggering neointimal hyperplasia (IH) and stenosis. This study proposes a semi-automated iterative computational fluid dynamics (CFD) framework to predict stenotic progression by correlating local hemodynamic triggers with virtual vessel wall remodeling.

**Method:** Three-dimensional AVF geometry was generated based on an idealized side-to-end anastomosis. Transient CFD simulations were performed under physiological pulsatile flow to quantify wall shear stress (WSS), oscillatory shear index, and relative residence time (RRT). We suggest a semi-automated iterative framework to simulate vascular remodeling in different stages. It involves identifying high-risk regions based on hemodynamic thresholds, following virtual geometry deformation in these regions to represent IH progression. Then, the flow is modeled again leading to further mesh morphing for the successive steps.

**Results:** Iterative simulations successfully identified high-risk hemodynamic zones correlating with clinical stenosis sites. The model specifically pinpointed the juxta-anastomotic vein and the venous "swing segment" as primary regions of disturbed flow, characterized by elevated RRT and low WSS. These findings align with longitudinal studies identifying these locations as highly susceptible to IH. Furthermore, the observed non-linear reduction in volume flow as stenosis progressed demonstrates the model's ability to accurately capture dynamic AVF maturation.

**Conclusion:** Incorporating iterative geometric transformations into CFD models provides dynamic predictions of AVF maturation superior to simulations of a specific progression state. This approach enables a deeper understanding of the risk associated with the vicious cycle mechanism during the AVF maturation process. This highlights the potential of patient-specific computational modeling as a robust clinical decision-support tool to aid surgeons in preoperative planning and optimize anastomosis configurations, ultimately enhancing long-term vascular access patency.

## Quantitative Assessment of Early Post-Type 2 Myocardial Infarction Remodeling

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**Background:** Myocardial infarction (MI) remains a leading cause of mortality worldwide. Unlike Type 1 MI, Type 2 MI (T2MI) arises from an imbalance between myocardial oxygen supply and demand, resulting in significant cardiac injury. This study aimed to characterize the early (4-day) pathophysiology of T2MI using a single high-dose isoproterenol (ISO) model in female mice, emphasizing quantitative cardiac-gated CT for microvascular dynamics alongside fibrosis, endothelial remodelling, and hematopoietic responses.

**Methods:** C57BL/6J female mice (8-12 weeks) received a single intraperitoneal ISO (160 mg/kg) or saline (control). At 4 days post-injection, cardiac-gated CT (MILabs Series7) with ExiTron nano contrast assessed vascular permeability via signal-intensity ratio (SIR Myo/LV) kinetics in septal/lateral walls. Hearts underwent Masson's trichrome for fibrosis and endomucin IHC for endothelial area (QuPath). Flow cytometry analyzed peripheral blood leukocytes and bone marrow hematopoietic stem/progenitor cells (HSPCs; BD LSRFortessa, FlowJo). Mann-Whitney U tests compared to groups (p<0.05).

**Results:** Gated-CT revealed impaired septal vascular permeability in MI: higher baseline SIR ( $0.370 \pm 0.0018$  vs. control  $0.284 \pm 0.00007$ ,  $p=0.0079$ ), but declining slope ( $-0.00090 \pm 0.00047 \text{ min}^{-1}$  vs. rising in control  $0.00182 \pm 0.00160 \text{ min}^{-1}$ ,  $p=0.0079$ ), indicating impaired permeability. Collagen area increased in MI ( $3.95 \pm 3.57\%$ ) vs. control ( $0.70 \pm 0.43\%$ ,  $p=0.0008$ ), signaling early fibrosis. Endothelial area rose ( $19.09 \pm 1.47\%$  vs.  $12.20 \pm 1.39\%$ ,  $p=0.0286$ ). Blood monocytes ( $1.266 \pm 0.684\%$  vs.  $4.352 \pm 1.668\%$ ,  $p=0.0159$ ) and neutrophils ( $3.602 \pm 0.669\%$  vs.  $6.256 \pm 0.773\%$ ,  $p=0.0079$ ) elevated; bone marrow LSK HSPCs reduced ( $0.497 \pm 0.037\%$  vs.  $0.423 \pm 0.046\%$ ,  $p=0.0303$ ), indicating stress-induced mobilization.

**Conclusion:** ISO-induced T2MI triggers early microvascular impairment, fibrosis, endothelial remodeling, myeloid expansion, and HSPC mobilization, highlighting dynamic post-injury responses amenable to targeted imaging and therapies.

# Intracellular Ca<sup>2+</sup> Modulates PKA Compartmentalization and Dynamics in Human iPSC-Derived Cardiomyocytes

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The automaticity of human induced Pluripotent Stem Cell-derived cardiomyocytes (hiPSC-CMs) is governed by coupled Ca<sup>2+</sup> and membrane clocks, coordinated through local Ca<sup>2+</sup> releases (LCRs) and cyclic adenosine monophosphate (cAMP)/protein kinase A (PKA) signaling.

We investigated the role of PKA in hiPSC-CM energetics by measuring its dynamics in the cytosol and mitochondria, and its crosstalk with Ca<sup>2+</sup>. We tested three hypotheses: (i) Ca<sup>2+</sup>-activated PKA signaling regulates energy balance; (ii) adenylyl cyclase activity correlates with spontaneous beating; and (iii) PKA compartmentalization is Ca<sup>2+</sup>-dependent.

We also compared hiPSC-CMs with rabbit sinoatrial node cells (SANCs). The key findings are: (i) PKA inhibition (H-89), Ca<sup>2+</sup> chelation (BAPTA), or mitochondrial Ca<sup>2+</sup> blockade (Ru360) led to energy imbalance; (ii) H-89 induced compartmentalized PKA activity in the cytosol, mitochondrial matrix, and outer mitochondrial membrane; (iii) Ca<sup>2+</sup> chelate via BAPTA reduced PKA activity globally; (iv) PKA dynamics and Ca<sup>2+</sup>-dependent regulation were similar in hiPSC-CMs and rabbit SANCs.

In conclusion, intracellular Ca<sup>2+</sup>-mediated PKA compartmentalization is present in hiPSC-CMs and rabbit SANCs.

# The Effect of Aortic Valve Stenosis on the Hemodynamic of the Coronary Arteries

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**Introduction:** Cardiovascular diseases, including coronary artery disease (CAD) and valvular disorders, are leading causes of morbidity and mortality. Aortic stenosis (AS) often coexists with CAD and can significantly reduce coronary flow reserve (CFR), increasing the risk of ischemia and sudden cardiac death.

While coronary dysfunction in AS is commonly attributed to increased resistance and altered wave reflections, aortic root hemodynamics may also play a key role. This study investigates time-dependent coronary flow by comparing AS, control valve, and post-TAVR (Evolut™) models to identify hemodynamic risk factors for CAD.

**Methods:** An in-vitro mock circulatory system was utilized, incorporating models of the aortic root, left and right coronary arteries (LCA, RCA), and a carotid artery. To simulate physiological conditions, the LCA was housed in a pressure sleeve synchronized with ventricular pressure to emulate heart-rate-dependent systolic resistance, and time-resolved measurements of ventricular, sinus, and aortic pressures, alongside aortic and coronary flow rates, were recorded. Both AS and post-TAVR (Evolut™) valve models were evaluated across varying heart rates (HR) and cardiac outputs (CO) to isolate valve-dependent hemodynamic effects.

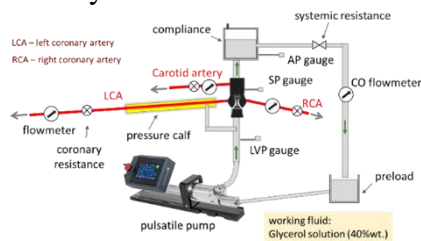


Figure 1. The in-vitro experimental system.

**Results:** Example results are shown in Figure 2 for the LV and aortic pressure and the arterial flow measured in the three arteries. A distinct difference in flow is observed between the three arteries: the LCA vs. RCA difference is due to increased systolic resistance from the pressure sleeve, while the RCA vs. carotid difference results from a local vortex in the aortic sinus.

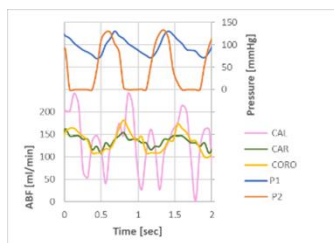


Figure 2. Example results of pressure and flow measured for 80 bpm.

**Discussion & Conclusion:** These findings may provide pure hemodynamical explanation to the altered coronary flow and the effect of valve structure on coronary flow and atherosclerosis progression.

## Beyond Glucose: Evidence that <sup>18</sup>F-FDG PET Underestimates Bone Marrow Activation in Diabetes

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**Introduction:** Vascular inflammation with elevated circulating white blood cell (WBC) counts drives cardiovascular disease, particularly in diabetes. The bone marrow (BM) is the primary WBCs source, and enhanced BM activity in cardiovascular risk states such as metabolic syndrome, and hypertension has been visualized as increased <sup>18</sup>F-fluorodeoxyglucose (<sup>18</sup>F-FDG) uptake on PET/CT imaging. However, in diabetes, no increase in BM <sup>18</sup>F-FDG uptake was observed (2). <sup>18</sup>F-FDG is a glucose analogue, hyperglycemia and insulin resistance may limit tracer uptake through substrate competition and altered glucose utilization. We therefore tested whether BM <sup>18</sup>F-FDG uptake in diabetes reflects hematopoietic activity under hyperglycemic conditions.

**Methods:** Patients with diabetes and age-matched controls (n=18/group) underwent <sup>18</sup>F-FDG PET/CT; BM activity was quantified in lumbar vertebrae using standardized uptake values, and circulating leukocytes were measured in peripheral blood. In parallel, male C57BL/6J diabetic and non-diabetic mice (n=5/group) underwent <sup>18</sup>F-FDG PET imaging. Peripheral leukocytes were quantified by flow cytometry. BM activation was quantified by hematopoietic stem/progenitor (LSK) frequency, Ki-67 proliferation, and BM cellularity. Cohorts were stratified by non-diabetic versus diabetic status.

**Results:** Diabetic patients displayed significantly lower BM <sup>18</sup>F-FDG uptake, with SUV mean difference of  $-0.3131 \pm 0.1216$  (p0.05), yet elevated circulating WBC counts compared with controls. Diabetic mice recapitulated this discordance, showing reduced BM <sup>18</sup>F-FDG signal, with SUV mean difference of  $-0.3489 \pm 0.1512$  (p0.05), but increased WBC leukocyte compared with controls. Direct BM analyses in mice demonstrated increased LSK frequencies (p 0.05), higher Ki-67 positivity (p 0.0001), and increased BM cellularity (p 0.05) - consistent with heightened hematopoietic activation despite attenuated glucose- PET readouts. P 0.05 (unpaired t-test) was considered significant.

**Conclusions:** Diabetes increases BM hematopoietic activation despite reduced BM <sup>18</sup>F-FDG uptake. These findings support metabolism-aware interpretation of BM PET signals and motivate development of non-glucose-based tracers to improve detection of BM activation in cardiometabolic disease.

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Novel K band wearable sensors and antennas for Healthcare, Telemedicine Systems, Internet of Things (IoT) systems, and communication sensors are presented in this paper. Only in few numbers of papers K band sensors are presented. One of the major goals in the evaluation of healthcare and telemedicine, and wireless communication devices is the development of wideband efficient compact low-cost antennas and sensors.

The development of wideband efficient antennas is significant to the evaluation of wideband and multiband efficient Telemonitoring, IoT, and medical wearable devices. The advantage of printed wearable antenna is that the feed and matching network can be etched on the same substrate as the printed radiating antenna. K band printed antennas and arrays are presented in this paper the sensors are compact, lightweight, efficient, and wideband.

The antennas design parameters, and comparison between computation and measured electrical performance of the antennas are presented in this paper. Fractal efficient antennas and sensors were evaluated to maximize the electrical characteristics of the communication and medical devices. This paper presents wideband printed antennas in frequencies from 16GH to 26GHz for Telemonitoring, Healthcare and IoT Systems.

The bandwidth of the K band fractal slot antennas and arrays ranges from 10% to 40%. The electrical characteristics of the new compact antennas in vicinity to the patient body were measured and simulated by using electromagnetic simulation techniques. The gain of the new K band fractal antennas and slot arrays presented in this paper ranges from 3dBi to 7.5dBi with 90% efficiency.

## Studying Fluorescent Properties of Olive Carbon Dots using Time-Resolved Fluorescence Measurements

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In the modern world, carbon derived nanoparticles (especially carbon dots - CDs) are revolutionizing biomedical nano-sensing and nanophotonic applications due to their unique properties (large surface area, tunable fluorescence, excellent biocompatibility, etc.).

CDs were synthesized from bio-renewable sources (olive tree leaves) via a hydrothermal route and studied in our experiments using time-resolved frequency domain fluorescence lifetime imaging microscopy techniques. These nanoparticles demonstrate relatively modest changes in fluorescence lifetime (FLT) values of  $5.0 \pm 0.2$  ns in water and glycerol solutions of different concentrations (0%, 30%, 60% and 80% glycerol) with fluorescence emission intensity increasing with the solution viscosity, i.e. glycerol concentration.

Fluorescence anisotropy decay measurements showed increasing steady state anisotropy  $r_{ss}$  values from  $0.058 \pm 0.03$  to  $0.3 \pm 0.03$ , while  $r_0$  remaining the same around  $0.38 \pm 0.02$  and rotational correlation time  $\theta$  growing significantly from  $1.01 \pm 0.02$  ns to  $16 \pm 0.1$  ns across all glycerol solutions with the increasing viscosity correspondingly.

The study indicates that CDs retain relatively stable FLT in glycerol solutions, while  $\theta$  shows evident changes in viscosity and is most beneficial for reflecting variations in local spatial properties.

# Vortex-Driven Perfusion: The Impact of Aortic Root Hemodynamics on Coronary Flow in Aortic Stenosis and Valve Replacements

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**Introduction:** Aortic stenosis (AS) frequently coexists with coronary artery disease (CAD), yet the mechanical influence of aortic root hemodynamics on coronary perfusion remains under-explored. While clinical models typically focus on myocardial workload, this study investigates how AS-induced high-velocity jets and vortex dynamics within the sinus of Valsalva dictate the pressure gradients necessary for coronary filling.

**Methods:** Using a physiological flow loop with a typically anatomical aortic root model and refractive index matching, we quantify hemodynamics via Particle Image Velocimetry (PIV). Models of AS and transcatheter aortic valve replacement (TAVR) are analyzed to assess the time-dependent flow field and coronary perfusion across low and high heart rate (HR) conditions.

**Results:** In the AS model at low HR, high-velocity jets induced distal vortex migration, shifting pressure gradients toward the coronary ostia and facilitating perfusion. Conversely, at high HR, this organized structure collapsed into turbulent dispersion, causing perfusion failure and reduced coronary flow reserve. These shifts suggest a mechanical driver for coronary atherosclerosis in AS. In contrast, TAVR models demonstrate re-established vortex stability and restored flow patterns.

**Discussion & Conclusion:** Coronary insufficiency in stenotic environments is governed by the interplay between valve geometry and heart rate, as mediated by vortex stability. The transition from beneficial vortex migration at low HR to turbulent collapse at high HR suggests that distal coronary disease is linked to global hemodynamic shifts act as primary drivers of distal CAD. These findings highlight vortex positioning as a critical regulator of perfusion and a vital consideration for patient-specific risk assessments in valvular interventions.

# End-to-End Joint Optimization of Z-Encoding Phase Mask and Z-Stack Reconstruction for Single-Shot 3D Fluorescence Microscopy

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Standard 3D fluorescent microscopy is often limited by slow scanning speeds and susceptibility to photobleaching, while faster volumetric modalities frequently impose prohibitive costs or significant resolution tradeoffs. We propose a scalable solution for snapshot 3D microscopy via the end-to-end joint optimization of an axial-encoding Point Spread Function (PSF) and a deep learning-based reconstruction algorithm. Building on our previous work demonstrating that a Deep Learning method for z-stack reconstruction can restore some axial range even from standard diffraction-limited images (which contain recoverable axial information via out-of-focus light), this study advances the approach by optimizing fabricable phase masks for superior depth encoding.

Our framework jointly teaches the optical element and the reconstruction network. To ensure physical realizability, we optimize the phase mask directly, utilizing a differentiable forward model to extract the resulting PSF at each iteration. The network is initialized with a known z-encoding PSF (e.g., Tetrapod) or an experimentally acquired phase-retrieved mask to inherently account for system-specific aberrations.

To facilitate training without requiring experimental data for every iteration of the evolving mask, we introduce a physics-based data synthesis pipeline. Standard fluorescent z-stacks are processed via a dehazing algorithm to isolate in-focus structures and remove out-of-focus haze. We then simulate the optical system by convolving the dehazed volume with the learned 3D PSF and summing the result, generating a single encoded 2D image. This forward imaging model preserves the visual characteristics of the original optical setup.

Upon convergence, the framework yields a design for a fabricable optical element. Following fabrication, the reconstruction network can be fine-tuned on a small dataset of experimentally captured images to correct for residual fabrication artifacts. Overall, our goal is for this approach to enable robust, single-shot 3D volumetric reconstruction using an optimally engineered depth-encoding phase mask.

# Integration of MRI and Computational Hemodynamic Modeling for the Assessment of Human Placental Vasculature and Function

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**Background:** The placenta is essential for fetal development, enabling oxygen and nutrient exchange between the mother and fetus. Placental insufficiency, the primary cause of fetal growth restriction, is associated with increased morbidity and mortality, however, its assessment remains challenging. While placental vasculature is associated with function, current imaging approaches provide limited functional information. Computational modeling offers a promising framework for deriving functional information from structural MRI. This study aims to integrate imaging and computational modeling for the quantitative assessment of placental vasculature and hemodynamics, with validation of in-vivo placental vasculature information through comparison with ex-vivo MRI.

**Methods:** Seven placentas were scanned in-vivo using Time-of-Flight MRI. Five cases were also scanned ex-vivo using high-resolution T1-weighted MRI. Umbilical cord insertion location was quantified using a centricity index, defined as the normalized distance between the cord insertion point and the placental center. Vascular trees were extracted and analyzed using skeletonization, bifurcation counts, and vessel diameter measurements. A reduced-order hemodynamic model estimated blood flow, pressure, and wall shear stress.

**Results:** In-vivo and ex-vivo placental vasculature were broadly similar, with more vascular branches detected in the ex-vivo placentas. Increased vascular complexity, reflected by higher branching and vessel density, was associated with distinct hemodynamic patterns. Placentas with marginal insertion demonstrated altered vascular organization and flow distribution compared to those with more central insertions. Computational modeling demonstrated spatial distributions in flow, pressure, and wall shear stress.

**Conclusion:** Integrating structural MRI and computational modeling enables quantitative assessment of placental vasculature and hemodynamics, with potential clinical relevance for evaluating placental function.

# Structural Motifs Promote Tear Resistance and Flaw Tolerance in Silk Fibroin–Alginate Biocomposites

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Soft fibrous tissues, including skin and tendons, represent a class of naturally occurring fiber-reinforced biocomposites whose mechanical robustness is rooted in hierarchical fibrous architectures.

This multiscale organization governs both deformation and fracturing processes, enabling exceptional resistance to tearing and reduced sensitivity to defects. Recent work has attributed this behavior to structural mechanisms such as crack-tip blunting, fiber bridging, and distributed energy dissipation, which collectively promote flaw tolerance. Despite these insights, the mechanics of tear initiation and propagation in soft fibrous tissues remain incompletely characterized, in part due to variability in experimental approaches across studies.

To address this gap, silk fibroin–alginate biocomposites with precisely controlled fiber orientations were engineered to reproduce fundamental structural motifs observed in soft fibrous tissues. Unidirectional ( $0^\circ$ ), cross-ply ( $0^\circ/90^\circ$ ), and angle-ply ( $\pm 30^\circ$ ) architectures were systematically investigated to evaluate their influence on tear-shielding behavior. Mechanical testing revealed that fiber architecture plays a decisive role in activating distinct fracture-mitigation mechanisms, resulting in tear tolerance comparable to that of native soft tissues.

Presence of structural motifs contributes to tear resistance and flaw insensitivity in fibroin-reinforced alginate biocomposites.

Fracture tests were conducted on precut specimens containing notches of varying lengths (30%, 50%, and 80% of specimen width). To directly visualize crack evolution, selected samples were stretched to prescribed stretch ratios ( $\lambda = 1.0\text{--}1.4$ ) using a custom miniature tensile device compatible with in situ scanning electron microscopy. Microstructural observations revealed progressive crack-tip blunting and fiber bridging during deformation, closely resembling tear-mitigating mechanisms reported in biological soft tissues.

By reverse engineering these fibrous architectures, this study elucidates key structural principles governing tear resistance and toughness, providing a design framework for fibroin-based biocomposites with enhanced flaw tolerance and tissue-like mechanical performance.

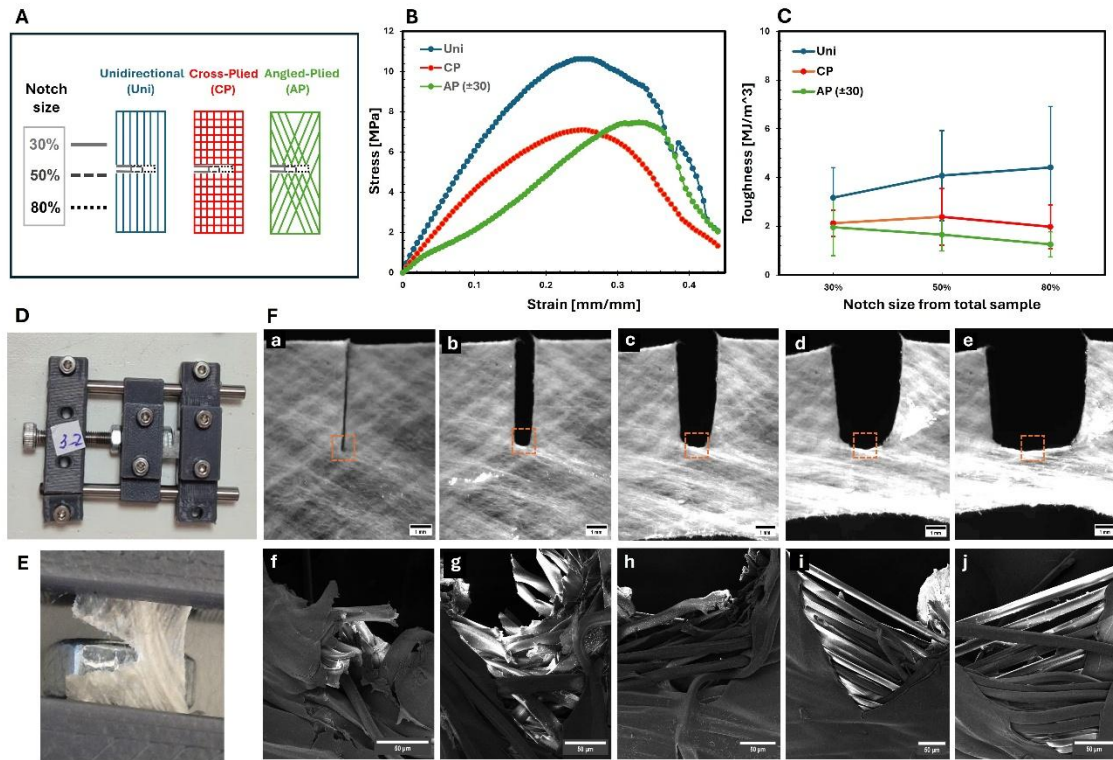


Figure 1- Biomimetic biocomposites demonstrated flaw insensitivity. (A) Precut biocomposites with varied fiber orientations and notch lengths. (B) Stress-strain curves for 30% notches. (C) Toughness versus notch length. (D,E) Miniature SEM stretching setup. (F) AP sample at stretch ratios  $\lambda = 1.0-1.4$  (af), (b,g), (c,h), (d,i), (e,j).

# An Abdominal Aortic Aneurysm Micro-Physiological Model for the Study of Localized Therapeutics

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**Background:** Abdominal aortic aneurysm (AAA) is a life-threatening vascular disease characterized by chronic inflammation, endothelial dysfunction, smooth muscle cell (SMC) apoptosis, and extracellular matrix remodeling. No pharmacological therapies are currently approved for AAA. Although nanoparticle-based drug delivery systems have shown promise in animal models, their clinical translation remains limited due to the lack of human-relevant validation platforms. This study aims to develop a human micro-physiological organ-on-chip model of AAA to enable controlled investigation of disease mechanisms and evaluation of localized nano-therapeutics.

**Method:** A polydimethylsiloxane (PDMS)-based microfluidic device is designed to support co-culture of human umbilical vein endothelial cells (HUVECs) under physiological flow and human aortic smooth muscle cells (HAoSMCs). Cells are cultured in separate upper and lower compartments, separated by a semi-permeable polyethylene terephthalate (PET) membrane. AAA-like inflammatory conditions are induced using tumor necrosis factor-alpha (TNF- $\alpha$ ), angiotensin II, and hydrogen peroxide. Pathological responses are assessed by measuring apoptosis, reactive oxygen species (ROS), elastin degradation, and calcification. Endothelial inflammatory activation is evaluated by quantifying neutrophil adhesion under flow and transmigration toward the SMC layer.

**Results:** Successful endothelial–SMC co-culture was achieved within the microfluidic platform. Endothelial cells formed a continuous monolayer under flow, while SMCs maintained characteristic marker expression. TNF- $\alpha$  stimulation significantly increased neutrophil adhesion to the endothelial layer under physiological shear stress, demonstrating a functional inflammatory response.

**Conclusion:** This human micro-physiological AAA model provides a controlled platform to investigate endothelial–SMC interactions and inflammatory mechanisms under pathological conditions. Ongoing work evaluates how endothelial–smooth muscle cell co-culture modulates the inflammatory response to AAA-related stimuli. Future studies integrate drug-loaded nanoparticles carrying agents with demonstrated anti-inflammatory, antioxidant, or aneurysm-suppressing effects to enable therapeutic assessment within the system. This platform serves as a human-relevant tool for mechanistic studies of AAA and for preclinical evaluation of localized nanoparticle-based. therapies.

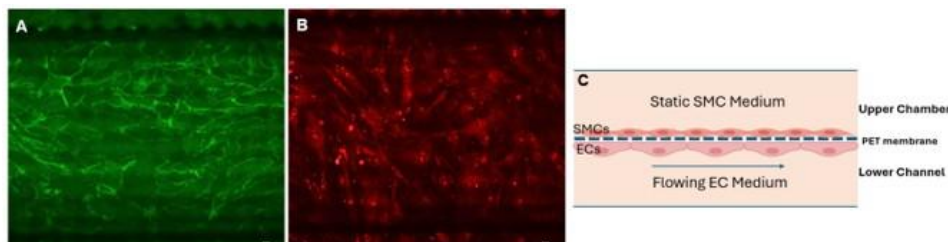


Figure 1 : Fluorescence images of the endothelial–smooth muscle cell co-culture for 24 hrs in the microfluidic device. (A) Endothelial cells (ECs, green, anti-CD31) forming a confluent layer. (B) Smooth muscle cells (SMCs, red, anti- $\alpha$ -SMA) cultured beneath the EC layer. (C) Schematic cross-sectional view of the co-culture microfluidic model, showing ECs exposed to flowing EC medium in the lower channel and SMCs maintained under static conditions in the upper chamber, separated by a semi-permeable PET membrane. Scale bar = 10  $\mu$ m.

# Automated Detection of Freezing of Gait in Complex Environments from Simple 2D Video using Spatiotemporal Graph Convolutional Networks

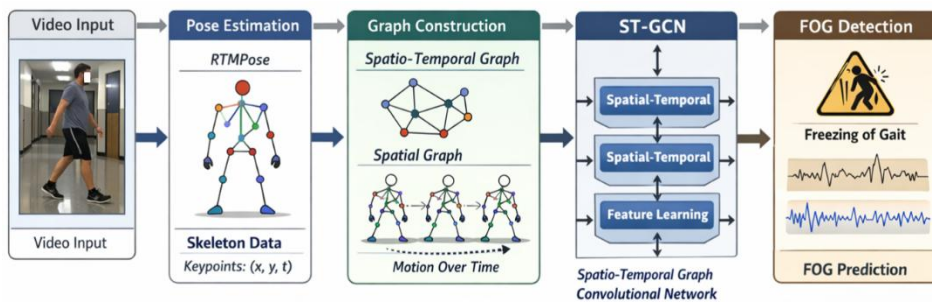
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**Aim:** To develop an automated, non-invasive method for detecting freezing of gait (FOG) from video recordings using computer vision and 2D pose estimation.

**Background:** Freezing of gait (FOG) is a debilitating symptom of Parkinson's disease (PD) associated with a high risk of falls. Current assessment methods rely on clinical observation or wearable sensors, which can be intrusive or limited in scope. Video-based analysis offers a promising alternative but is often hindered by complex environments, occlusions, and the presence of multiple individuals. Recent advances in pose estimation and graph convolutional networks (GCNs) allow for the modeling of spatiotemporal relationships in gait without the need for physical markers.



**Methods:** Video datasets from 35 participants with PD and FOG were collected at TLVMC (Ichilov) (mean age  $71.3 \pm 8.8$  years; 12 women; NFOGQ  $19.3 \pm 4.4$ ). These videos captured complex clinical environments, presenting significant tracking challenges such as frequent occlusions, dynamic backgrounds, and the presence of multiple individuals. A computational image processing pipeline was developed, which integrates YOLOv11 for person detection and StrongSORT for robust multi-object tracking and target subject isolation. 2D skeletal keypoints were extracted and processed using a novel Spatiotemporal Graph Convolutional Network (ST-GCN). This architecture captures both spatial (body posture) and temporal (movement dynamics) features to classify sequences as "FOG" or "No-FOG"

**Results:** The ST-GCN model demonstrated superior performance compared to baseline methods (vanilla YOLO and StrongSORT). The system achieved an AUC of 0.86, accuracy of 0.83, and an F1-score of 0.83. Specifically for FOG events, the model achieved a sensitivity (recall) of 0.94 and a precision of 0.75.

Parameter / Metric	Value
<i>Dataset Specifications</i>	
Total Subjects ( <i>n</i> )	35
Total Videos	~ 120
Total Frames	~ 720,000
Frame Rate	25 fps
<i>Data Partitioning</i>	
Training Set	70%
Validation Set	20%
Test Set	10%
<i>Overall Model Performance</i>	
AUC-ROC	0.86
Average Precision (AP)	0.71
Accuracy	0.83
Precision (Macro)	0.84
F1-Score (Macro)	0.83
<i>FOG Detection Metrics</i>	
Sensitivity (Recall)	0.94
Precision (PPV)	0.75
F1-Score	0.83

**Table 3. Preliminary Automated FOG Detection Results.** A summary panel reporting early subject independent FOG detection performance from video derived RTMPose skeletons and spatiotemporal graph convolutional modeling. Across 35 Parkinson’s participants, results show AUC-ROC 0.86, accuracy 0.83, macro-F1 0.83, and strong FOG sensitivity (0.94) with precision 0.75 in clinically realistic environments.

**Conclusions:** The proposed ST-GCN framework effectively detects FOG events from standard video recordings, even in challenging environments. High sensitivity (0.94) suggests strong clinical utility for automated gait assessment. Future work will focus on deploying this tool for large-scale analysis of archived video data to further characterize FOG triggers.

## A robotic platform for surgical site infection simulation

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**Background/Aim:** Surgical site infections (SSIs) remain common postoperative complications and are strongly influenced by local wound microenvironment conditions. Existing preclinical models often lack physiological realism and standardized quantitative assessment of bacterial behavior. The aim of this study was to develop a robotic wound simulation platform enabling controlled investigation of bacterial adaptation under clinically relevant wound pH conditions.

**Method:** A life-sized robotic wound care patient (RWCP) was developed to simulate SSI conditions under controlled laboratory settings. The system incorporates soft tissue simulants, a laparotomy incision, controlled simulated wound fluid (SWF) delivery, respiration-like motion, and temperature regulation. SWF inoculated with *Lactobacillus delbrueckii* subsp. *bulgaricus* was continuously delivered through the incision at clinically relevant flow rates.

Two wound microenvironment conditions were investigated: acidic SWF (pH 5.8) and near-neutral SWF (pH 6.8), with three independent replicates per condition. After 24 h of exposure, wound dressings were collected for scanning electron microscopy (SEM) analysis. Automated image analysis included deep learning-based bacterial segmentation (Cellpose), morphometric quantification in FIJI, and custom Python-based topology analysis for detection of bacterial chain formation and aggregation.

**Results:** The RWCP enabled reproducible SSI simulation under controlled environmental conditions. Bacterial counts were significantly higher at pH 5.8 compared to pH 6.8. In addition, bacteria exposed to the acidic environment demonstrated altered morphology characterized by elongation, reduced circularity, and increased aspect ratio. Topological analysis further revealed greater chain formation and bacterial aggregation under acidic conditions.

**Conclusion:** This study presents a robotic SSI simulation framework integrating biomechanical wound simulation with automated quantitative microbiological analysis. The RWCP enables standardized investigation of bacterial adaptation to wound microenvironment conditions and may support future preclinical evaluation of wound care materials, dressings, and infection prevention strategies.

## Skeletal Muscle-Derived Extracellular Vesicles and Their Impact on Glucose Regulation in Type 2 Diabetes

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Type 2 diabetes (T2D) is wide-spread chronic disorder marked by insulin resistance and disrupted cellular communication, leading to inflammation and metabolic dysregulation. Conventional treatments for T2D focus on symptoms rather than underlying intercellular signaling deficits. Extracellular vesicles (EVs), which transport crucial molecular cargo, could revolutionize therapeutic strategies. Tissue engineering of skeletal muscle has emerged as a promising approach to harness EVs for T2D intervention.

We previously demonstrated that engineered skeletal muscle overexpressing GLUT4 (G4OE-EMC) significantly improves diabetic indicators in Diet-Induced Obesity (DIO) mice, enhancing blood glucose levels, insulin sensitivity, and cytokine profiles. In this study, we isolated EVs from GLUT4-overexpressing 3D muscle constructs and characterized them using morphological and functional assays. When applied to wild-type myotubes, G4OE-EMC derived EVs increased glucose uptake; in vivo studies in diabetic mice, showed improved glucose tolerance and response. Proteomic and microRNA analyses revealed that these EVs modulate key metabolic pathways namely IGF-1 and insulin signaling partly through downregulation of specific MiRs, including MiR-122, MiR-486, and MiR-16.

These findings suggest that EVs derived from engineered skeletal muscle can transmit metabolic benefits to recipient tissues, helping explain the systemic improvements observed after implanting even a small construct. By targeting the root causes of T2D-related dysfunction, this tissue engineering strategy could offer a powerful platform for developing EV-based therapies that go beyond conventional interventions.

## Acunex Vascular Systems: A Catheter-Delivered Continuous Suturing System for Durable EVAR Graft Fixation

**Areen Shtewe**, Yathreb Asaad Hillo  
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**Need:** Every year, 200,000 patients die from abdominal aortic aneurysm. Endovascular Aneurysm Repair (EVAR) transformed how we treat this disease, but it left one critical problem unsolved: Up to 40% of patients develop Type I endoleaks and 30% suffer graft migration, both stemming from poor fixation: current available fixation methods including hooks, barbs, and staples grip at scattered points and leave the circumference unprotected. Patients return for reinterventions costing up to \$50,000 each, with overall post-procedural expenditure rising by 50%. Decades of iteration on the same discrete-fixation concept have yielded diminishing returns. What the field needs is not a better anchor; it needs a different principle entirely.

**Market:** The global EVAR market stands at \$3.5 billion, growing at 8% annually toward \$5 billion by 2030, driven by over 200,000 procedures per year. The opportunity is not a niche; it is the entire market, because every single one of those procedures carries this unresolved fixation problem.

**Technology:** Acunex is pursuing what no minimally invasive device has achieved: replicating the durable fixation of open surgical repair through a catheter-based approach. In open surgery, the graft is directly sutured to the aorta, effectively forming a single unified structure. Acunex delivers this endovascularly through a unidirectional needle that penetrates both the EVAR graft and the aortic wall, sewing them together continuously and circumferentially.

**Achievements:** Acunex has moved from principle to proof. A 21-gauge needle prototype was validated in vitro, demonstrating unidirectional graft penetration with anchors maintaining firm fixation against detachment, the first physical evidence that continuous endovascular suturing is mechanically achievable. A provisional patent application has been filed to protect the core technology. This progress builds on iterative CAD development, formal feasibility validation with a leading medical device engineering firm, and clinical input from five vascular surgeons across Israel and Canada who confirmed no adequate solution exists.

## Bioengineered Human Neurovascular Unit: A Perfusable In-Vitro Platform

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Yehuda Wexler<sup>2</sup>, Asaf Silverstien<sup>1</sup>, Orit Bar-Am<sup>1</sup>, Dina Safina<sup>1</sup>,  
Yifat Herman-Bachinsky<sup>1</sup>, Nitsan Dahan<sup>3</sup>, Moria Maman<sup>4</sup>, Malka  
Nissim-Rafinia<sup>4</sup>, George M Church<sup>5,6</sup>, Lior Gepstein<sup>2</sup>, Eran Meshorer<sup>4</sup>,  
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The blood-brain barrier (BBB), together with neurons and immune cells form the neurovascular unit (NVU), which maintains proper central nervous system (CNS) function but restricts drug delivery. To investigate NVU function, pathology, and drug delivery, we developed a physiologically relevant in vitro human NVU model integrating BBB multi-scale vasculature with functional neurovascular spheroids.

We engineered a multi-scale vascular tissue (MSVT) with macro- and micro-vasculature from BBB derived cells. In MSVT, self-assembled microcapillaries connect with prepatterned macrovessels on a 3D scaffold creating a perfusable hierarchical vascular network. The macrovessels functionality was confirmed by distinct response to angiogenic factors, formation of intact endothelium, key extracellular matrix expression, and barrier integrity. Capillary networks displayed in vivo-like organization and BBB characteristic markers expression. Integration between macro- and microvessels was verified by fluorescent beads perfusion.

Engineered induced pluripotent stem cells (iPSCs) overexpressing neural or endothelial markers under doxycycline induction differentiated to vascularized neurospheres. Neuronal activity was confirmed by calcium imaging and immunolabeling. Upon integration with the multi-scale vascular network, the neurovascular spheroids showed extensive neural sprouting and vascular connections, confirming successful formation of NVU-MSVT model.

Perfusion through macrovessels in a custom bioreactor promoted macrovessel's endothelial maturation. Consistent with in vivo, treatment with permeability altering agent resulted in a reversible barrier opening. In addition, NVU-MSVT recapitulated inflammatory hallmarks upon Tumor Necrosis Factor - $\alpha$  (TNF- $\alpha$ ) treatment, including elevated permeability, and upregulation of TNF- $\alpha$  and Intercellular Adhesion Molecule 1 (ICAM-1) levels. Lastly, perfusion of the neuroactive drug 4-aminopyridine increased calcium wave frequency, confirming drug delivery and neural activation.

Together, the NVU-MSVT provides a functional human model that can be used as a platform for investigating NVU physiology, pathology, and targeted drug delivery.

## Architected Hybrid Scaffolds for Patient-Specific, Mechanically Compliant Breast Tissue Engineering

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Inbal Michael, Shulamit Levenberg  
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Breast cancer is the most common malignancy among women worldwide. Many patients undergo mastectomy followed by implant-based reconstruction using silicone devices. However, current implants present significant limitations, including excessive weight, high stiffness, and a substantial risk of long-term complications or failure.

Tissue engineering offers a promising alternative; however, replicating the mechanical behavior of native breast tissue remains a major challenge.

Here, we present a bio-fabricated breast construct based on the assembly of modular tissue components composed of hybrid scaffolds. This strategy enables the creation of a hierarchical, biomimetic architecture that more closely reproduces the structural and mechanical characteristics of native tissue.

The hybrid scaffolds are produced using high-resolution 3D printing of a stiff, biocompatible material arranged in an architected elastic geometry that yields bulk soft-tissue-like mechanical behavior. This is combined with injection molding of a secondary material optimized for cellular growth and integration. Each component is systematically tuned to achieve defined mechanical properties, permeability, and biological performance. Optimization is guided by computational simulations, mathematical modeling, and experimental validation.

By integrating advanced design methodologies with reproducible fabrication workflows, this work establishes a practical pathway toward improved reconstructive solutions for women requiring breast implants, enabling the fabrication of living, stable, patient-specific, biomimetic tissue constructs.

# Macroscopic Fourier-Based Spectral Imaging for Biopsy Analysis and Diagnosis

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In recent years, the use of artificial intelligence (AI) in medical applications has rapidly expanded, particularly in histopathology. However, despite promising research outcomes, most AI-based solutions have not yet transitioned into routine clinical practice. One of the primary barriers is the high sensitivity of medical decision-making to errors, which demands robust, reliable, and information-rich data sources.

Previous studies have demonstrated the advantages of spectral imaging, which captures significantly more information than conventional imaging systems and can improve analytical performance. Nevertheless, research on spectral imaging-based histopathology remains limited, mainly due to technical challenges in acquiring high-quality spectral images within practical timeframes suitable for training AI models.

In recent years, we have developed an optical imaging system based on Fourier microscopy that enables acquisition of histological spectral images at speeds comparable to standard imaging systems. Using this platform, we have demonstrated the benefits of spectral imaging for multiple AI-driven applications, including virtual staining and cancer nuclei segmentation, showing improved performance compared to conventional imaging approaches.

These results highlight the potential of fast macroscopic Fourier-based spectral imaging as a practical and scalable foundation for next-generation computational pathology tools.

# Toward Distortion–Perception–Balanced MRI Reconstruction with Rectified Flow

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Accelerated MRI reconstruction must balance two goals: fidelity to the acquired k-space measurements and perceptual realism of anatomy. Deterministic deep reconstructions trained mainly with pixel-wise losses often optimize PSNR/SSIM but blur fine structures.

Perceptual objectives can improve sharpness but may add anatomy-inconsistent details, especially under aggressive under sampling. Our goal is to use MRI’s known acquisition physics during refinement, while keeping PMRF’s separation between a distortion-optimal anchor and a transport toward realism.

We build Posterior-Mean Rectified Flow (PMRF) for MRI reconstruction. PMRF first learns the posterior mean, a distortion-optimal, measurement-anchored estimate. It then learns a rectified flow that transports posterior-mean reconstructions toward the clean-image distribution. MRI has a known acquisition model: masked Fourier encoding. This exposes structured measurement cues in k-space. Using these cues naively in the refinement stage can break PMRF’s guarantees.

We therefore add physics cues while preserving PMRF’s separation. We propose Endpoint-Neutral Gauge Rectified Flow (ENGRF). ENGRF changes the intermediate flow dynamics but keeps the endpoints fixed.

We validate on the fast MRI knee single-coil dataset across several acceleration factors. ENGRF improves distortion metrics and anatomical realism over PMRF and other baselines under multiple acceleration settings. ENGRF improves results while keeping PMRF’s posterior-mean anchor and the balance between fidelity and realism.

# Engineering a Fetal-Like Wound Microenvironment: Controlled TGF- $\beta$ 3 Delivery via FibMA Hydrogel Reduces Adult Skin Fibrosis

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Acute and chronic skin defects present significant challenges due to prolonged healing, excessive scarring, and impaired skin function. Unlike adult wounds, early fetal wounds heal without scarring. While mechanisms remain unclear, TGF- $\beta$ 3, a pro-regenerative cytokine, is essential for scarless fetal healing. In contrast, adult wounds exhibit reduced TGF- $\beta$ 3 and increased TGF- $\beta$ 1 levels, contributing to fibrosis. We hypothesize that scarless healing can be enhanced in adult wounds by exogenously restoring this factor. To accomplish this, we propose using a methacrylated fibrinogen (FibMA) hydrogel dressing as a controlled release depot for bioactive recombinant TGF- $\beta$ 3, aiming to simulate the fetal wound environment.

Human TGF- $\beta$ 3 was recombinantly produced in HEK293 cells and encapsulated within FibMA hydrogels in different formulations. Release kinetics were evaluated using fluorescence methods. Bioactivity was assessed in vitro using 2D scratch assays and a 3D gel-in-gel migration model with fibroblasts and keratinocyte cells. Subsequently, in vivo, full-thickness dorsal skin wounds in rats were treated with FibMA hydrogels (containing active, latent, or no TGF- $\beta$ 3) and compared to untreated wounds and healthy skin. Healing assessment included histology (H&E, Sirius Red), immunofluorescence, and RT-qPCR analysis.

Hydrogel formulations demonstrated a sustained release profile, achieving 80% cumulative protein release over 28 days. In the scratch assay, TGF- $\beta$ 3 accelerated keratinocyte wound closure, with stronger effects for the active form, whereas fibroblasts showed no significant response. In the gel-in-gel model, both active and latent TGF- $\beta$ 3 enhanced outgrowth in both cell types. Preliminary in vivo results showed higher CD31 expression and significantly reduced alpha-SMA in treated wounds compared to control. RT-qPCR indicated significant VEGFA upregulation and a significant decrease in Collagen I/III ratio in treated wounds.

The results suggest that FibMA hydrogel system effectively delivers bioactive TGF- $\beta$ 3 and has the potential to reduce fibrosis and support a regenerative healing process in adult wounds.

# Cell-Cell Interactions in Bioprinted Vascularized Composite Soft Tissue Flaps with an Integrated Arterial-Venous Loop

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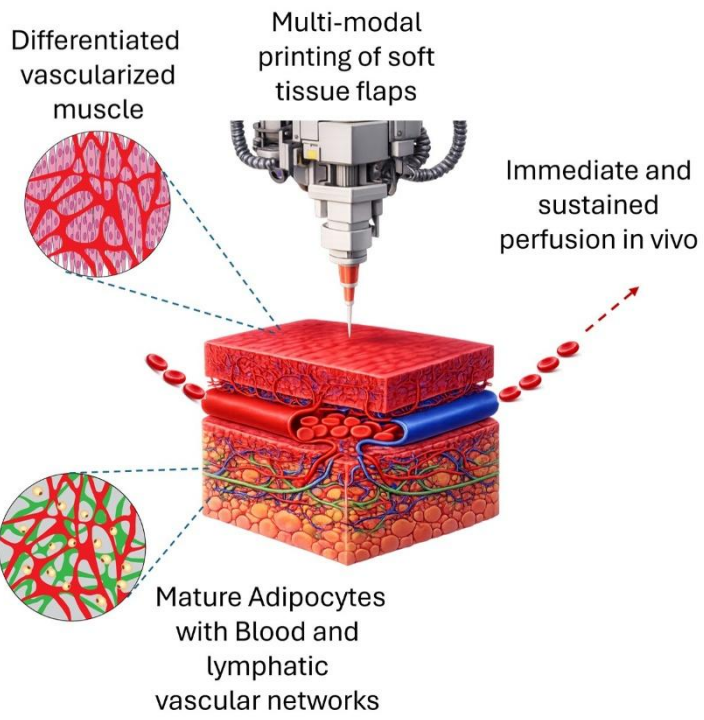
Severe soft-tissue defects remain major clinical challenges, as current reconstructive strategies rely on autologous flap transplantation, which is limited by donor-site morbidity and tissue availability.

This research advances the field of regenerative medicine by developing scalable, perfusable, and functionally integrated engineered composite soft-tissue flaps. The successful engineering of functional, clinically relevant tissues depends on an understanding of intercellular interactions that govern tissue organization, maturation, and integration.

The ongoing approaches in tissue engineering and bioprinting technologies primarily rely on printing single tissue constructs with microvasculature rather than designing a multi-tissue construct with feeding vessels branching deep within the composite flap.

This work expands toward clinically relevant composite soft-tissue reconstruction by engineering bio printed muscle–adipose flaps with integrated blood and lymphatic vasculature, interconnected by a continuous vasculature composed of a 3D-printed feeding arteriovenous loop and bio printed microvasculature. The printed feeding vessels within the flaps were micro surgically anastomosed to the femoral artery and vein, demonstrating immediate flow recovery, ensuring nutrient supply and waste drainage. Following implantation, the flaps exhibited myogenic differentiation while preserving a mature adipocyte phenotype. Direct attachment to both arterial and venous systems, alongside vascular and lymphatic ingrowth, promoted tissue survival and integration.

These findings highlight the potential of multi-modal printing utilizing human-derived cells to generate composite, perfusable soft tissue flaps with both vascular and lymphatic networks, providing a foundation for future patient-specific reconstructive.



applications.

# Improving Ligamentum Flavum Haptic Rendering in a Bimanual Epidural Needle Insertion Simulator

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Epidural anesthesia is a blind needle insertion procedure that relies primarily on haptic feedback to identify the epidural space after passing through several tissues, among which the ligamentum flavum is the most rigid.

Failure to identify these mechanical cues is a leading cause of failed epidurals and accidental dural punctures, particularly among inexperienced clinicians. Existing epidural simulators often rely on simplified or static force models that do not accurately capture these tissue-specific mechanical cues. To address this, our work builds an existing haptic bimanual simulator for epidural needle insertion that renders resistive forces using two haptic devices, with a focus on improving the ligamentum flavum texture.

Based on experimental evidence and prior biomechanical studies, the ligamentum flavum can be modelled as a nonlinear, fiber dominated structure, in which puncture arises from progressive fiber rupture rather than purely elastic deformation.

Accordingly, the needle-tissue interaction forces are decomposed into stiffness and cutting components with localized rupture events. Our aim is to generate a haptic response that reproduces pre-puncture resistance, puncture and post-puncture loss-of-resistance sensations consistent with reported experimental data, thereby improving training realism and skill acquisition

## Simulations and Classification of Flow Fields in Different Umbilical Cord Models

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The umbilical cord (UC) is the vital physiological link between the mother and fetus, enabling the exchange of respiratory gases, nutrients and metabolic waste, which are essential for normal fetal development. Structural abnormalities of the UC, including excessive cord length, abnormal coiling and true umbilical cord knots (TUCK), may adversely affect fetal well-being and are associated with serious perinatal complications. Despite their clinical importance, current noninvasive diagnostic methods remain limited, heavily reliant on operator skill and often inadequate for reliable prenatal detection.

Doppler ultrasound (DUS) of the UC is the standard clinical method for fetal monitoring; however, its diagnostic capabilities are limited. As pregnancy advances, visualizing the UC becomes increasingly challenging, especially in cases of posterior placenta, fetal movement, or highly convoluted cord morphology, which makes consistent measurements at a uniform Doppler angle difficult. Despite advances in high-resolution and 3D ultrasound, prenatal detection of cord abnormalities such as TUCK remains limited and prone to errors. Additionally, Doppler monitoring of growth-restricted fetuses provides only limited hemodynamic information, lacking key details on flow patterns, pressure gradients and wall shear stress.

To address these limitations, this study developed a novel integrative computational framework that combines computational fluid dynamics (CFD) with machine learning (ML) to improve the detection of UC structural abnormalities. Three-dimensional UC models were built in SolidWorks, representing normal geometry, abnormal coiling and TUCK. CFD simulations were performed in ANSYS Fluent under steady-state, laminar-flow conditions. To create velocity-field datasets, CFD simulations were run across all UC models, normal and abnormal, with systematically varied inlet flow conditions for each geometry, yielding a large and diverse set of velocity-field images. This dataset was then used for ML-based classification, providing a potential computational tool for prenatal monitoring and clinical decision-making.

# Clinical Progression of Dystrophinopathies: Exploring the Role of Autonomic Nervous System Activity and Machine Learning Models

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**Background:** Dystrophinopathies, including Duchenne and Becker muscular dystrophies (DMD and BMD), are progressive neuromuscular disorders characterized by substantial heterogeneity in clinical course and rate of functional decline. Loss of independent ambulation (LoA) represents a major clinical milestone associated with accelerated morbidity and long-term adverse outcomes; however, the timing of LoA varies widely between individuals and remains difficult to predict at the patient level. This study aims to develop an integrated, longitudinal framework for modeling clinical progression in dystrophinopathies, with a focus on predicting time to loss of independent ambulation.

**Method:** Analyses were conducted using a nationwide real-world clinical registry comprising longitudinal functional, genetic, treatment, and sociodemographic data. Survival-based modeling approaches were applied to characterize ambulatory trajectories and identify predictors of LoA. Threshold-based analyses were used to examine the temporal relationship between decline in key functional measures and subsequent LoA. The proposed doctoral research further extends this framework by incorporating machine learning-based trajectory modeling and physiological biomarkers, including autonomic nervous system function assessed via heart rate variability (HRV) and wearable sensor-derived physical activity measures.

**Results:** Preliminary survival analyses demonstrate marked heterogeneity in ambulatory trajectories according to functional performance, genetic features, treatment exposure, and sociodemographic context. Threshold-based analyses indicate that decline in key functional measures precedes LoA by variable, patient-specific intervals, supporting the presence of distinct progression tempos rather than a uniform pattern of disease decline.

**Conclusion:** By integrating longitudinal survival analysis, trajectory-based machine learning models, and physiological biomarkers within a time-aware analytical framework, this research aims to improve individualized prognostic assessment and enhance understanding of disease heterogeneity in dystrophinopathies. The incorporation of HRV and wearable-derived measures offers a novel, non-invasive approach to monitoring disease progression and may support personalized clinical monitoring and intervention strategies.

# End-to-End Deep-Learning-Based Discovery of Quantitative Molecular MRI Acquisition Protocols

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**Introduction:** Saturation transfer (ST) MRI is a molecular imaging technique that has shown promise for a variety of biomedical applications [1]. However, in its commonly applied form, ST measurements are influenced by various confounding factors, which challenge the interpretation of the observed phenomena [1,2]. Quantitative methods, such as magnetic resonance fingerprinting (MRF), may improve the specificity of ST imaging, yet they require long scan times and are highly sensitive to the exact acquisition parameters used [3].

Here, we developed an automated deep-learning-based framework for designing and discovering optimized and clinically compatible ST-MRF acquisition protocols.

**Methods:** An automated computational framework (AutoPulst, Fig. 1) was developed in JAX capable of accurately simulating the saturation transfer signal. The method optimized the data acquisition and analysis in parallel by representing the underlying biophysical process as a computational graph and conjugating it to a deep quantification network. Validation was performed using in-vitro phantoms and human volunteers at 3T and 7T clinical MRI scanners.

**Results and Discussion:** In-vitro, AutoPulST produced quantitative parameter maps with more than 50% higher signal quality and accuracy (p0.001) compared to randomly designed protocols. In human brain imaging at 3T (Fig. 2), AutoPulST consistently improved the image quality and quantification accuracy compared to random protocols (p0.001), while shortening the scan times by up to 7.5-fold (requiring merely 19–77 s). As optimization was limited to two acquisition parameters (saturation pulse power and frequency), we expect that expanding the approach to include additional radiofrequency properties will further improve performance and enable the imaging of additional metabolites.

**Conclusion:** An end-to-end optimization pipeline was developed, facilitating a rapid, accurate, and clinically relevant imaging of quantitative molecular parameters.

# A Novel Approach for Electrophysiological Profiling of Cardiac Organoids Using Spatiotemporal Analysis and Beat Rate Variability

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**Background:** Accurate evaluation of cardiac electrophysiology is critical for translational research and preclinical drug-safety testing. For that purpose, cardiac organoids provide a valuable platform, promoting the study of physiological and pathophysiological processes affecting heart rate and rhythm. Multi-electrode arrays (MEA) are widely used for high-throughput electrophysiological assessments. Despite the widespread use of MEA technology in cardiac research, current biomarker analysis tools are limited, focusing primarily on one-dimensional electrophysiological biomarkers and on averaged inter beat intervals calculation. Thus, we aimed to develop innovative algorithms for standardized biomarker calculation, spatiotemporal biomarker dynamics assessment, and comprehensive Beat Rate Variability analysis of cardiac organoids.

**Methods:** We recorded electrograms from spontaneously beating cardiac organoids (n=14), generated from human-induced pluripotent stem cell derived cardiomyocytes, using 8x8 electrode MEA plates. We developed novel algorithms for R-, S-, and T-peak detection as well as advanced two-dimensional electrical signal processing tools of these biomarkers. These algorithms were implemented on the open-source PhysiMEA platform.

**Results:** Cardiac organoids exhibited a high degree of similarity among biomarker distributions under basal conditions, indicated by their coefficients of variation (p-value 0.2). Additionally, comprehensive analysis of Beat Rate Variability in cardiac organoids is presented for the first time, revealing high very low frequency content (78.21%) in cardiac organoid inter-beat intervals spectra compared to low- and high-frequency components (11.11% and 10.68%, respectively).

**Conclusions:** PhysiMEA provides robust and accessible tools for translational electrophysiology, enhancing cardiac tissue characterization and improving detection of drug-induced electrophysiological disturbances. Its advanced analytics support early-stage safety screening experiments and mechanistic studies in cardiovascular research.

## A High-Throughput Perfusable Platform for Generating Vascularized Tissues

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Engineering vascularized human tissues that are physiologically relevant and scalable remains a persistent challenge in drug development. Widely used 2D cultures and animal models often fail to predict human responses, contributing to high attrition rates and rising development costs.

Although organ-on-chip and perfusion technologies have improved physiological relevance, many remain difficult to scale or integrate into workflows suited for large experimental datasets and industrial use.

This work introduces a high-throughput perfusion platform designed to support parallel culture and testing of multiple engineered tissues. The system is built around a modular microfluidic device fabricated using 3D printing, allowing rapid iteration and compatibility with standard laboratory practices. Engineered tissues are created with hierarchical vasculature that combine larger perfusable vessels with surrounding microvascular networks, enabling controlled fluid flow through tissue constructs.

The platform supports parallel perfusion across multiple samples and standardized experimental conditions, enabling systematic investigation of transport and barrier function.

Initial implementation demonstrated reliable perfusion across multiple tissue units and successful formation of vascular networks within engineered constructs. Flow exposure produced clear cellular responses consistent with vascular maturation, and the platform enabled consistent, parallel operation across multiple samples. These early results indicate that perfused tissue culture can be scaled while maintaining biological relevance and experimental reproducibility.

Overall, this work presents a scalable strategy for producing perfusable human tissue models suited for pharmacological testing. By combining hierarchical vascularization, high-throughput experimentation, and 3D-printing-based fabrication, the technology aims to bridge the gap between tissue engineering and the practical needs of pharmaceutical and biotechnology industries. This platform offers a more human-relevant alternative to animal testing for drug screening, toxicity assessment, and even inter-organ interactions in preclinical research.

# Predicting Subject-Specific fMRI Activation Maps from Cognitive Profiles using a Spatial Basis Decomposition

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Individual differences in cognitive skills are reflected in different fMRI activation patterns, yet most analyses treat cognitive abilities as covariates rather than a signal that can predict brain-wide responses. The goal of the current study is to build and validate a model that predicts subject-specific fMRI activation maps from cognitive and behavioral measures, enabling interpretable links between cognition and functional brain organization.

We used multi-session fMRI datasets with block-design task conditions and accompanying cognitive profiles obtained from six-year-old children (n=33) and adults (n=14). For each subject and condition, first-level GLM contrast maps serve as prediction targets. Cognitive features were used as inputs together with task-condition encoding. To overcome the computational challenge of predicting hundreds of thousands of voxels from limited samples, we implemented a spatial basis decomposition framework. Rather than predicting individual voxels directly, target maps are projected onto a lower-dimensional subspace using various spatial basis functions.

Machine learning models were then trained to map the cognitive and task inputs to the coefficients of these spatial bases, enabling the reconstruction of full 3D activation maps. The spatial fidelity of reconstructed maps across different basis configurations, ranging from unsupervised anatomical parcellations to supervised, task-driven decompositions was assessed.

Preliminary evaluations indicate that predicting activation via a lower-dimensional basis subspace mitigates the overfitting typically seen in direct voxel-wise prediction. Our findings reveal that a principled selection of basis vectors adequately covers the target map space, yielding a highly expressive model. Additionally, employing non-linear mapping for predictions results in superior reconstruction quality, outperforming standard methods that are mostly limited to linear models.

The framework of the current project demonstrates the feasibility of generating subject-specific functional maps from behavioral and cognitive data. By framing whole-brain prediction as a basis-coefficient mapping problem, this approach provides a scalable, computationally efficient tool for predicting the neural correlations of individual cognitive differences.

# Combined Discrete Wavelet Transform and Machine Learning from Reflectance Spectra for Screening Types of Skin Cancer in Patients

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**Background/Aim:** Skin cancer diagnosis currently relies on visual inspection and invasive, time-consuming biopsies. This study aims to develop a non-invasive, automated platform using diffuse reflectance spectroscopy (DRS) for real-time detection and classification of healthy versus cancerous tissue, specifically differentiating between malignant melanoma (MM), basal cell carcinoma (BCC), and squamous cell carcinoma (SCC).

**Method:** Diffuse reflectance spectra (400–1000 nm) were acquired in vivo and ex vivo from 11 patients (MM=4, BCC=5, SCC=2). Preprocessing included outlier removal and Kaiser-Bessel filtering. Discrete Wavelet Transform (DWT) with a DB4 mother wavelet decomposed signals into five levels, from which ten features (e.g., entropy, kurtosis) were extracted. Classification was evaluated using various machine learning algorithms (SVM, k-NN, Random Forest, Naïve Bayes) via two approaches: a multi-class ECOC-SVM model and a two-stage classification process.

**Results:** The hybrid DWT-ML framework demonstrated high performance across all metrics. The multi-class ECOC-SVM approach achieved a top accuracy of 98%. Overall results showed accuracy exceeding 95%, an average Area Under the Curve (AUC) of 0.99, and a false negative rate below 5%. Notably, the model achieved 100% accuracy in differentiating between SCC and BCC.

**Conclusion:** The integration of DWT and machine learning provides an effective, rapid, and non-invasive platform for skin cancer screening. The high accuracy and low false-negative rates highlight the potential of this technology to assist medical professionals in early detection and significantly reduce the need for invasive biopsies.