Standing-Wave Induced Regeneration of Otic Neurites (SIRON)

M3

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The Problem

Degeneration of spiral ganglion neurons (SGNs) and synapses occurs in sensorineural hearing loss.
Approximately 20% of deaf infants with cochlear implants are unable to use the device optimally [1].Neuronal loss creates a physical separation between cochlear implant (CI) electrodes and target neurons. **Commercial CIs do not restore natural hearing and do not repair damaged biological structures.**

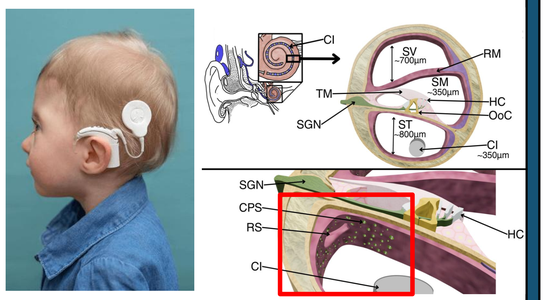

Figure 1: (a) Child using cochlear implant **(b)** 3D-Cochlear micro-anatomy and Canaliculi Perforantes of Schuknecht (CPS) in relation to a cochlear implant (CI) and retrocolumnar space (RS)

The Solution: Integrated Physical and Chemical Guidance

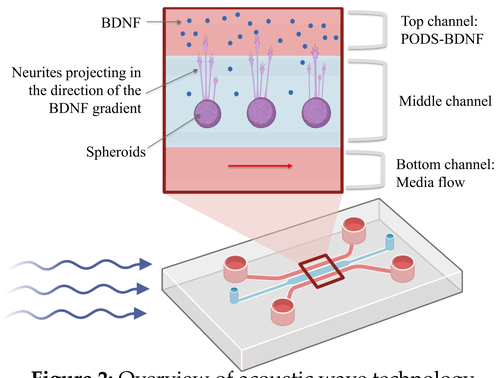

Figure 2: Overview of acoustic wave technology

1) Acoustic waves position and anchor neural spheroids near CI electrodes
2) Long-lasting brain-derived neurotrophic factor (BDNF) concentration gradient
3) Stable neurotrophic signaling
4) Promotes directed neurite growth across electrode–neuron gap

Results

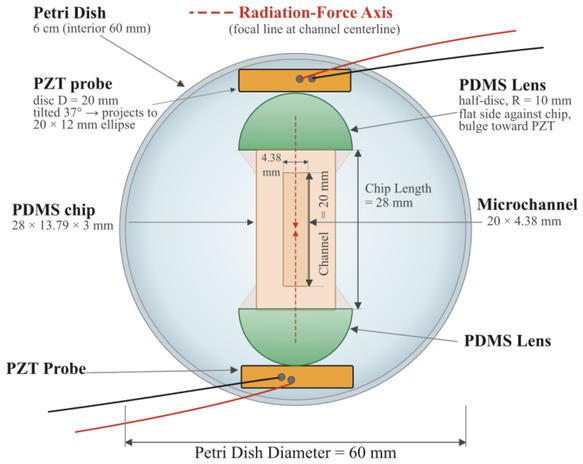

Figure 3: Top view of experimental set up using PDMS microfluidic chips, PDMS lens, and 2 lead zirconium (PZT) transducers

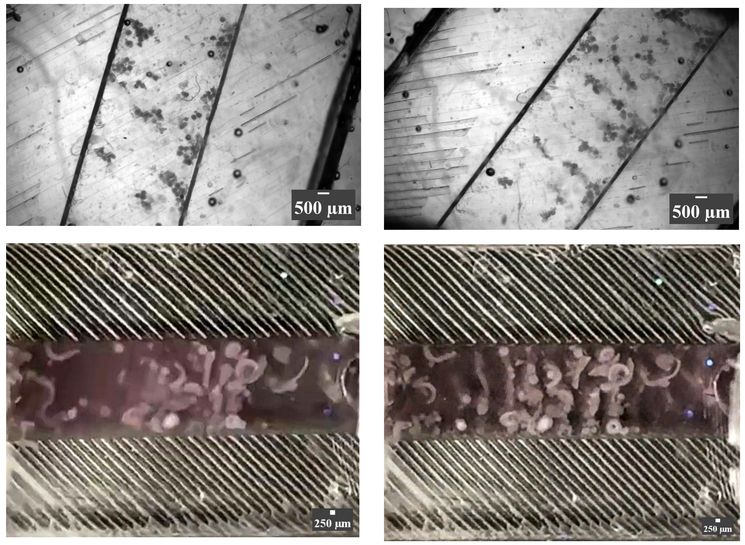

Figure 4: Parallel set of PZT transducers was placed on either end of center channel at 750 kHz frequency. Human embryonic kidney (HEK) spheroids accumulated at nodes 1.2 mm apart.

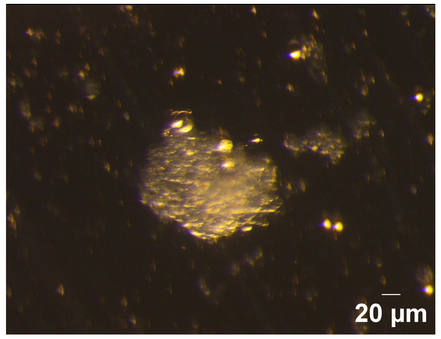

Figure 5: Close-up image of single spheroid.

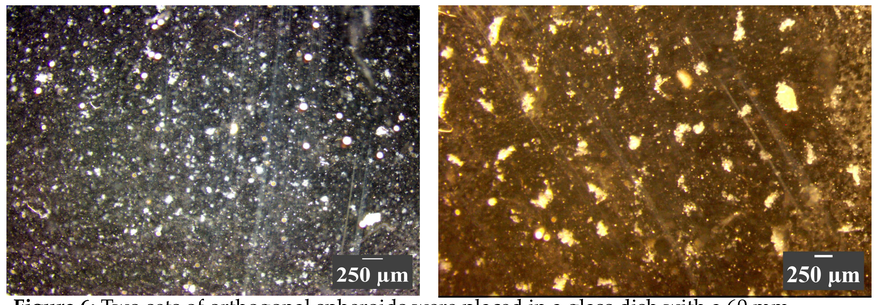

Figure 6: Two sets of orthogonal spheroids were placed in a glass dish with a 60 mm diameter. 2.5 x 10^6 HEK cells were suspended in 10 mL of solution, and cells accumulated at equally spaced nodes.

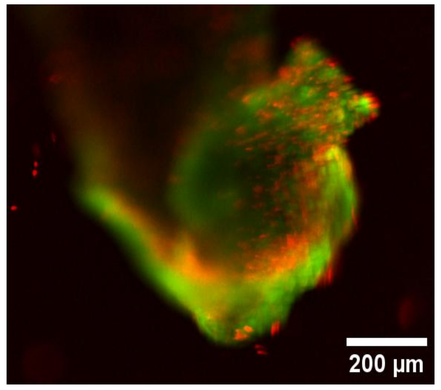

Figure 7: Live-dead staining of ESGN spheroids embedded in Vitrogel for 1 week shows >80% live cells (green), with sparce dead cells (red), demonstrating that spheroids remain viable in hydrogel over our device's therapeutic window.

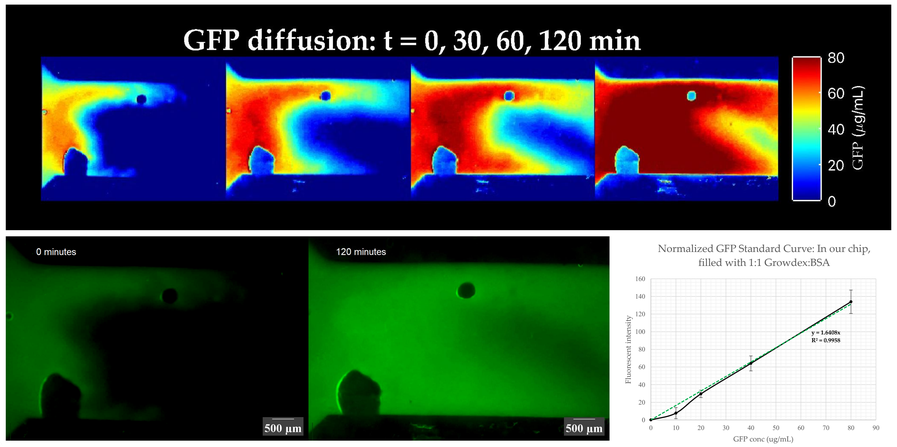

Figure 8: 60 μg/mL free GFP in Bovine Serum Albumin (BSA) reservoir diffusing through 1:1 GrowDex®/BSA over 2 hours. GFP standard curve is calculated using 5 GFP concentrations: 0, 10 μg/mL, 20 μg/mL, 40 μg/mL and 80 μg/mL in 1:1 GrowDex®/BSA injected into PDMS-cast chips

Conclusions

1) The microfluidic device successfully spaces spheroids at clinically relevant node distances to align with electrodes using bulk acoustic waveforms

2) A concentration gradient was established in the microfluidic chip, experimentally verified using GFP

3) Spheroid formation was achieved through two sets of orthogonal PZT, enhancing the experimental workflow.

4) Overall, this work supports sustained neurotrophic signaling and improved structural integration in subsequent biohybrid cochlear implant prototypes.

Future Work

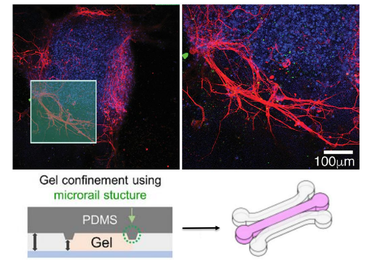

Figure 9: (a) Neurite projection from ONP spheroids[2] **(b)** Pinning of fluid to middle channel of microfluidic chip using microrails (left)[3] and hydrophilicity conferred by laminar flow (right)

Acknowledgments

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References: 1] Matsuoka, A.J., et al. *In Prep*, Biohybrid cochlear implants: Neural interfaces, regenerative pathways, and translational benchmarks.
2] Chang, H., et al. (2020), An engineered three-dimensional stem cell niche in the inner ear by applying a nanofibrillar cellulose hydrogel with a sustained-release neurotrophic factor delivery system.
3] Lee, M.S., et al. (2025), Synovium-on-a-Chip Reveals Fibroblast–Macrophage Crosstalk Underpinning Joint Homeostasis and Evaluation of Gout Therapies.