Safety of Wireless Brain Implants - A Systematic Review

Nelson Lee Angels and Atef Elsherbeni

nelsonangels@mines.edu, aelsherb@mines.edu

ELECTRICAL ENGINEERING
COLORADO SCHOOL OF MINES

ARC Antennas, RFID, and Computational Electromagnetics Group

WARNING: SENSITIVE CONTENT

Brain implants research involve invasive surgical medical procedures on human and/or animal subjects. For educational purposes, images of some of these procedures will be shown, that some may find unsettling.

Viewer discretion is advised.

The Headlines

Elon Musk's Neuralink brain chip tests kills 15 monkeys out of 23, company accused of causing 'extreme suffering', says report

ET THE ECONOMIC TIMES Feb 15, '22

Brain Implants Allow Paralyzed Man to Walk Using His Thoughts

The New York Times Feb 15 , 2022

'Neural revolution': Royal Society calls for inquiry into new wave of brain implants

The Guardian Sep 10, '19

Paralyzed patients communicate thoughts via brain-computer interface

FOX NEWS Feb 1 , '17

'The greatest feeling in the world': Deep brain stimulation helps stroke survivor regain independence

CNN Aug 14, '23

Lawmakers Push For SEC Probe Into Elon Musk's Neuralink For Claims About Brain Implant Safety

Forbes Nov 22, '23

Elon Musk's Neuralink wins FDA approval for human study of brain implants

REUTERS May, 2023

What We'll Discuss Today

- **The Why: Purpose of Review & Key Findings**
- **The Technology**
- **The Risks**
- **The Biological Effects**
- **Biocompatibility**
- **Research Results**
- **Conclusions**
- **Future Outlook: Where Are We Going?**
- **Questions & Discussion**

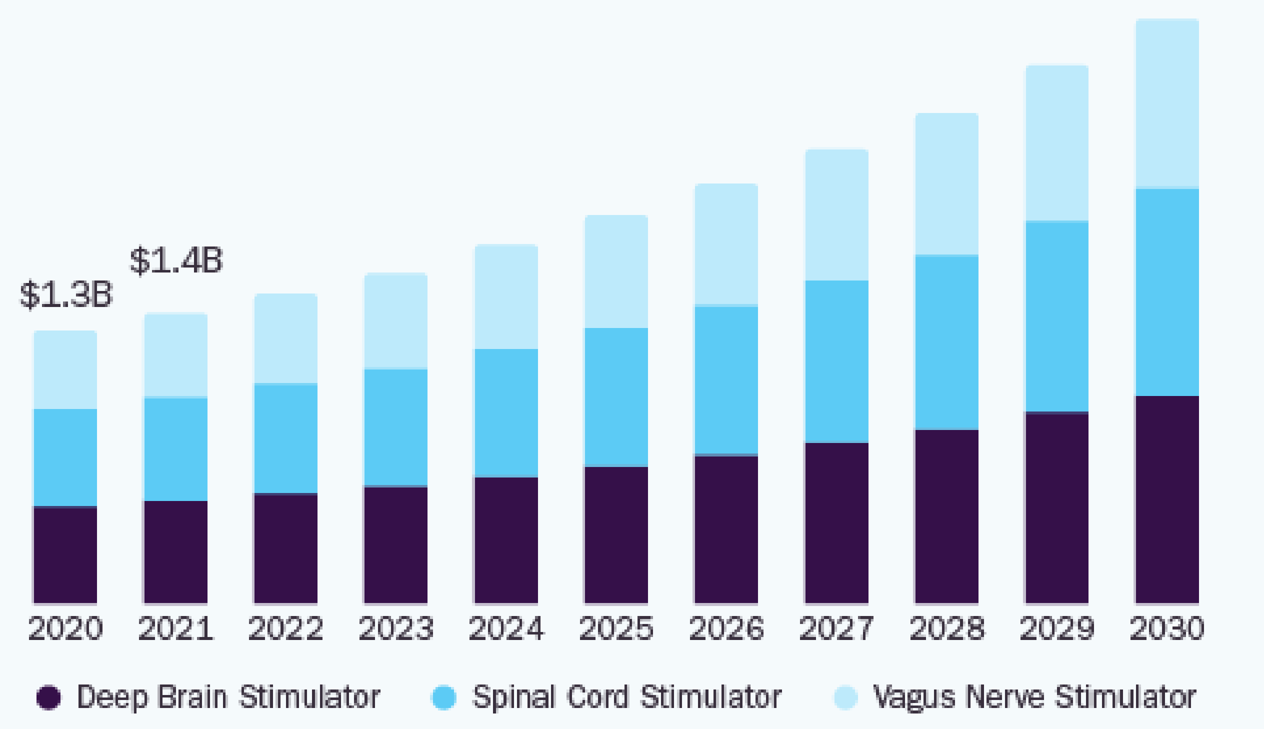
The Why

…it's where the money is going

- **Brain Implants Market Size is Expected to Exceed $ 14.24 B in 2032**

  - **As commercial market swells the research funding is following**

North American Brain Implants Market
Size, by Product, 2020-2030 (USD Billion)



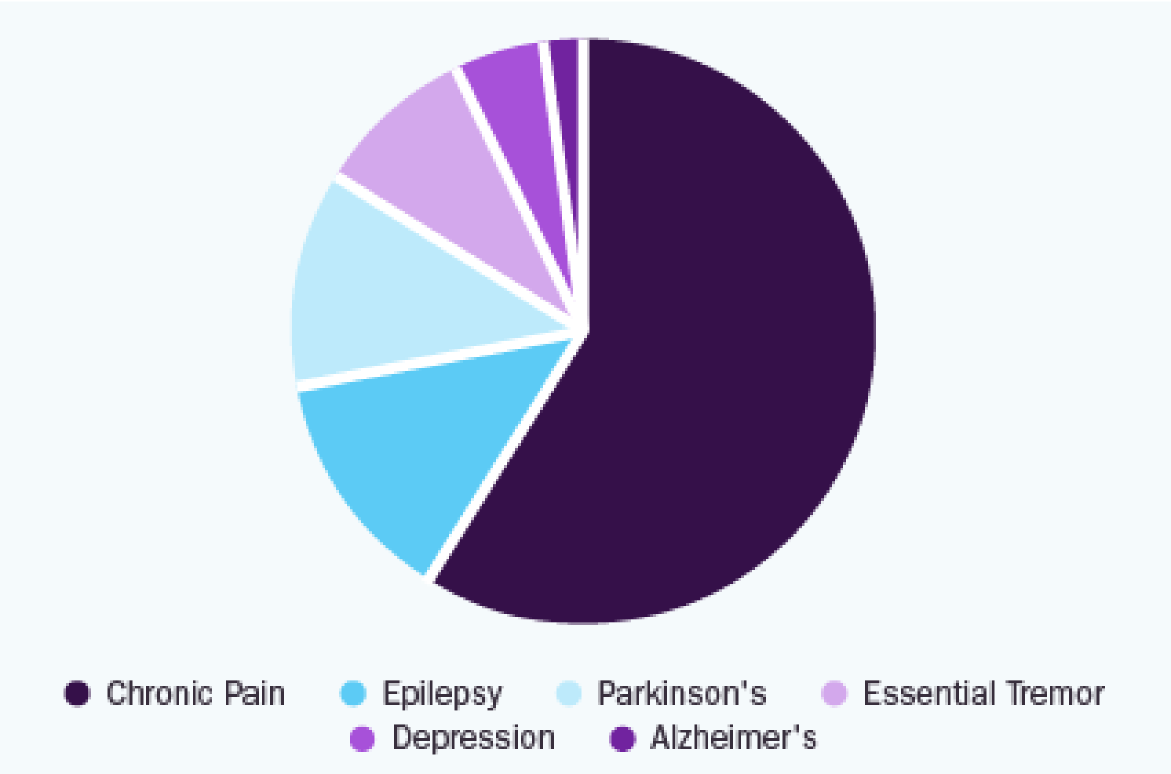
Source: Grand View Research (GVR)

The Why

Major factors driving the growth

- Increasing incidence of neurological conditions driving commercial growth and research interest
- Parkinson's, Alzheimer's, and epilepsy, c
- Increased awareness of brain implant benefits
- Increased positive research outcomes

Global Brain Implants Markey
Share, by Application, 2022 (%)



Source: Grand View Research (GVR)

The Why: Purpose of this Research Review

Increasing incidence of neurological conditions

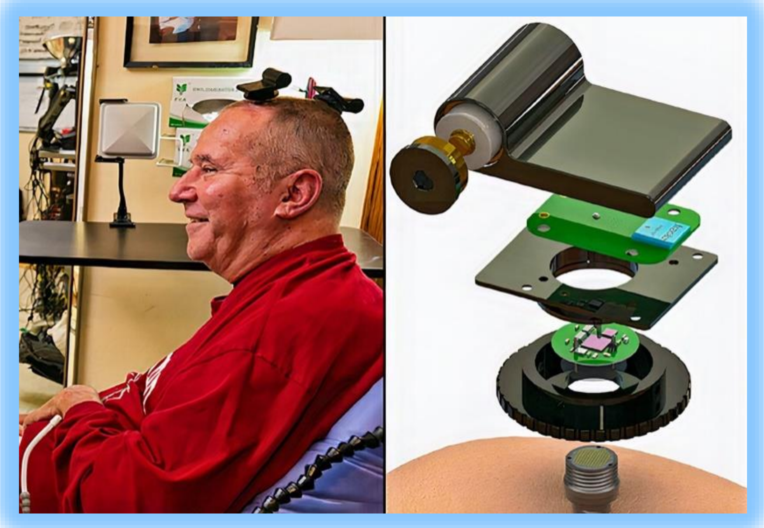
Increased prevalence of Brain Computer Interfaces (BCI)

Increased Wireless Modality

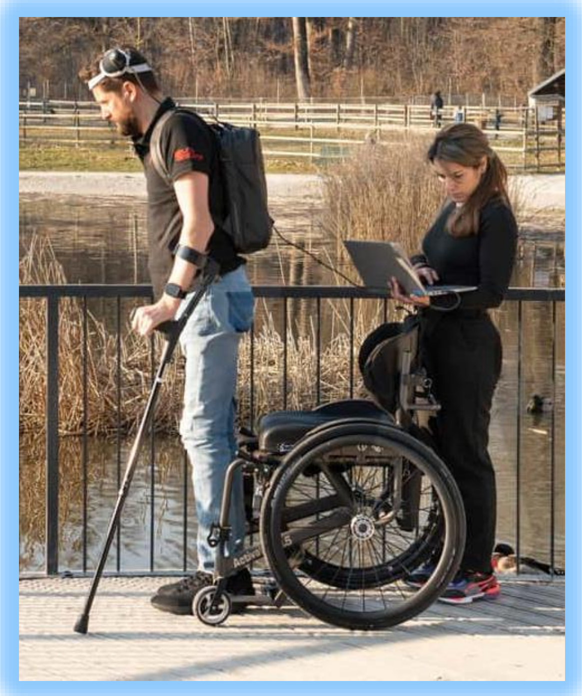
Impending need for research to test the chronic safety implications of these new devices

The Why: Exponential Growth of Wireless BCIs

- **Wireless BCIs increasingly becoming viable treatment option**
  - **Limited and Potentially Outdated Safety Standards**



A participant in a clinical trial uses wireless transmitters that replace the cables normally used to transmit signals from sensors inside the brain. Source: BrainGate



A digital bridge between the brain and spinal cord helps an individual with paralysis to walk naturally. Source: CHUV/Gilles Weber

A research participant in a study of speech neuroprostheses is connected to computers that translate her brain signals into the speech and facial movements of an avatar. Source: Berkeley Engineering | Photo by Noah Berger

The Why: Key Findings

Literature on BCI is substantial but wireless modality is scare

Acute Medical Complications are rare

Chronic safety implications largely unknown

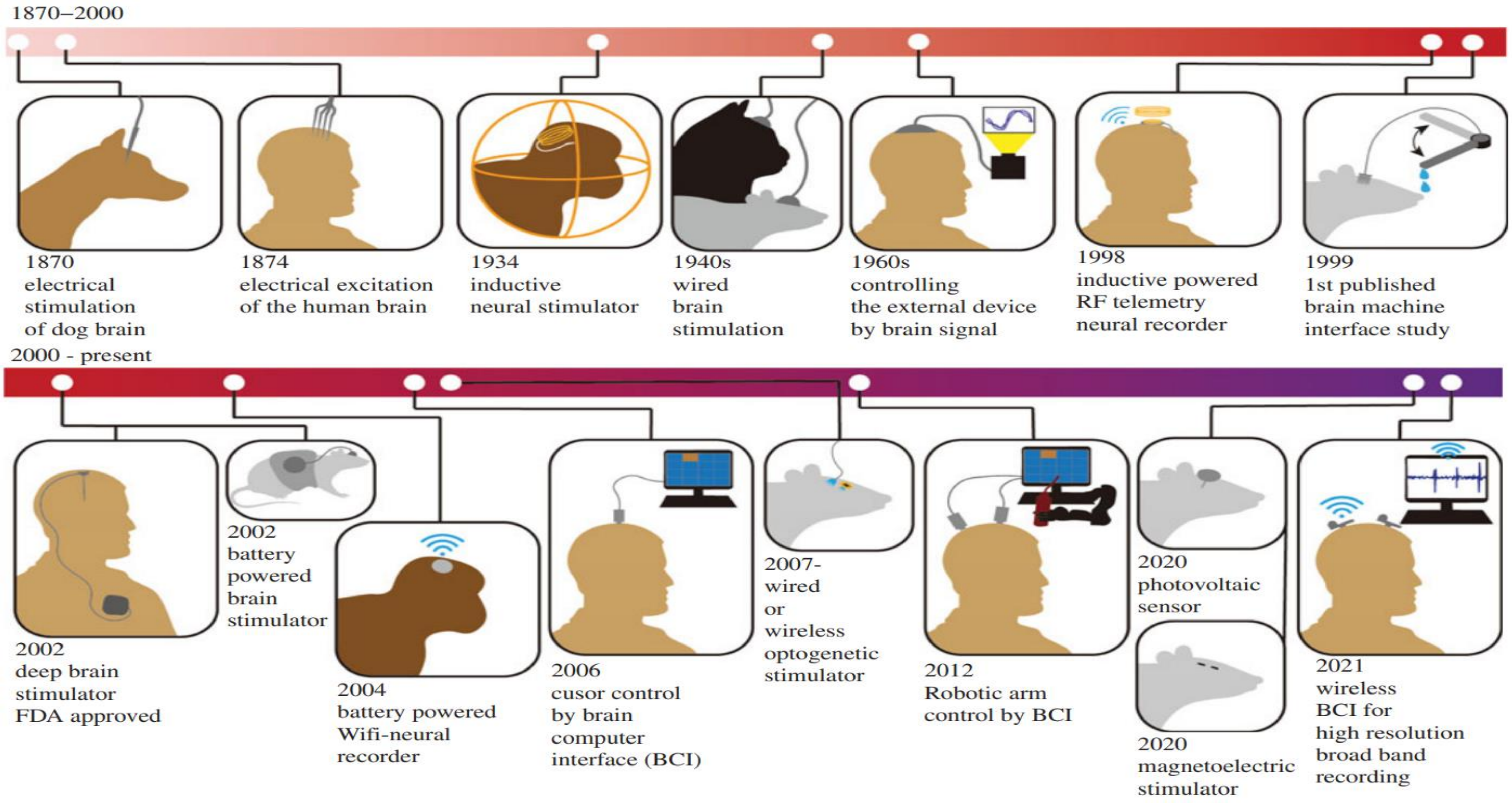
Biocompatibility materials breakthroughs show promise, specifically in ceramics

Lack of clarity around wireless device induced psychological stress

Other than SAR, lack of uniform biological safety testing consensus

Considerable caution needed until quality of experimental methodology improves

The Technology: Timeline

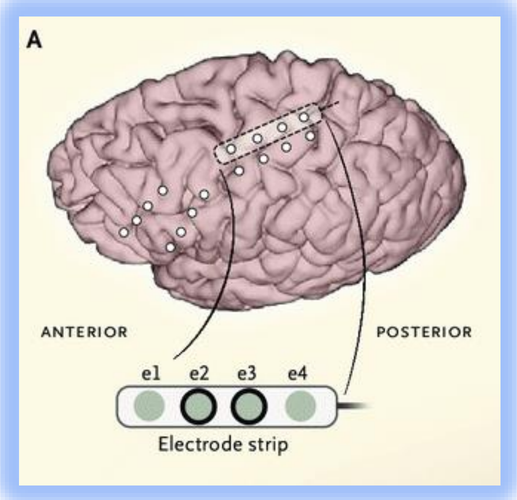


Source: Han-Joon Kim et al. Nick. (2022). *The Royal Society Publishing*

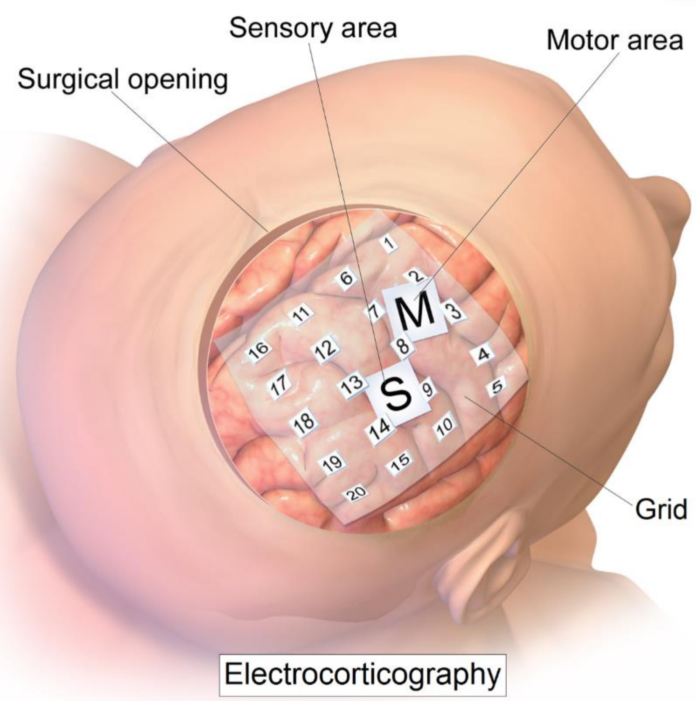
The Technology: BCI Overview

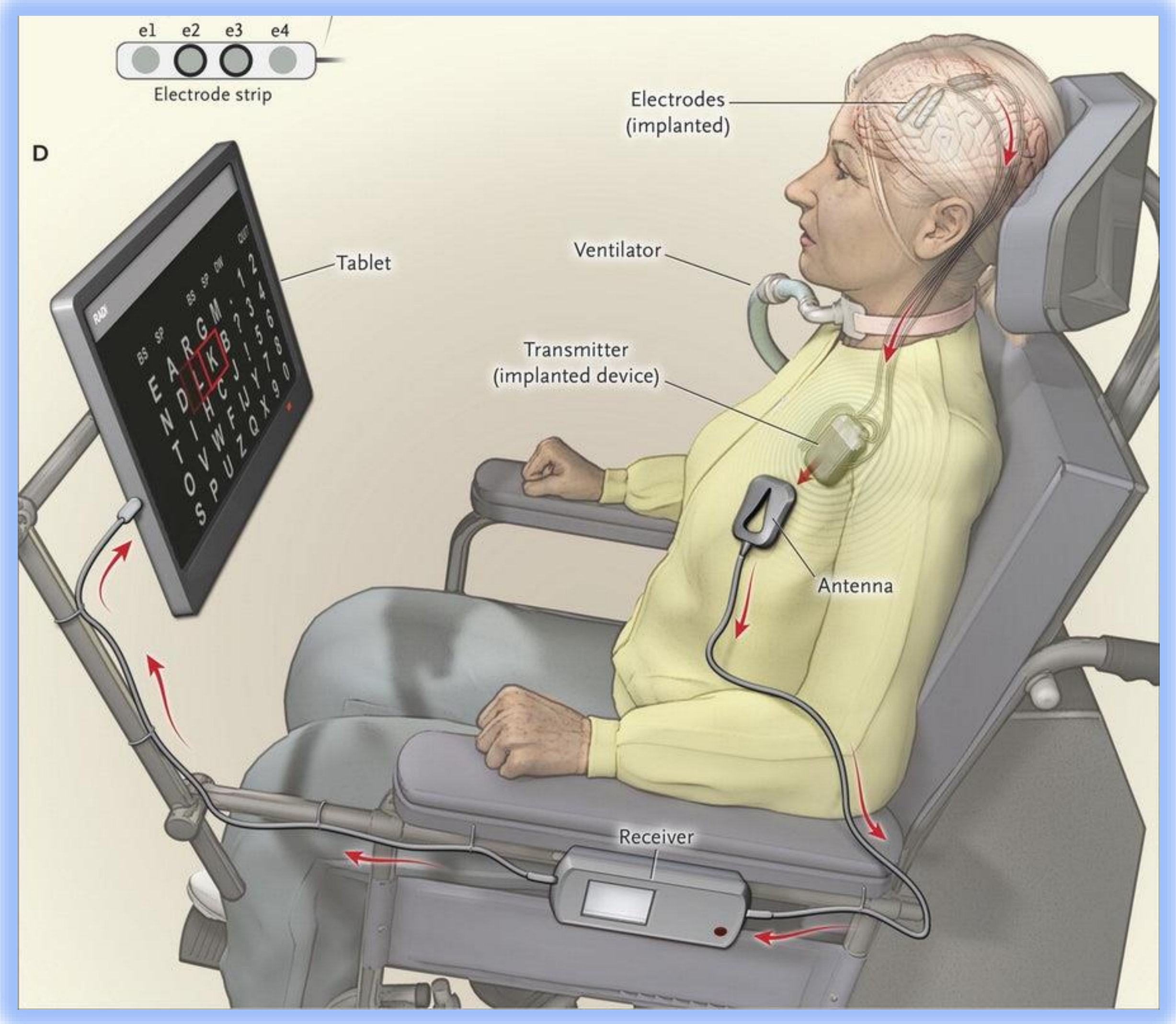
Subdural Electrode Over Motor Cortex

with extracranial subcutaneous transmitter



Electrode placement on the brain

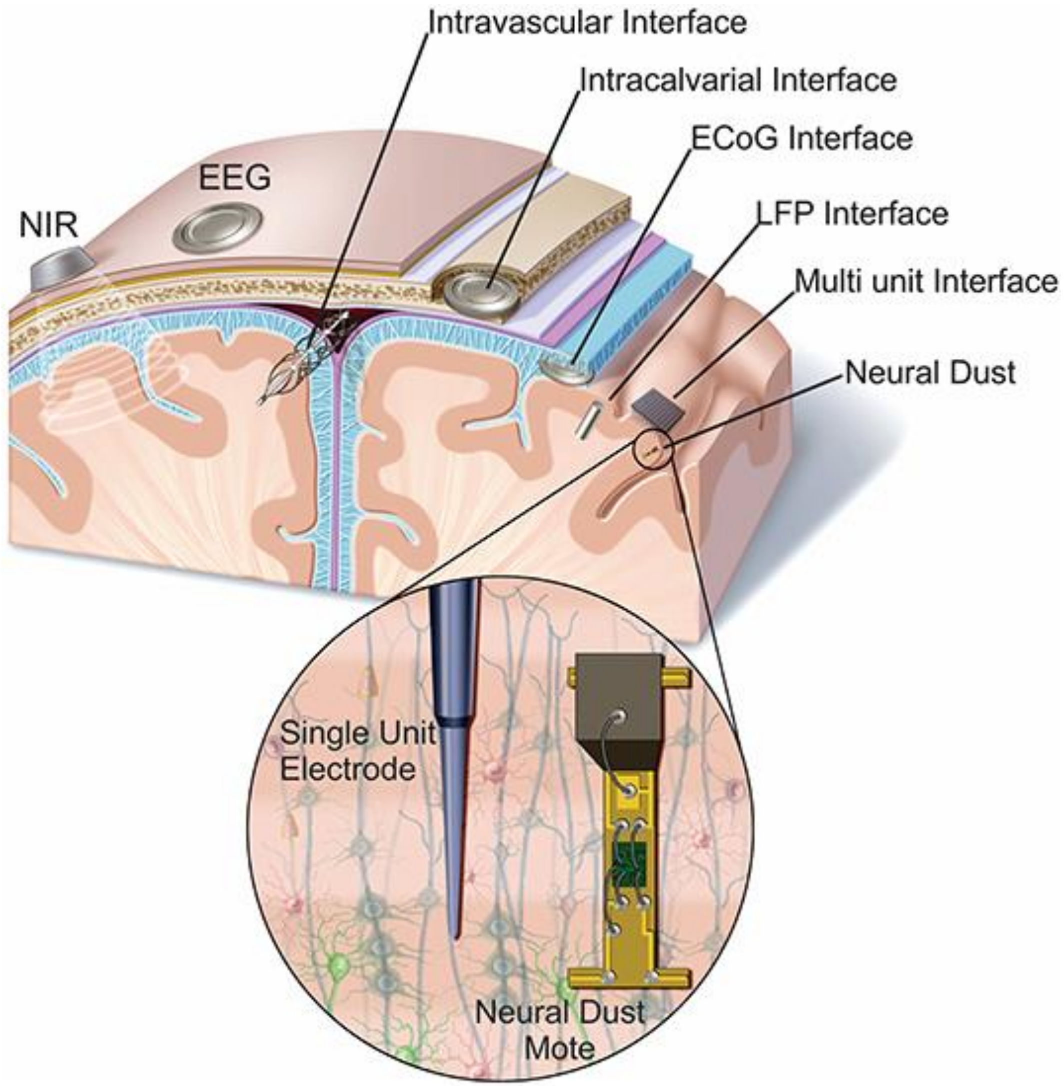




Fully Implanted Brain–Computer Interface in a Locked-In Patient with ALS

Source: Vansteensel et al. Nick. (2016). New England Journal of Medicine

The Technology: Location Options



Anatomic locations of representative BCI sensors

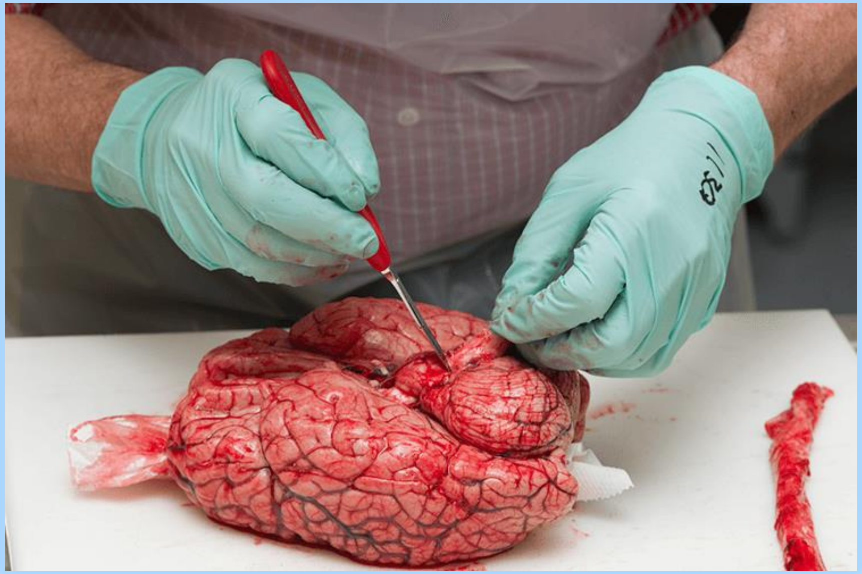
- Diverse number of locations
- Varying degrees of invasiveness
- On or above the surface of the scalp (near infrared, EEG, and MEG)
- EEG, electroencephalography
- NIR, near infrared
- ECoG, electrocorticography;
- LFP, local field potential

Source: Leuthardt EC, Moran DW and Mullen TR (2021) Defining Surgical Terminology and Risk for Brain Computer Interface Technologies

The Technology: Going Wireless

Neurophysiological Advancements

- Interdisciplinary birth of science
- New brain research pathways
- Neural network complexity “known”



Fully intact human brain, donated, for medical research

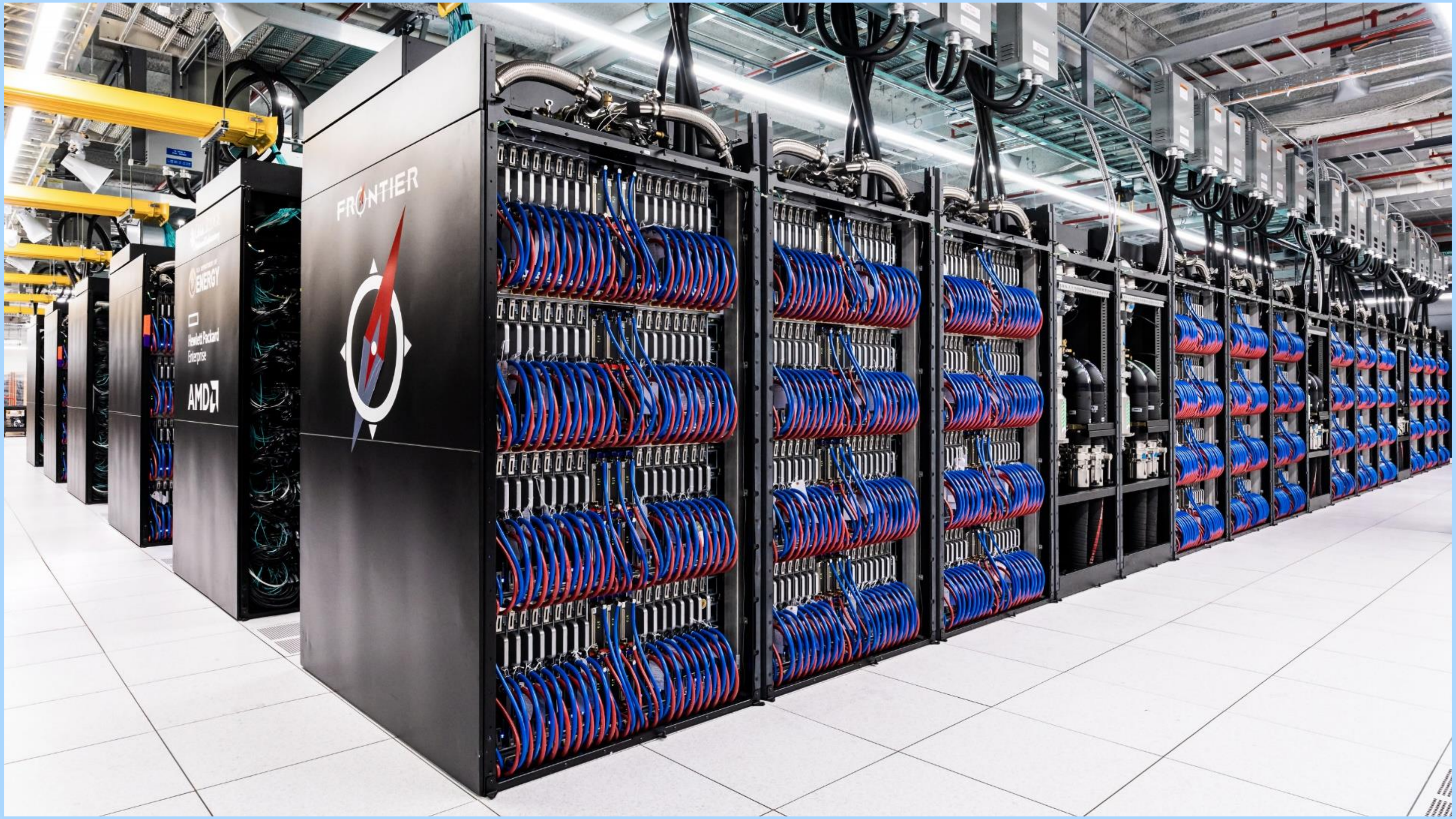
Neuroscientist carefully slices and arranges cross-sections of a brain for freezing

Source: Calgary Brain Bank, *Alexis Wnuk*

The Technology: Going Wireless

Computational Advancements

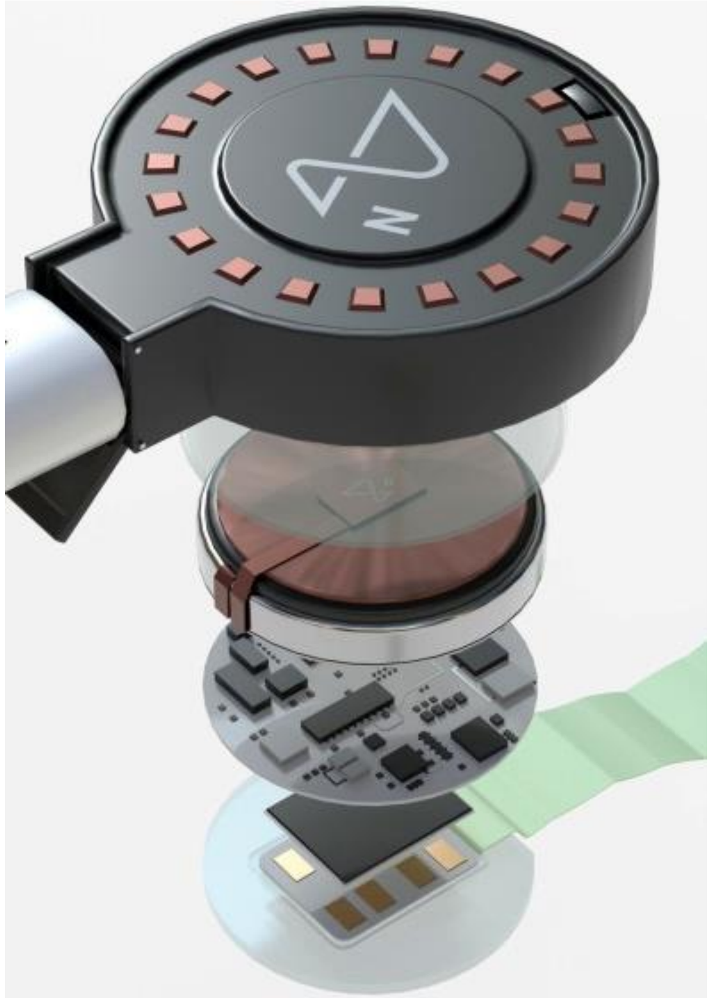
- 100 billion (1×10^{11}) neurons in dataset
- Exascale computing
  - exaFLOPS (quintillion 10^18 FLOPS)
- Cloud computing
  - Biomedical engineering boom
- UWB Transmitter with 1.66 Gb/s
- Transdural link >250 Mbps data rate demonstrated

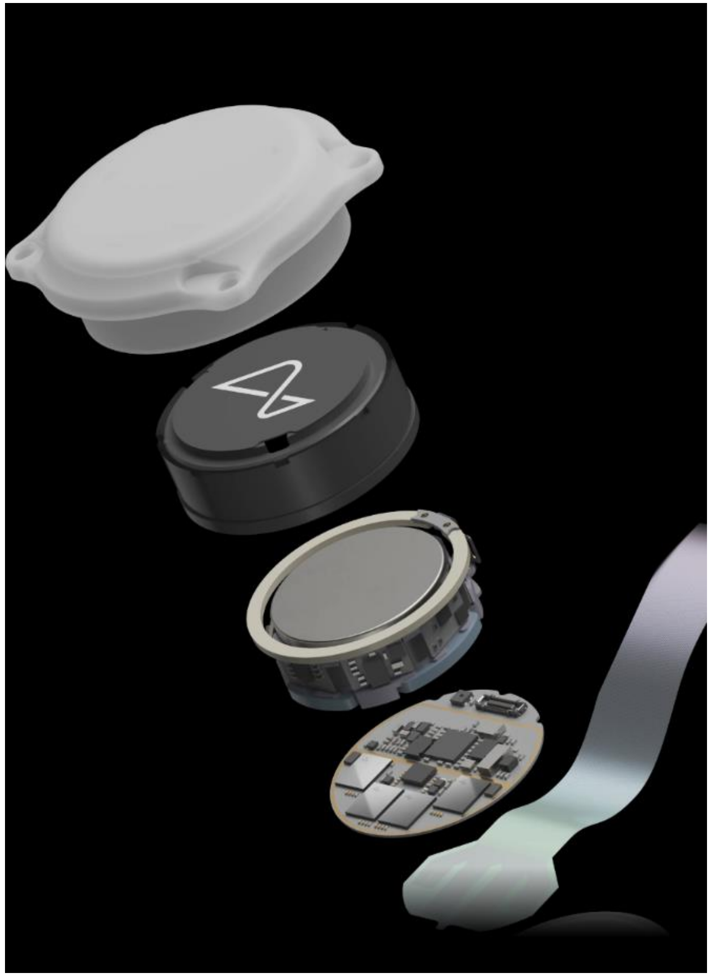


View of ‘Frontier’, an exascale-class machine

Source: Oak Ridge National Laboratory, *Technology Review*

The Technology: Wireless





Neuralink wireless brain implant device connected to charger

Going Wireless

Technological advancements have enabled wireless modality of BCIs

- Self-Powering
- Wireless Power Transfer
- Elon Musk's *Neuralink* leading cultural interest in its commercial viability

Neuralink wireless brain implant in hand

Source: Neuralink.com

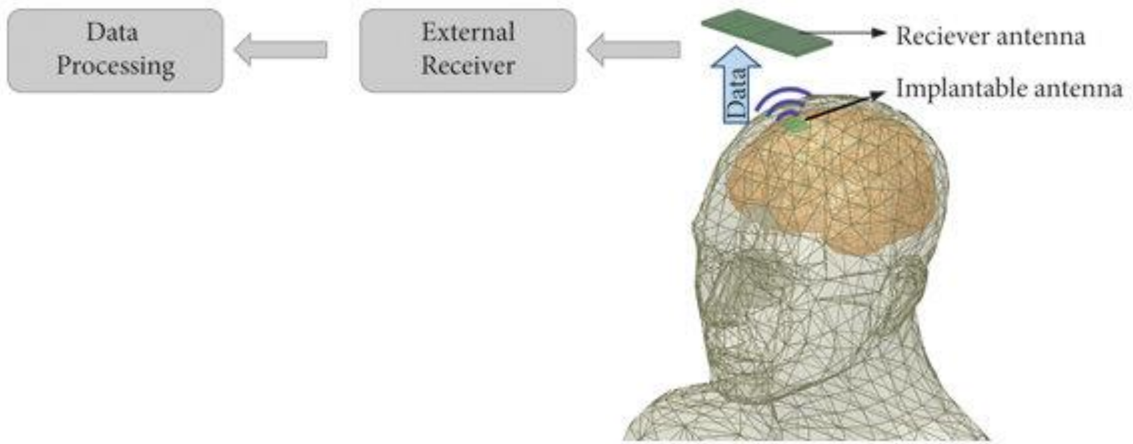
The Technology: Wireless

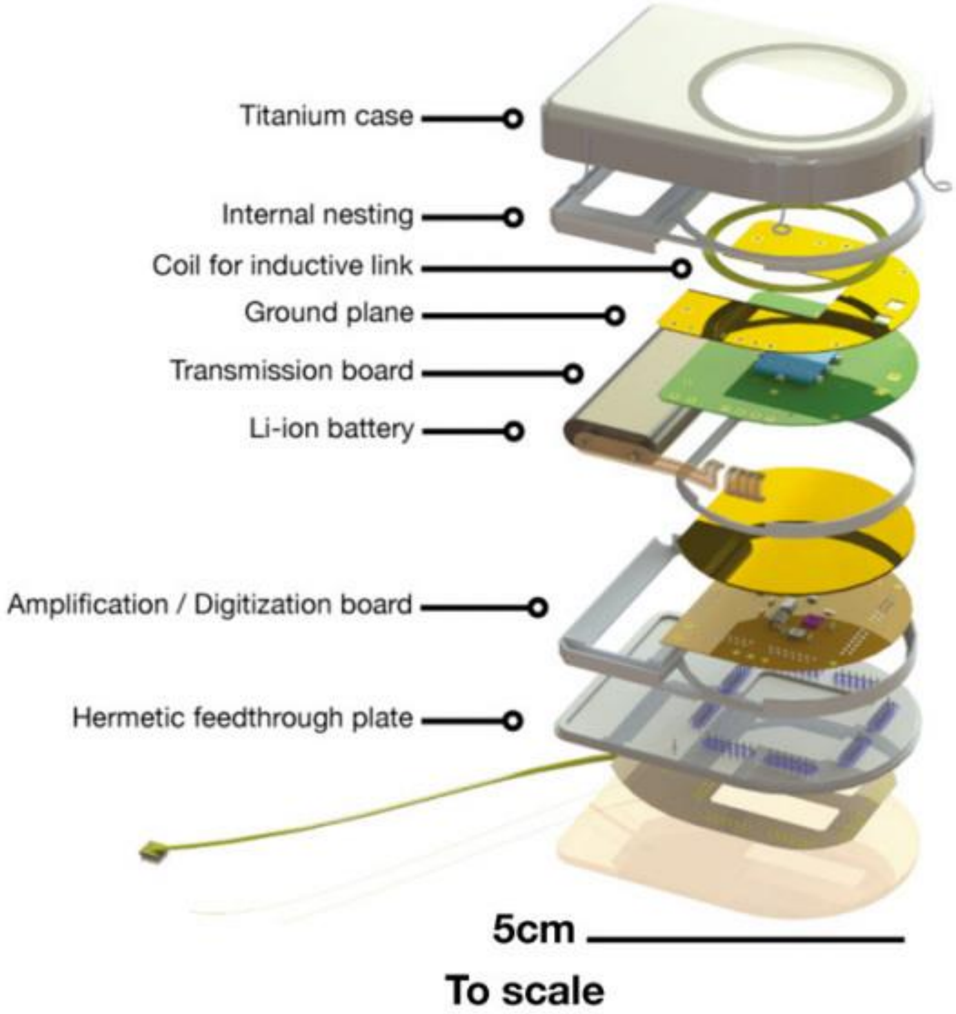
Source: Neuralink.com

The Technology: Wireless

Going Wireless

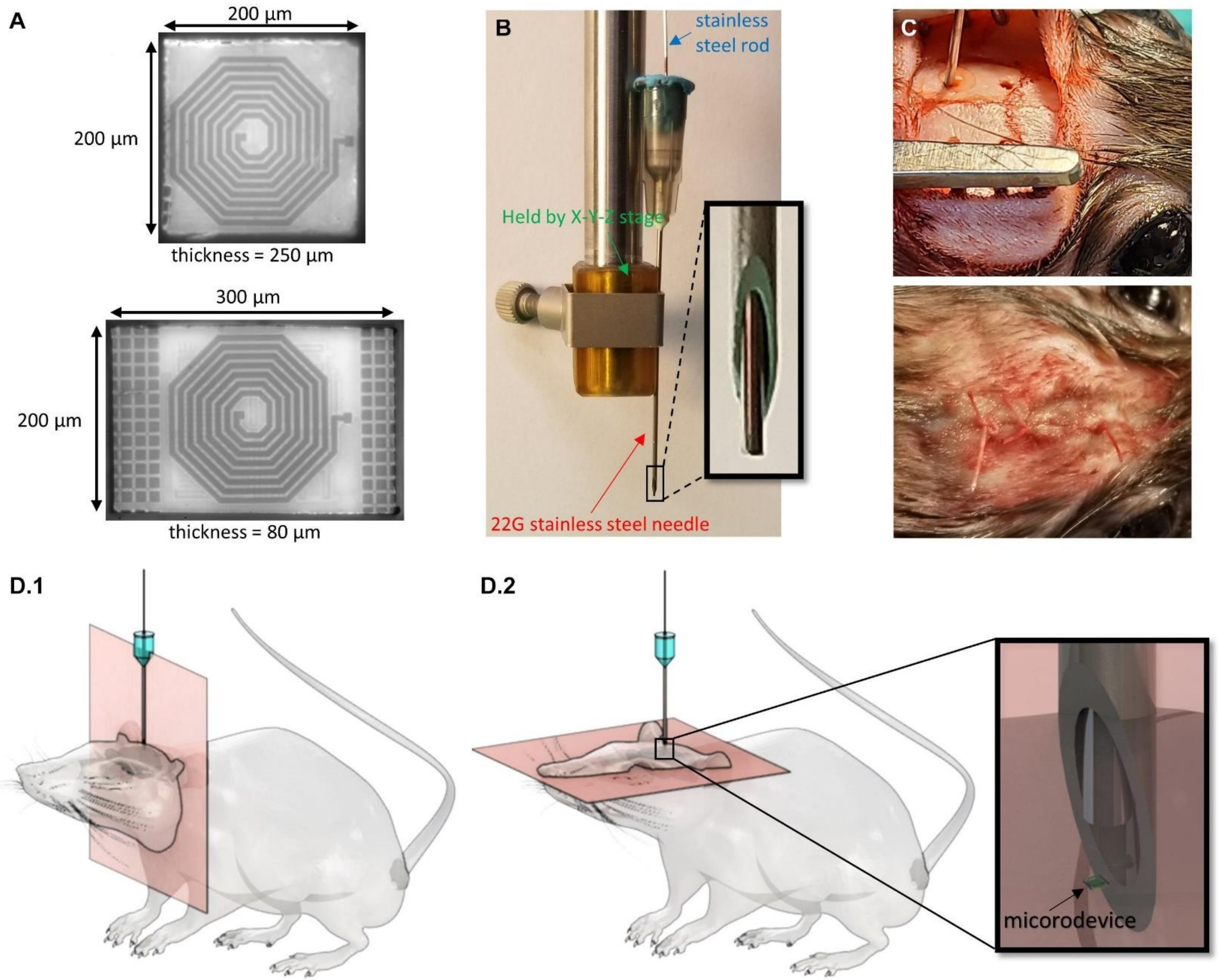
- **2013: Brown University creats first wireless BCI**
- **Hermitic sealing key in allowing breakthrough**
- **100 mW Power Consumption**
- **2023: Purdue first to demonstrate high-bandwidth wireless communication between neural implants and wearable devices**





Source: David A Borton *et al* 2013 *J. Neural Eng.*

The Risks & Biological Effects



Implant Migration

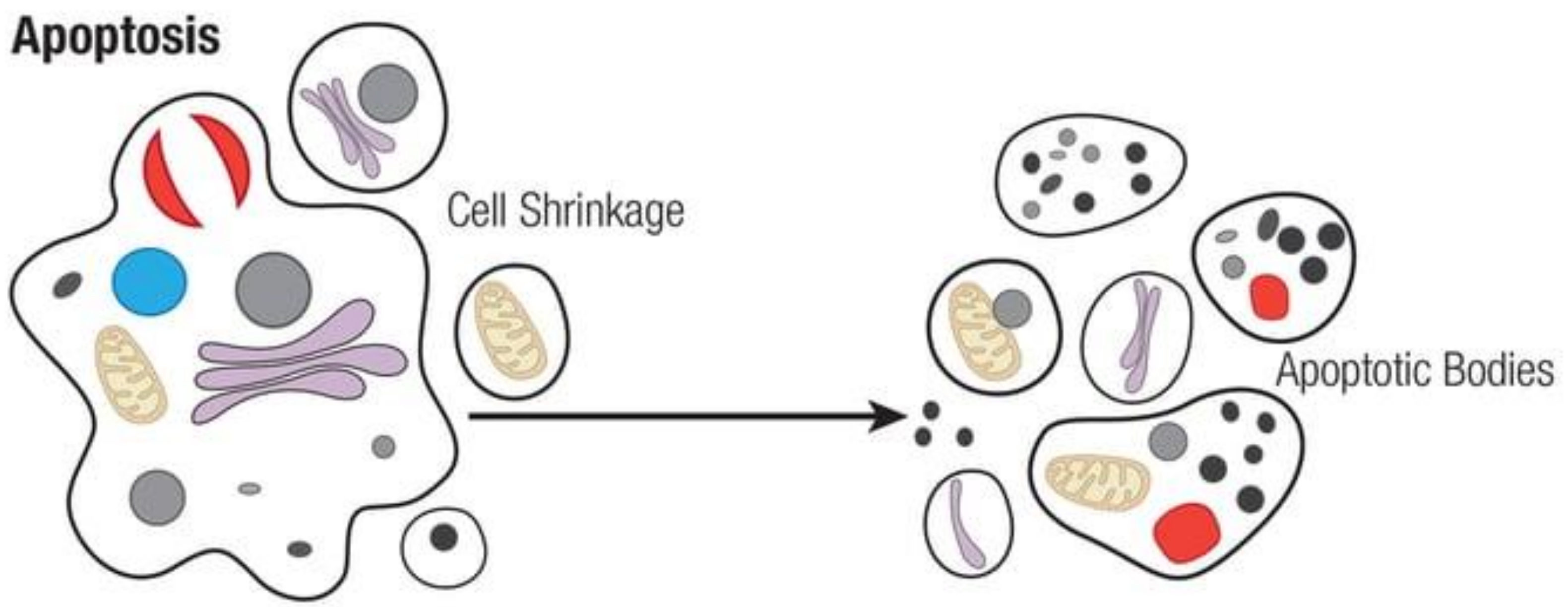
Employing leadless brain implants result in novel risks such as implant migration

- Most studies on animals
  - Harvard University – rodents (*Rattus* norvegicus), weakly applicable
- Auckland Study – sheep (*Ovis* Aries), stronger applicability to humans

(A) Micrographs of two microdevices (B) picture of injection tool with close-up of 22G needle and rod tip (C) Picture of rat during microdevice injection and after suturing (D) MR images taken using (D.1) coronal orientation and (D.2) axial orientation.

Source: Adam, Khalifa *et al* 2021 *Neural Technology*

The Risks - Physical



Apoptosis in a cell resulting in apoptotic bodies

Physical Side Effects

Tissue damage, psychological damage, cellular response represent the categories of interest

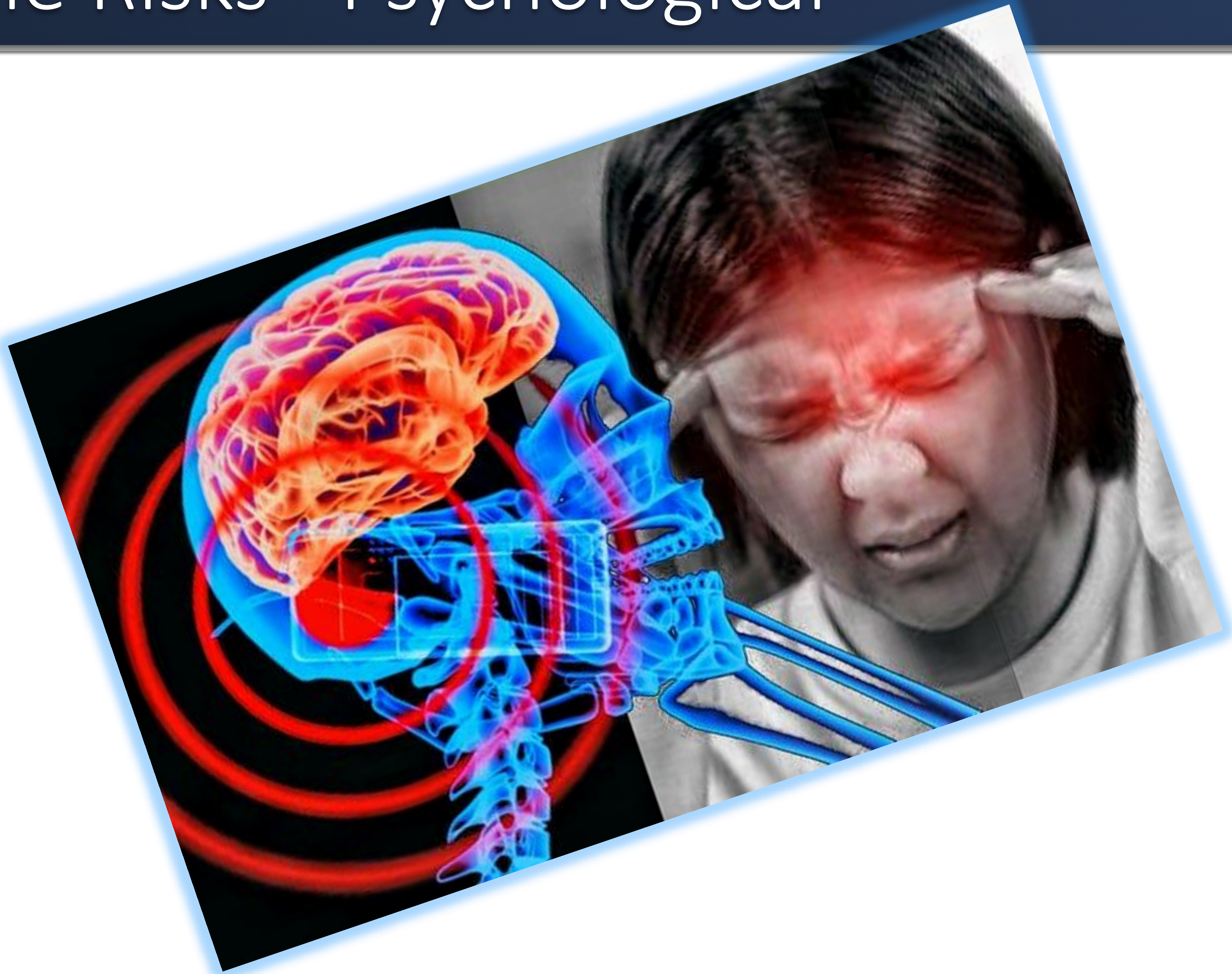
- Biological Markers used to demarcate tissue response
- RF-EMF exposure evaluated
- Cell damage investigated for apoptosis

The Risks - Psychological

Psychological Side Effects

Low-level RF-EMF induced psychological stress of concern

- 50+ years of relevant research work
- International Commission on Non-Ionizing Radiation Protection's (ICNIRP) set specific absorption rate (SAR) threshold < 2 W/kg



Dramatization of EMF induced psychological stress

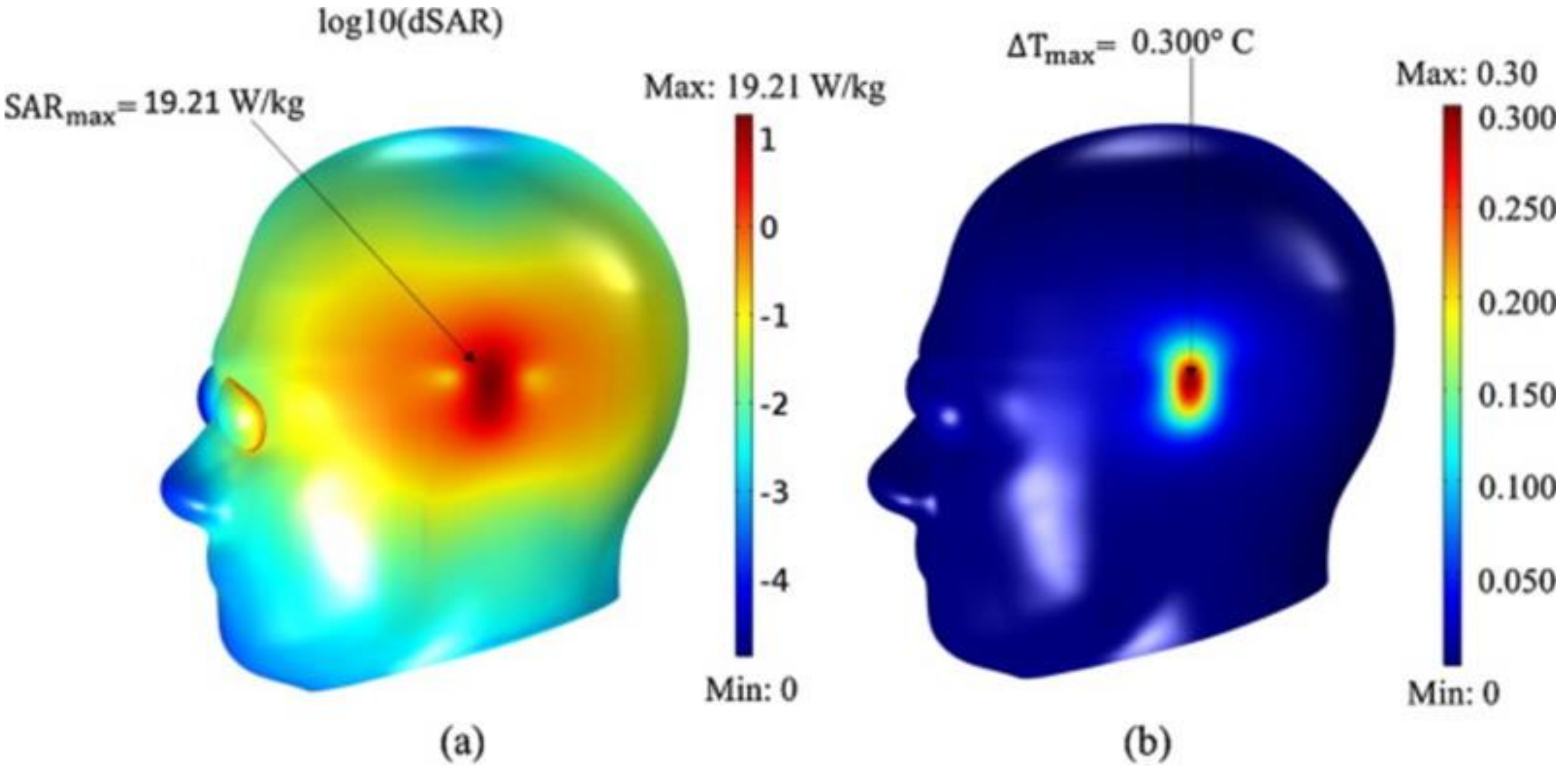
Source: Julie Grisham, Stock Images

The Risks - Human Head Simulations & SAR

Psychological Side Effects

SAR: Specific Absorption Rate, key metric for assessing safety of electromagnetic exposure in implants

- Accurate simulations require advanced techniques, specialized expertise
- Research on computational methods explored



MATLAB simulation SAR model. Dramatized with artist rendition

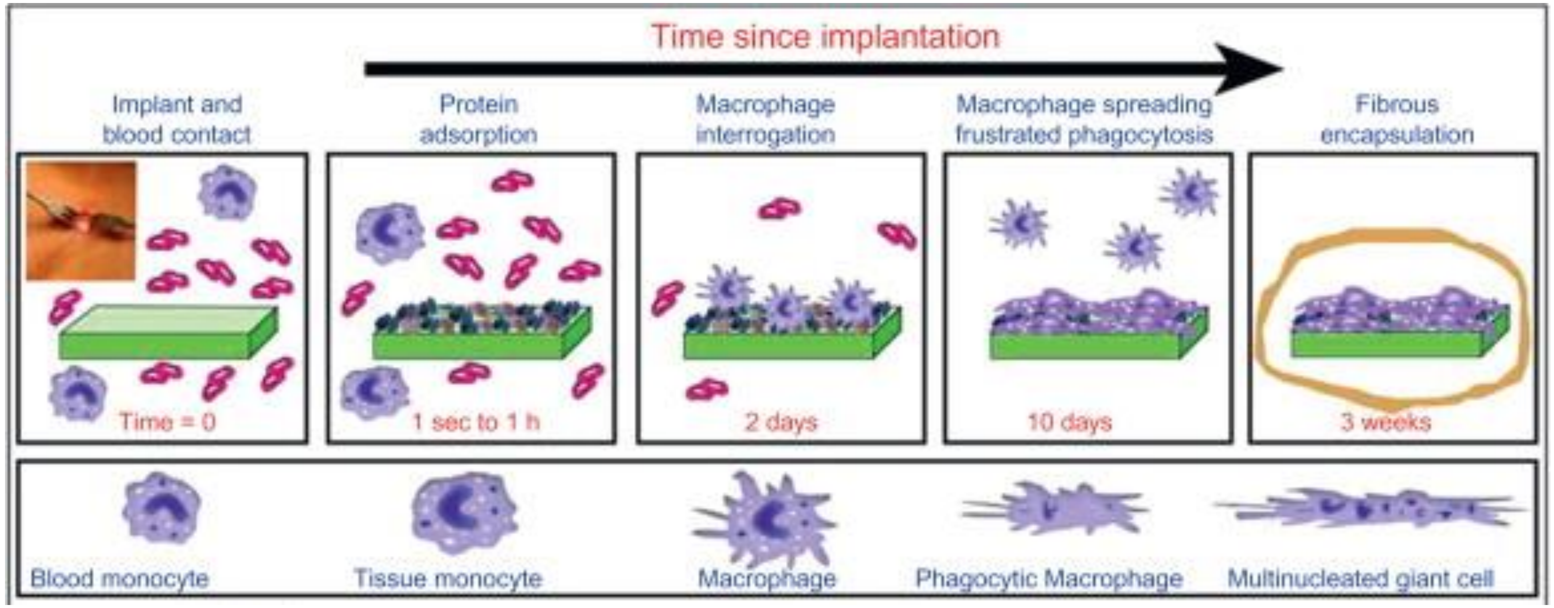
Source: National Frequencies Agency, LiveSafe.in

Biocompatibility

Localized, Observable Foreign Body Response

Biocompatibility of encapsulating material is lifetime-limiting component

- **Expanded Definition:** managing responses to foreign bodies and energy emissions (heat and radiation) over long-term
- **Critical Component**: Biocompatibility of encapsulating materials essential for longevity implants, device performance and safety
- **Challenges and Innovations**: body's hostile environment requires miniaturization, increasing electrode density while maintaining functionality.



Fibrous response to implantation over 3 weeks

Source: National Frequencies Agency, LiveSafe.in

Biocompatibility - Materials

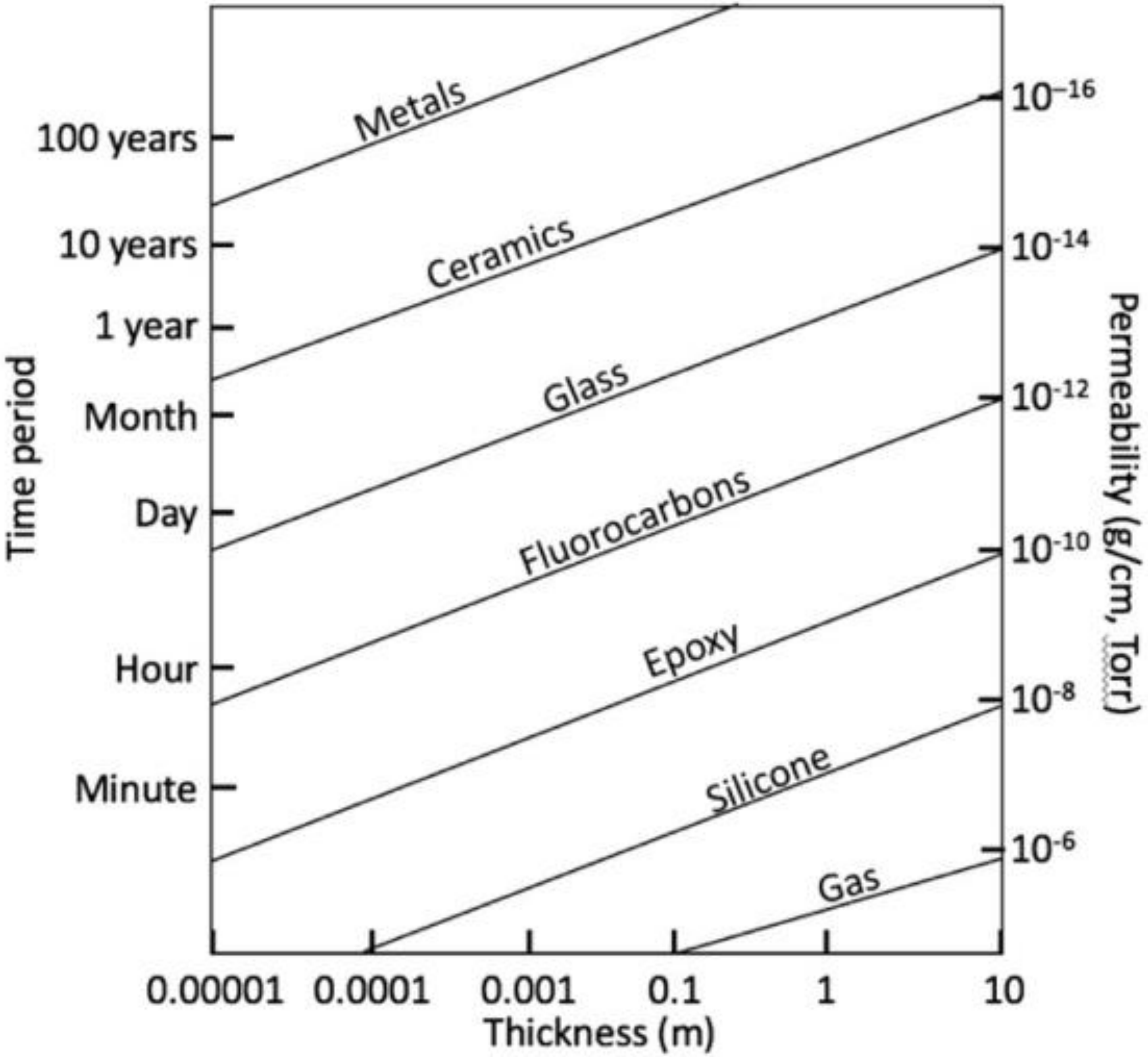
Localized, Observable Foreign Body Response

Encasing materials in wireless brain implants must ensure long-term biocompatibility and impermeability, guided by ISO 10993 and FDA standards

•**Material Interaction**: Encasing materials (metals, polymers, ceramics) interact with neural tissue

•**Standards and Regulations**: ISO 10993 and FDA guidance provide frameworks

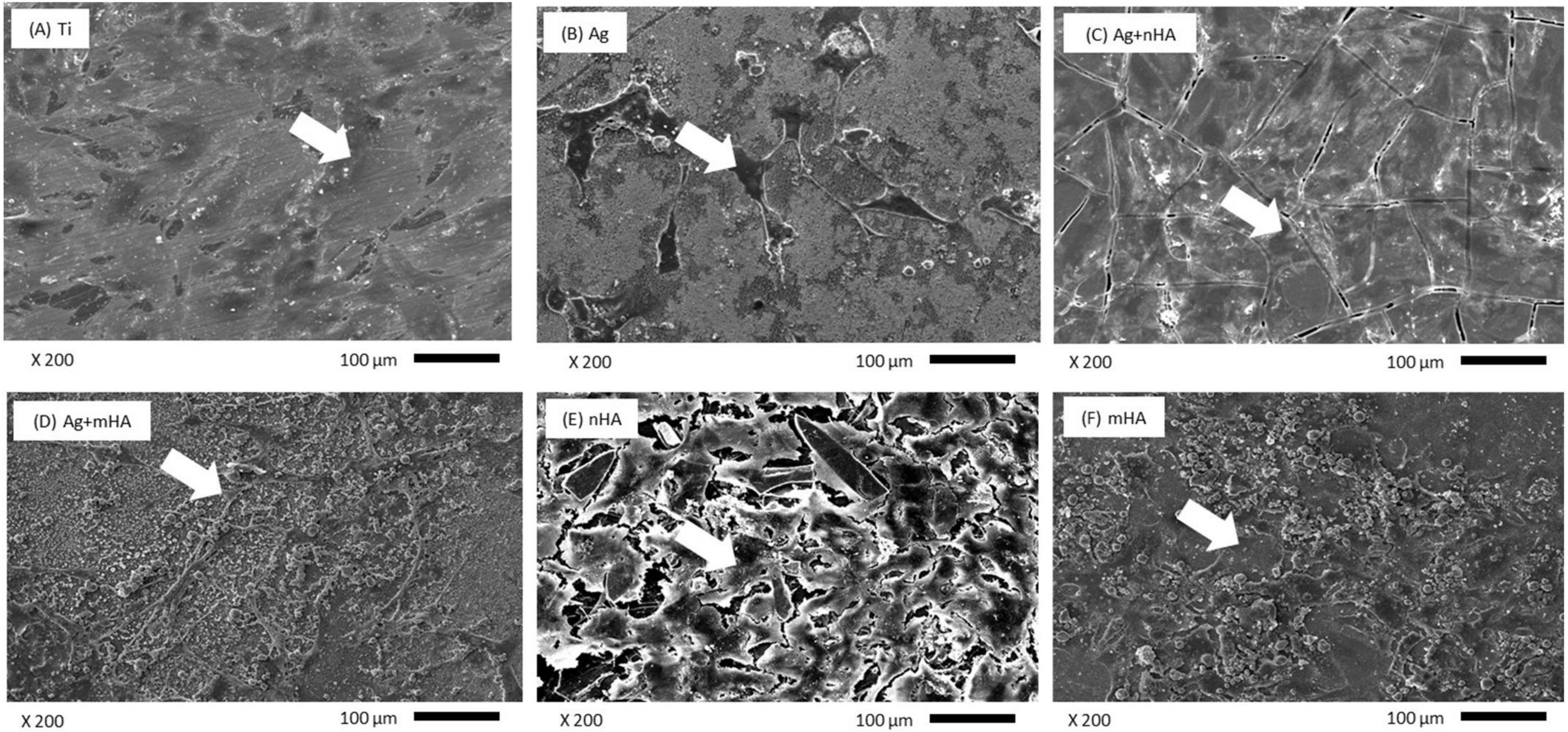
•**Seal Integrity**: Impermeable barriers prevent internal components from migrating into the body



Source: Joung YH, "Development of implantable medical devices: from an engineering perspective," Int Neurourol J, vol. 17, no. 3, pp. 98-106, Sep. 2013

Biocompatibility - Materials

SEM images of human primary osteoblast cells grown on titanium discs after 7 days



(A) uncoated Ti, (B) Ag,(C) Ag + nHA, (D) Ag + mHA, (E) nHA, (F) mHA

Source: Ranj, Nadhim Salaie et al, Science Direct

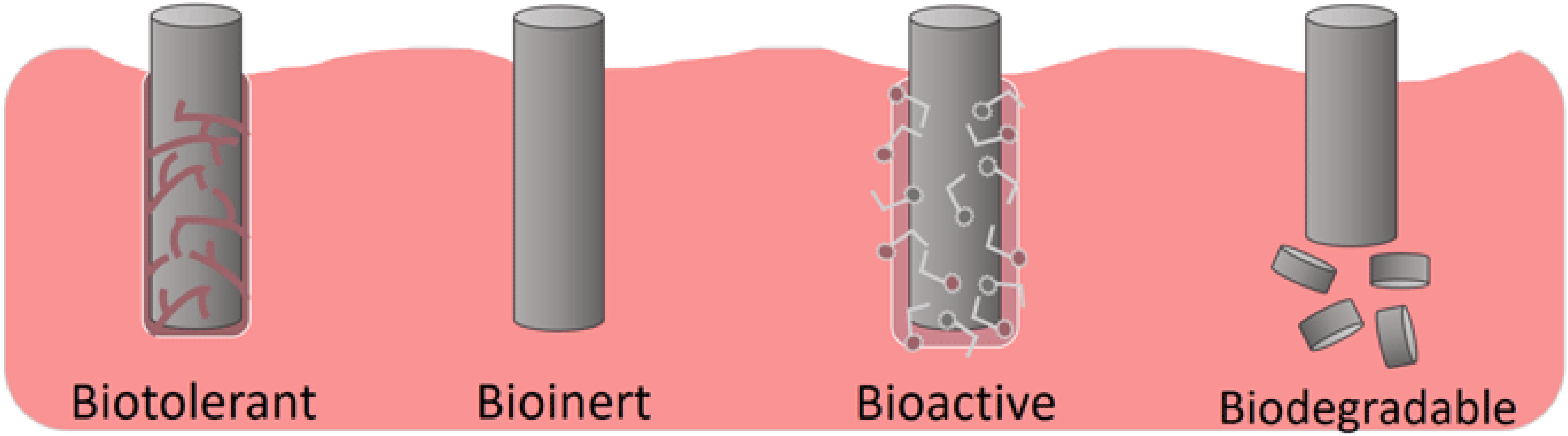
Biocompatibility - Materials

Metals in Wireless Brain Implants

- **Biocompatibility**: Metals (titanium and cobalt alloys) highly biocompatible due to bio-inertness and corrosion resistance

- **Usage**: Commonly used in electrodes for deep brain stimulation (DBS) and neurovascular interventions

- **Challenges**: Metal encapsulation can disrupt wireless energy transfer , larger device footprint



Source: Joung YH, "Development of implantable medical devices: from an engineering perspective," Int Neurourol J, vol. 17, no. 3, pp. 98-106, Sep. 2013

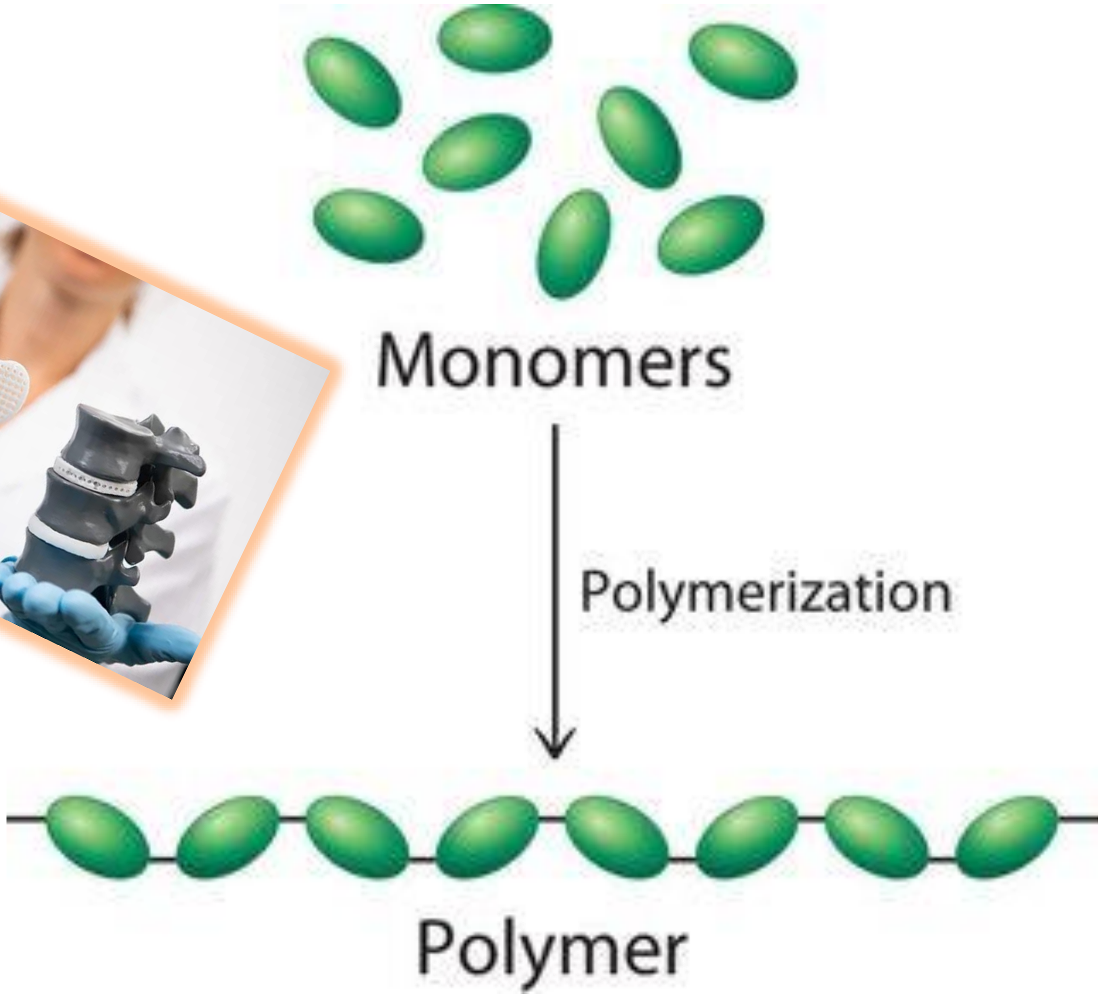
Biocompatibility - Polymers

Polymers in Wireless Brain Implants

Polymers are crucial in implant technology but face challenges like water permeability for long-term use

•**Versatility and Application**: Synthetic polymers (e.g., silicones, epoxy, polyimide) are versatile, commercially viable, and can be precisely tailored

•**Natural Biopolymers**: Offer bioactivity, biodegradability, and better cell adhesion, but may have reduced mechanical strength and potential for immune reactions

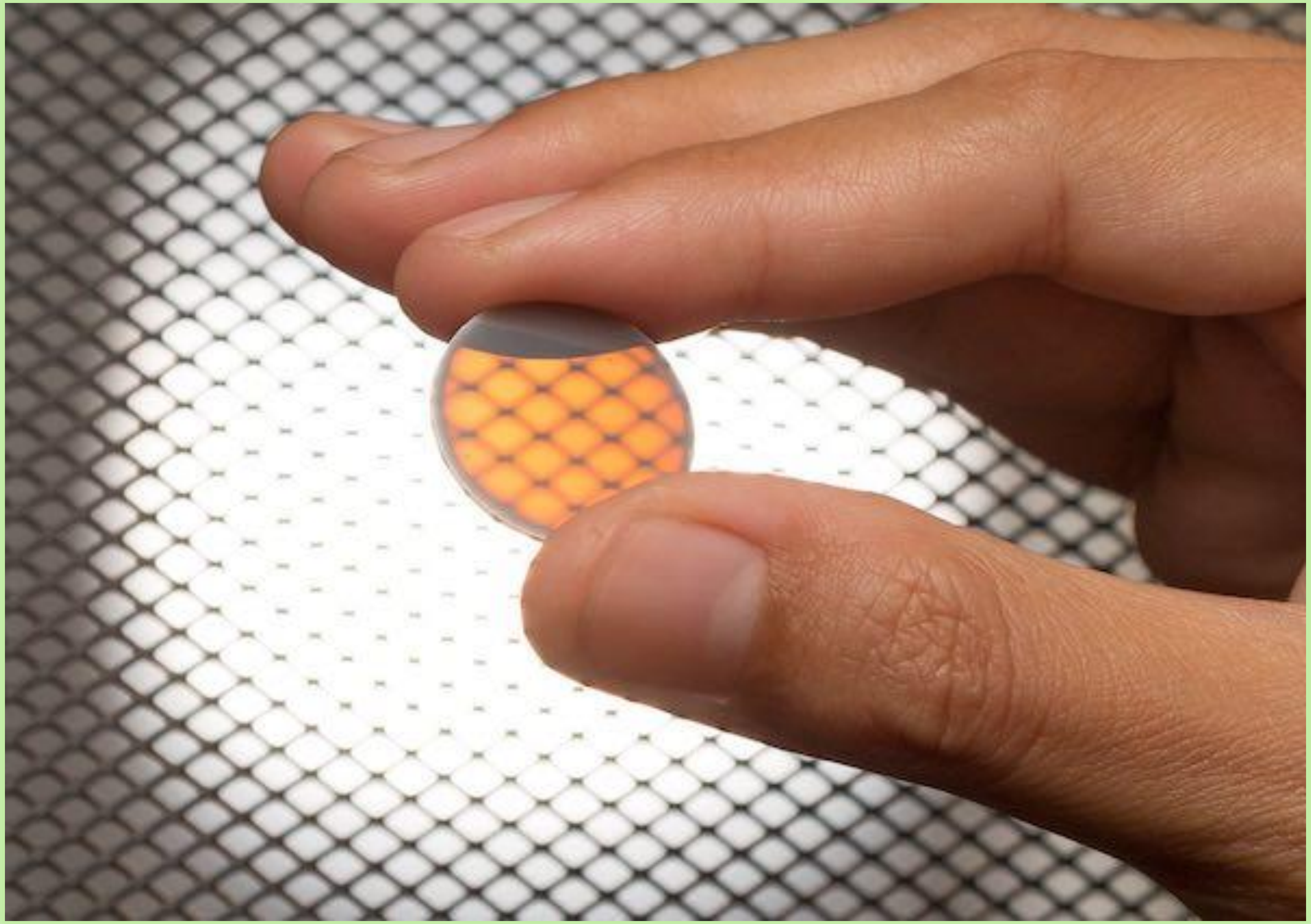


Source: Joung YH, "Development of implantable medical devices: from an engineering perspective," Int Neurourol J, vol. 17, no. 3, pp. 98-106, Sep. 2013

Biocompatibility - Ceramics

Ceramics in Wireless Brain Implants

Ceramics, known for their strength, electrical properties, and biocompatibility, face brittleness challenges but thin-film advancements are expanding their potential in wireless brain implants



- **Material Properties**: Ceramics are inorganic, hard, brittle, and resistant materials with high strength, excellent electrical properties, biocompatibility, and corrosion resistance

- **Challenges and Usage**: Brittle nature and shape resistance limit use, though certain technologies are enhancing potential

Source: Joung YH, "Development of implantable medical devices: from an engineering perspective," Int Neurourol J, vol. 17, no. 3, pp. 98-106, Sep. 2013

Frequency Bands

Frequency Bands and Flexibility in Wireless Brain Implants

Material Advancements: Innovations in ceramic thin films and liquid metal antennas have improved wireless interface flexibility - expanded frequency bands

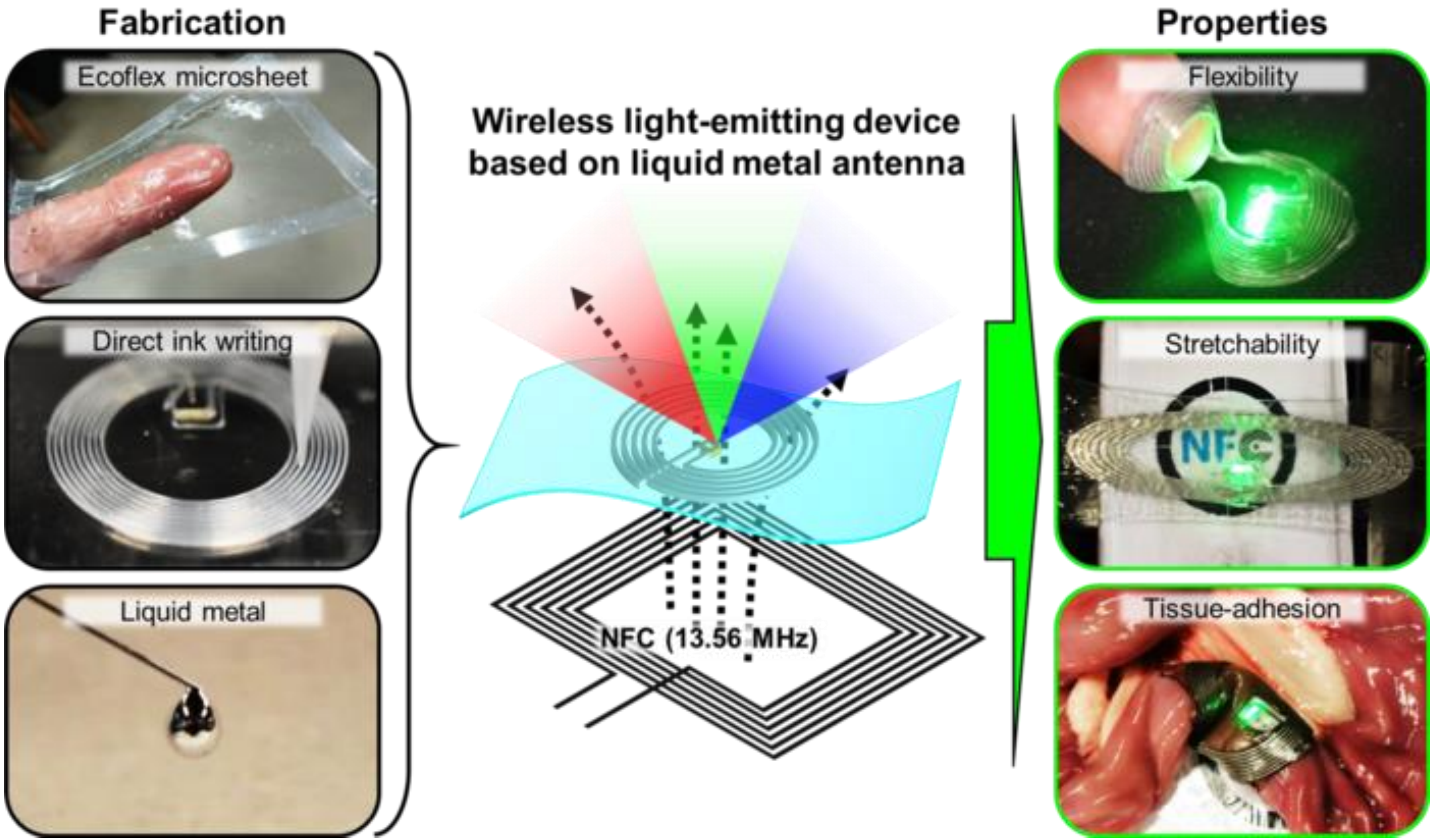
Enhanced Antennas: Liquid metal antennas in elastomeric encapsulants and multilayer flexible screen-printed coils now support far beyond previous limits of 100-200 channels. Efficient power transmission at low frequencies (<1 kHz)

Conductive Materials: Gallium alloys (e.g., GaIn, Galinstan) and stretchable polymer diodes demonstrate high mechanical compliance and conductivity, crucial for flexible, high-performance

MATLAB simulation SAR model. Dramatized with artist rendition

Source: Ranj, Nadhim Salaie et al, Science Direct

Frequency Bands



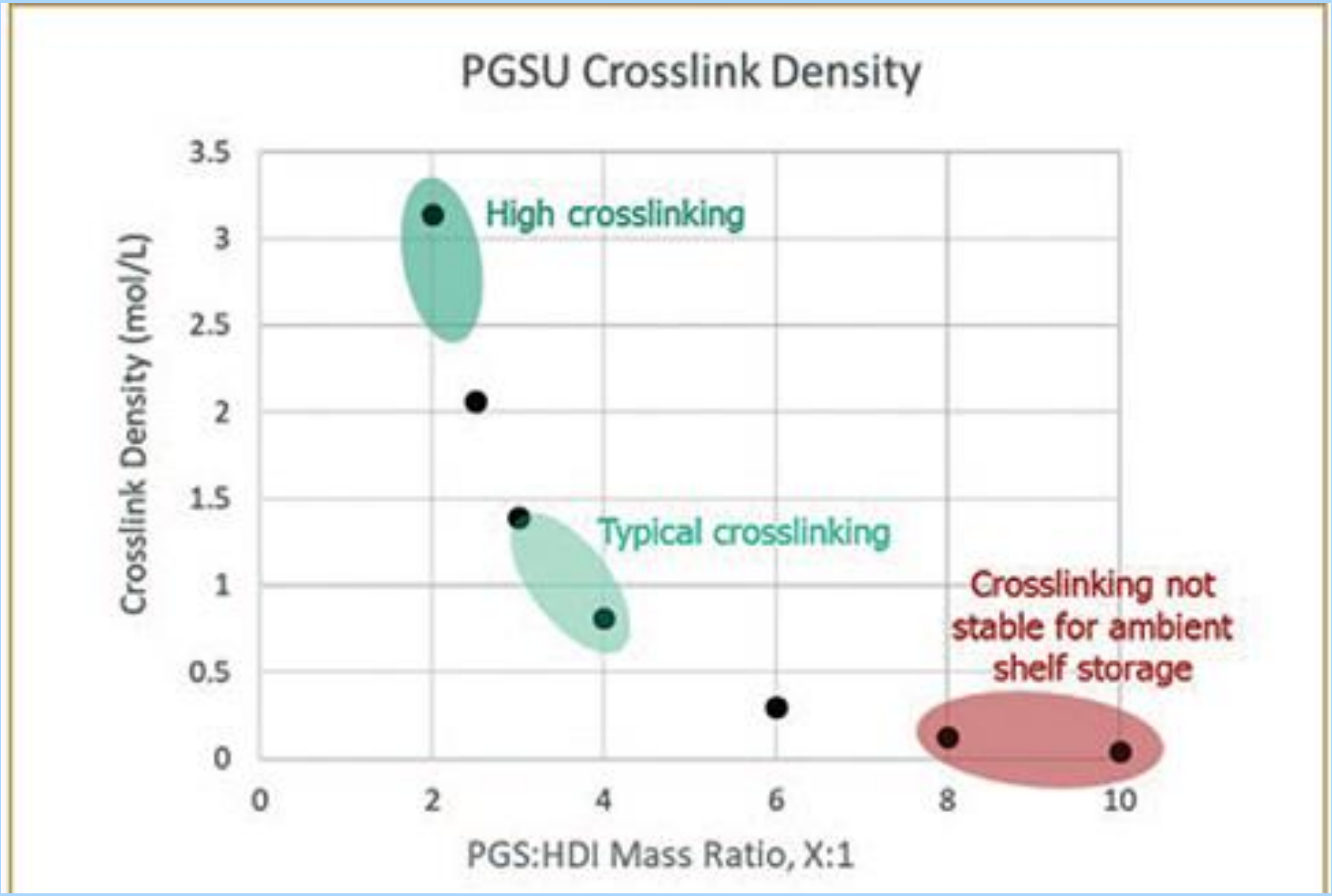
Development of a wirelessly powered light-emitting device based on a liquid metal microfluidic antenna.

Source: SINGAPORE UNIVERSITY OF TECHNOLOGY AND DESIGN

Frequency Bands

Polymeric Delivery System

Mass ratio of PGS: hexamethylene diisocyanate (HDI), which can be converted to isocyanate: hydroxyl stoichiometric ratio if the polyol's hydroxyl value is known, dictates the cross-linking density obtained with PGSU



Source: SINGAPORE UNIVERSITY OF TECHNOLOGY AND DESIGN

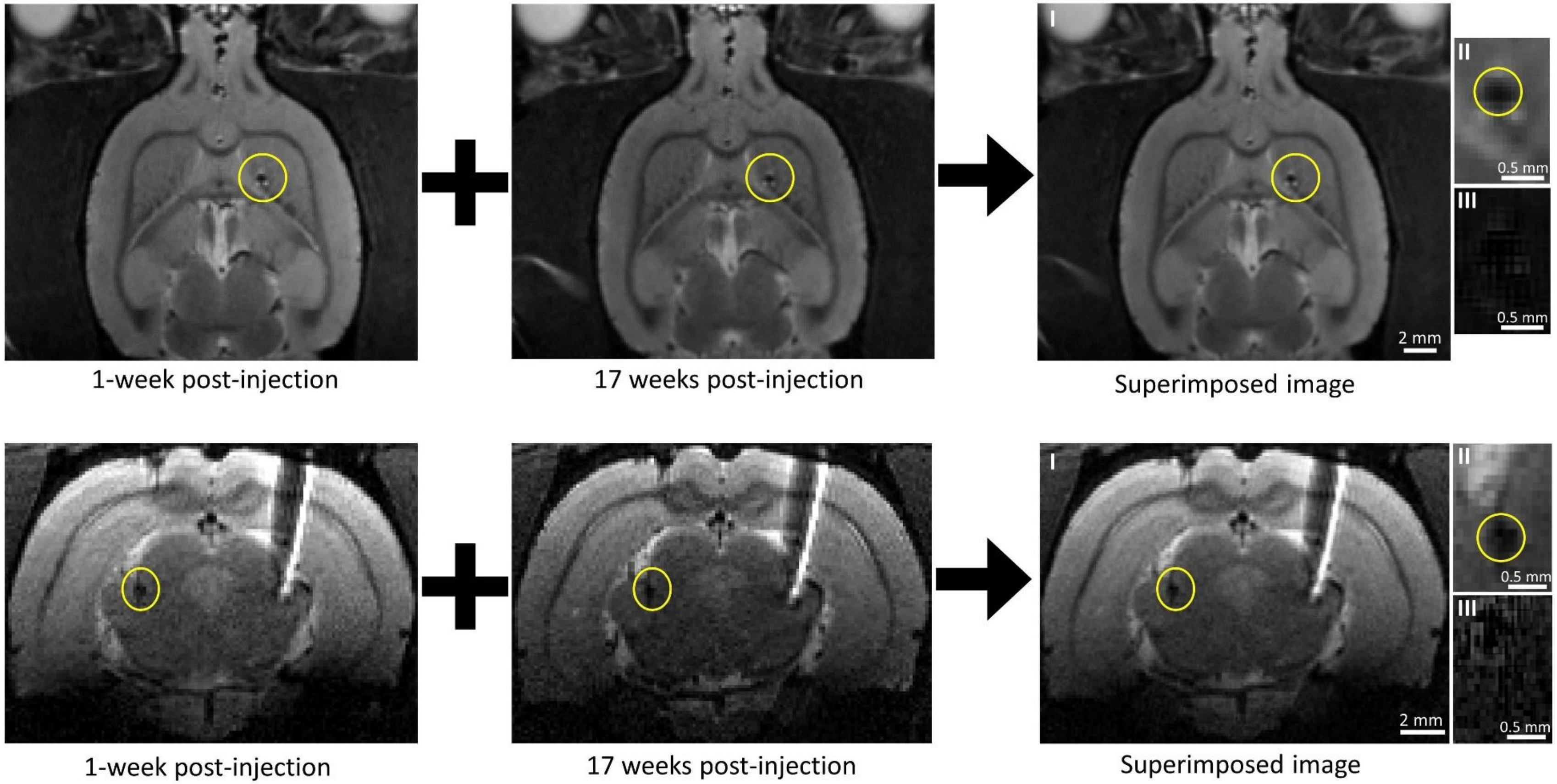
Review Results

Study Selection: Out of **42** initial studies, 10 unique studies were selected after review, with additional hand-searching increasing the total to **14 studies**

Geographical Distribution: Studies include two global multicenter studies and 12 others conducted in the US, South Korea, Australia, Japan, Canada, and India

Research Gaps: Significant gaps in literature were identified, particularly concerning long-term safety and RF-EMF induced psychological and physiological effects, necessitating further comprehensive research.

Review Results – Implant Migration Effects



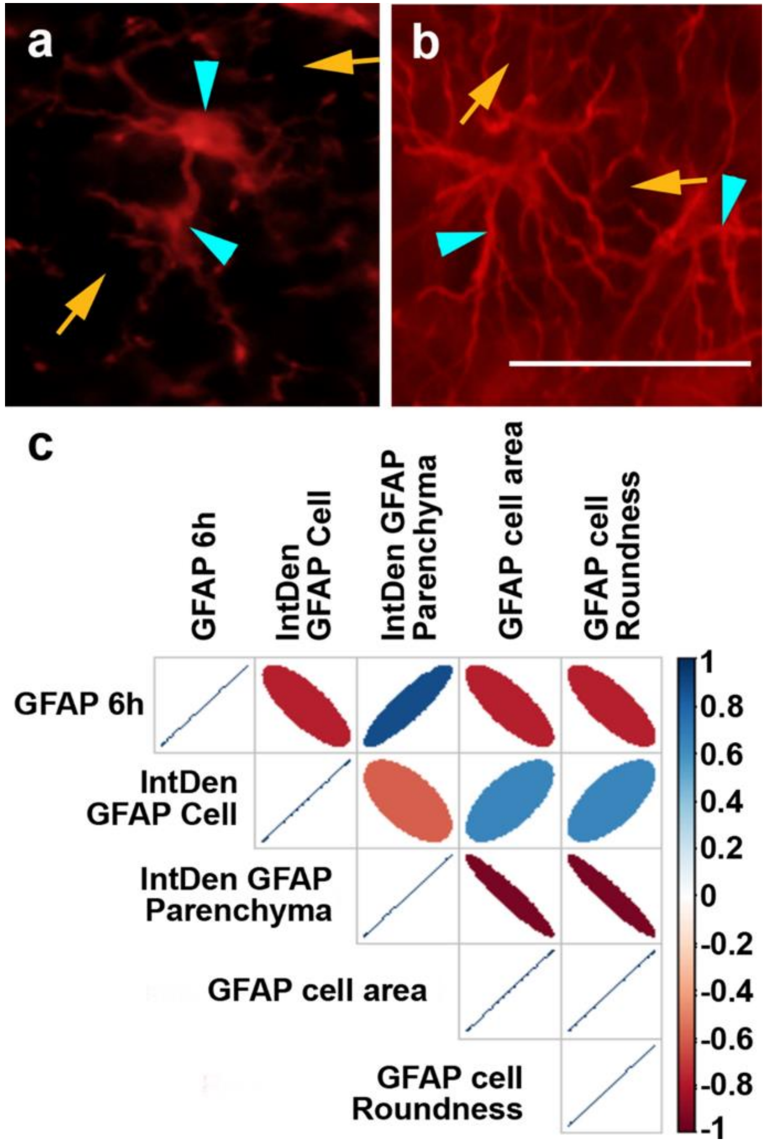
Tracking microdevice migration in the rodent brain using a 9.4T MRI scanner. (*Top row*) Two axial MR images, brain (*Bottom row*) Two coronal MR images, Images II show a close-up of the microdevice taken from images I, and images III show a close-up view of the microdevice with subtraction done instead of superimposition.

Review Results

2 High-Quality Studies in the Literature Examining Implant Migration

- Harvard University rodents with < 0.01 mm^3 device show **no migration**, severe glial scar formation
- Auckland Study observed movement of up to **4.6 mm** in subset of implants in first 3 months, no movement in any implant during 3–6 months
- **No evidence of a migration track or tissue damage** in subsequent histological analyses

Review Results – Physical Effects



Review Results

•**Auckland Study Findings**: GFAP and IBA-1 histological analysis showed no statistically significant difference between implanted tissue and control

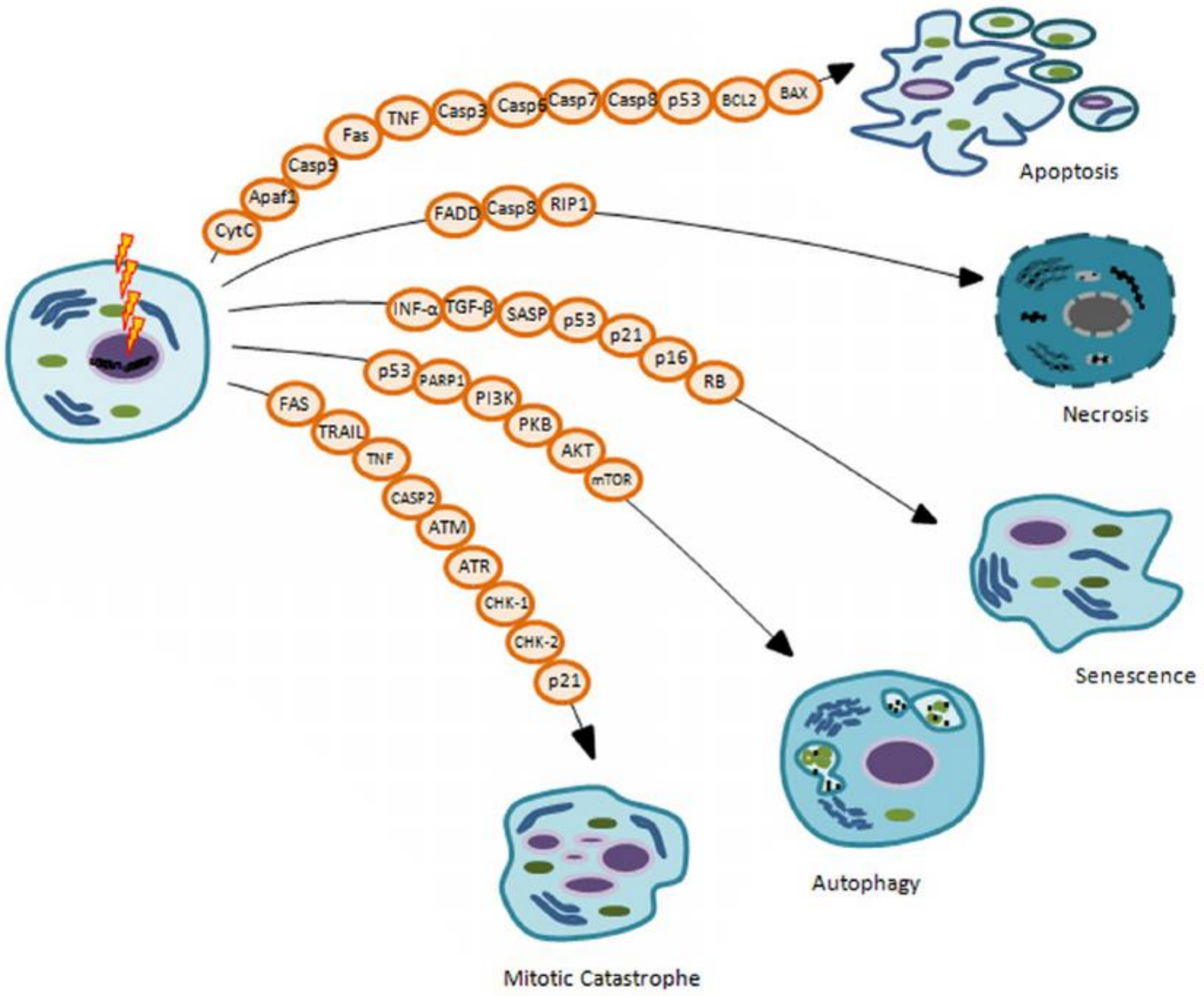
•GFAP and IBA-1 only two bio markers used

•**Lack of Comprehensive Data**: Insufficient data on RF-EMF induced biological risks, particularly for markers sensitive to low-level RF-EMF exposure (less than 100 MHz), including neuronal cell apoptosis and psychological stress

•**Challenges and Conclusions**: Difficulty in translating experimental frequency ranges to intracorporeal environments, but scoping reviews provide evidence suggesting potential RF-EMF induced cell death and psychological stress warrant further investigation.

Source: Lafrenaye, A.D., Mondello, S., Wang, K.K. *et al.* Circulating GFAP and Iba-1 levels are associated with pathophysiological sequelae in the thalamus in a pig model of mild TBI. *Sci Rep*

Review Results – Cellular Effects



Review Results

Cellular Response to RF-EMF Exposure

•**Gene Expression**: 2005 study showed EMF exposure transiently affects genes related to apoptosis and cell cycle control, but compensatory mechanisms prevent detectable changes in cell physiology

•**Methodological Flaws**: 2015 scoping review found many studies on RF-EMF induced apoptosis had flaws in their experimental methodologies regarding EM and biological requirements

•**Guideline Adherence**: No sufficient data indicates undue concern about RF-EMF induced apoptosis in the head and trunk if international guidelines are appropriately followed

Review Results – Psychological Effects

Results: Psychological Response to RF-EMF Exposure

Evidence of Neuropsychiatric Effects: Studies indicate that non-thermal microwave EMF exposures can cause insomnia, headache, depression, vertigo, and memory changes, potentially linked to voltage-gated calcium channels (VGCCs) in the brain

Correlation Challenges: Difficulties exist in correlating study frequencies with the lower frequencies emitted by wireless brain implants (<20 Hz)

Outdated Safety Standards: The ICNIRP's SAR threshold of <2 W/kg in the head and trunk area has not been updated since 1998, necessitating cautious interpretation of RF-EMF related BCI safety findings

Source: Julie Grisham, Stock Images

Review Results - Human Head Simulations & SAR

Results: Human Head Simulations & SAR

Simulation Importance: Accurate human head simulations crucial for assessing SAR

Advanced Techniques: Methods like finite-difference time-domain (FDTD) integrated with the Debye model and the Pennes bioheat equation provide comprehensive SAR and temperature distributions up to 100 GHz.

Expertise Gap: Complexity of these simulations and the need for precise human head models require specialized expertise, highlighting a notable gap between demand and availability of skilled professionals

United States projected to require 5,100 broadcast engineers over next decade due to retirements of 6,200 existing professionals. This anticipated shortage is particularly pronounced in the RF knowledge domain. Factors contributing to the absence of new entrants include:

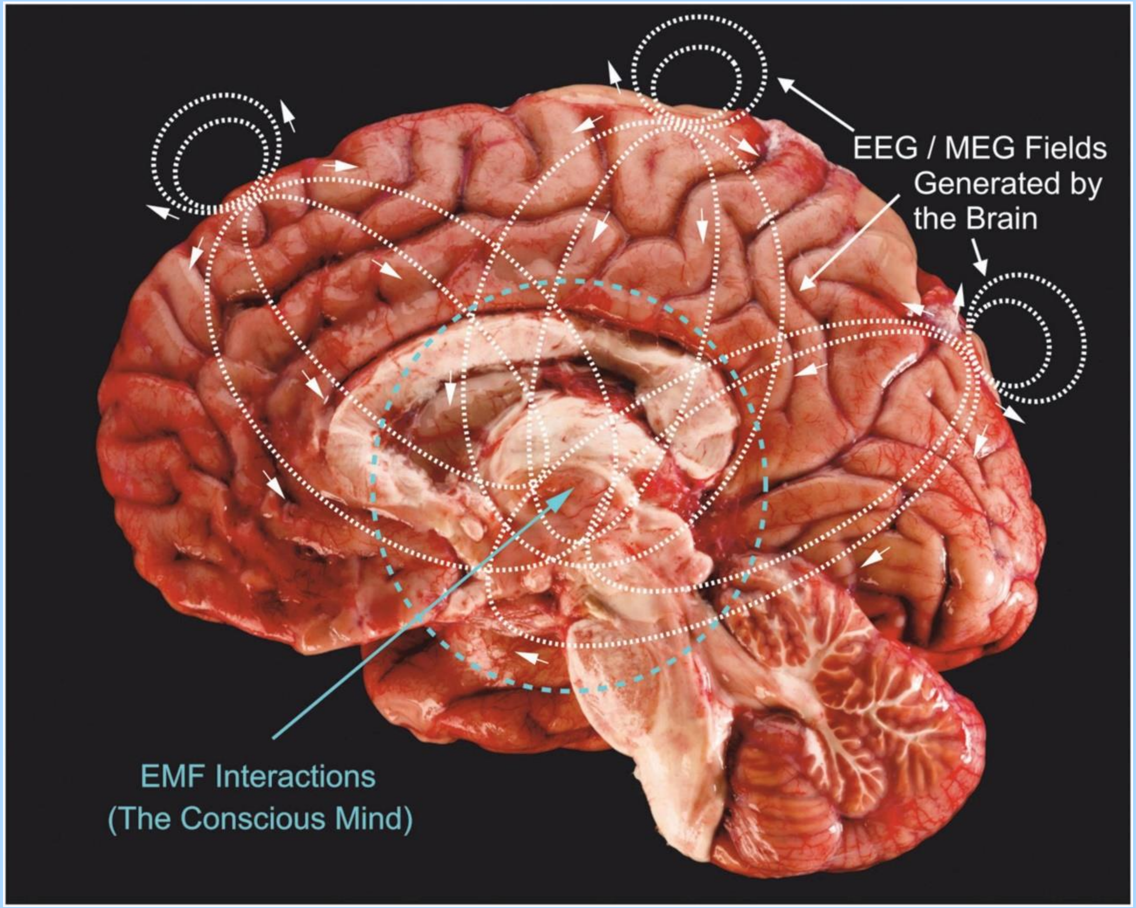
•The allure of competing technical fields offers higher pay and more straightforward work conditions.

•Broadcast engineering requires a broad knowledge base.

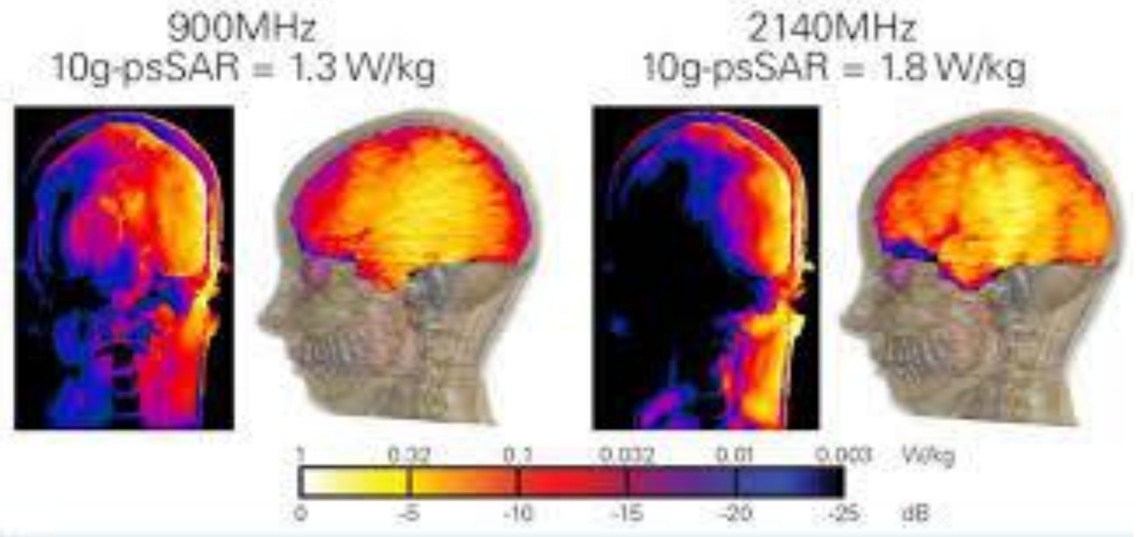
•There is a need for more awareness among major stakeholders.

Source: Dave Edwards, Consultant (Dave Edwards Media)

Results: Human Head Simulations & SAR



RF EMF appears to interfere with the brain's natural EEG/MEG signals by inducing currents and altering the electromagnetic environment, which may disrupt normal neural activity and brain function



Frequency dependent nature of SAR in simulation

Source: Julie Grisham, Stock Images

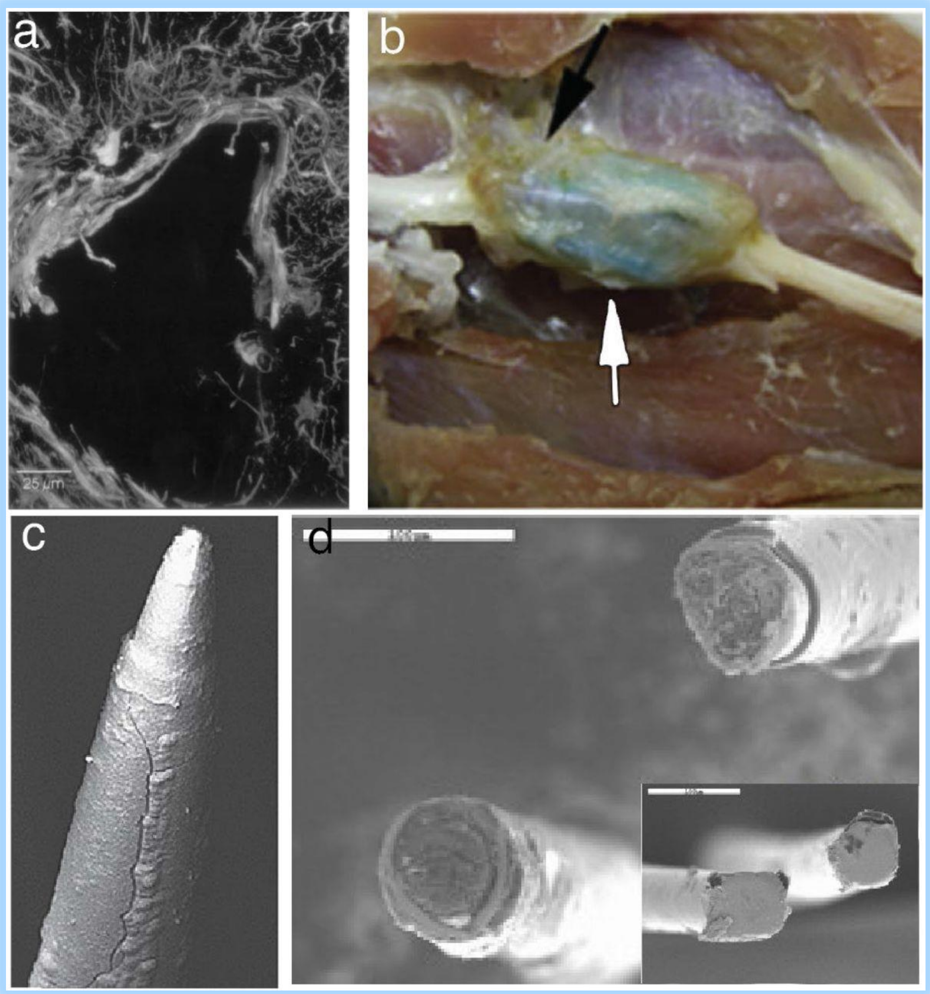
Review Results – Materials Effect

Biocompatibility of Wireless Brain Implant Materials

Metals: Metals offer excellent biocompatibility and durability but can trigger immune responses and disrupt wireless energy transfer

Polymers: polymers are versatile and tunable but face challenges with water permeability

Ceramics: ceramics provide high strength, biocompatibility, and RF transparency but are brittle and challenging to shape for brain-computer interfaces



Failure modes of neural implants

a) Stain for glial fibrillary acidic protein (GFAP) in rats after 12 weeks b) Formation of a fibrotic capsule in the cat sciatic nerve after 5-6 weeks c) Cracks in the parylene encapsulation of a microelectrode array after 554-days of non-human primate d) Corrosion in tungsten microwires after 87 days post-implantation in rat cortex. Source: Ceramic Packaging in Neural ImplantsKonlin Shen, Michel M. Maharbiz

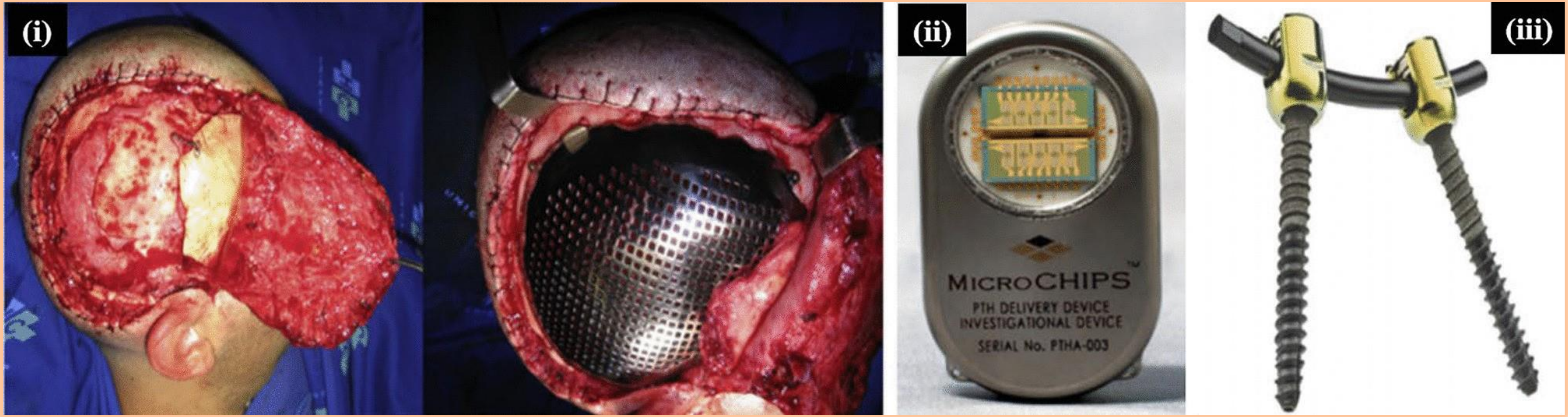
Review Results – *Metals* Materials Effect

Biocompatibility of Metal Encapsulation in Wireless Brain Implants

High Biocompatibility: Titanium, cobalt alloys; bioinert, corrosion-resistant.

Immune Reactions: TLR4 signaling; blood-brain barrier permeability; axonal dieback.

Technical Challenges: Disrupts wireless energy transfer; MRI eddy currents; tissue heating.



(**i**) Titanium alloy cranial implant, (**ii**) Wirelessly controlled drug-delivery implantable chip, and (**iii**) Carbon fiber pedicle screws with a titanium polyaxial head and carbon-fiber-reinforced rods

Source: Davis, R., Singh, A., Jackson, M.J. *et al.* A comprehensive review on metallic implant biomaterials and their subtractive manufacturing. *Int J Adv Manuf Technol*

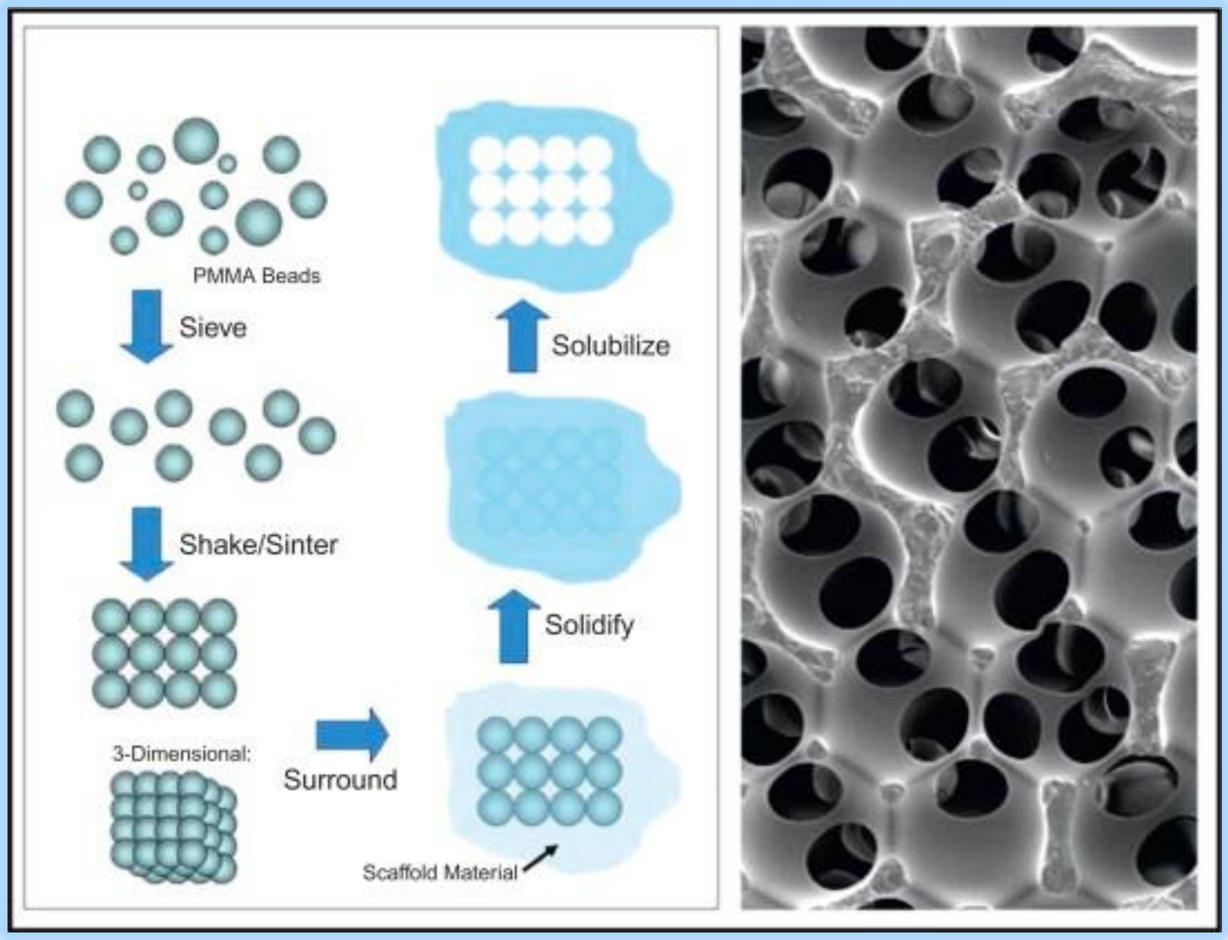
Review Results – *Polymers* Materials Effect

Biocompatibility of Polymer Encapsulation in Wireless Brain Implants

Versatile Materials: Synthetic polymers like silicones, epoxy, polyimide; tunable properties; extensive use in implants

Challenges: Unacceptable water permeability for chronic use; reduced mechanical strength; potential immune responses

Natural Biopolymers: Bioactivity, biodegradability; better cell adhesion; risk of compromising long-term integrity



sphere-templating process for preparing porous biomaterials with uniform-sized pores

Source: Buddy D. Ratner, Chapter 3 - The Biocompatibility of Implant Materials, Academic Press, 2015

Review Results – *Ceramics* Materials Effect

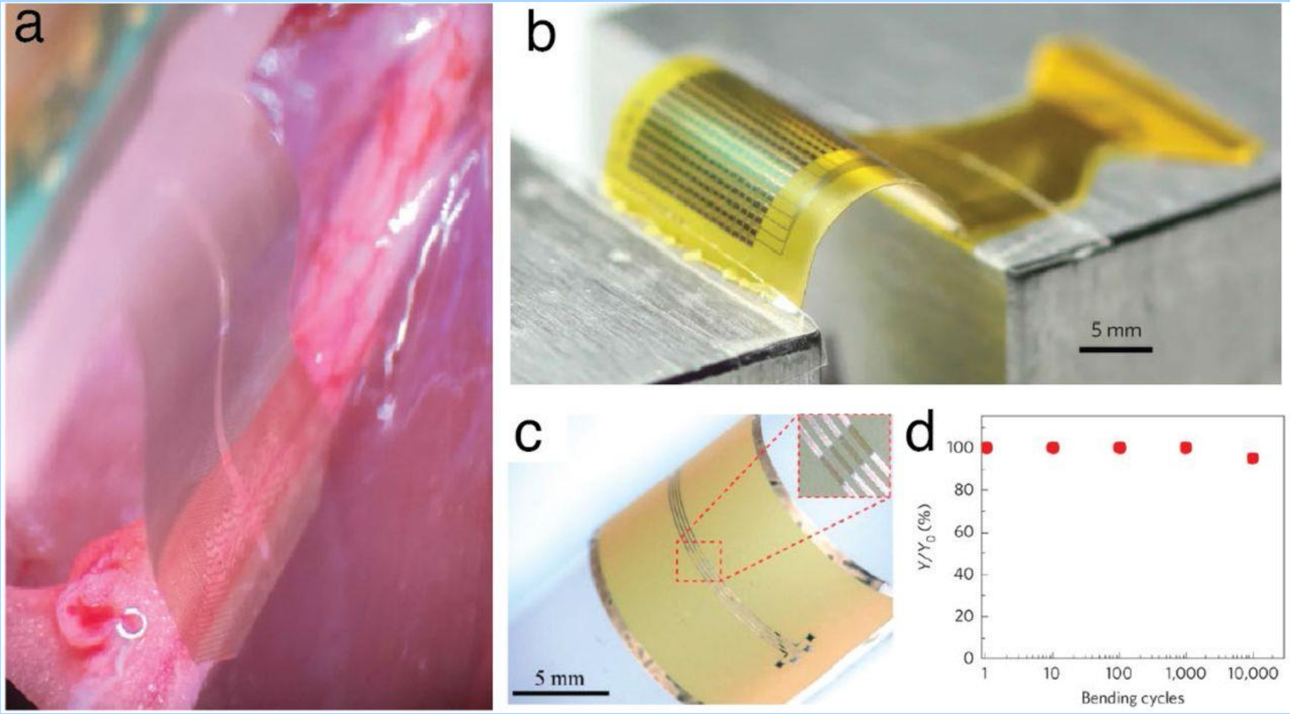
Thin-film ceramics, known for high strength, low dielectric constant, and corrosion resistance, offer advanced flexibility and functionality (e.g., RF transparency, optical transmission) but remain limited by brittleness and shaping

- **Material Properties**: Inorganic, hard, brittle; non-metallic oxides, carbides, nitrides; high strength, low dielectric constant, corrosion-resistant.

- **Technological Advancements**: Thin-film ceramics (SiC, SiO2, SiN); fractions of a nanometer to micrometers; bipolar conductivity; flexibility; RF field transparency.

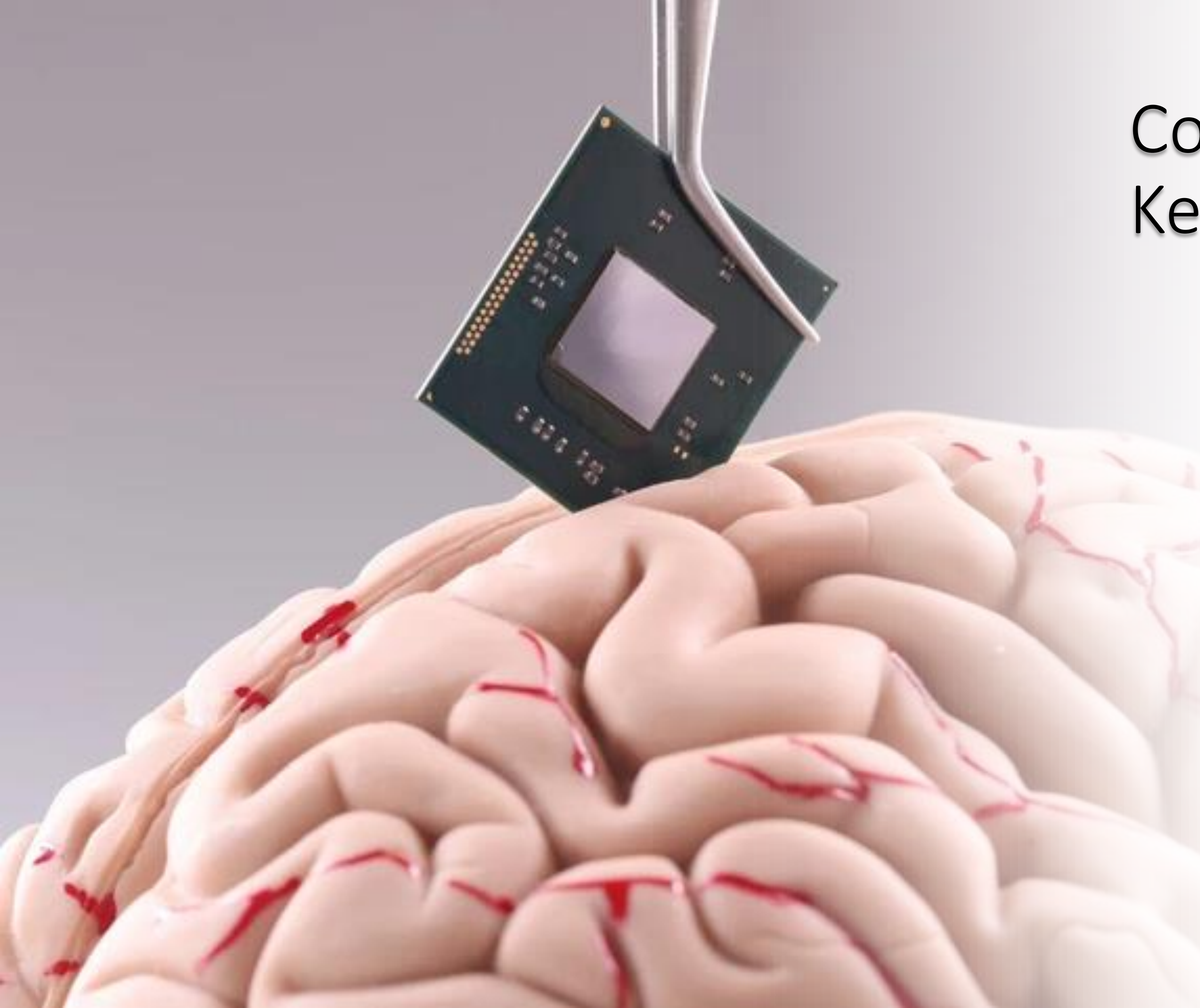
- **Functional Ceramics**: Barium titanate (BaTiO3), lead zirconate titanate (PZT); optical transmission, ultrasonic sensing; mechanical power harvesting; potential for acoustic and optical detection technologies.

Ceramics



Flexible ceramic-encapsulated electronics enabled by thin films

a) SiC ECoG wrapped around sciatic nerve of a rat b) Thermal oxide encapsulated electrode array for cardiac monitoring c) SiC encapsulated electronics wrapped around curved surface (radii 6 mm) d) percentage of working electrodes after bending cycles (bent to a radius of curvature of 5 mm) showing that the electronics are not compromised after bending cycles. Source: Ceramic Packaging in Neural ImplantsKonlin Shen, Michel M. Maharbiz



Conclusions & Key Findings

- **Research Gaps**: Significant gaps in understanding wireless functionality and safety implications of brain-computer interfaces (BCIs), particularly regarding RF-EMF induced psychological effects and potential tissue/cell impacts

- **Safety Concerns**: Current SAR thresholds from the 1990s may not adequately ensure safety, especially concerning psychological stress; need for more comprehensive and rigorous research methodologies

- **Research Needs**: Urgent need. Improved methodologies; consensus on biological endpoints; comprehensive safety evaluations

Conclusions & Key Findings

Emerging Trends: Growing interest in miniaturization, higher-bandwidth wireless data transfer, thin-film ceramics, biodegradable biopolymers, flexible/liquid metals, and non-electromagnetic energy transfer (acoustic/optical)

Future Focus: Combining RF, acoustic/ultrasonic, and optical energy transfer technologies; importance of accurate human head modeling and highly skilled engineers for EM simulations; need for specialized RF expertise

Regulatory Impact: Limited impact of current safety research until FDA/ISO updates guidelines; importance of developing a universal testing consensus to guide safety protocols

Conclusions

Current regulatory frameworks focused on SAR thresholds **might not adequately ensure the safety** of wireless brain implants.

Future research should explore combining **electro-optical, electroacoustic, and radio-frequency technologies housed in thin-film ceramics** to address safety concerns and enhance device functionality.

Until the FDA/ISO provides a **universal testing consensus**, the impact of safety research will be limited.

Nevertheless, **ongoing exploration and development hold promise** for creating safer and more effective WBCIs, potentially revolutionizing applications in medicine and neuroscience.

Future Outlook

Where Are We Going?

BREAKING

Lawmakers Push For SEC Probe Into Elon Musk's Neuralink For Claims About Brain Implant Safety

Forbes Nov 22, '23

Questions, Comments, Discussion

Thank you for attending!