Neural implant insertion system using ultrasonic micro-vibration to improve penetrating microelectrode array insertion mechanics: In vitro and in vivo evaluations

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NeuralGlider™ CORTICAL
Neural Implant Insertion System

Introduction

Penetrating electrode arrays provide localized access to neural stimulation and recording sources, and they are a valuable neuroscience research tool. Neuroscientists and researchers developing future clinical applications continually seek to increase information transfer potential by implanting electrode arrays with higher numbers of shanks at greater density. Successful insertion of penetrating electrode arrays into brain tissue remains a significant challenge, and outcomes are often heavily reliant on surgical skill and technique. During insertion, electrode arrays apply forces to the neural tissue resulting in significant compression (dimpling) at the implant site and strain on local tissues. Shallow insertions (< 1 mm) targeting the upper cortical layers are especially difficult. Electrode arrays may need to be over-inserted past the target depth to ensure puncture of meningeal membranes, or be fired in at very high velocity, limiting accuracy and possibly increasing implantation trauma.

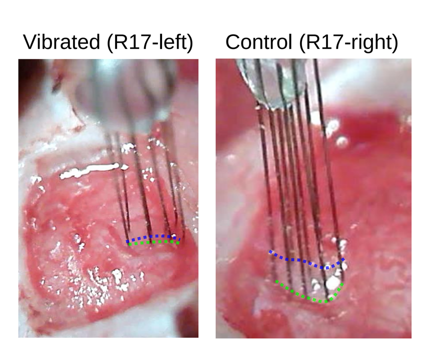
+ **NeuralGlider-Cortical™ uses ultrasonic micro-vibration to reduce the insertion force and dimpling during microelectrode array implantation.**

NeuralGlider-Cortical™ System

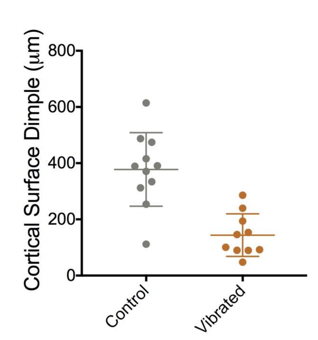
+ Ultrasonic actuator produces axially-directed micro-vibrations in shanks as array is inserted
+ Stereotaxis mountable closed loop micro-positioner stage, 0.5 µm resolution
+ Omnetics-compatible, detachable coupler for reliable transmission of ultrasonic vibration to the neural implant
+ RoHS compliant control box
+ Low profile USB microscope camera, with user-positioned mount to the stereotaxic instrument
+ LabVIEW-based GUI for control of the micro-positioner and actuator while recording position data

Prior Research

+ Initial *in vivo* study:
  - Utilized custom-built 8-channel tungsten microwire arrays (50 µm diameter with 250 µm spacing)
  - Bi-lateral barrel cortex implants
  - All insertions through pia (dura removed) at 50 µm/s
  - 2-week survival (N=10); recordings and histology
+ Ultrasonic micro-vibration of penetrating electrode arrays during insertion substantially reduces insertion forces and dimpling of brain tissue
+ Initial short-term studies supported safety of approach; no significant difference in recording quality or histology



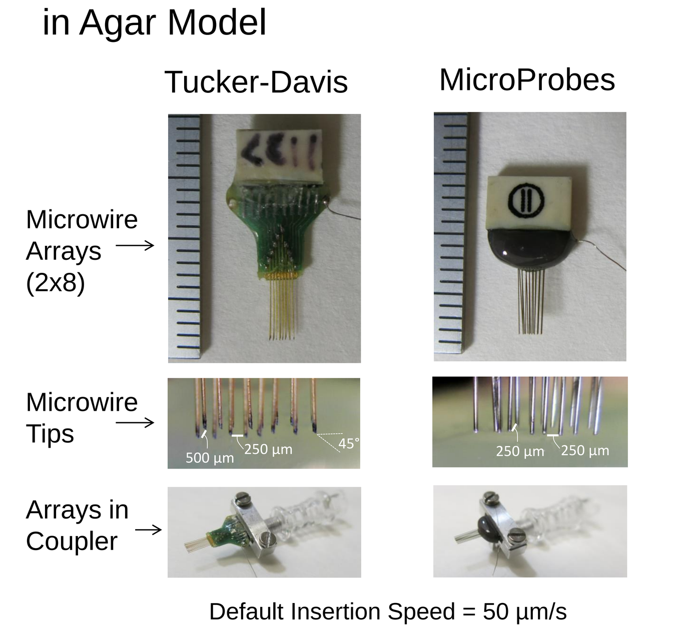
8-ch arrays inserted with (left) and without (right) ultrasonic vibration into rat barrel cortex. Dashed lines: brain surface at initial contact (Blue) and at target insertion depth (Green).

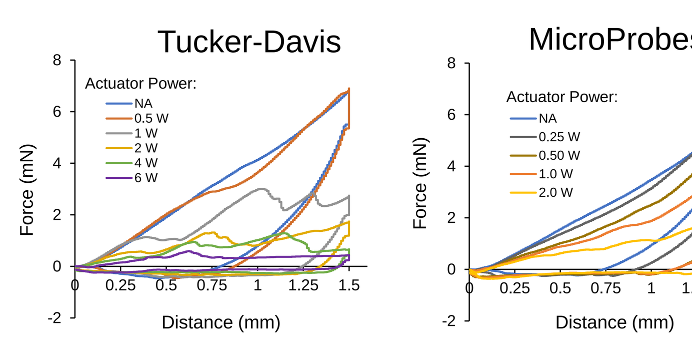


Maximum dimple, estimated from analysis of insertion videos. (* p<0.001; n=10)

Improving Insertion Mechanics of Commercial Microwire Arrays

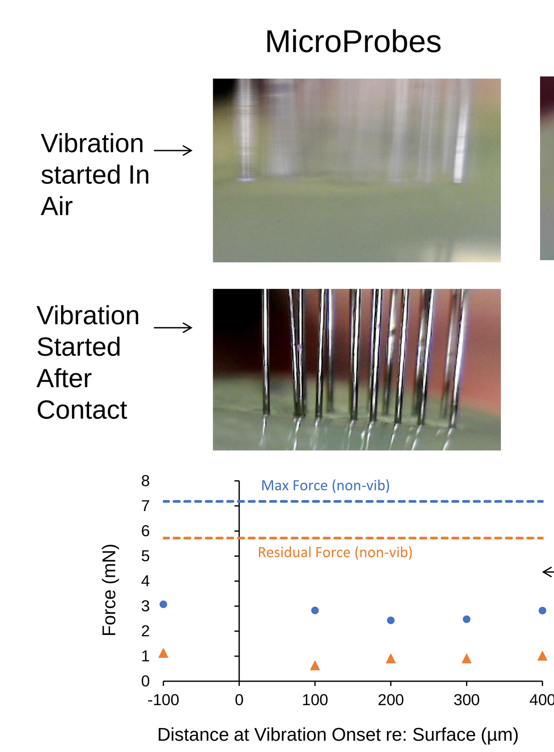
+ Reduced Insertion Force Demonstrated in Agar Model





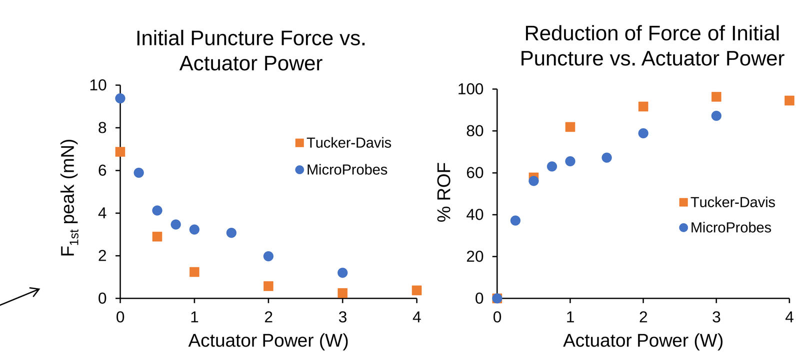
Above: Examples of agar insertion force vs. insertion distance profiles for both Tucker-Davis and MicroProbes arrays.

Right: Summary analysis of initial puncture force (1st peak in force vs. insertion distance plot) vs. actuator power.

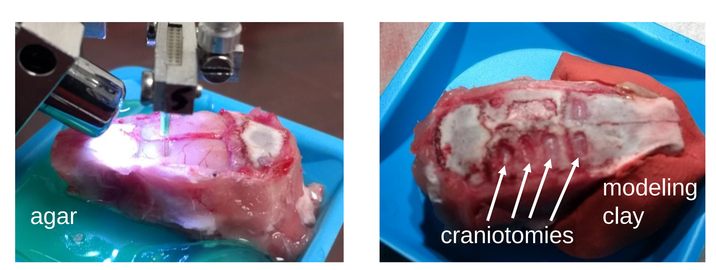


Substantially more "off-axis" vibration was observed with MicroProbes (top) arrays when actuated in air as compared to Tucker-Davis. Delaying vibration until tips make initial contact avoids off-axis vibration (middle).

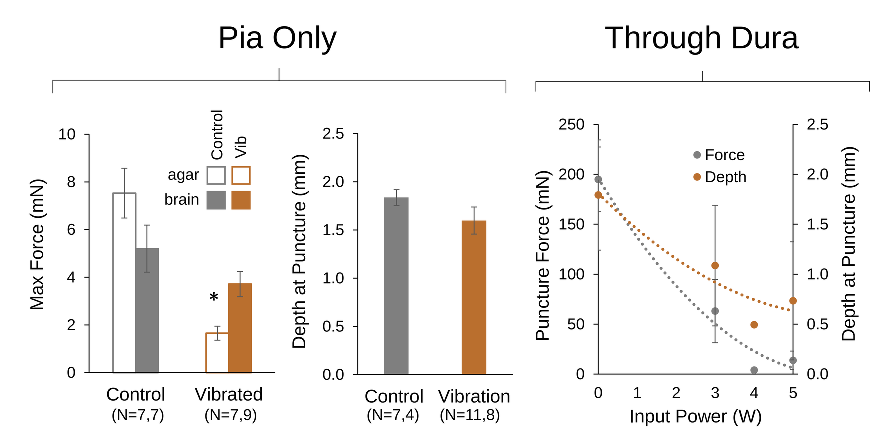
Delaying vibration until the tips were partially advanced into the model did not greatly impact performance.



+ Insertion Force and Dimpling Reduction: *Ex Vivo* Evaluations

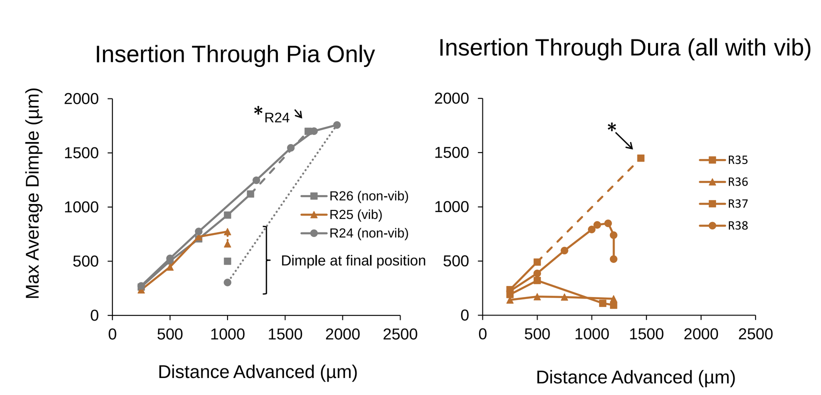


Examples of *ex vivo* insertion force testing sample preparations. Left: sample with large craniotomy on bed of agar for pia-only insertions. Right: Example of preparation with small craniotomies for testing dura insertion approach.



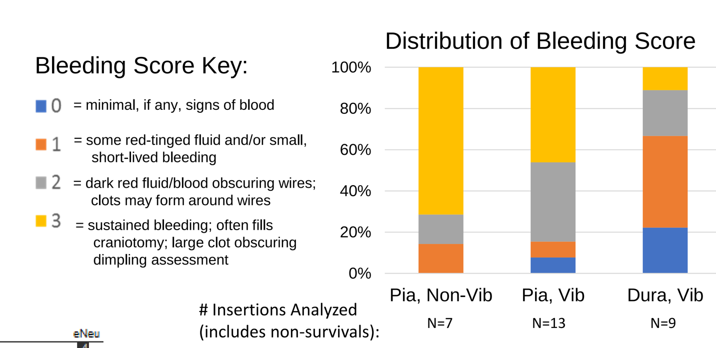
Ex vivo insertion force summary for insertion of Tucker-Davis arrays through pia only vs. through intact dura (control = non-vibrated). With ultrasonic vibration, insertion through dura generated comparable forces as insertion through pia only. Insertion through small craniotomy with intact dura yielded less dimpling.

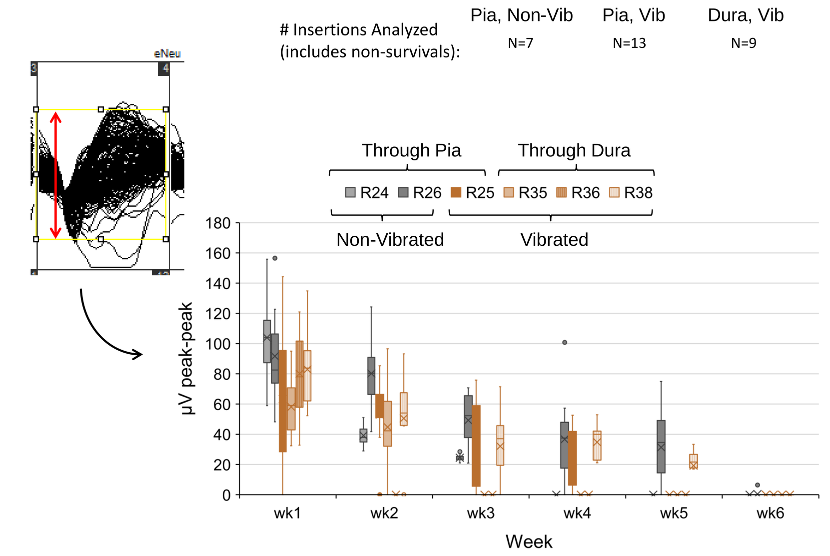
+ Demonstrated Safety and Efficacy of Ultrasonic Vibration-aided Insertion, Including Through Dura



Video frames corresponding to 250 µm intervals during insertion process were extracted and analyzed. Average brain surface dimple determined from averaging exposed lengths of visible wires relative to tip positions when brain first contacted (Image-J).

* Max dimple estimated by total distance array was advanced as blood obscured video and/or rupture (and subsequent brain relaxation) was not clear.

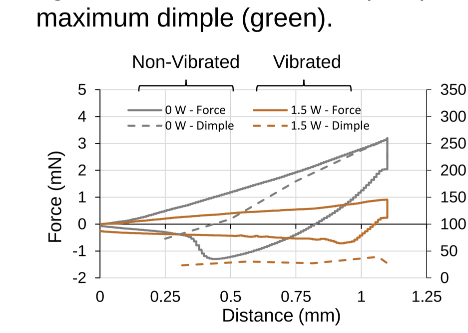


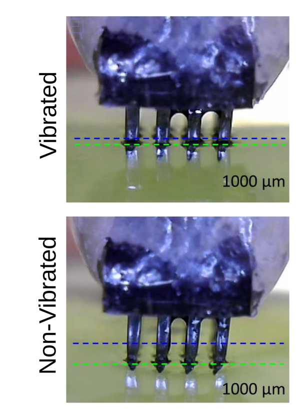


Compatibility with Many Array Types

+ Blackrock

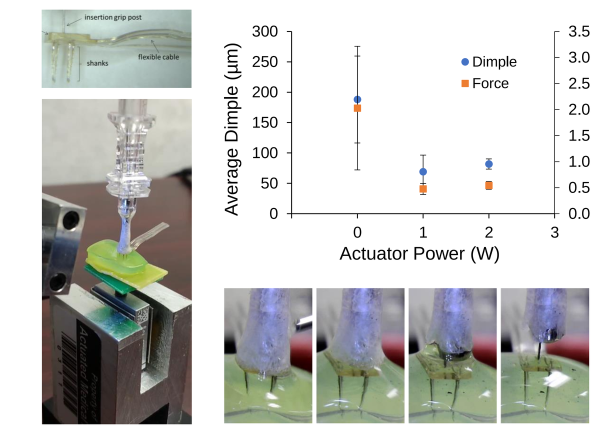
Poly-ethylene glycol (PEG) was used to attach unwired 4x4 array to actuator coupler. *Below:* Plots of insertion force and dimpling vs. distance for representative vibrated and non-vibrated insertions. *Right:* Video frames from same insertions extracted after advancing 1000 µm. Dashed line marks surface of agar model at initial contact (blue), and at maximum dimple (green).





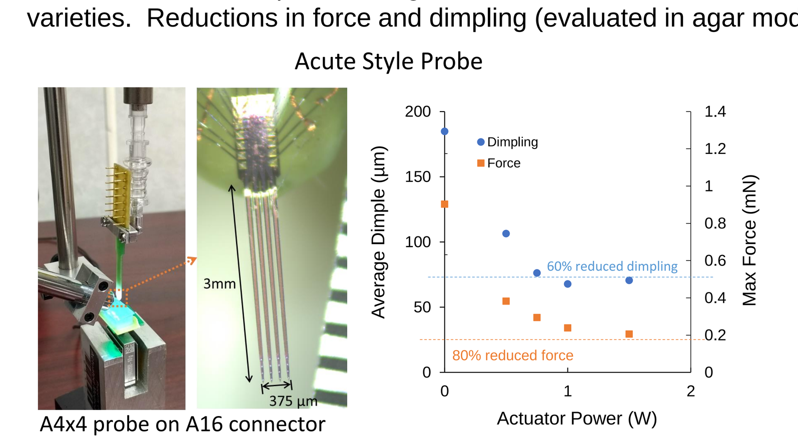
+ N-Form

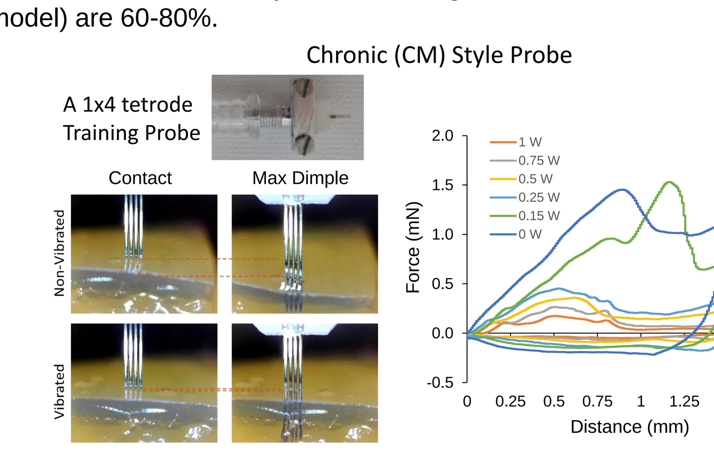
PEG was also used to attach a 2x2 array with portion of ribbon cable to actuator coupler. Insertion force measurement setup with agar test sample resting on force sensor is shown in lower left photo. Insertion force and dimpling could be reduced by 75% and 60%, respectively. PEG can be dissolved with water to release array.



+ NeuroNexus

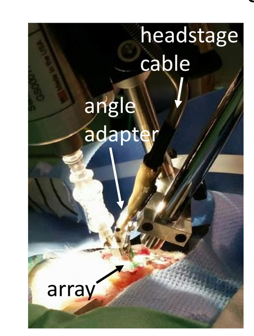
Several NeuroNexus probe configurations have been evaluated with the NeuralGlider system, including both acute and chronic varieties. Reductions in force and dimpling (evaluated in agar model) are 60-80%.





Additional System Capability

+ Neural Recording During Insertion

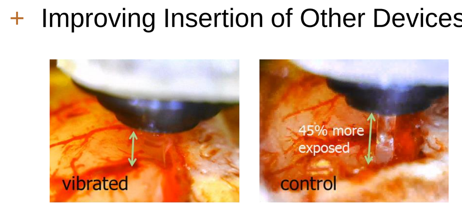


With custom angle adapter to couple headstage amp to array, it is possible to obtain neural recordings at points during the insertion process

+ Compatibility with TDT's ZIF Connector

Demonstrated compatibility of NeuralGlider with Tucker-Davis Technology's (TDT) patented ZIF-connector arrays, popular among researchers

+ Improving Insertion of Other Devices



Ex vivo pilot study demonstrated that NeuralGlider may improve Inscopix GRIN lens insertions (deeper penetration with less brain compression)

Conclusions and Future Directions

+ Ultrasonic micro-vibration by the NeuralGlider neural implant system safely improves insertion of microwire arrays and many other array types on the market
  - 60-80 % reductions in tissue dimpling and insertion force are typical
+ The NeuralGlider system enabled the insertion of microwire arrays through dura, which may simplify future neural implant procedures for some devices
+ The system is shown to be compatible with many electrode array types; also could have application in the placement of other non-electrode devices
+ Future *in vivo* studies required for evaluating potential for improving chronic results and for evaluating performance with non-microwire devices

Acknowledgments

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