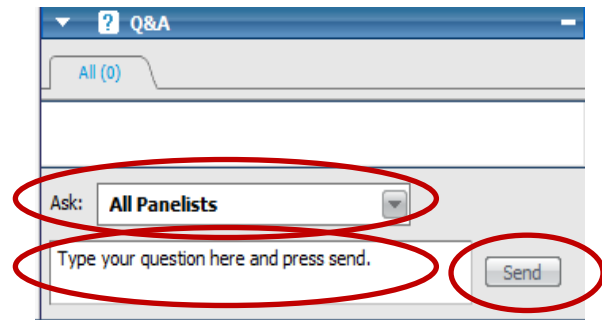
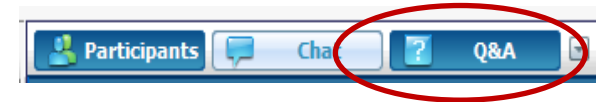


# First, a Few Housekeeping Points

- Slides advance automatically
- Question and Answer period at end
- Submit questions at any time
  - Q&A panel is on the lower right side (If you don't see it, click the "Q&A" button in the upper right)
  - Type a question into the lower section of the Q&A panel that appears
  - Ask "All Panelists" and click "Send"
- A copy of the presentation is posted at [paradigmcorp.com/webinars](http://paradigmcorp.com/webinars); a copy of the replay will also be emailed
- **In order to receive CCMC credit**, after the closing comments, close out of the WebEx window. Two windows will pop up with 1) the WebEx feedback survey and 2) the **CCMC credit survey**. Upon completion of the CCMC survey, you will be redirected to a copy of the CCMC Verification of Completion certificate.
- If you experience computer broadcast audio problems, please use the dial-in number posted in the Chat panel





PARADIGM<sup>®</sup>

OUTCOMES



# Imagination to Innovation: The Future of Medical Technologies

*Michael C. Choo, MD MBA FACEP FAAEM*

*Paradigm Chief Medical Officer*

## Michael Choo, MD, MBA, FACEP, FAAEM Paradigm Chief Medical Officer



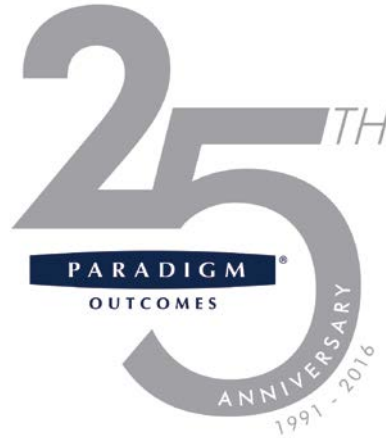
- Maintains Paradigm's relationships with network of physicians and centers of excellence. Responsible for enhancing clinical operations, research, and development.
- Teaches emergency medicine, internal medicine and family practice residents at the Wright State Boonshoft School of Medicine.
- BA and MD from Boston University's six-year accelerated honor's program in medicine and an MBA from the University of Tennessee School of Business Administration.
- Fellow of the American College of Emergency Physicians and a fellow and board member of the American Academy of Emergency Medicine.

# Paradigm Outcomes

*Journey through medical innovations*

## PAST

- 1976 – 1<sup>st</sup> CT scanner
- 1978 – 1<sup>st</sup> ATLS training
- 1980 – 1<sup>st</sup> Implantable cardioverter defibrillator
- 1980 – 1<sup>ST</sup> MRI
- 1981 – 1<sup>st</sup> Pulse oximeter
- 1982 – Human insulin
- 1995 – Medical lasers



## PRESENT

- Functional electrical stim
- Myoelectric prosthesis
- Exoskeletons
- Laser therapy for scars
- Targeted Muscle Reinnervation

## FUTURE & BEYOND



# The Future of Catastrophic Injury Care?

## *The future and beyond*

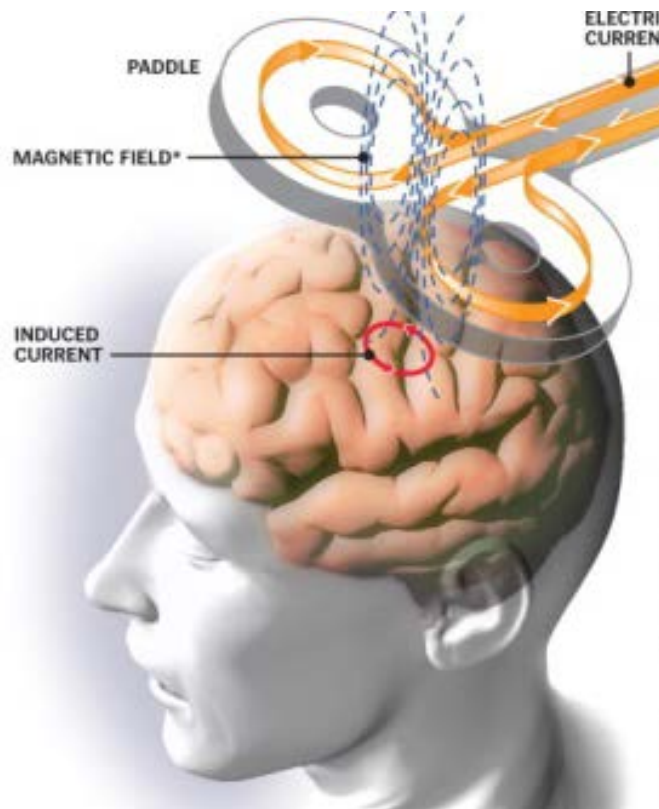
### ***Dr. Choo's Top 10 Medical & Technological Innovations***

1. Repetitive Transcranial Magnetic Stimulation (r-TMS)
2. Neuro-spinal scaffolds
3. Acute Intermittent Hypoxia
4. Brain-Computer-Interface (BCI) with machines
5. Brain-Computer-interface (BCI) with limb reanimation
6. Brain-Computer-interface (BCI) with endovascular sensor
7. Optogenetics
8. 3-D Bio-Printing (ITOP)
9. Prosthetics – Sensory Feedback – Electronic Skin
10. Genetic therapy

# ABI/TBI Care: Repetitive Transcranial Magnetic Stimulation (r-TMS)

*Improving motor and gait in TBI patients and coma states via electromagnetic induction*

1



## The Principles

- Electrochemical cells
- Neuronal pathways
- Neuroplasticity

## The Science

- Magnetic field
- Brain anatomy
- Stimulation = Practice

# ABI/TBI Care: Repetitive Transcranial Magnetic Stimulation (r-TMS)

*Improving motor and gait in TBI patients and coma states via electromagnetic induction*

## Motor recovery

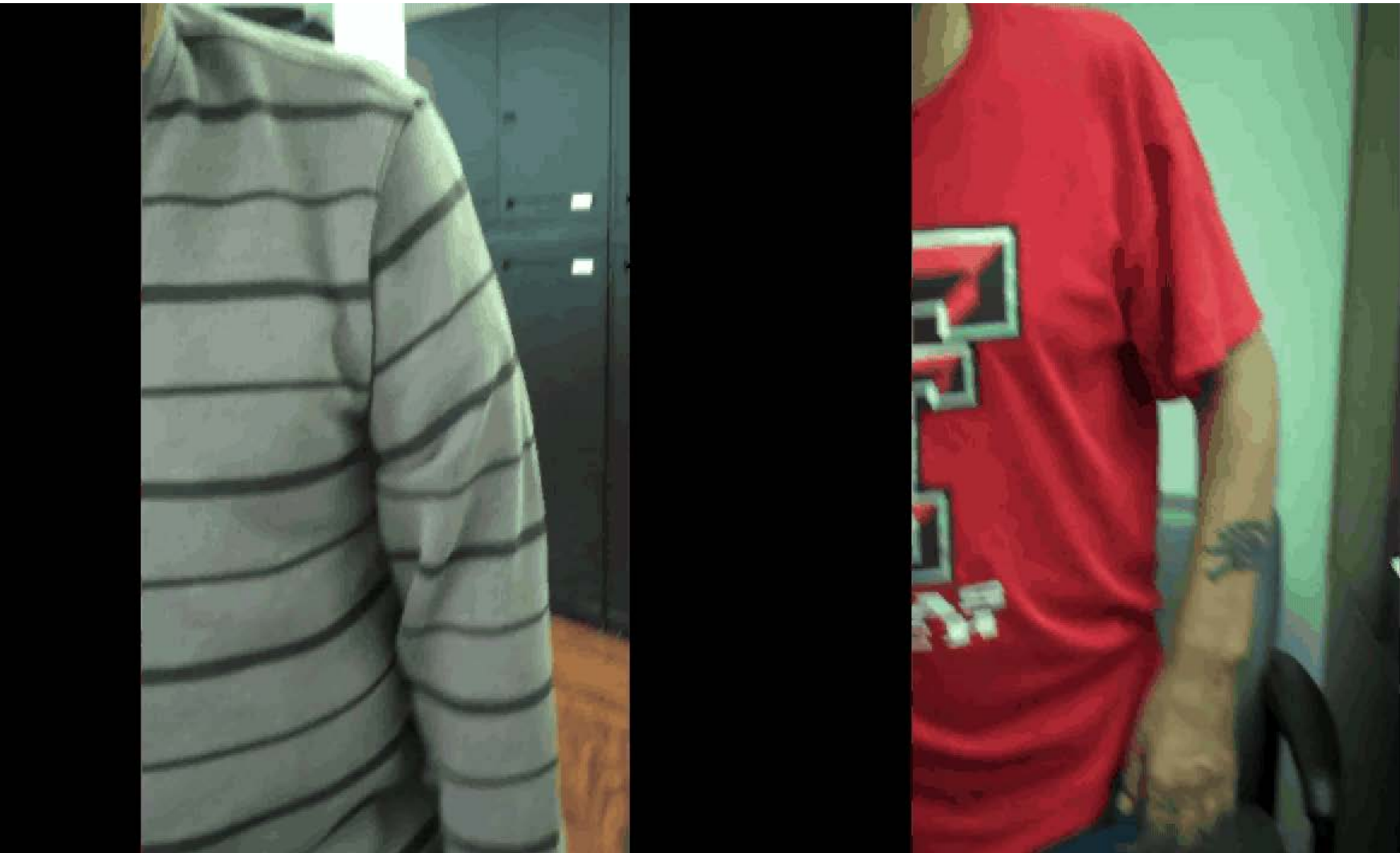
- Direct stimulation
- Modulating interhemispheric inhibition

## Application in stimulation of brain excitability

- Minimally conscious
- Vegetative state

# ABI/TBI Care: Repetitive Transcranial Magnetic Stimulation (r-TMS)

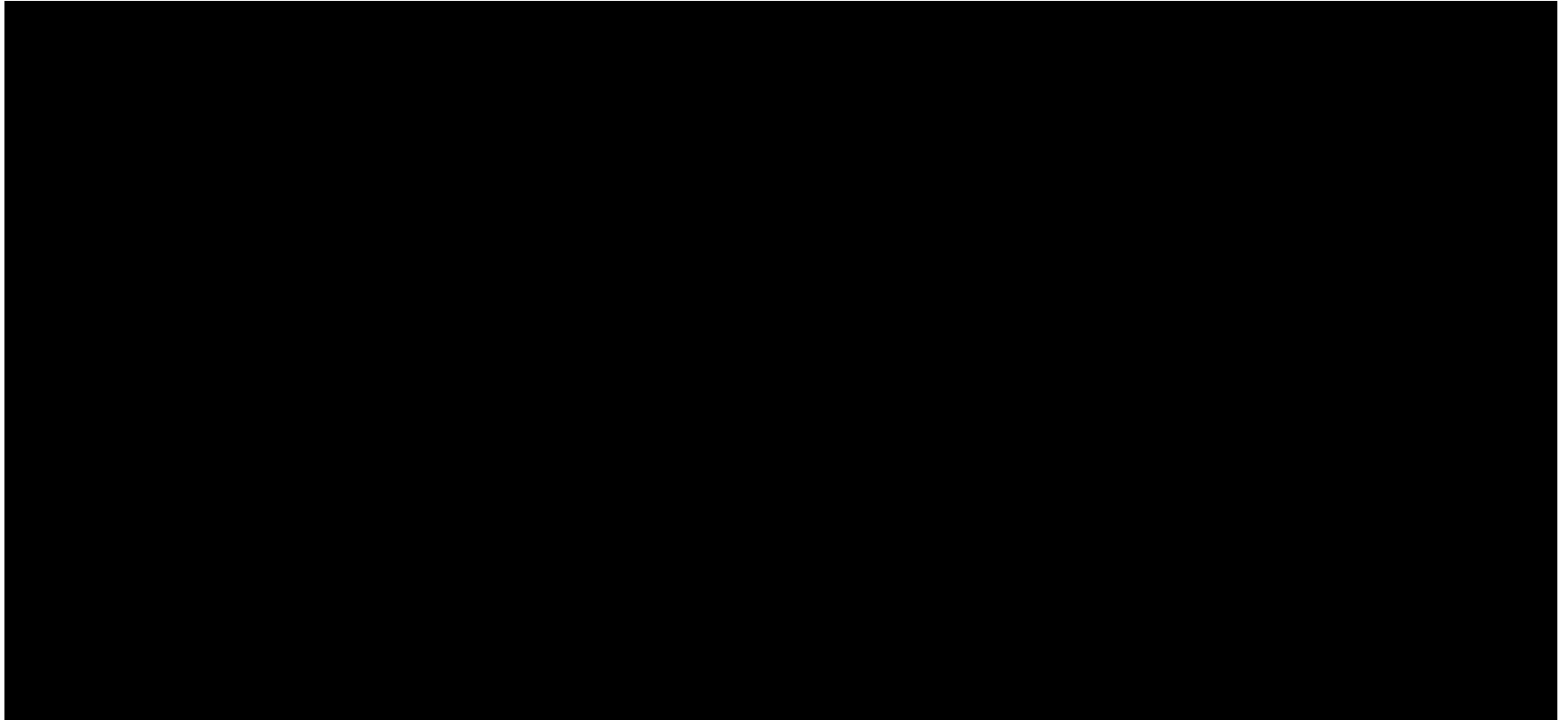
*Improving motor and gait in TBI patients via electromagnetic induction*





# Repetitive Transcranial Magnetic Stimulation (r-TMS)

*Improving motor and gait in TBI patients via electromagnetic induction*



# SCI Care: Neuro-spinal scaffolds

*InVivo Therapeutics Inc.- stem cell with PLGA scaffolds*

2

**Acute  
Injury**

**Neuro-Spinal  
Scaffold:  
PLGA  
Poly-L-Lysine**

**Appositional  
SCI Healing**

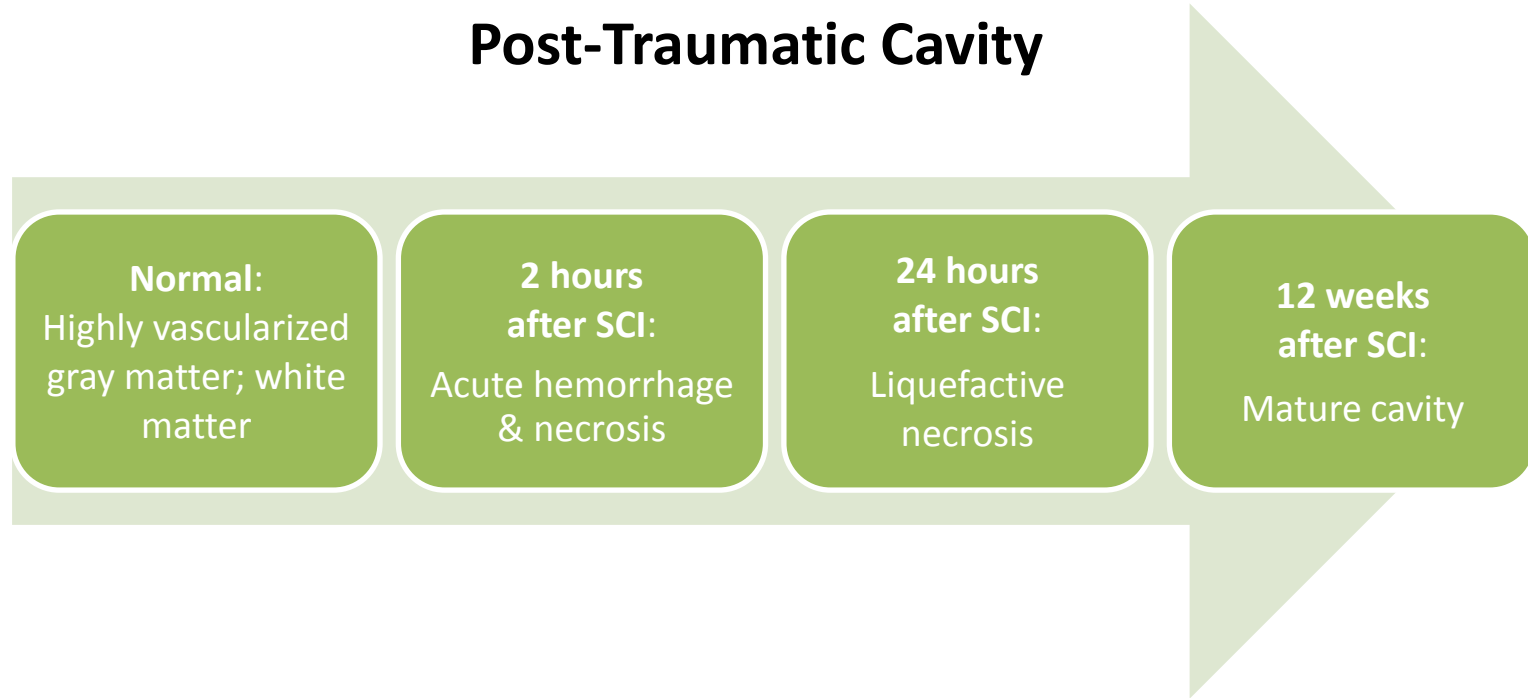
## Reference Image

(1) <http://www.invivotherapeutics.com/research-clinical-development/pipeline/neuro-spinal-scaffold/> (InVivo Therapeutics website, Pipeline: Neuro-Spinal Scaffold)

# SCI Care: Neuro-spinal scaffolds

*InVivo Therapeutics Inc.- stem cell with PLGA scaffolds*

## Progression of Acute SCI to Post-Traumatic Cavity



### Reference Article

(2) [http://www.invivotherapeutics.com/wp-content/uploads/2016/03/InVivo\\_Corporate\\_Presentation\\_3-6-16-FINAL.pdf](http://www.invivotherapeutics.com/wp-content/uploads/2016/03/InVivo_Corporate_Presentation_3-6-16-FINAL.pdf) (InVivo Therapeutics, Presentation: Innovative Products for Spinal Cord Injury, Page 8)

# SCI Care: Neuro-spinal scaffolds

*InViVo study of probable benefit of the neuro-spinal scaffold for safety and neurologic recovery in subjects with complete thoracic ASIA A spina cord injuries (INSPIRE)*

## INSPIRE Trial

### Inclusion Criteria:

- 18 - 65 years
- T3-T12/L1; **ASIA A within 21 days**
- Non-penetrating contusion injury
  - 4 mm diameter and limited to two contiguous vertebral levels

### Outcome Measures:

- Safety
- Change in ASIA, sensory scores, motor scores, bladder and bowel function, neurological tests, and SCIM III

**Warning:**  
graphic video on  
the next slide

# SCI Care: Neuro-spinal scaffolds

*InVivo Therapeutics Inc.- stem cell with PLGA scaffolds*

**Warning:**  
graphic video

## **Video:** **First Human Implantation of a Bioresorbable Polymer Scaffold for Acute Traumatic Spinal Cord Injury**

### **Reference Video**

(3) <https://www.youtube.com/watch?v=LOXzZG1ULw0> (YouTube)

# SCI Care: Neuro-spinal scaffolds

*InVivo Therapeutics Inc.- stem cell with PLGA scaffolds*

## First Patient Report at 3 Months

“...progressed from a complete AIS A injury to an incomplete AIS C injury with motor, sensory, bowel, and bladder *function improvements*.”

- *Return of active movement* of the hip flexors against gravity and palpable contractions of the knee extensors
- Sacral sensory sparing at *S4-5*

# Acute Intermittent Hypoxia: A Novel SCI Therapy

*Improves both respiratory and non-respiratory motor neurons*

3

NON-INVASIVE

SPINAL PLASTICTY PROMOTION

HYPOXIC EPISODES = phrenicLTF

# Acute Intermittent Hypoxia: A Novel SCI Therapy

*Improves both respiratory and non-respiratory motor neurons*

EPISODIC SEROTONIN RECEPTOR ACTIVATION

BDNF- BRAIN DERIVED NEUROTROPHIC FACTOR

SPINAL PLASTICITY OF MOTOR NEURONS



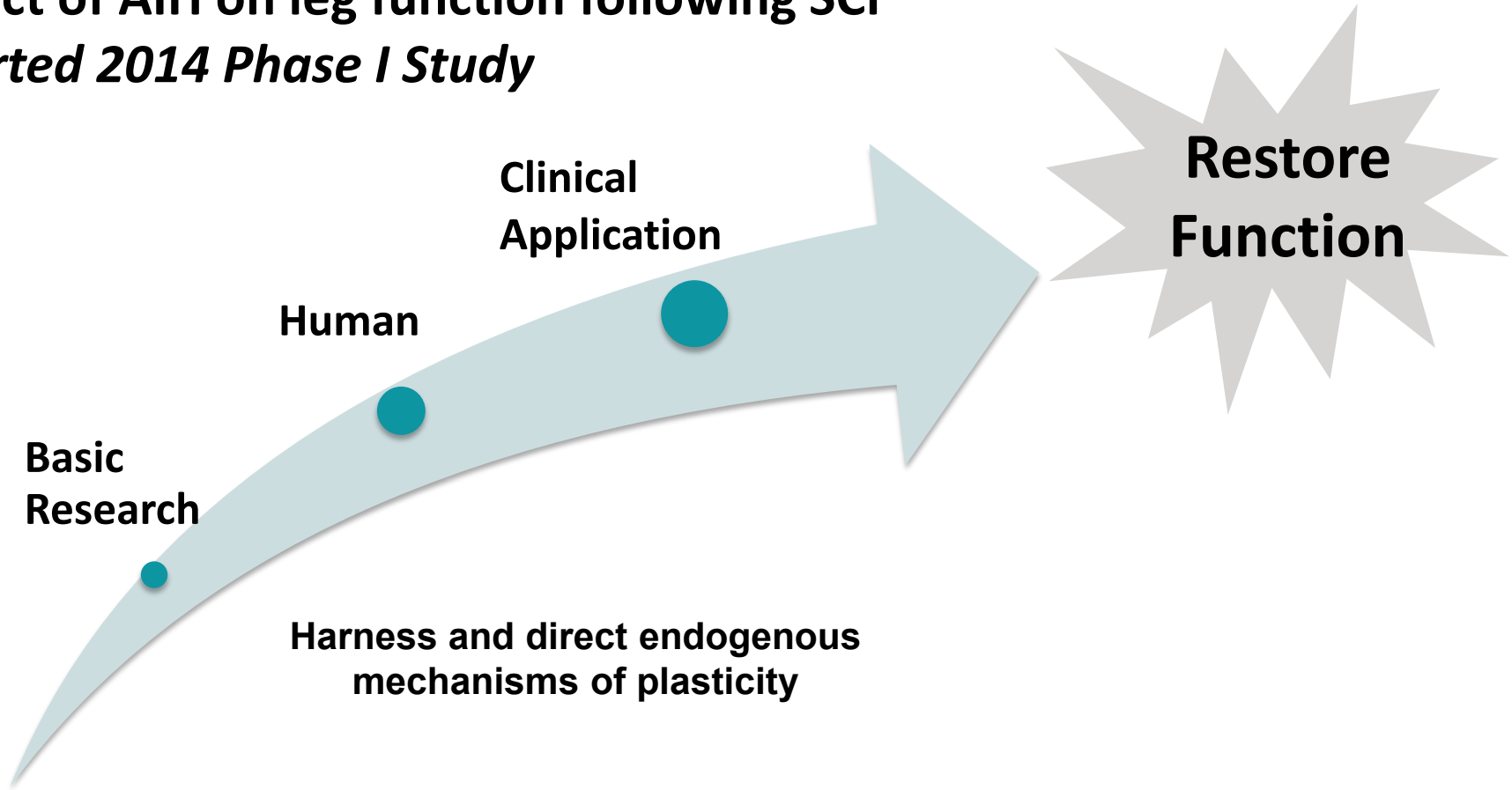
# Acute Intermittent Hypoxia: A Novel SCI Therapy

*Potential spinal plasticity promotion for SCI rehabilitation*

**Emory University:**

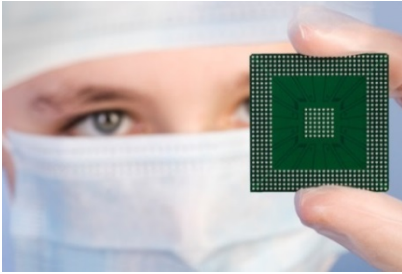
**Effect of AIH on leg function following SCI**

***Started 2014 Phase I Study***

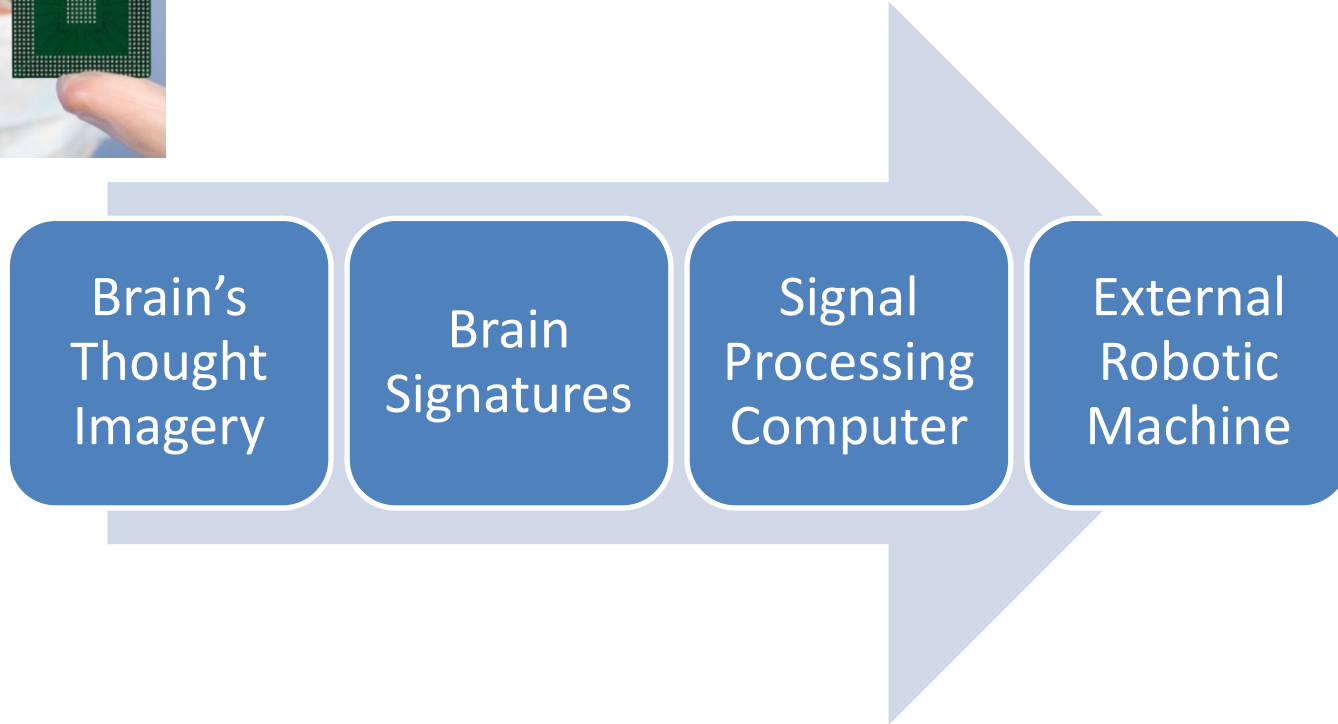


# SCI Care: Brain Computer Interfaces (BCI) and Robotics

*Gateway for the brain for paralyzed patients*



4



## Reference Image

(4) <https://news.brown.edu/articles/2012/05/braingate2> (Brown University, Article: People with paralysis control robotic arms using brain-computer interface)

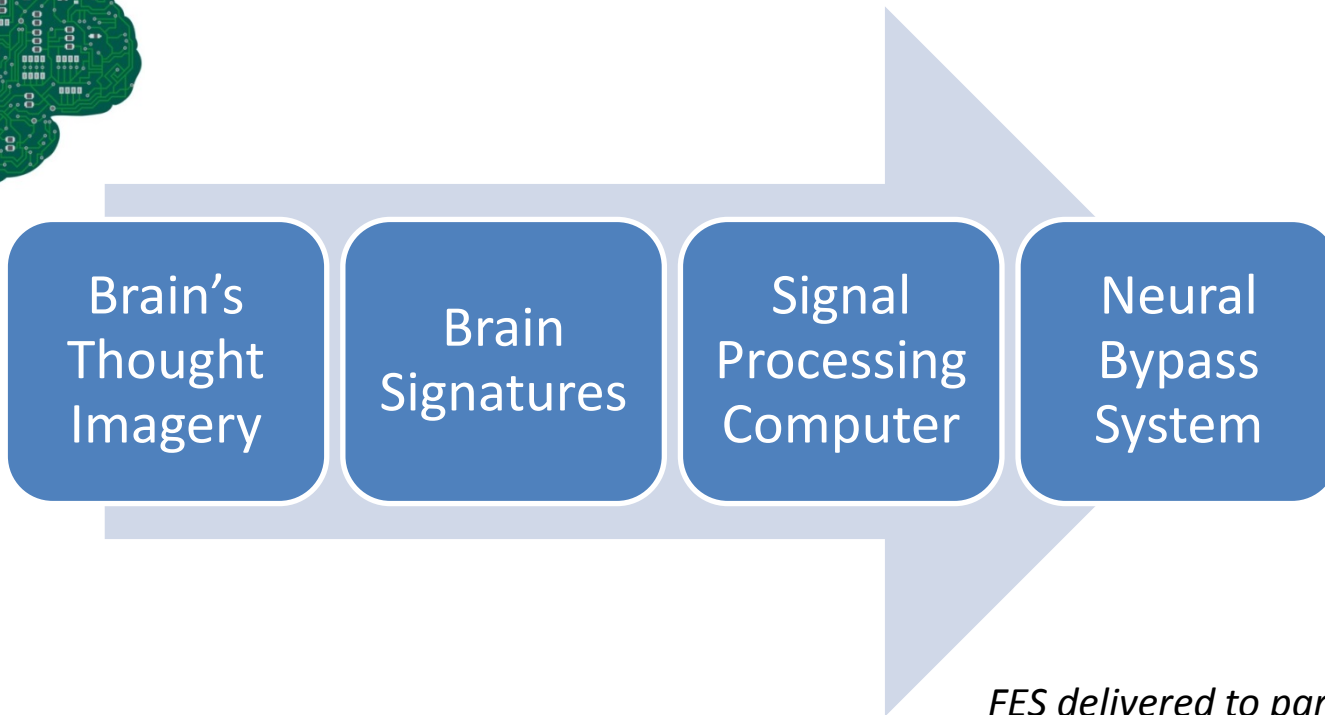
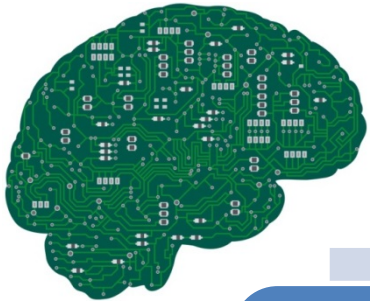
# SCI Care: Brain Computer Interface (BCI) with Limb Reanimation

*Brain Spinal Interface Technology- neural bypass, FES*

5

Article:

*Restoring cortical control of functional movement in a human with quadriplegia*



# SCI Care: Brain Computer Interfaces (BCI) with Limb Reanimation

*Gateway for the brain for paralyzed patients*

**Video:**  
**Ohio Man Receives  
'Brain Chip' in  
Human-Computer  
Interface**

## Reference Video

(5) <https://www.youtube.com/watch?v=d8sUuBbp7hY> (YouTube)

# SCI Care: Brain Computer Interfaces (BCI) & Robotics

*Gateway for the brain for paralyzed patients*

**Wireless, implantable,  
rechargeable, long-term  
brain-computer interface**

## Reference Images

(6) <http://www.extremetech.com/extreme/149879-brown-university-creates-first-wireless-implanted-brain-computer-interface> (Extreme Tech, Article: Brown University creates first wireless, implanted brain-computer interface)

# SCI Care: Brain Computer Interface (BCI) with Nerve Stimulation

*Brain Spinal Interface Technology using Wireless BCI & Epidural Spinal Stimulation*

**Video:**  
**Primates regain  
control of paralyzed  
limb**

## Reference Video

(7) <https://www.youtube.com/watch?v=1sjeytKmlCk> (YouTube)

# SCI Care: Brain Computer Interface (BCI)

*Brain Spinal Interface Technology- neural control via Stentrode*

6



BIOSCIENCE TECHNOLOGY

STENTRODE

ENDOVASCULAR PLACEMENT

# SCI Care: Brain Computer Interface (BCI) with Endovascular Sensor

*Brain Spinal Interface Technology- neural bypass*

**Video:**  
**Stentrode**  
**in Action**

## Reference Video

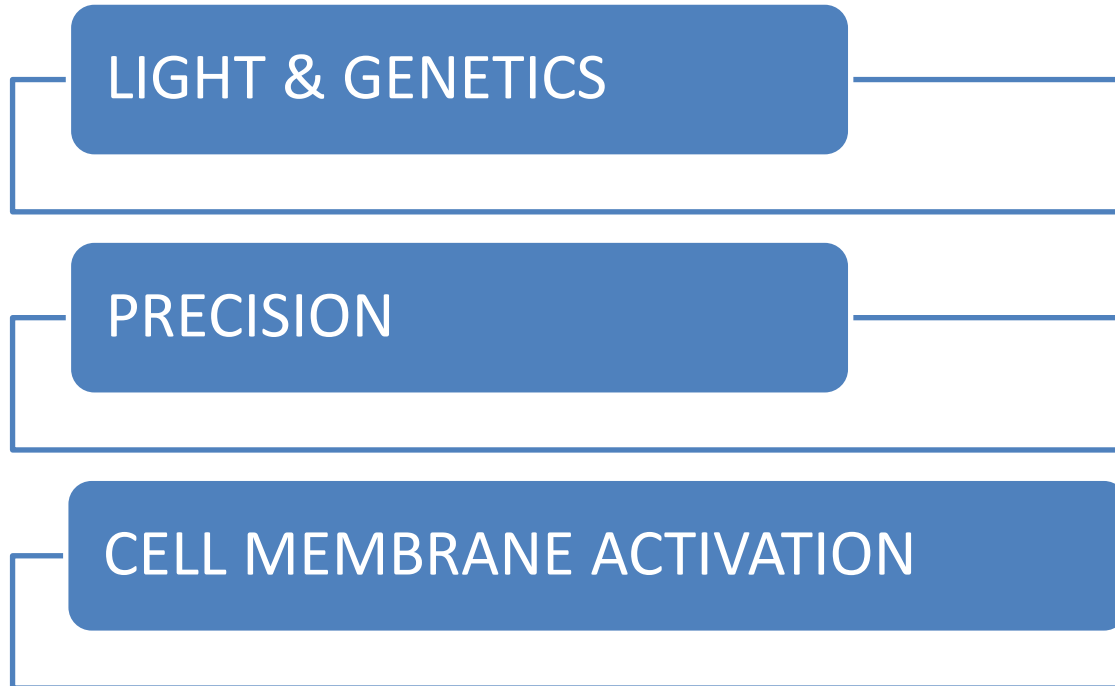
(8) <https://www.youtube.com/watch?v=hB3H3wHwO24> (YouTube)



# Optogenetics: A Novel Technique for Neuroscience

## *Brain and SCI applications*

7



### Reference Images

(9) [http://www.nature.com/neuro/journal/v18/n9/fig\\_tab/nn.4091\\_F1.html](http://www.nature.com/neuro/journal/v18/n9/fig_tab/nn.4091_F1.html) (Nature Neuroscience, Article: Optogenetics: 10 years of microbial opsins in neuroscience, Figure 1)

# Optogenetics: A Novel Technique for Neuroscience

*Neuronal activation*

## Optogenetics: Putting the pieces together

### Reference Images

(10) [http://www.nature.com/neuro/journal/v18/n9/fig\\_tab/nn.4091\\_F2.html](http://www.nature.com/neuro/journal/v18/n9/fig_tab/nn.4091_F2.html) (Nature Neuroscience, Article: Optogenetics: 10 years of microbial opsins in neuroscience, Figure 2)

# Optogenetics: A Novel Technique for Neuroscience

*Neuronal activation: precision and specific action in TBI and SCI*

## Brain Discoveries:

- Insights into neural circuits
  - Behavioral (addiction)
  - Cognition
  - Movements

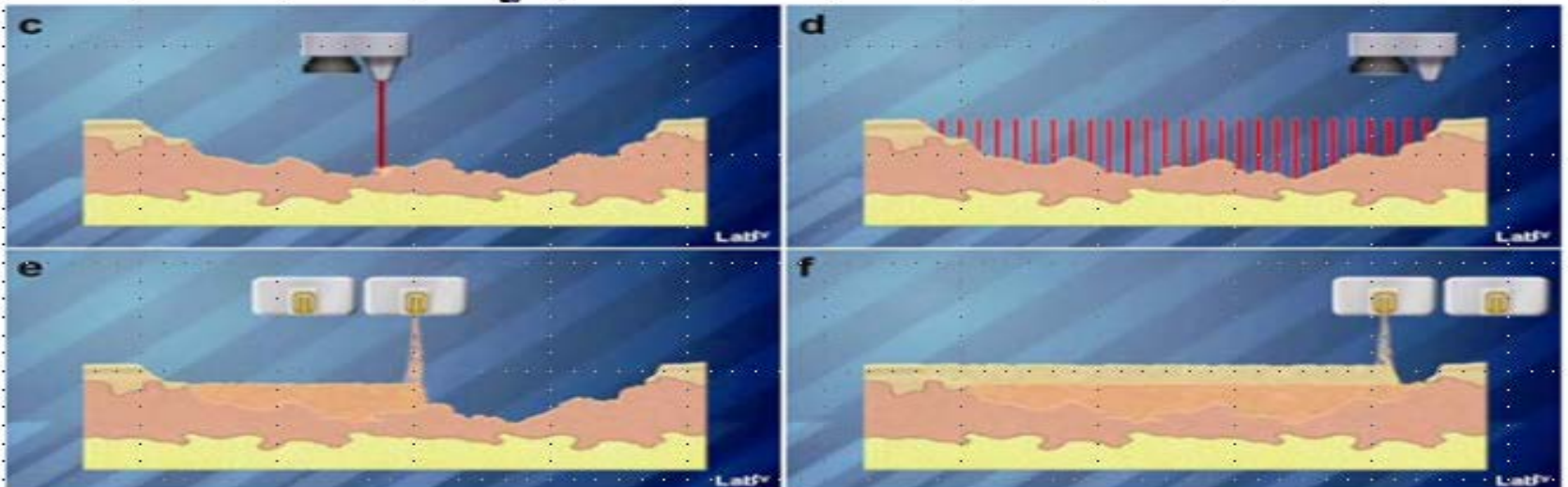
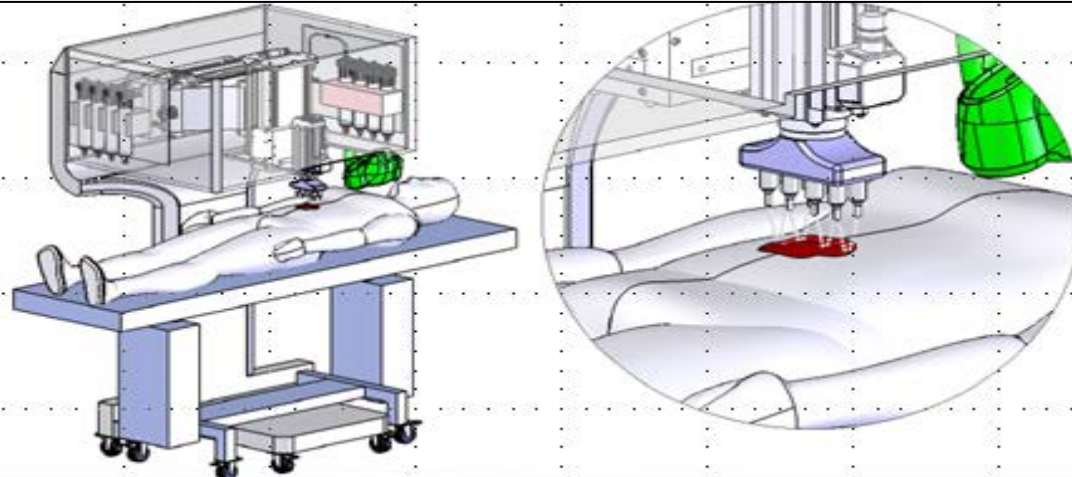
## Motor Neuron Activation:

- Restoration in SCI
  - Respiratory function
  - Bladder function
  - Muscle function

# Burn Care: 3-D BioPrinting (ITOP)

## Bioprinting of Skin Cells for Skin Reconstruction of Burn Wounds

**Mohammad Z. Albanna**, Sean Murphy, Weixin Zhao, Idris B. El-Amin, Josh Tan, James H. Holmes  
John D. Jackson, Anthony Atala and James J. Yoo



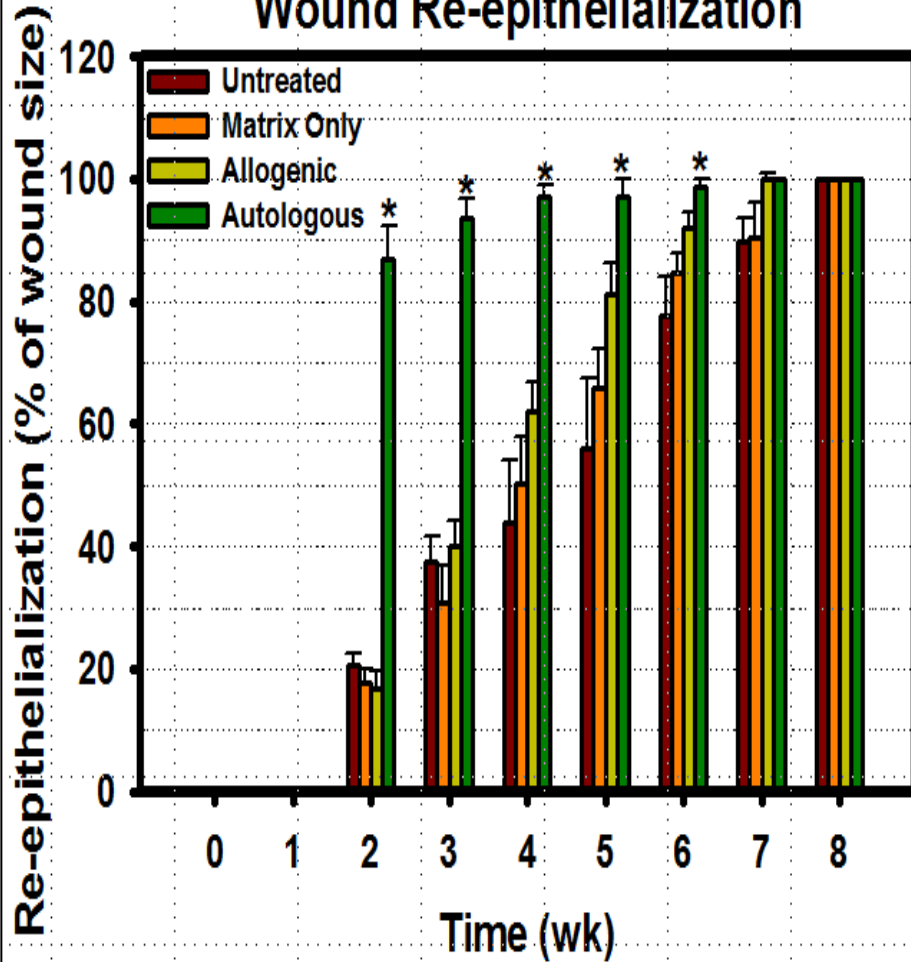
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# Burn Care: 3-D BioPrinting (ITOP)

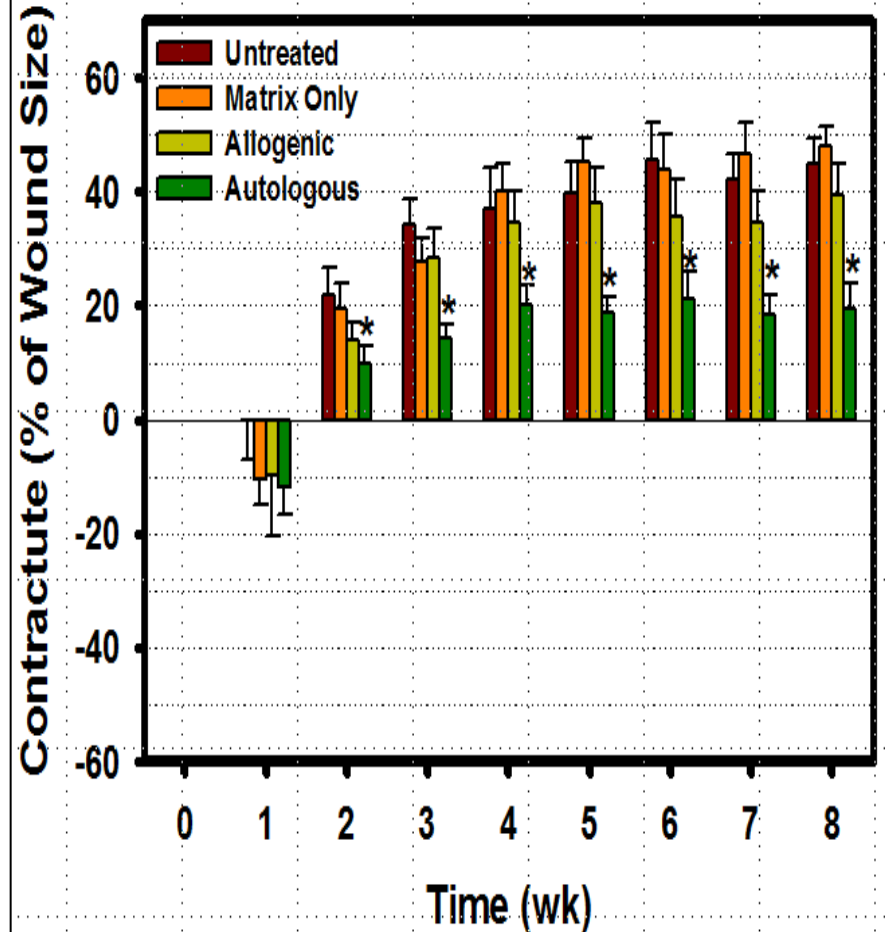
## Bioprinting of Skin Cells for Skin Reconstruction of Burn Wounds

**Mohammad Z. Albanna**, Sean Murphy, Weixin Zhao, Idris B. El-Amin, Josh Tan, James H. Holmes  
John D. Jackson, Anthony Atala and James J. Yoo

### Wound Re-epithelialization



### Wound Contracture



Used with permission from Wake Forest School of Medicine

## Electronic skin for prosthetics

### Reference Images

(11) <https://www.technologyreview.com/s/602092/how-to-give-fake-hands-real-feeling/> (MIT Technology Review, Article: How to Give Fake Hands Real Feeling)

# Genetic Therapy: CRISPR

*Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)*

10

GENE EDITING SYSTEM

RNA ENZYME DEFENDER

CAS9 & CAS3

ANTIMICROBIAL SOLUTION?

# Paradigm's Medical Innovation Position Papers

*Bridging cost of therapy and functional outcome benefits*

**Our positions: *help, hope, hype***

The image displays four cover pages of Paradigm Outcomes position papers, arranged in a 2x2 grid. Each cover features the Paradigm Outcomes logo at the top and a title for a medical innovation. The top-left cover is titled 'Medical and Rehabilitation Innovations' and 'Functional Electrical Stimulation Ergometer (FES BIKE)'. The top-right cover is titled 'Medical and Rehabilitation Innovations' and 'Exoskeletons in Spinal Cord Injury 2014'. The bottom-left cover is titled 'Medical and Rehabilitation Innovations' and 'Hyperbaric Oxygen Therapy for Traumatic Brain Injury'. The bottom-right cover is titled 'Medical and Rehabilitation Innovations' and 'Neuro-Endocrine Screening and Hormone Replacement Therapy (HRT) in Trauma related Acquired Brain Injury 2014'. Each cover also includes a copyright notice for Paradigm Management Services, LLC.





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<https://www.surveymonkey.com/r/medicalinnovations>

Tip: If your work computer has blocked Survey Monkey, access the link via your home computer.

# Question and Answer Session

*Submit your questions in the Q&A panel on the right of your screen.*

Michael Choo, MD, MBA, FACEP, FAAEM  
Paradigm Chief Medical Officer



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*Please use the toll-free dial-in number: 1-877-668-4490, access code 666 795 698 # #*



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