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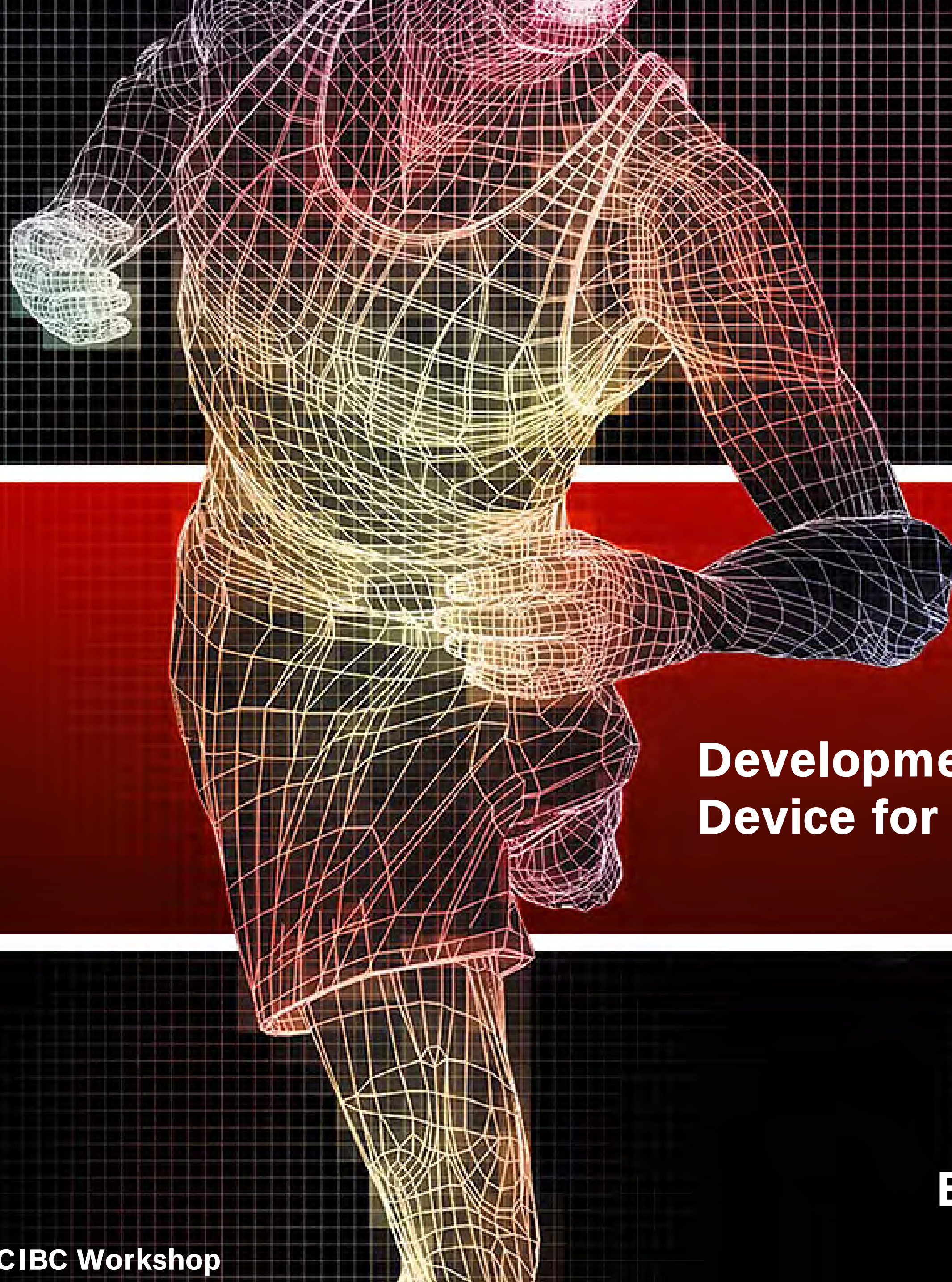

Development of an Electrical Stimulation Device for Osseointegrated Amputees

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University of Utah

Bone and Joint Research Lab

Introduction: Issues with Prosthetic Implants

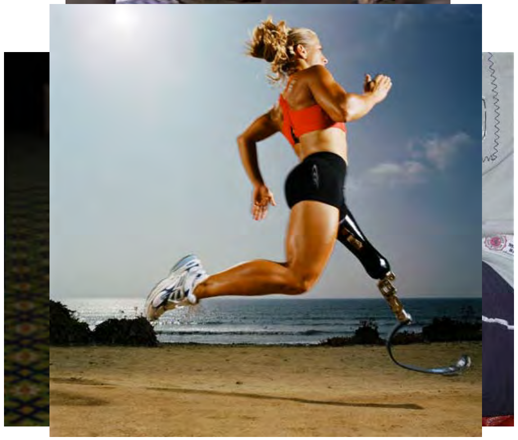
- Concerns
  - Fixation mechanism
  - Rehabilitation
  - Limited residual limb
  - Debilitating diseases
  - Improved mobility
  - Comfort

- 1000 war-related amputations from OIF/OEF[1]

1. *American war and military operations casualties: Lists and statistics*, in *CRS report for Congress*. 2007, Congressional Research Service. p. CRS1-25.

Introduction: Initial Focus

- Osseointegration
- Socket Complications
  - Osteoporosis on amputated limb[2]
  - 3x increase in osteoarthritis on contralateral limb[2]
- Osteopenia
  - Affects 34 million Americans annually
- Osteoporosis
  - Affects 10 million Americans annually



2. Kulkarni et al. *Clin. Rehabil.* 1998 Aug;12(4):348-353.

Introduction: Osseointegration

Physical

- Improved mobility[3]
- Reduced pressure sores[3]
- Ability to walk on challenging terrain[3]
- Reduced energy for ambulation[4]

Psychological

- Proprioception[5]
- Depression[6]
- Integration

3. Hagberg, K., & Branemark, R. (2001). *Prosthet. Orthot. Int., 25*(3), 186-194.
4. Couch NP et al. American Journal of Surgery 1977 Apr;133(4):469-473.
5. Jacobs R & Van Steenberghe D. Journal of Oral Rehabilitation 2006 Apr;33(4):282-292.
6. Kashani JH et al. J Clin Psychiatry 1983 Jul;44(7):256-258.

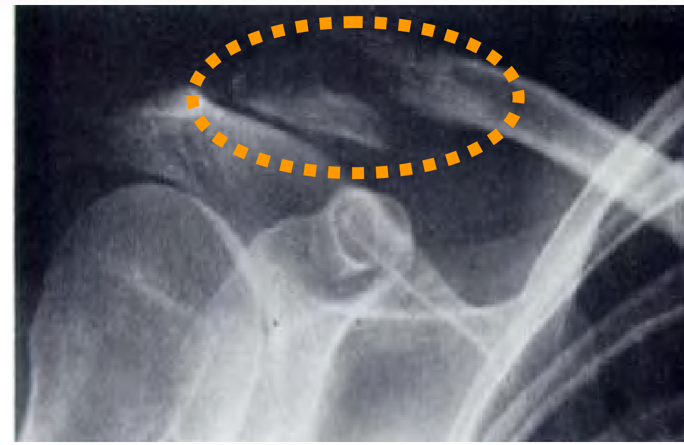
Research Aim

<u>The Big Picture:</u>

So how do we help the warrior and veteran amputees?

Research Aim

- Empirical results <u>not</u> standardized
- What can we learn
  - Electric Field
    - 1-10 V/cm[7-8]
  - Current Density
    - <2 mA/cm^2 [7-8]
- What is our hypothesis
  - Strain responsive (osteocytes)
  - Electrochemical reaction at cathode



Friedenberg et al. JBJS (1974)
Brighton et. al. JBJS 1975.

7. Ferrier, J. et al. (1986) *J Cell Physiol.* 129(3): p. 283-8.
8. Noda, M. & A. Sato. (1985) *Clin Orthop Relat Res*, 193: p. 288-98.

Methods: Sample Population

- N = 4
  - 2 Amputees
  - 2 “Artificial” Amputees
- Large standard deviations selected to account for variety in anatomy
- Required absent of metal to prevent image artifact

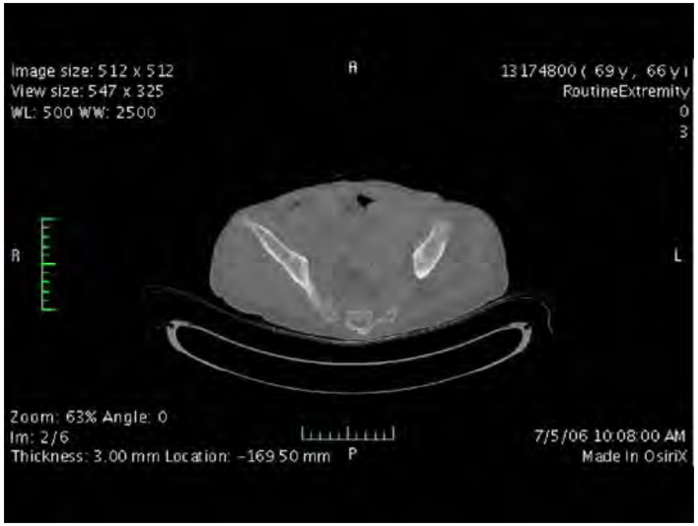
Table 1: Patient Demographics

Patient	Sex	Amputee	Age	Height [cm]	Weight [kg]
1	M	No	60	185.4	79.9
2	F	No	28	157.5	50.1
3	F	Yes	80	152.4	45.5
4	M	Yes	68	160.0	56.9

Mean	59.00	58.10	163.83
Median	64.00	53.50	158.75
SD	22.24	15.27	14.73

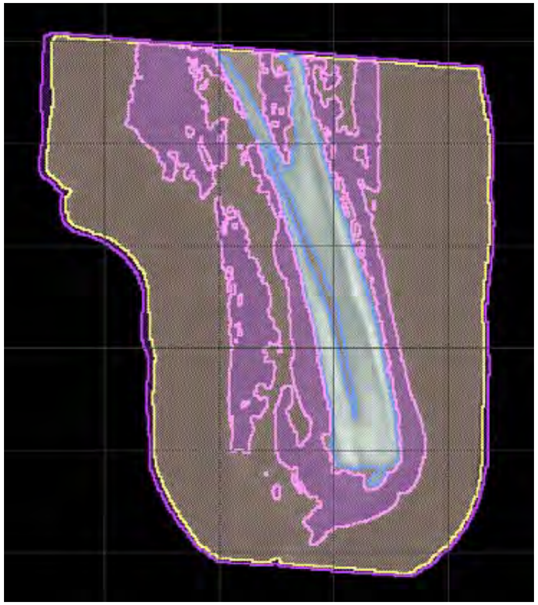
Methods: Computational Modeling Progression

- Authorization
  - University of Utah IRB
  - HIPAA
  - WRAMC
- Amputee Reconstruction
  - Computer Tomography (CT) scans
    - High frequency
    - Reduced motion artifact



Methods: Seg3D

- **Threshold CT Images**
  - Bone
  - Bone Marrow
  - Adipose Tissue
  - Musculature
- **Confidence Connected Filter**
  - Musculature
- **Dilate/Erode Filter**
  - Skin (2mm)[9]
- **Manual Inspected**
- **Combined hierarchy into a single label map for Finite Element Analysis**



Sagital View: Amputee Residual Limb

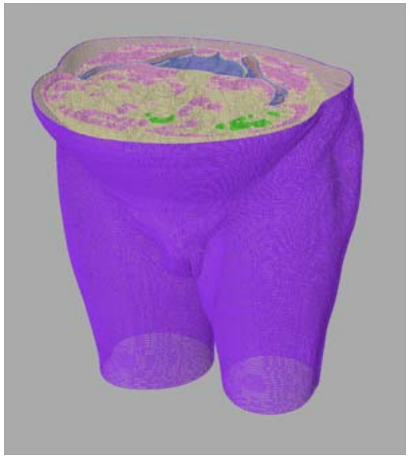
9. Tortora, J. & Nielsen M. (2008). *Principles of Human Anatomy* (11th ed). United States: John Wiley & Sons.

Methods: Seg3D Hierarchy Map

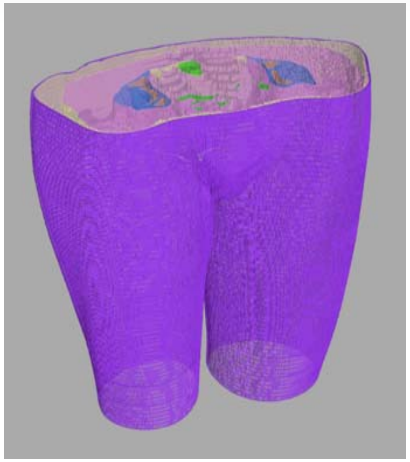
- 6 Layer Hierarchical Map
  - Skin
  - Adipose Tissue
  - Muscle
  - Bone
  - Bone Marrow
  - Organs

- Conductivities(10-12):

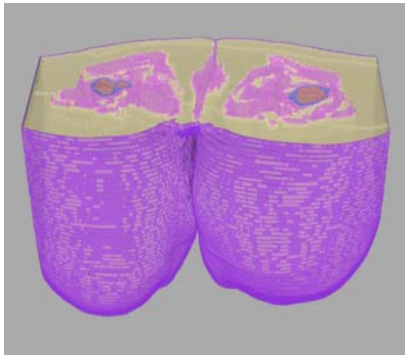
Tissue Type	Conductivities [S/m]
Skin	0.26
Muscle	0.25
Adipose	0.09
Organ	0.22
Cortical Bone	0.02
Bone Marrow	0.07



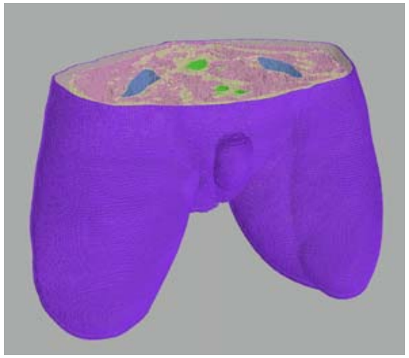
Amputee 1



Amputee 2



Amputee 3



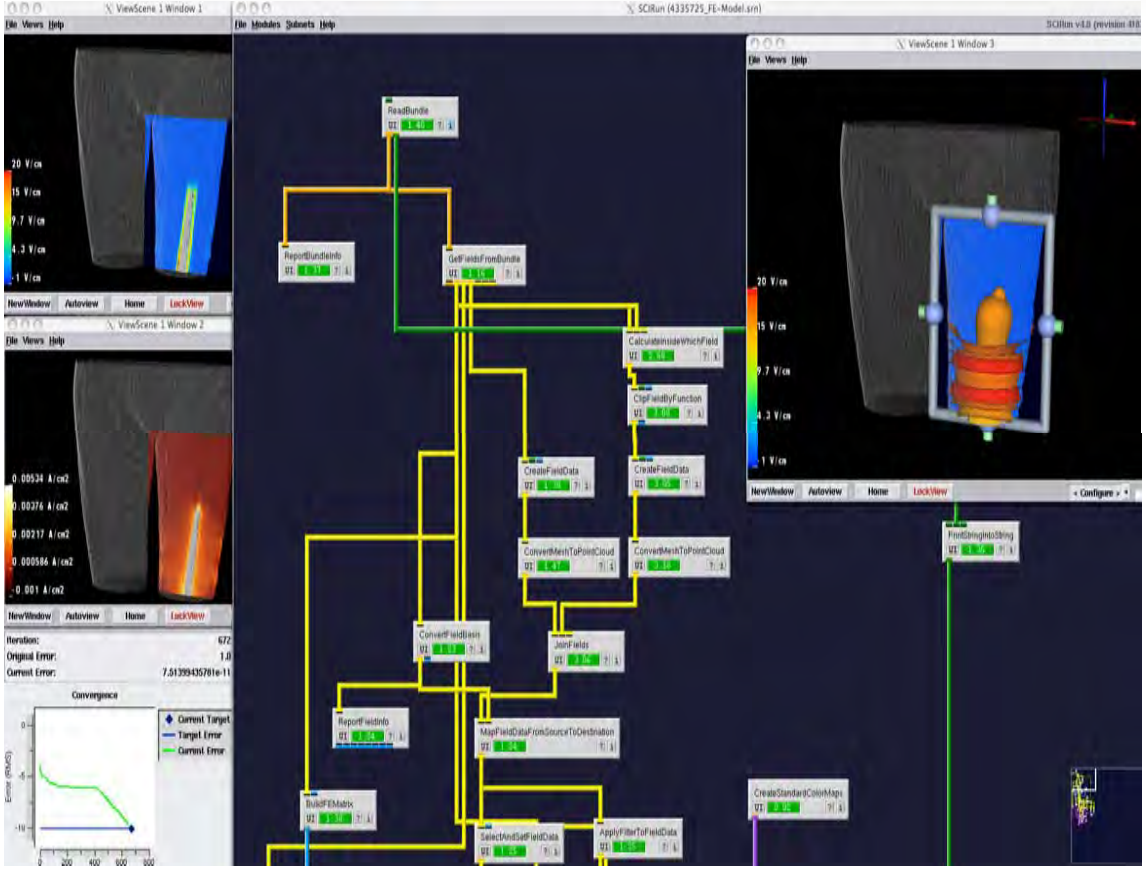
Amputee 4

10. Chiu, R. S., & Stuchly, M. A. (2005). *IEEE Trans Biomed Eng, 52*(6), 1103-1109.
11. Gabriel, S. Et al. (1996). *Phys Med Biol, 41*(11), 2271-2293.
12. Stinstra, J. G et al. (2007). *IEEE Engineering in Medicine and Biology Conference*.

Methods: SCIRun

SCIRun Platform

1. Patient specific finite element model
2. Interactive interface
3. Boundary Conditions



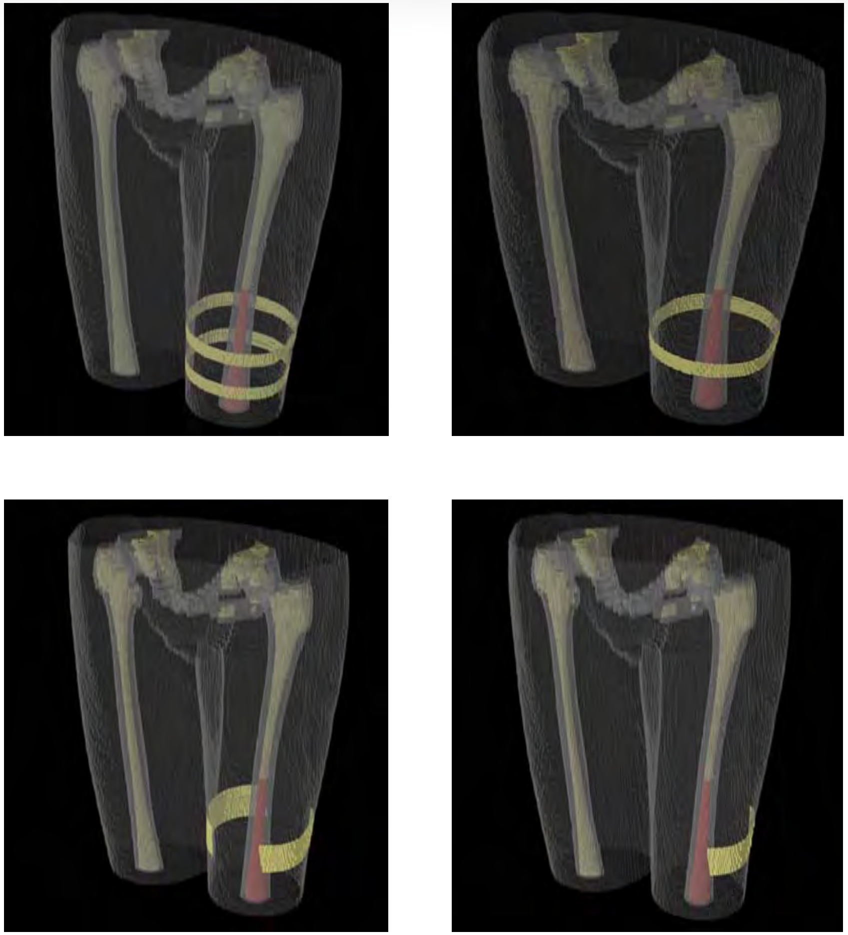
SCIRun Schematic for Amputee 2

Methods: Electrode Configuration

- Electrode Design
  - 2 Band
  - 1 Band
  - 2 Patch
  - 1 Patch

- Electrode Size
  - Band: 1.6cm
  - Patch: 3 cm

- Osseointegrated Implant
  - Set to the endosteal wall
    - Gaps > 50-75 μm may lead to fibrous encapsulation[13,14]



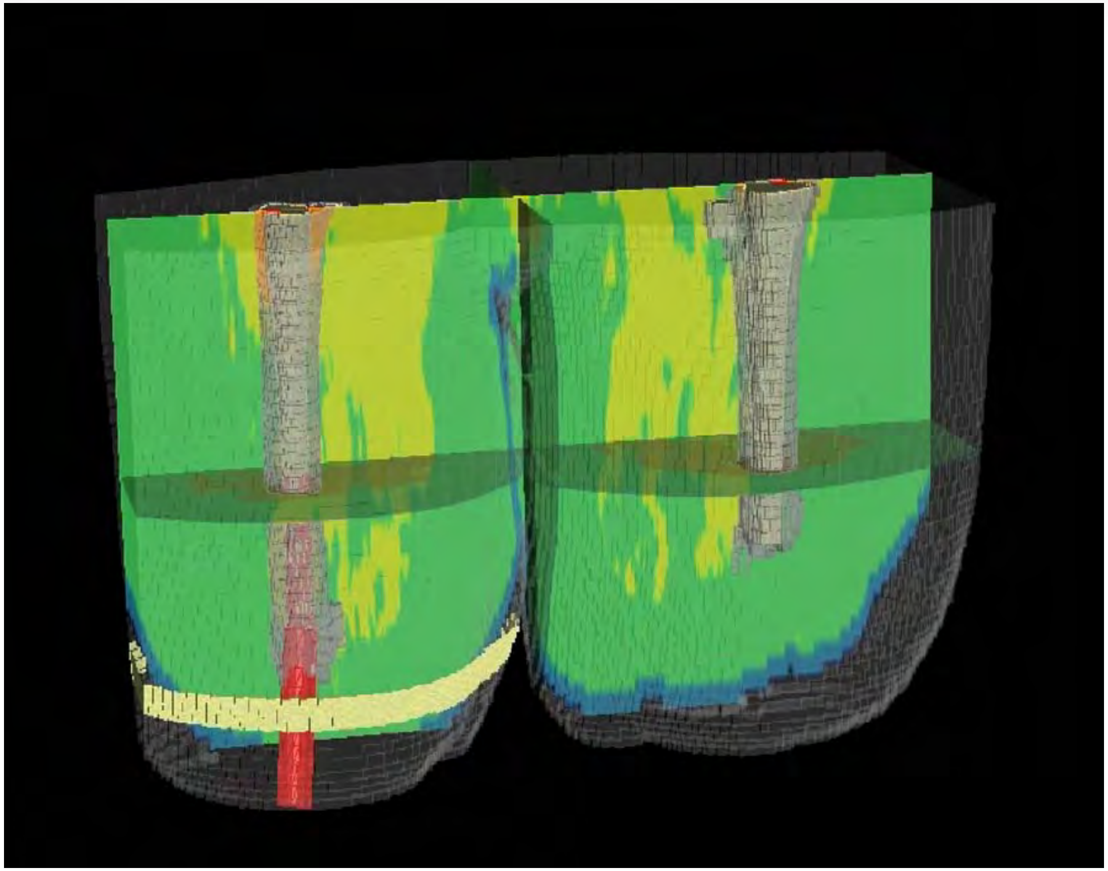
Electrode Configuration for Artificial Amputee 2

13. Bloebaum et al. (1994). *J Biomed Mater Res, 28*(5), 537-544.
14. Hofmann, A. et al. (1993). *J. Arthroplasty, 8*(2), 157-166.

Methods: Electrode Placement

Modeling Approach

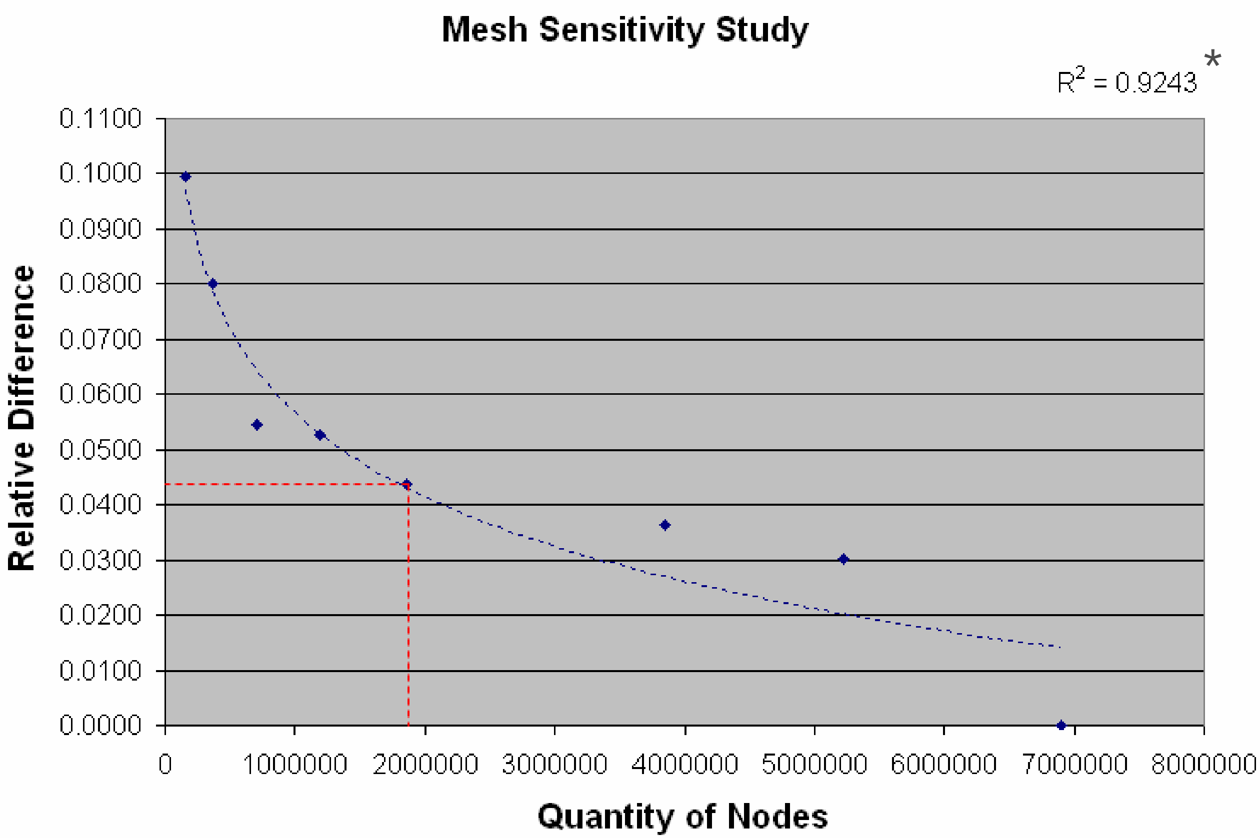
- Model developed from Seg3D segmentation
- Anatomically accurate
- Real time electrode manipulation



Electrode Placement on Amputee 3

Methods: Mesh Sensitivity Study

Mesh	# Elements	# Nodes	RD
100 100 50	149089	161131	0.0995
125 125 75	350180	371472	0.0802
150 150 100	673032	706082	0.0545
175 175 125	1146778	1194044	0.0527
200 200 150	1796690	1860772	0.0439
250 250 200	3745038	3850202	0.0364
275 275 225	5097243	5226587	0.0301
300 300 250	6742588	6898729	0.0000



15. Hinkle , D. (2003). *Applied Statistics for the Behavioral Sciences* . Boston : Houghton Mifflin Company.

* Denotes very high positive correlation[15]

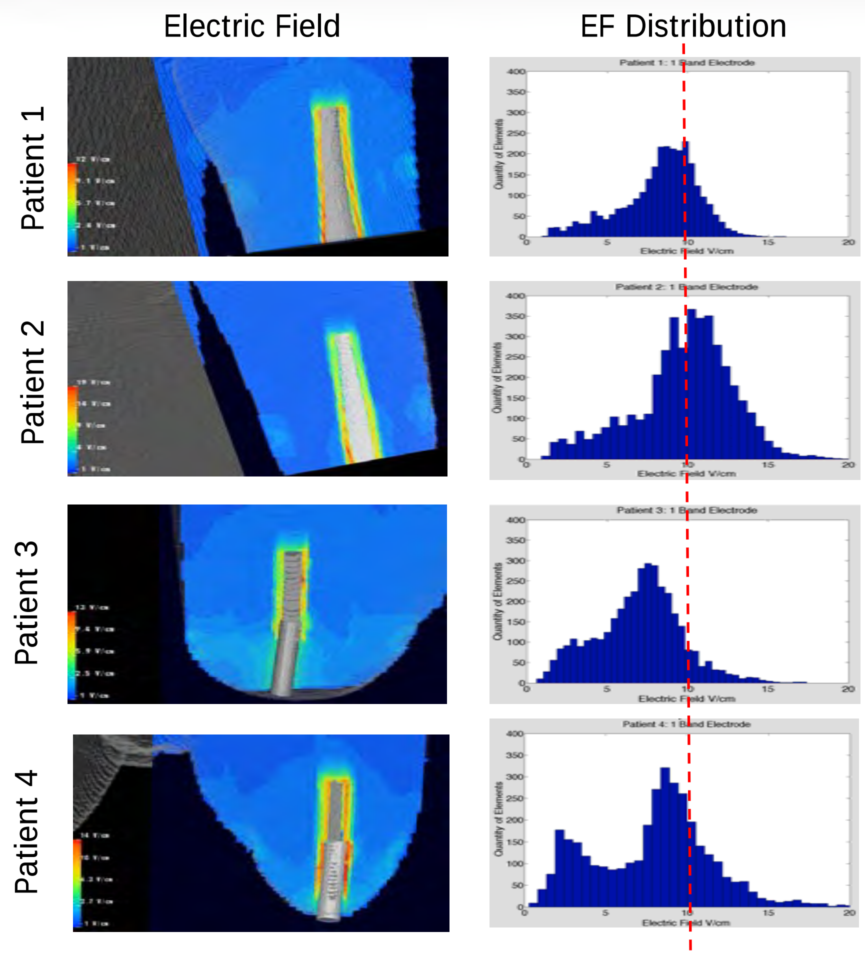
Methods: Null Hypotheses

Hypotheses:

1. No need for patient specific model
2. All electrode configurations will produce similar electric field and current density distributions
3. “Artificial” and actual amputees will produce similar electric metrics

Results: Isolated Case

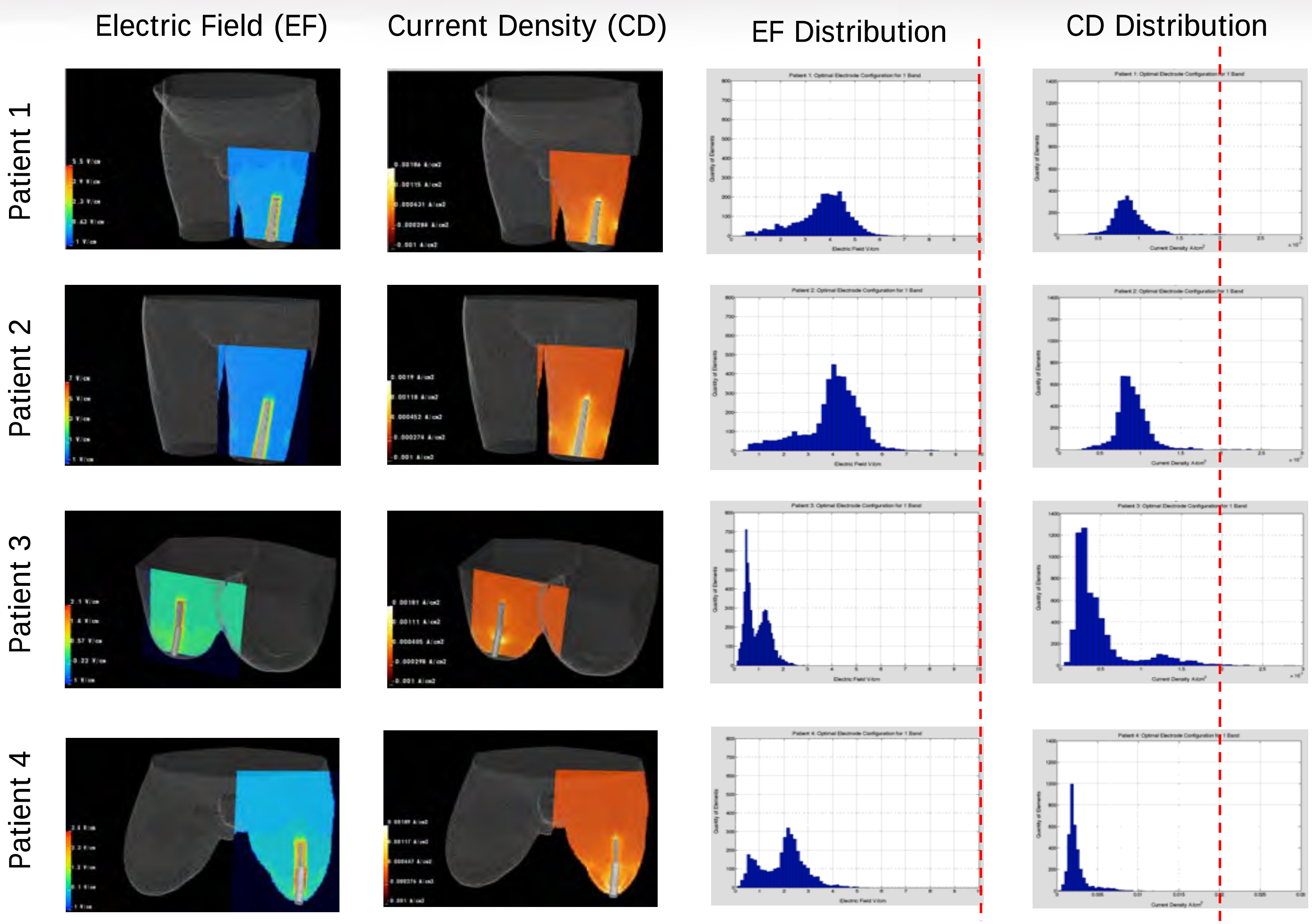
- Initial Approach
- Potential: 9v
- Histograms: ~ 6000 elements surrounding the implant site
- Broad variation among patients
- Gaussian or Skewed Peaks
- Random level of homogeneity



Electric Field Of Amputee Residual Limbs

Results: Patient Specific Modeling Requirement

- **New Potential**
  - 1.0-4.5v
- **Patient 1**
  - 4.00 V
  - 1.86 mA/cm^2
- **Patient 2**
  - 3.50 V
  - 1.90 mA/cm^2
- **Patient 3**
  - 1.50 V
  - 1.81 mA/cm^2
- **Patient 4**
  - 2.25V
  - 1.89 mA/cm^2

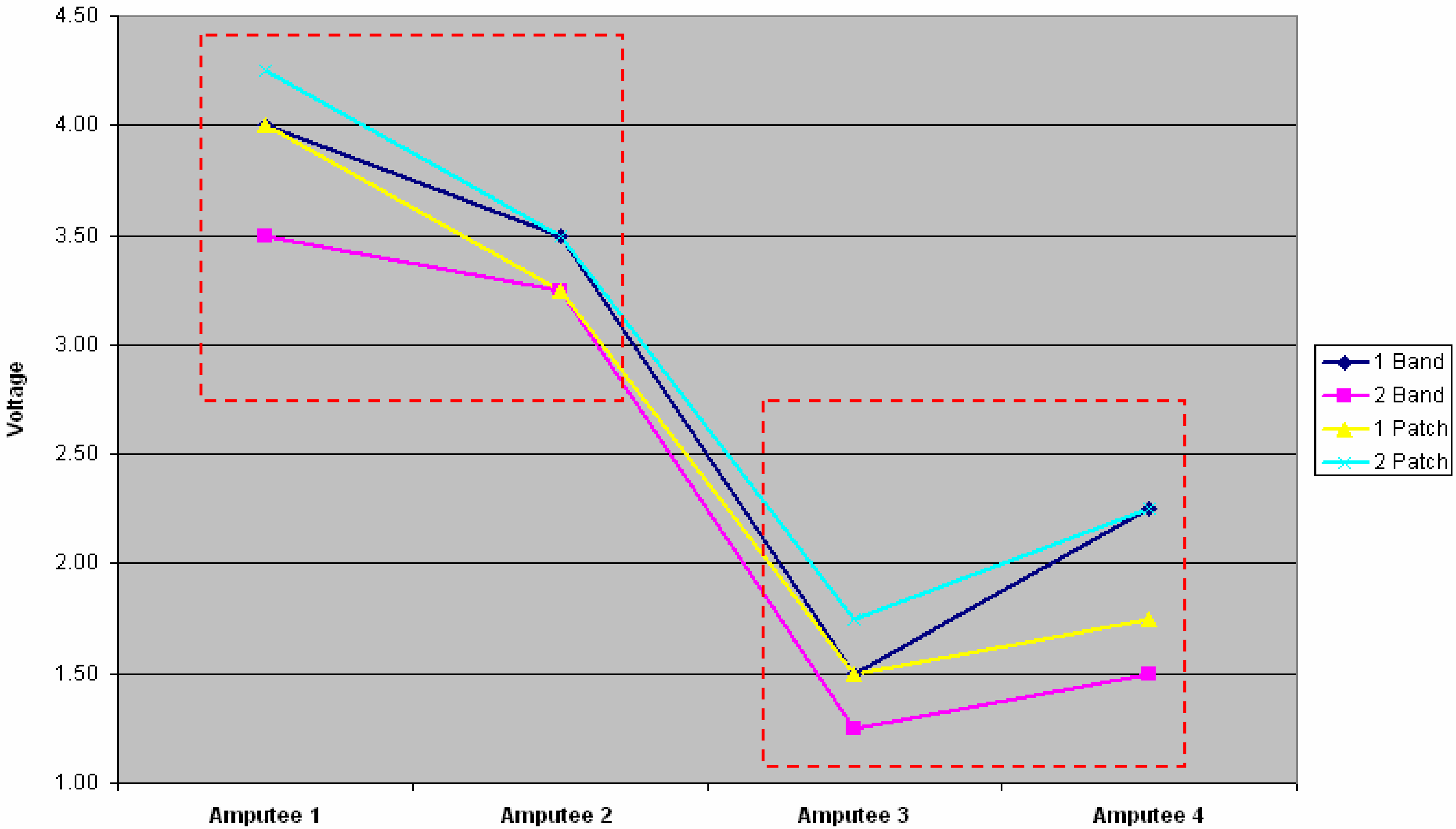


Optimal Potential in 1 Band Configuration for all Amputees

Results: Electrode Recommendations

	Amputee 1	Amputee 2	Amputee 3	Amputee 4
1 Band	4.00 V	3.50 V	1.50 V	2.25 V
2 Band	3.50 V	3.25 V	1.25 V	1.50 V
1 Patch	4.00 V	3.25 V	1.50 V	1.75 V
2 Patch	4.25 V	3.50 V	1.75 V	2.25 V

Results: Electrode Recommendations



Results: Does Bone Mineral Density Matter?

Bone: 0.02 to 0.01 S/m

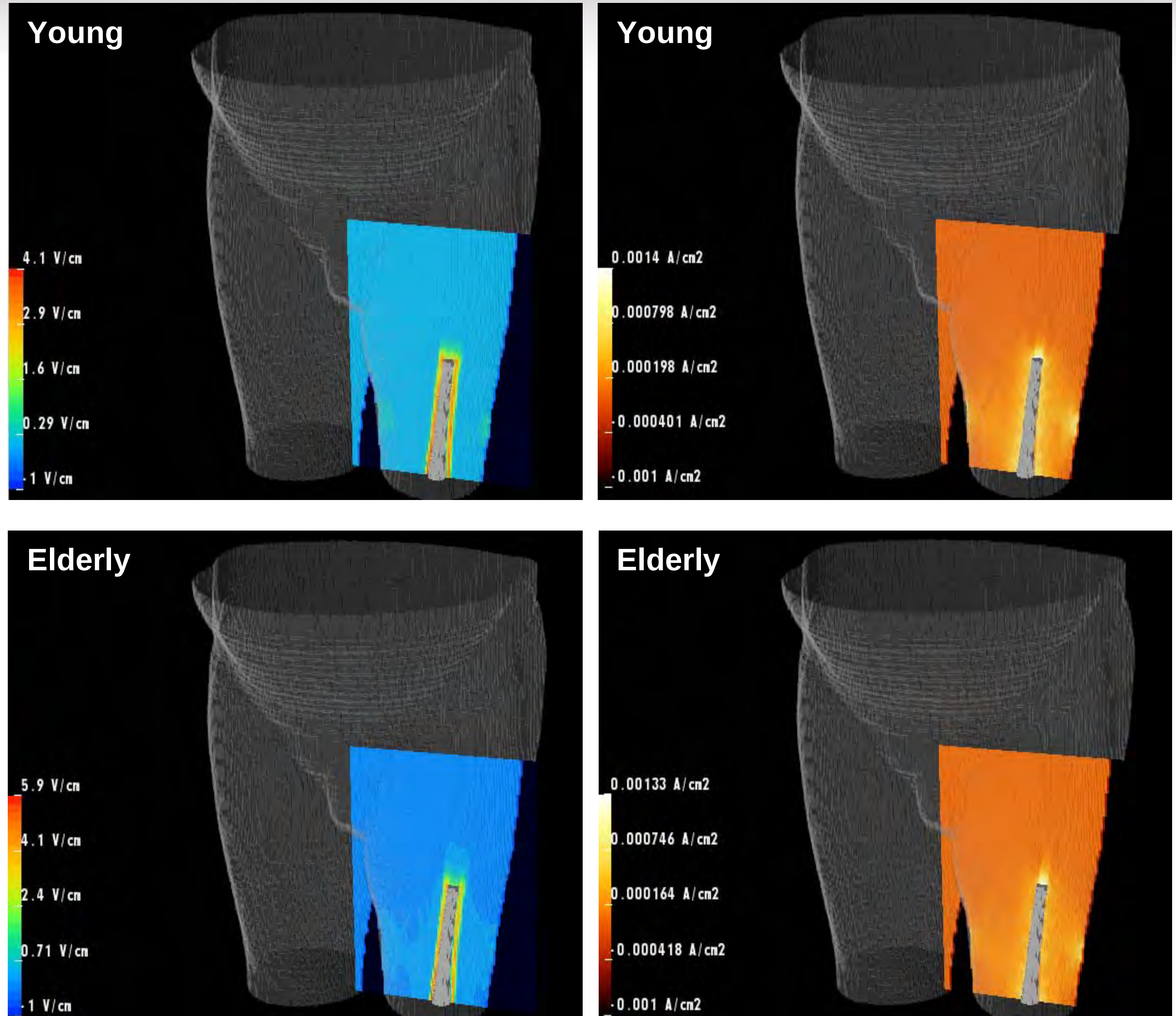
- **Amputee 1 – Young Patient**
  - $J = \sigma E$
  - $0.0014\ \text{A/cm}^2 = \sigma \cdot 4.1\ \text{V/cm}$
  - $\sigma_{average} = 0.034\ \text{S/m}$

- **Amputee 1 – Elderly Patient**
  - $J = \sigma E$
  - $0.00133\ \text{A/cm}^2 = \sigma \cdot 5.9\ \text{V/cm}$
  - $\sigma_{average} = 0.023\ \text{S/m}$

- **Amputee 2**
  - $\sigma_{average:}$ 0.027 S/m to 0.020 S/m

- **Amputee 3**
  - $\sigma_{average:}$ 0.084 S/m to 0.070 S/m

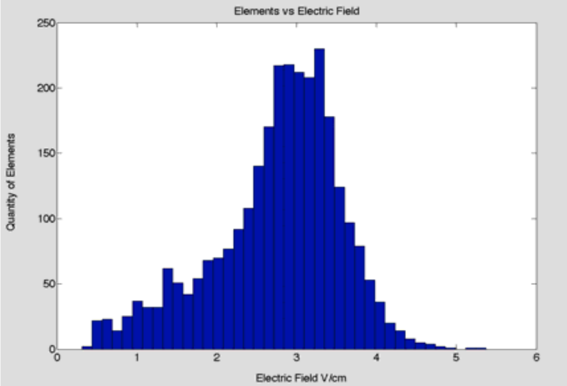
- **Amputee 4**
  - $\sigma_{average:}$ 0.055 S/m to 0.051 S/m



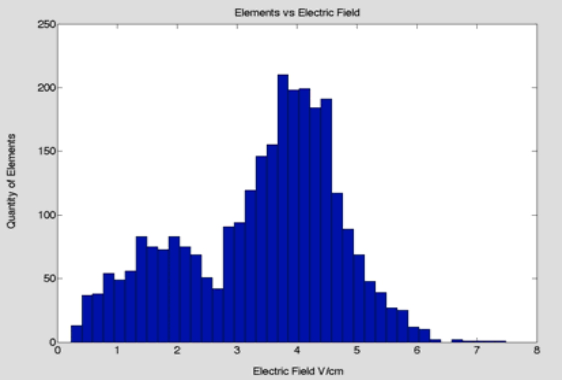
16. Nyman, J.S. et al. (2006). *J Biomech*. **39**(5): p. 931-8.
17. Ke, Z. et al. (2007). *Chin. Phys. Lett.*, *24*(1), 187-190.

Results: Does Bone Mineral Density Matter?

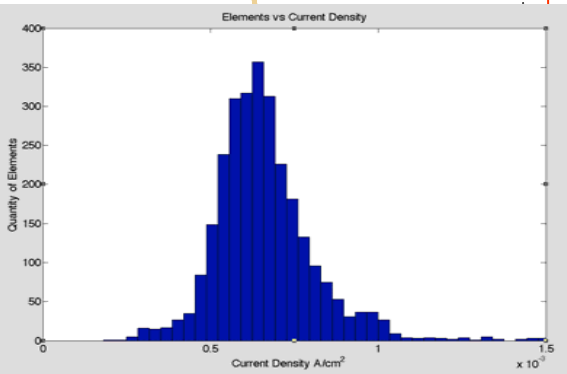
- **Amputee 1**
  - $\sigma_{average}$ = 0.034 S/m to 0.023 S/m
- **Amputee 2**
  - $\sigma_{average}$ = 0.027 S/m to 0.020 S/m
- **Amputee 3**
  - $\sigma_{average}$ = 0.084 S/m to 0.070 S/m
- **Amputee 4**
  - $\sigma_{average}$ = 0.055 S/m to 0.051 S/m
- **What caused this?**
  - Increased resistivity → decreased current density
  - Voltage divider



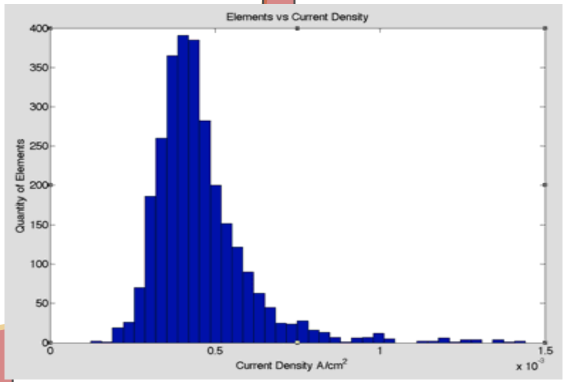
Young Patient 1 Electric Field Distribution



Elderly Patient 1 Electric Field Distribution



Young Patient 1 Current Density Distribution

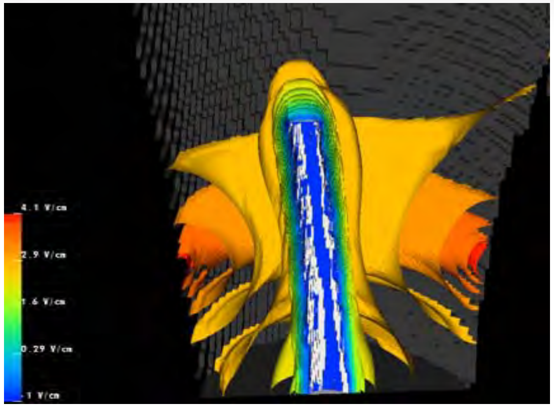


Elderly Patient 1Current Density Distribution

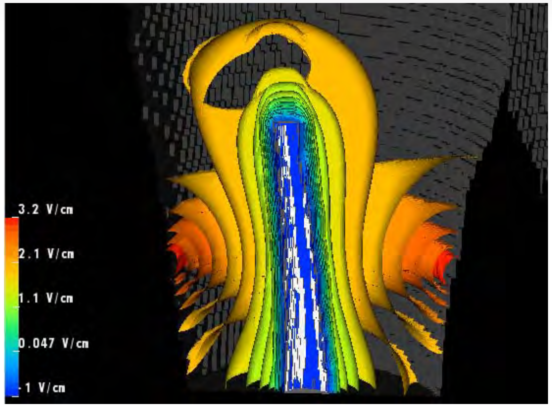
Results: Does Muscle Orientation Matter?

Muscle: 0.25 to 0.10 S/m

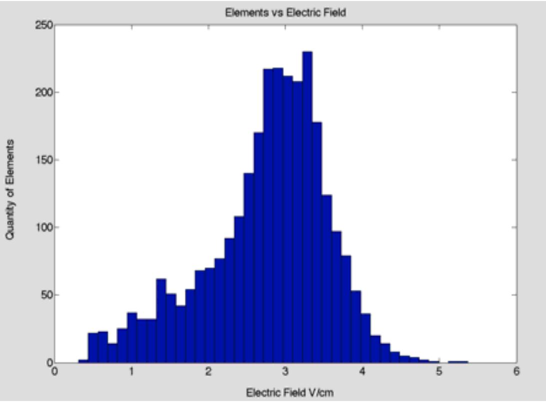
- **Amputee 1 – Longitudinal Muscle**
  - $J = \sigma E$
  - $0.0014 \text{ A/cm}^2 = \sigma \cdot 4.1 \text{ V/cm}$
  - $\sigma_{average} = 0.034 \text{ S/m}$
- **Amputee 1 – Transverse Muscle**
  - $J = \sigma E$
  - $0.00124 \text{ A/cm}^2 = \sigma \cdot 3.2 \text{ V/cm}$
  - $\sigma_{average} = 0.039 \text{ S/m}$
- **Amputee 2**
  - $\sigma_{average:}$ 0.027 S/m to 0.034 S/m
- **Amputee 3**
  - $\sigma_{average:}$ 0.084 S/m to 0.087 S/m
- **Amputee 4**
  - $\sigma_{average:}$ 0.055 S/m to 0.053 S/m



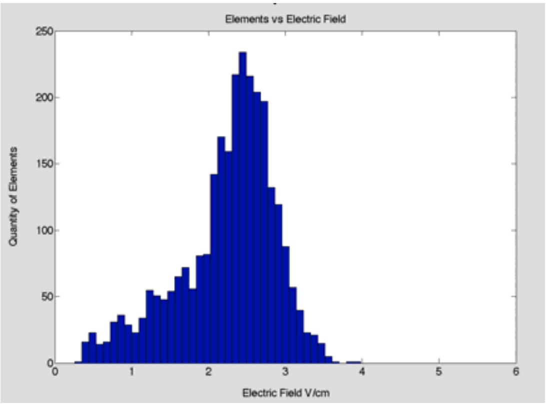
Electric Field 3D Representation:
Subject 1 Longitudinal Muscle



Electric Field 3D Representation:
Subject 1 Transverse Muscle



Electric Field Distribution:
Patient 1 Longitudinal Muscle



Electric Field Distribution:
Patient 1 Transverse Muscle

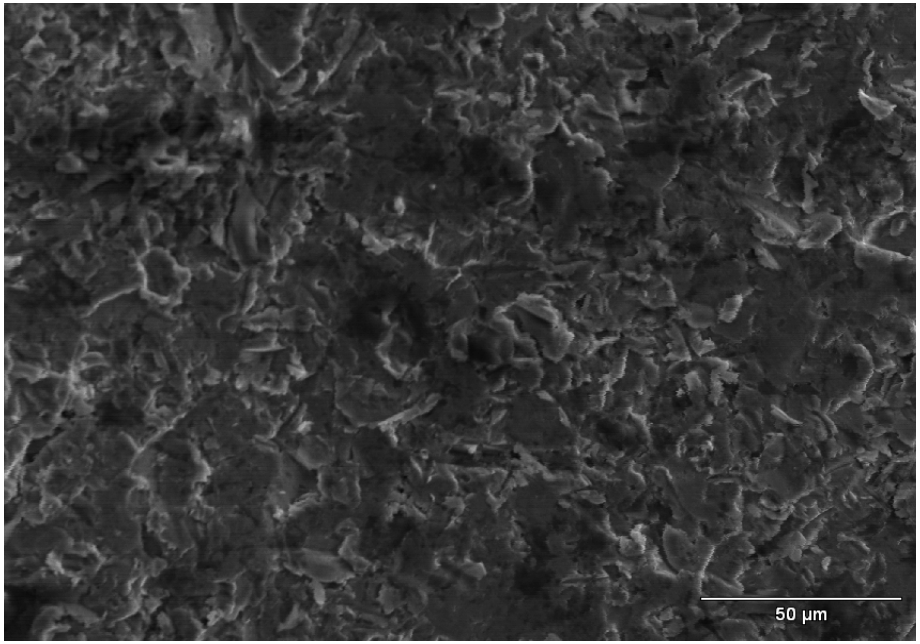
Conclusion

- All null hypothesis rejected
- Variations due to anatomy / amputee type
- Bone mineral density vs. Muscle Orientation

Amputee Anatomical Differences

Future Application

- **Implant Porosity**
  - Conductivity and porosity have an inverse relationship[17]
- **Vascularity**
  - Resistivity of around bone approximately 80x less resistive[18]
- **Validation** of electrical model with in vivo electrode array
- **Model confirmation** with small animal model

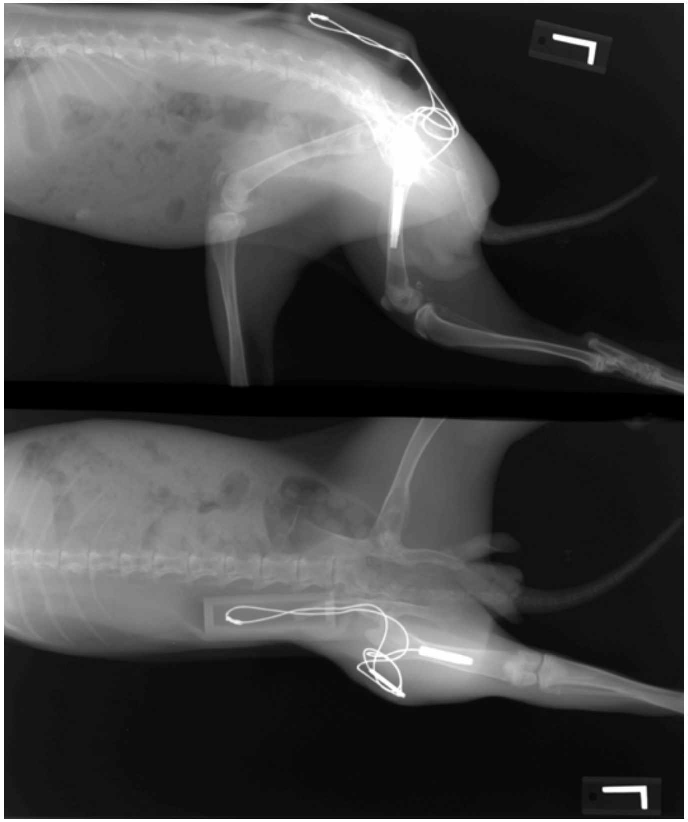


SEI with SEM of Implant Porosity

17. Ke, Z. et al. (2007). *Chin. Phys. Lett.*, *24*(1), 187-190.
18. Hassler CR et al. *Clin Orthop Relat Res* (1977) May(124):9-19.

In vivo Confirmation

- IACUC Approved Study
- Initiated: October 2008
- Goal: Improve localized bone response with controlled electrical stimulation
- Modality: DC Configuration



Control: 10.17.2008

Methods: Null Hypotheses

Hypotheses:

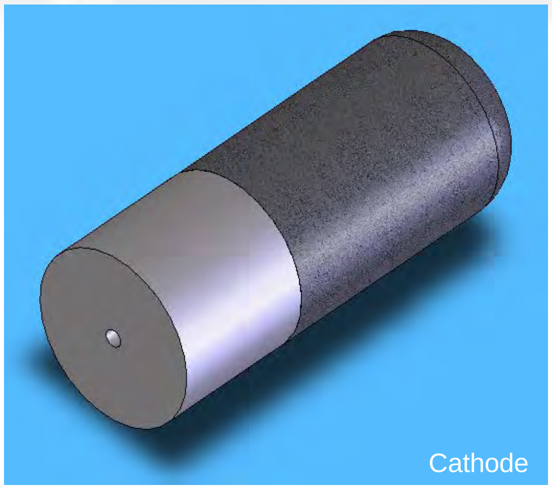
1. Electrical stimulation will not increase bone ongrowth when compared to the control group

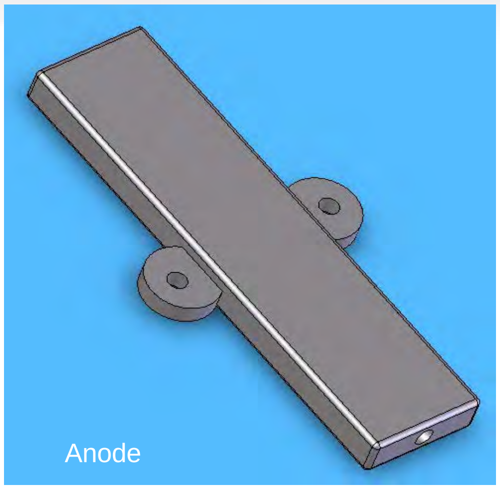
2. Electrical stimulation will not increase cortical thickness of the proximal femur when compared to the control group

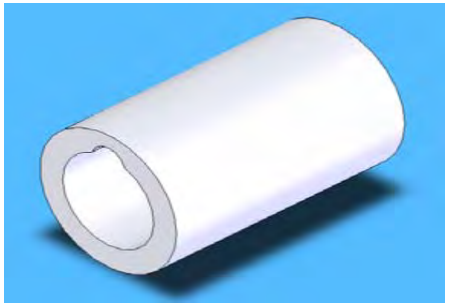
3. Osteoblast migration will not be visible in peri-cathode region

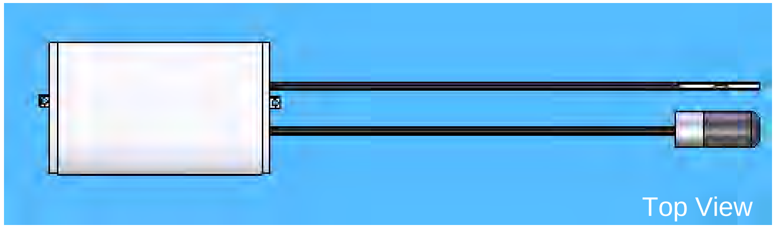
4. Implant removal will not require higher forces for the electrical stimulation group during mechanical testing

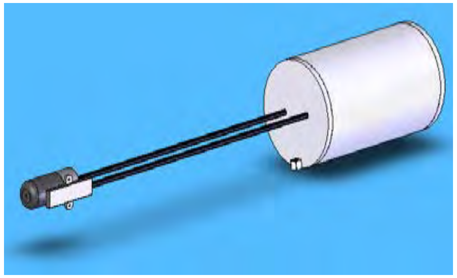
Methods: 3D Design Components

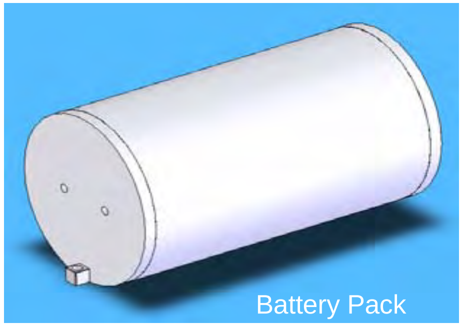








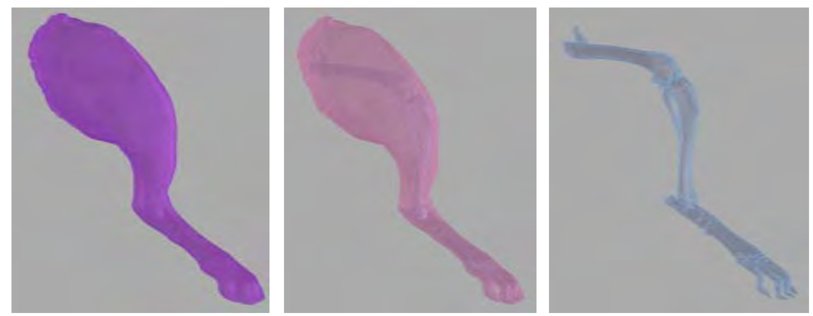




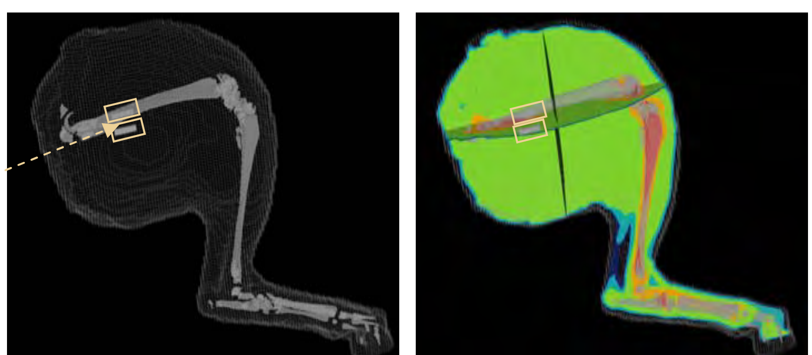
Methods: Electrical Stimulation Steps

- Controlled electric fields & current densities may expedite osseointegration and reduce rehabilitation rates
- IACUC Approved

Step 1: Obtain CT Files



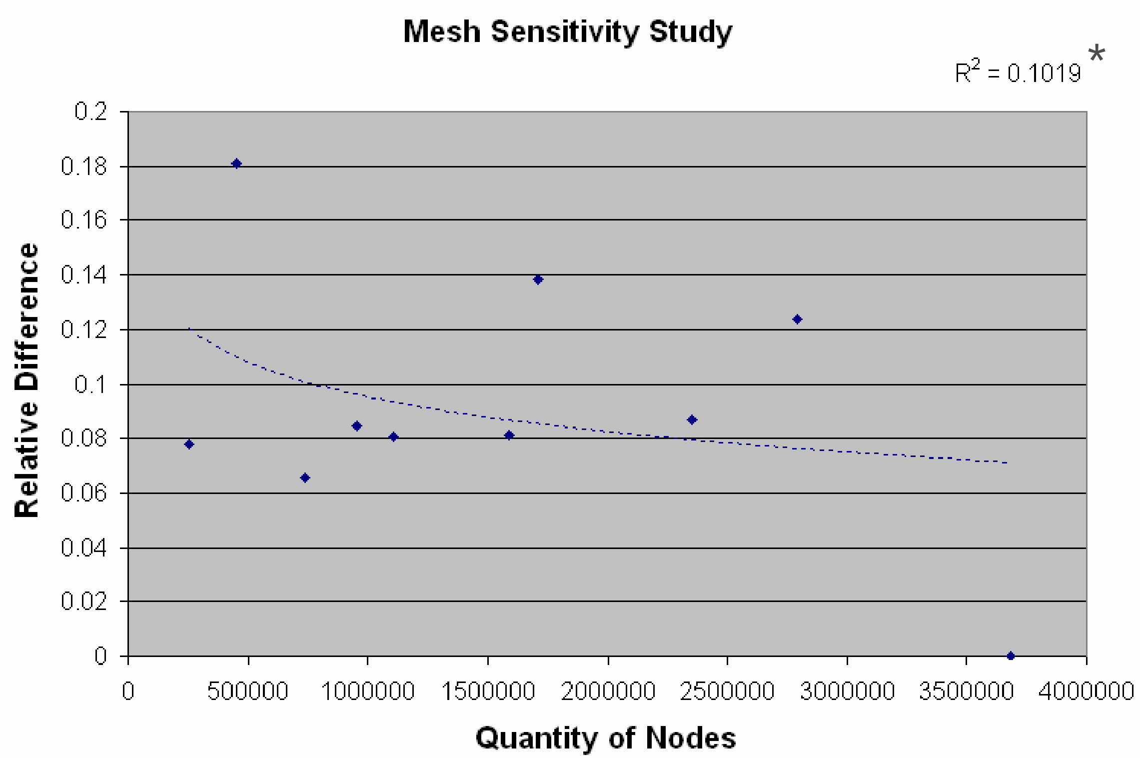
Step 2: Construct Segmentations



Step 3: Electrode Placement

Methods: Mesh Sensitivity

Mesh	# Elements	# Nodes	RD
125 125 100	236,923	256,955	0.0777
150 150 125	423,524	453,074	0.1808
175 175 150	693,458	734,842	0.0656
200 200 150	904,105	952,891	0.0844
200 200 175	1,053,357	1,108,277	0.0808
225 225 200	1,518,128	1,588,441	0.0812
250 250 175	1,641,348	1,713,507	0.1386
275 275 200	2,263,338	2,353,063	0.0870
300 300 200	2,691,912	2,792,024	0.1237
325 325 225	3,559,189	3,680,336	0.0000

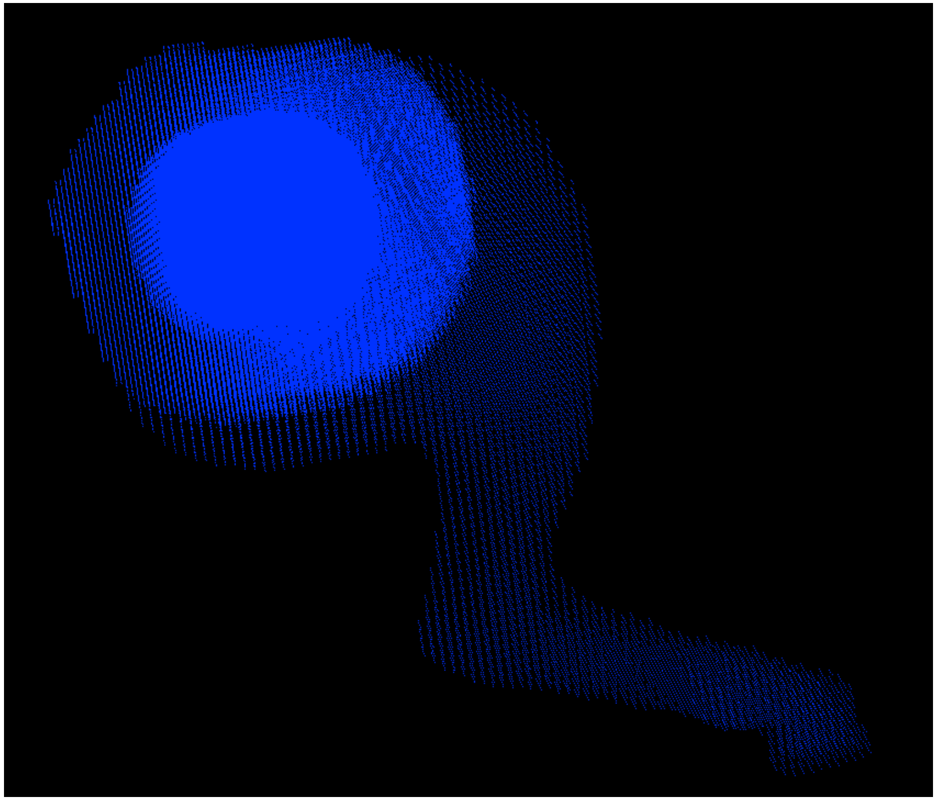


15. Hinkle , D. (2003). *Applied Statistics for the Behavioral Sciences* . Boston : Houghton Mifflin Company.

Denotes little to no positive correlation[15]

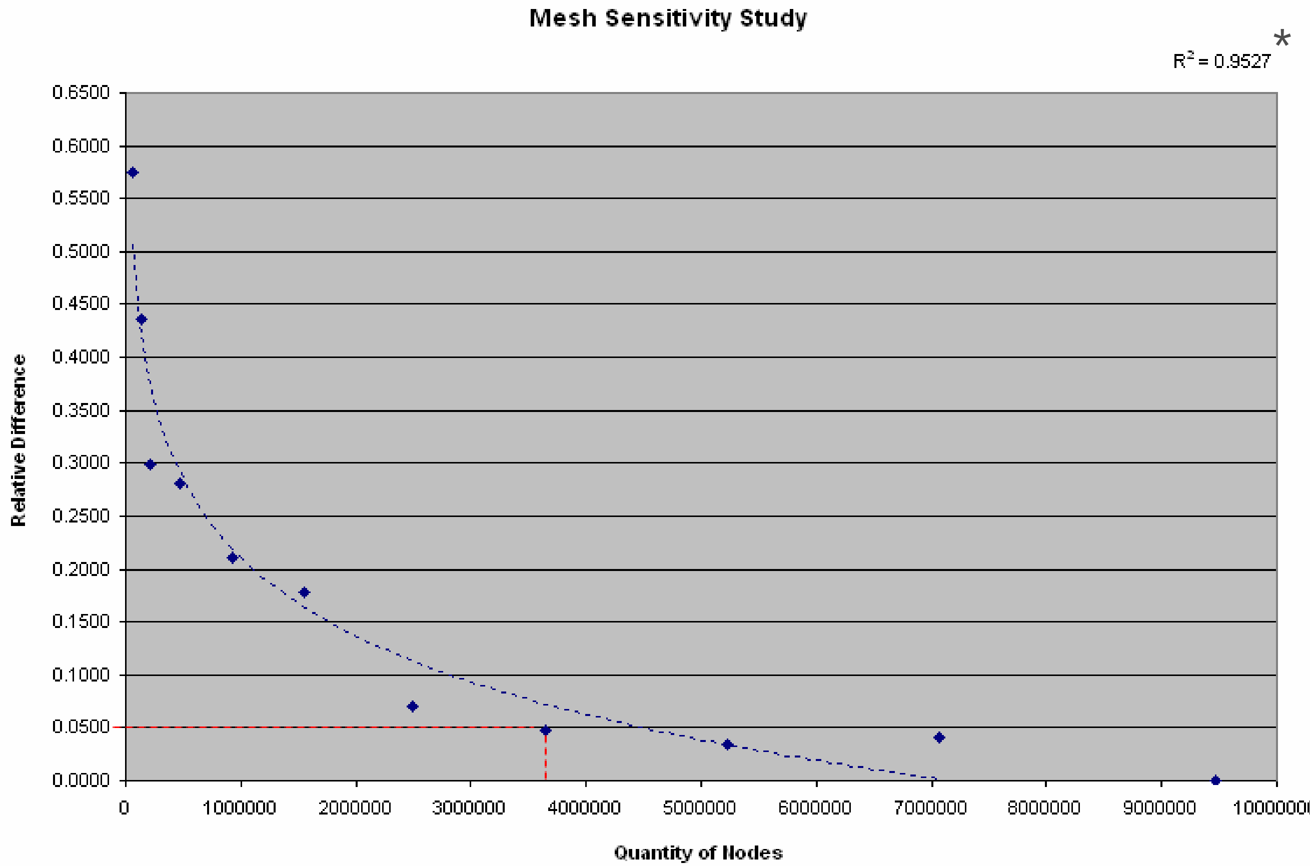
Methods: Mesh Refinements

- Increased mesh density between electrodes
- Reduced element density in z axis
- Mesh changed from hexahedral elements to tetrahedral elements due to the limb geometry



Methods: New Mesh Sensitivity

Mesh	# Elements	# Nodes	RD
50 50 10	339664	62582	0.5751
65 65 13	757569	136959	0.4357
75 75 15	1167283	209345	0.2982
100 100 20	2644620	469005	0.2812
125 125 25	5253734	924153	0.2111
150 150 30	8875334	1553662	0.1781
175 175 35	14282627	2490617	0.0703
200 200 40	20947529	3643599	0.0481
225 225 45	30095588	5222433	0.0346
250 250 50	40798231	7068842	0.0406
275 275 55	54699423	9462728	0.0000



15. Hinkle , D. (2003). *Applied Statistics for the Behavioral Sciences* . Boston : Houghton Mifflin Company.

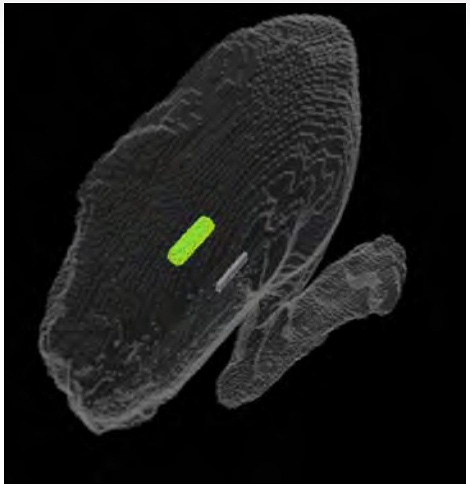
* Denotes very high positive correlation[15]

Methods: Selecting a Potential

Using a 200 200 40 Mesh…

Voltage [V]	EF [V/cm]	CD [mA/cm^2]	Current [mA]
1.00v	2.1	3.31	1.252
0.70V	1.5	2.32	0.876
0.65V	1.4	2.15	0.813
0.60V	1.3	1.99	0.751
0.55V	1.2	1.82	0.688
0.5V	1.1	1.66	0.626

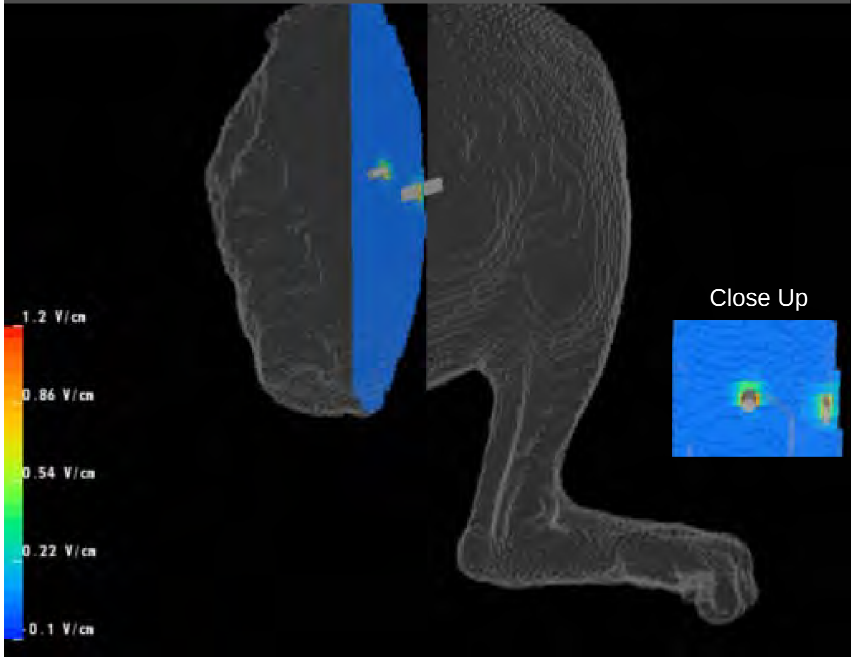
- Elements around Implant ~ 6,000
- Total Elements in Model ~ 20.9 million



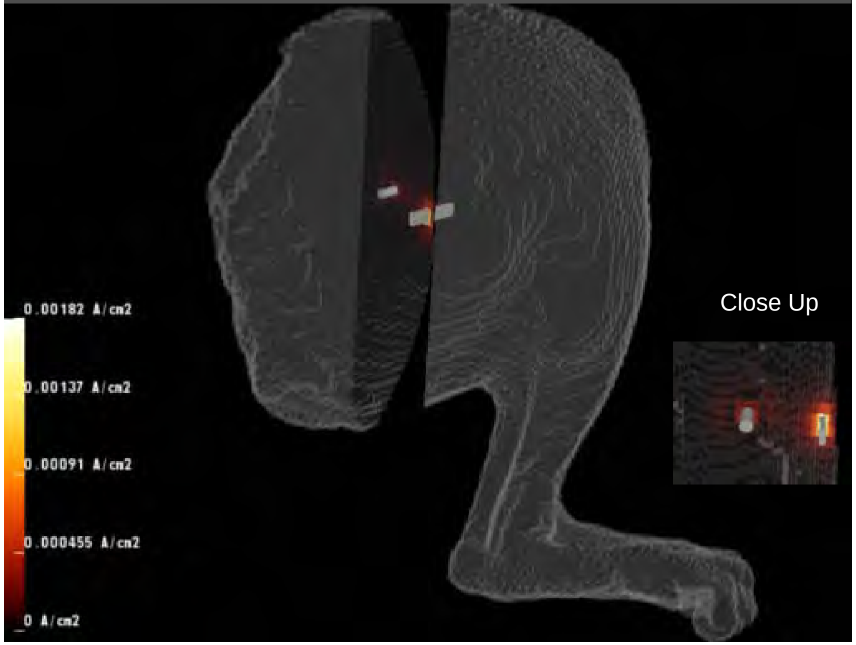
Rabbit Electrode Placement

Methods: Finite Element Analysis

Electric Field Distribution



Current Density Distribution



Methods: Battery Selection

<u>Capacity for t=3 weeks</u>

= 0.688mA * 21 days * 24 hours

= 346.75 mAh

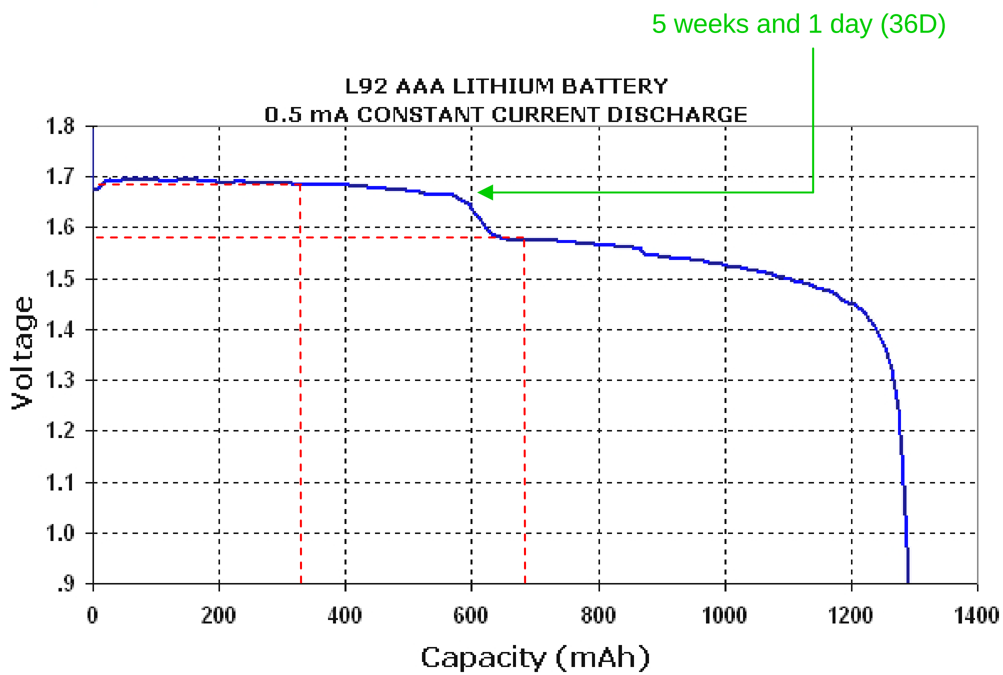
- Expected decrease in voltage 0.2 V or 1.18%

<u>Capacity for t=6 weeks</u>

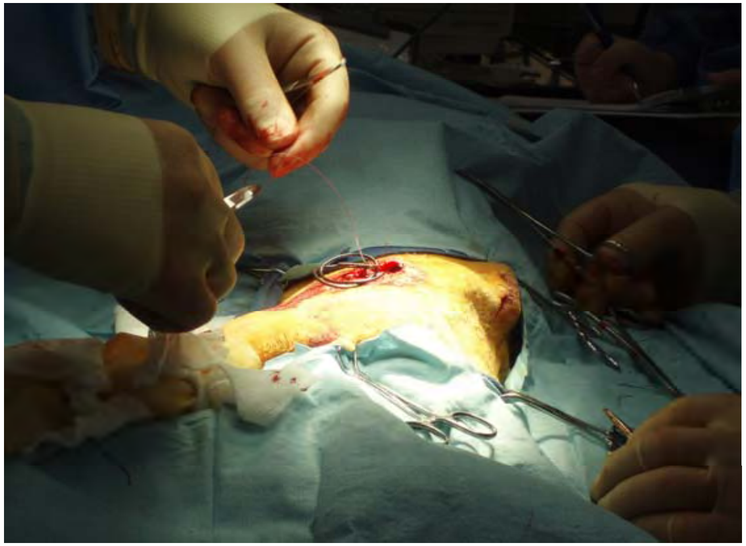
= 0.688 mA * 42 days *24 hours

=693.50 mAh

- Expected decrease in voltage 1.2V or 7.06%



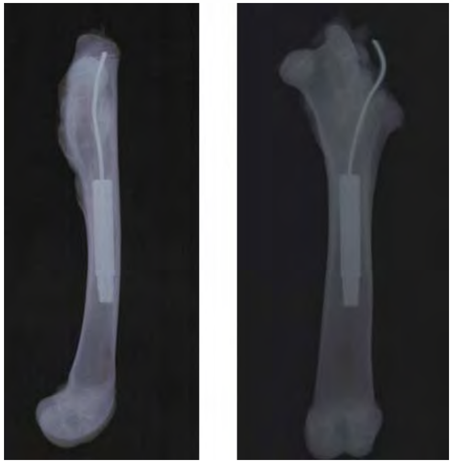
In vivo Confirmation



In vivo Confirmation

Preliminary Progress

- **Preliminary Work**
  - Gross Photography
  - Radiographs
- **Future Work**
  - Contact Radiographs
  - SEM
  - ABI
  - Tetracycline Labeling
  - H&E Stain
  - Mechanical Testing
  - Resonance Frequency Testing



Radiographs of Control Rabbit Post Euthanasia

Rabbit Battery Pack

Gross Measurement of Rabbit Femur

Pronounced Remodeling of Control Rabbit

Blood Collection Results

- **Low Counts**
  - WBC: 3.3 [6.4-14.1 thou/µL]
  - Absolute Lymphocyte: 2112 [3776-12267 /µL]
  - Total Protein: 4.6 [6.1-6.8 g/dl]
  - Potassium: 4.1 [4.8-5.8 mEq/L]

- **High Counts**
  - Alkaline Phosphate: 156 [106-134 iU/L]
  - Phosphorus: 6.4 [3.7-4.6 mg/dL]
  - Glucose: 124 [50-93 mEq/L]

- **Normal Counts**
  - RBC: 6.35 [6.01-7.63 mil/µL]
  - HGB: 13.4 [13.3-16.3 g/dL]
  - Calcium: 11.9 [5.8-14.4 mg/dL]

Post-Operative Electrical Rabbit
11.12.2008

Conclusions: Overall

- All null hypothesis in amputee study rejected
- Electrode band recommendation: 2 Band configuration
- Minor adjustments necessary on a patient specific basis
- Improved bone stock may be possible (In vivo results pending)

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Q & A

Additional Slides if Needed

- Specific Boundary Conditions
- Implant Surface Topography Analysis
- Influence of Dry vs. Hydrated Skin
- Battery Selection

Methods: SCIRun Computation

Boundary Conditions

1. $\varphi_{(r)}\big|_{\partial G_{bone}} = \varphi_{(r)}\big|_{\partial G_{muscle}}$ → Nodes are continuous between two tissue types

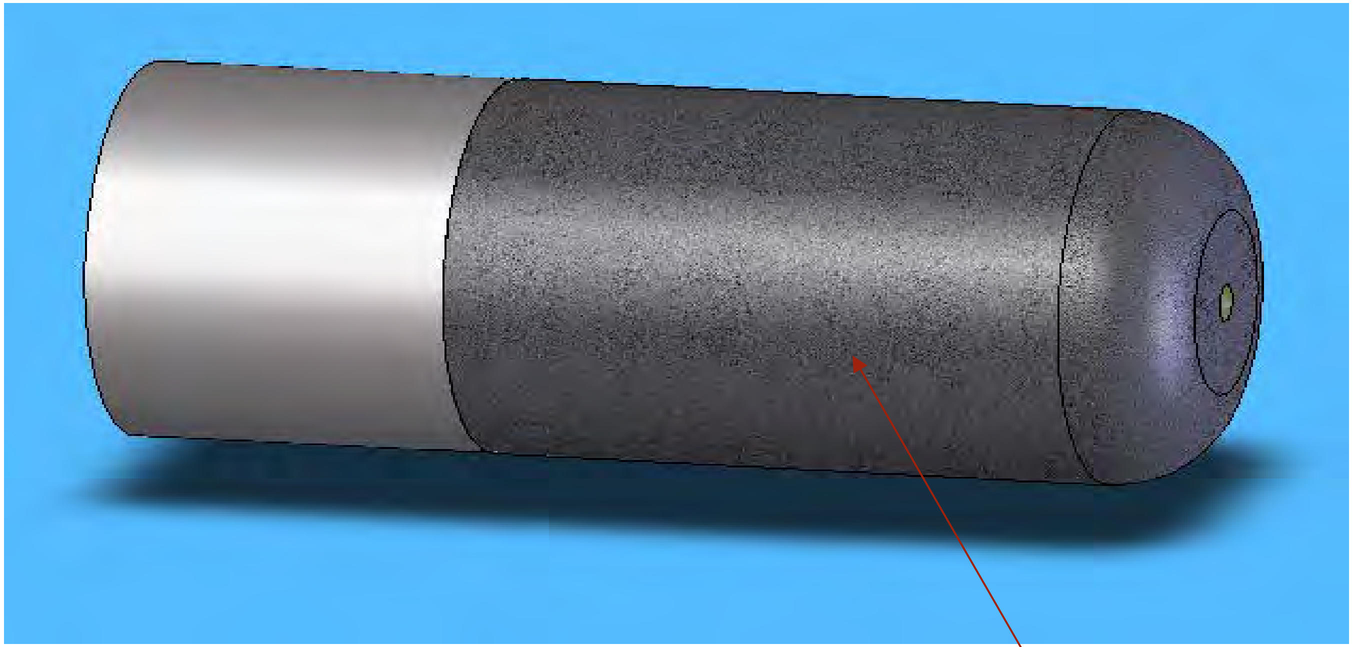
2. $\sigma_{bone} \nabla \varphi_{(r)}\big|_{\partial G_{bone}} \cdot \vec{n} = -\sigma_{muscle} \nabla \varphi_{(r)}\big|_{\partial G_{muscle}} \cdot \vec{n}$ → Current of the bone = current of muscle

3. $\sigma_{skin} \nabla \varphi_{(r)} = 0$ → Current flowing out of skin = 0

4. $\sigma \nabla \varphi \cdot \vec{n} = 0$ → Obeys Kirkoff's Voltage Law

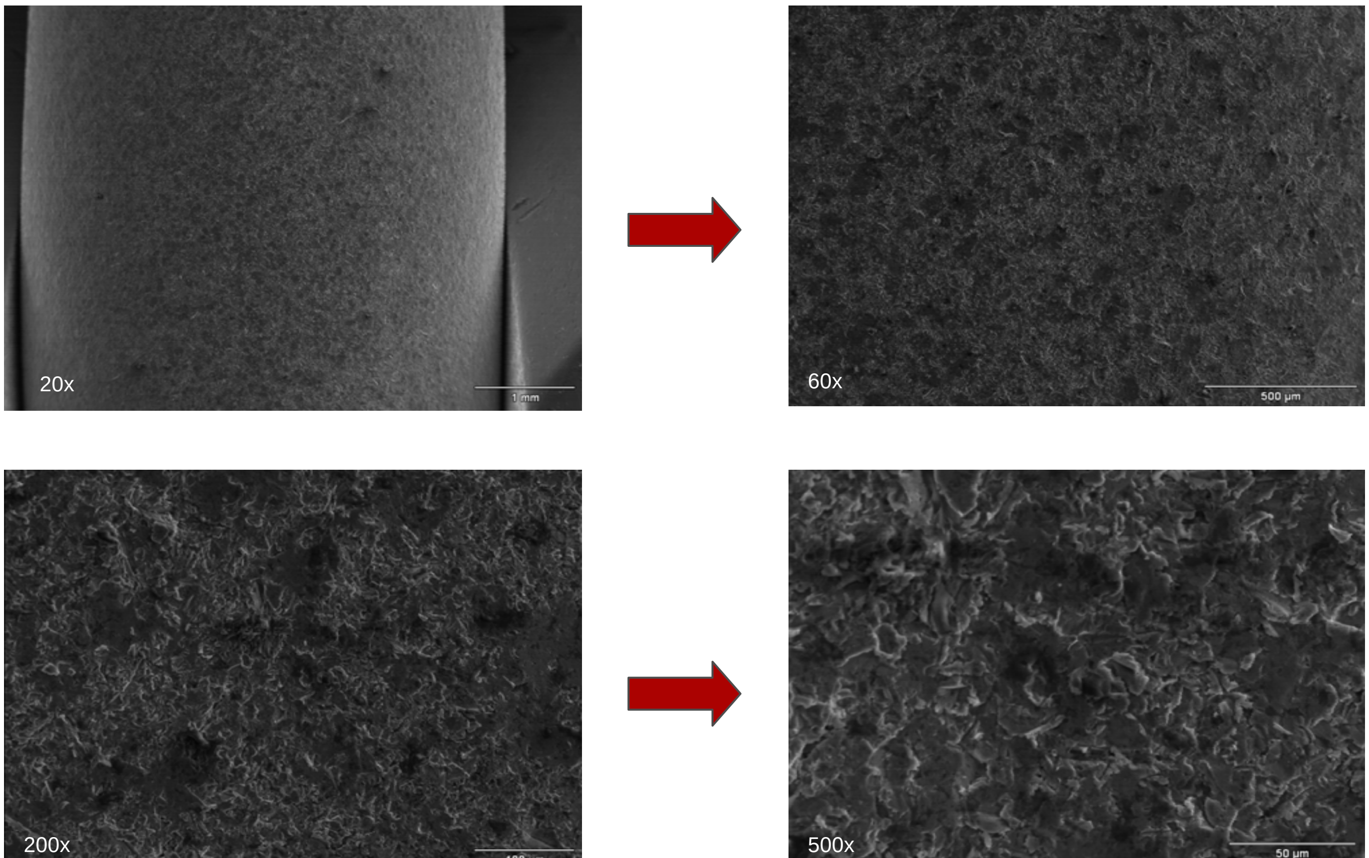
5. $\varphi =$ constant for electrodes → Constant potential at the electrodes

Methods: Grit Blasted Assessment with SEM

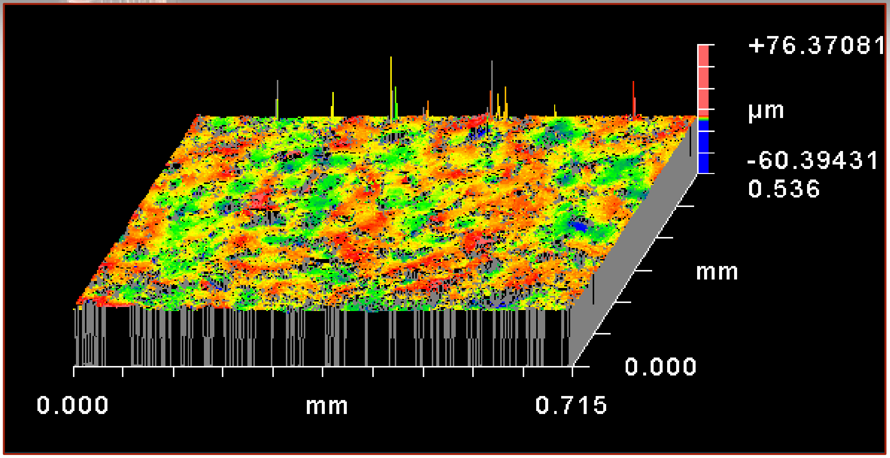


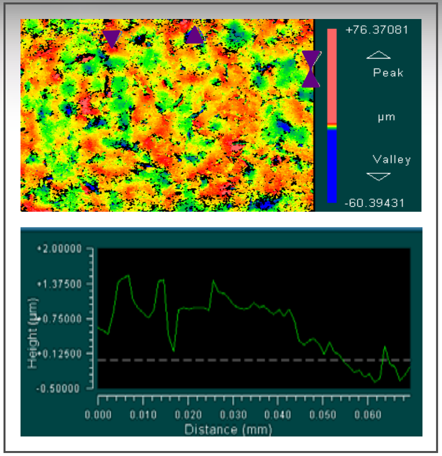
Let's Take a Closer Look…

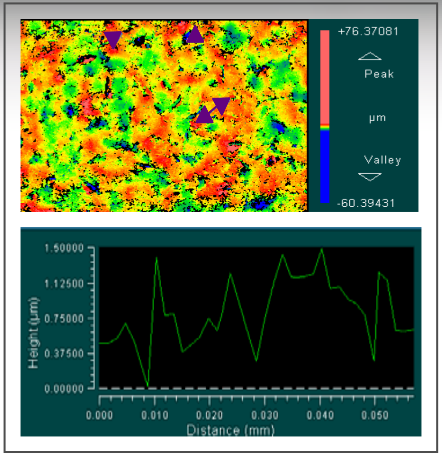
Methods: SEM Images of Grit Blasted

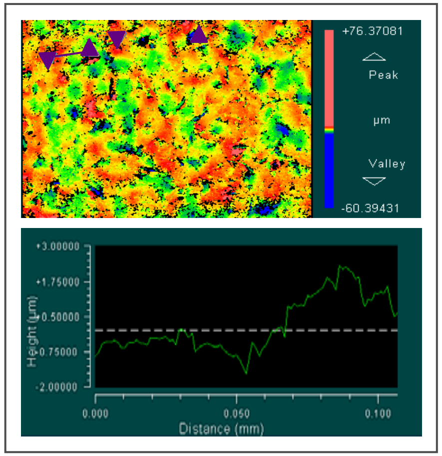


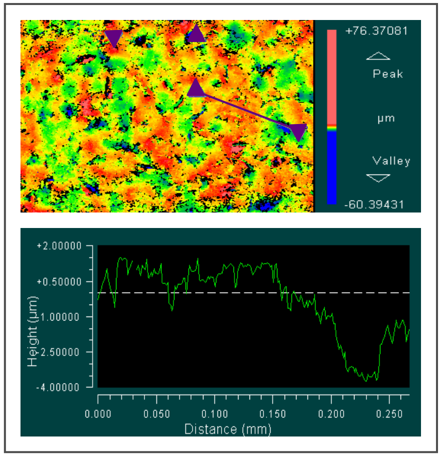
Methods: Optical Profilometer Assessment

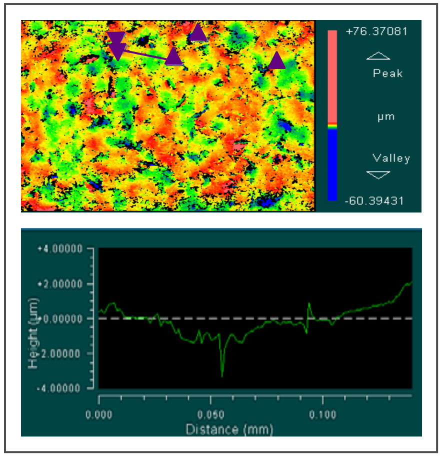


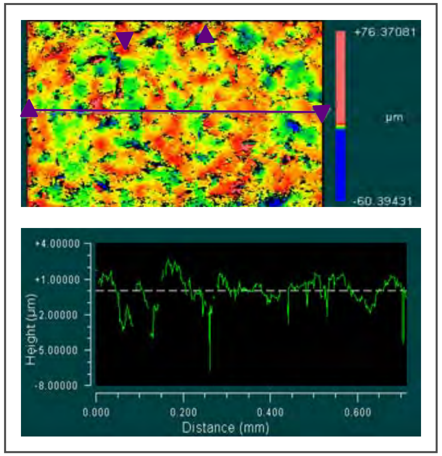








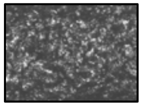




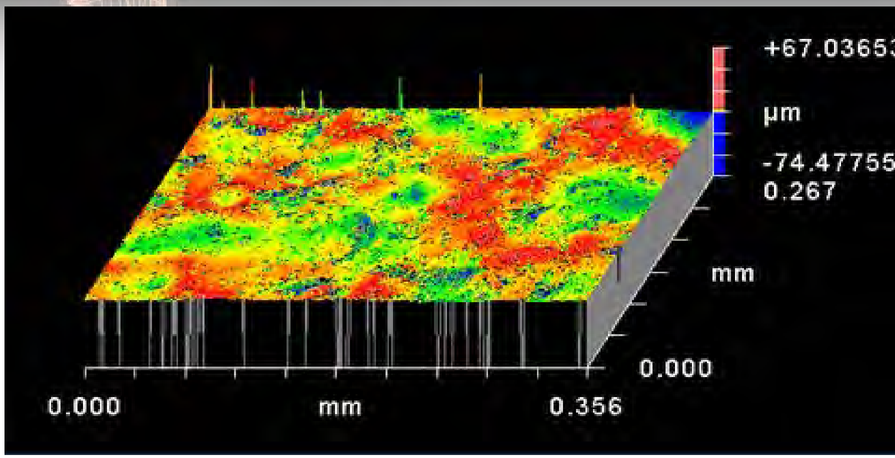
Results:

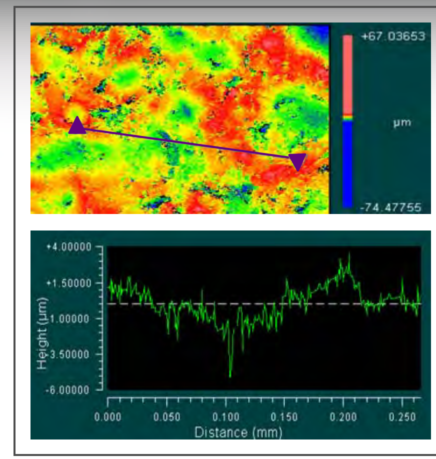
Ra ~ 0.841 μm

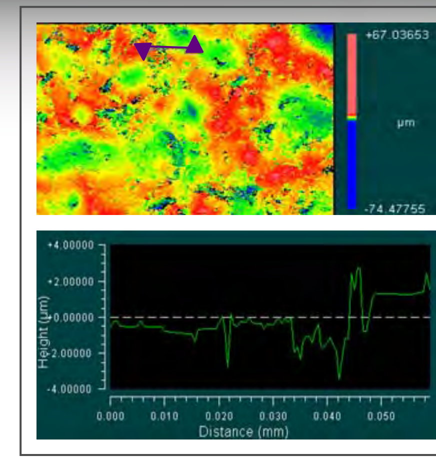
Apv ~ 2.8 μm to – 3 μm → (5.8 μm)

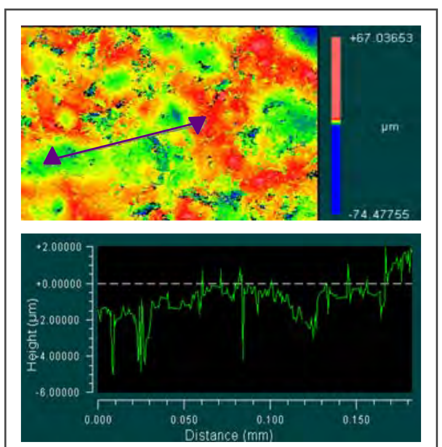


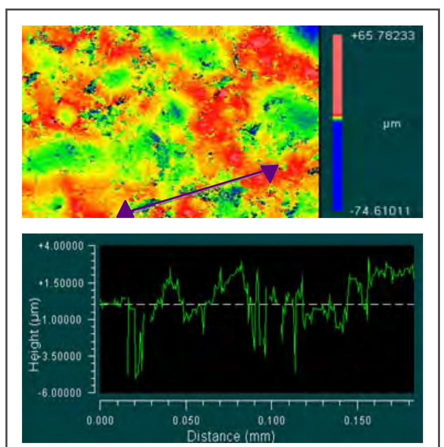
Methods: Optical Profilometer Assessment

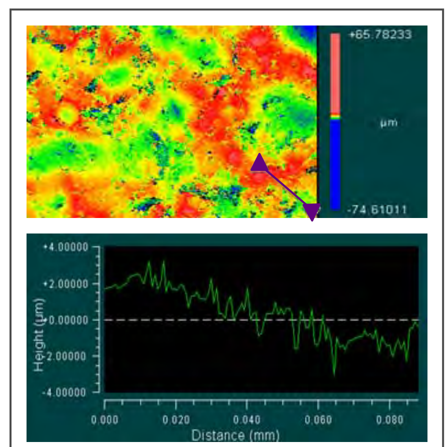


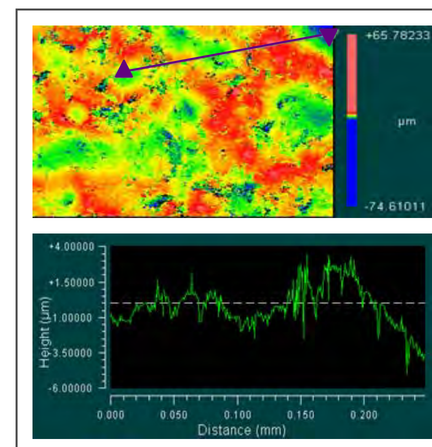












Results:

Ra ~ 1.024 µm

Apv ~ 3.7 µm to – 5.3 µm → (9 µm)