

Precision in Practice:

Exploring Bioinks and Adipose Grafting for the Next Generation of Soft Tissue Repair

Supported by an educational grant from Tides Medical

Faculty

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Faculty Disclosures

- **Michael N. Desvigne, MD, FACS, CWS, FACCWS, MAPWCA**
Advisory Board: Sanara Med Tech, Solventum, Tides Medical; Consultant/Speakers
Bureau: Aroa Biosurgery, Integra, Moleculight, Inc., MTF Biologics, Sanara Med Tech,
Solventum, Tides Medical, Urgo Medical North America.
- **Vincent Li, MD, MBA**
Nothing to disclose in relation to this activity
- **Munier Nazzal, MD, MBA, M Ed, FRCS, FACS, DFSVS, FACCWS**
Nothing to disclose in relation to this activity

Disclosures

- Faculty have been informed of the responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)
 - Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
 - This activity has been independently reviewed for balance

This continuing medical education activity includes device or medicine brand names for participant clarity purposes only. No product promotions or recommendations should be inferred.

Learning Objectives

- Explore the potential of micronized adipose tissue for regenerative medicine, including how tissue micronizing devices function and the composition, properties, and applications of bioinks in 3D bioprinting for soft tissue repair
- Assess current scientific research, device innovations, and clinical outcomes associated with the use of 3D-printed adipose tissue matrix grafts and future implications in wound care and reconstructive surgery
- Analyze real-world case studies demonstrating the application of adipose tissue grafting techniques across diverse wound types and clinical treatment settings

Adipose-Derived SVF-Enriched Bioink for Angiogenesis and Wound Healing

Vincent W. Li, MD, MBA

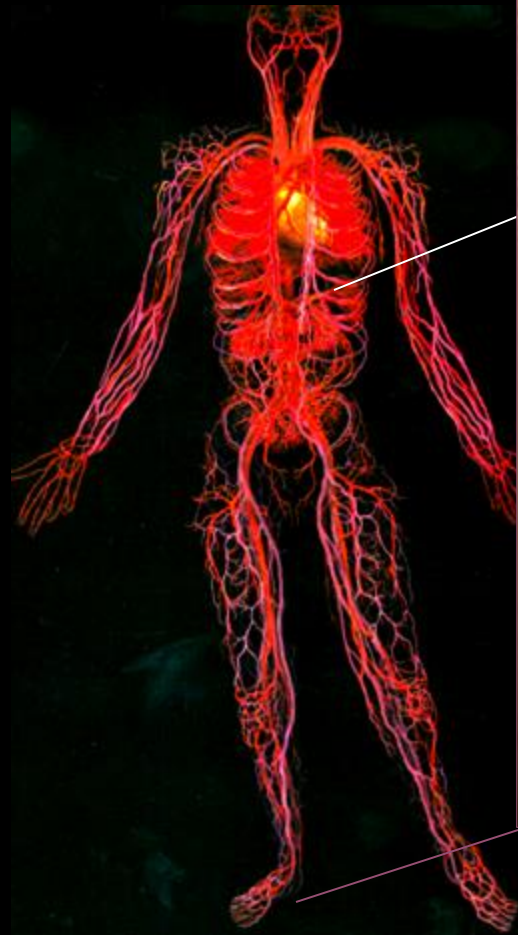
Scientific Director and COO, The Angiogenesis Foundation

Medical Director, Angiogenesis & Wound Healing Center, Mass General Brigham

Assistant Professor, Harvard Medical School

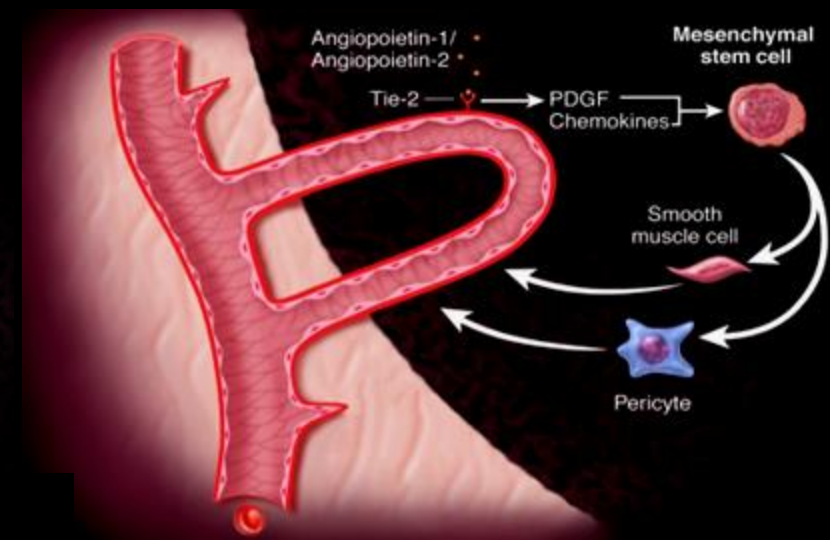
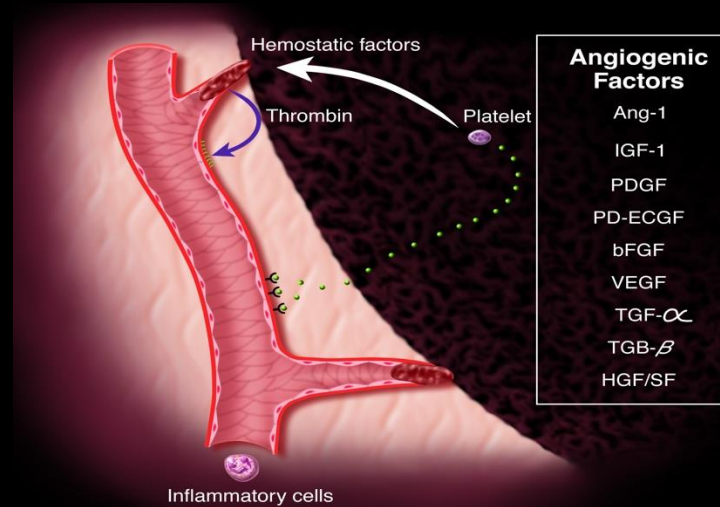
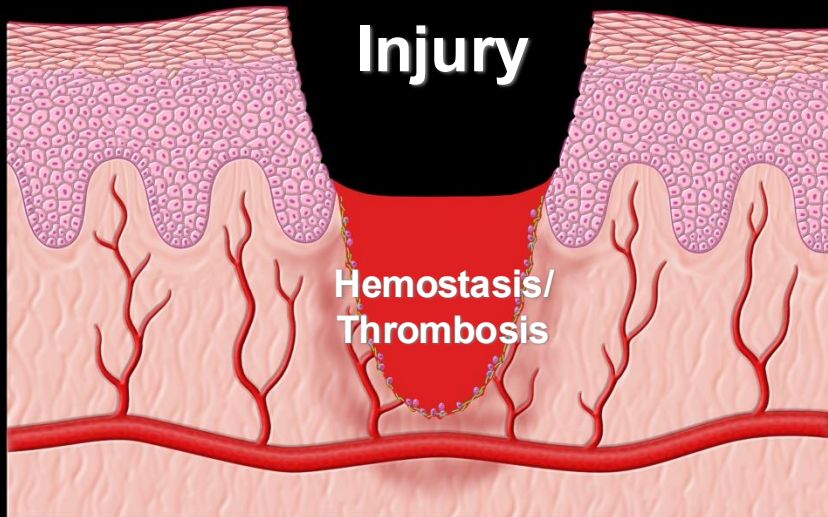
Boston, MA

Angiogenesis

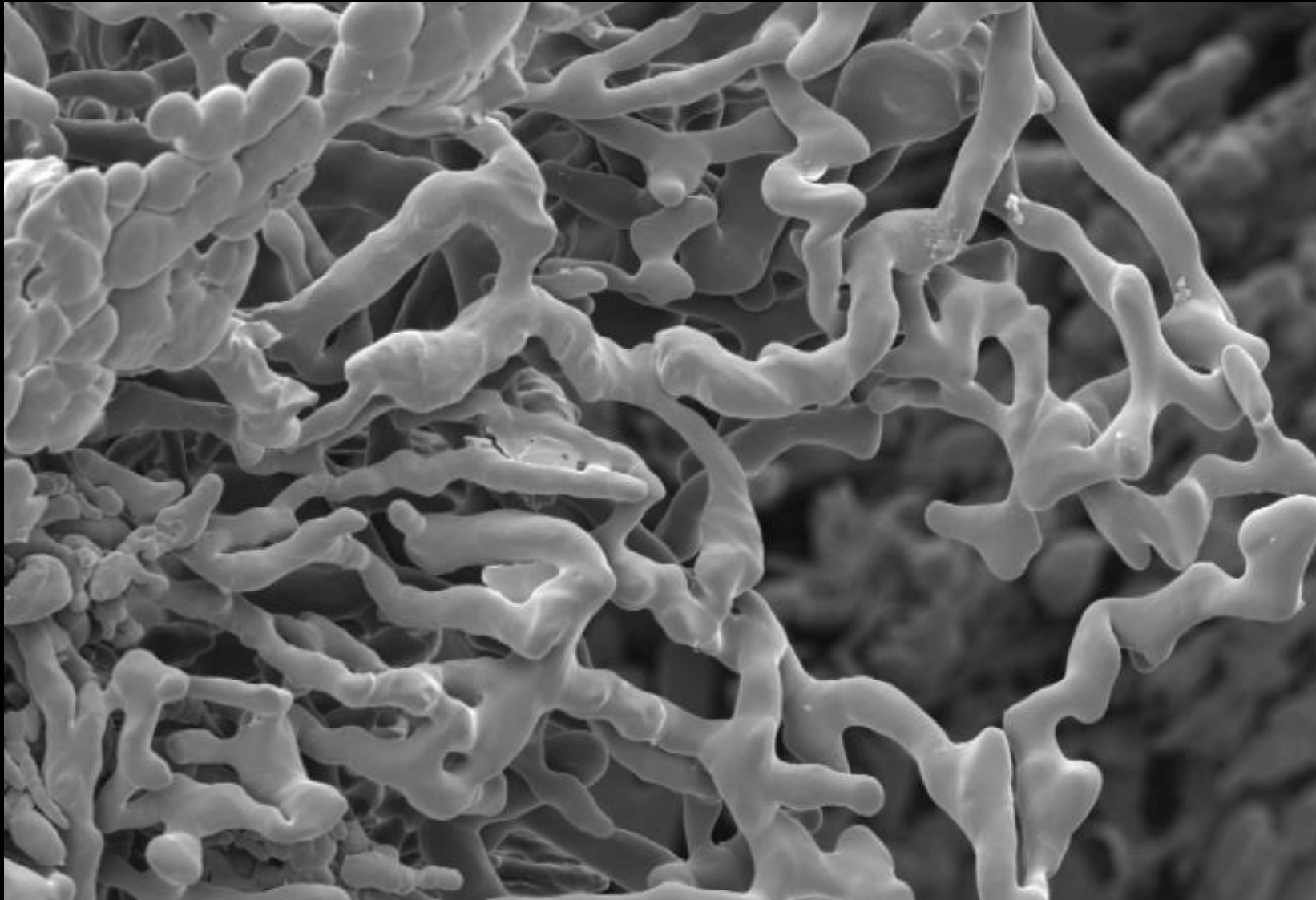


Required for Granulation...

Angiogenesis in Wound Healing

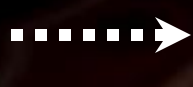


Vessels in the Wound Bed



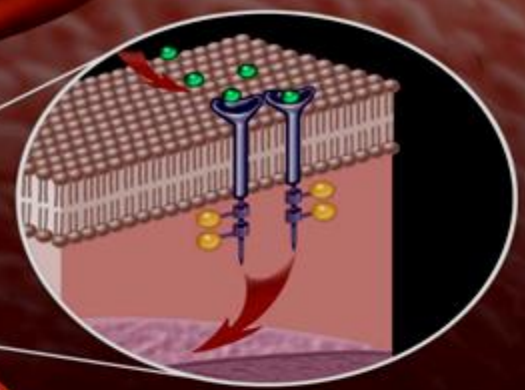
Wound Angiogenesis

Hypoxia/HIF1-alpha
Inflammation
Platelets



Angiogenic
Factors

Receptor
Binding



ARTERIO-VEINOUS
PATTERNING

INVASION

PROLIFERATION

MIGRATION

TUBE
FORMATION

VESSEL
MATURATION

Endothelial Progenitor
Cells (EPC)

HOMING

Smooth muscle cells
pericytes

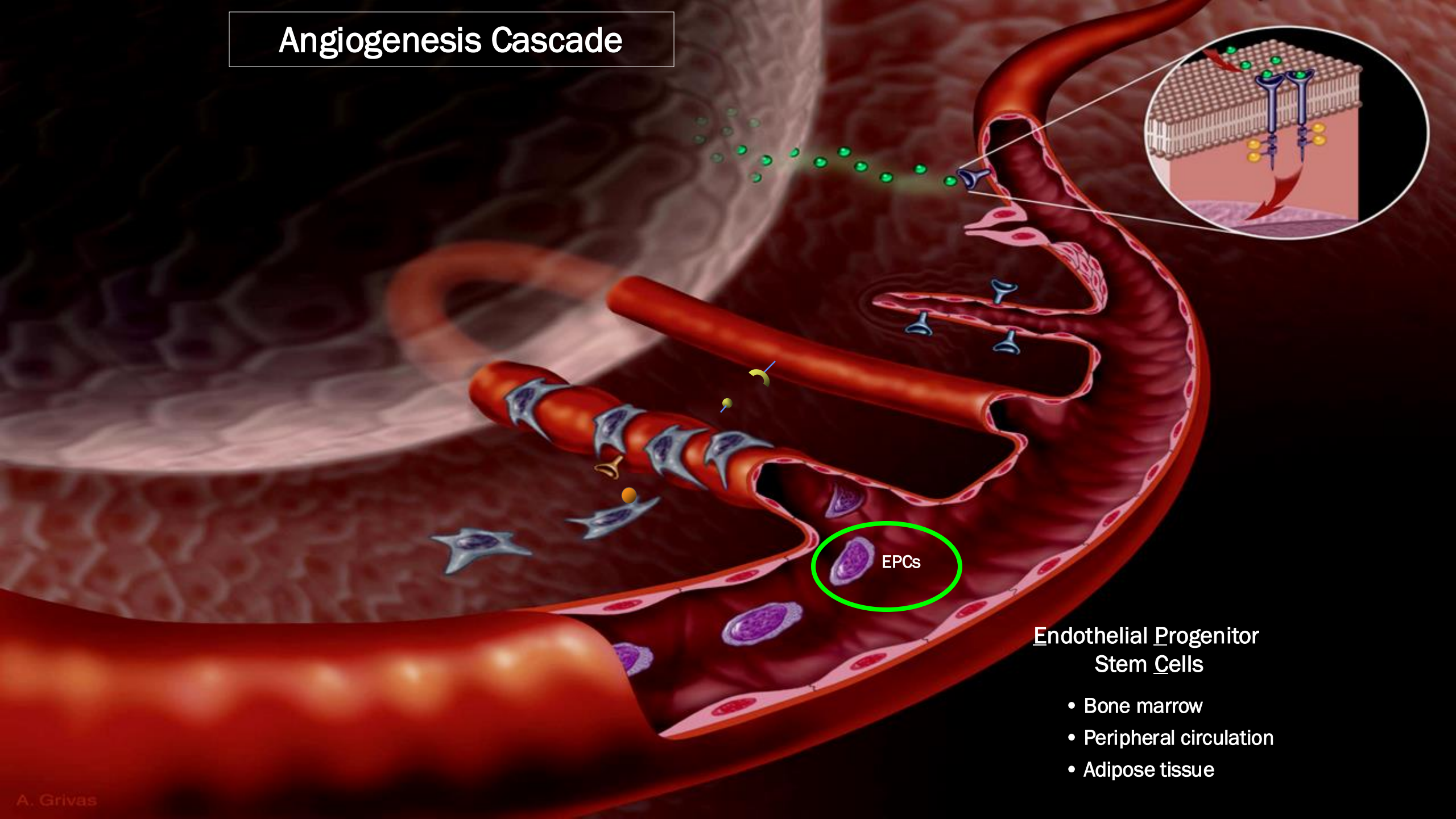
eph/EphB2

$\alpha_v\beta_3$

$\alpha_v\beta_5$

$\alpha_5\beta_1$

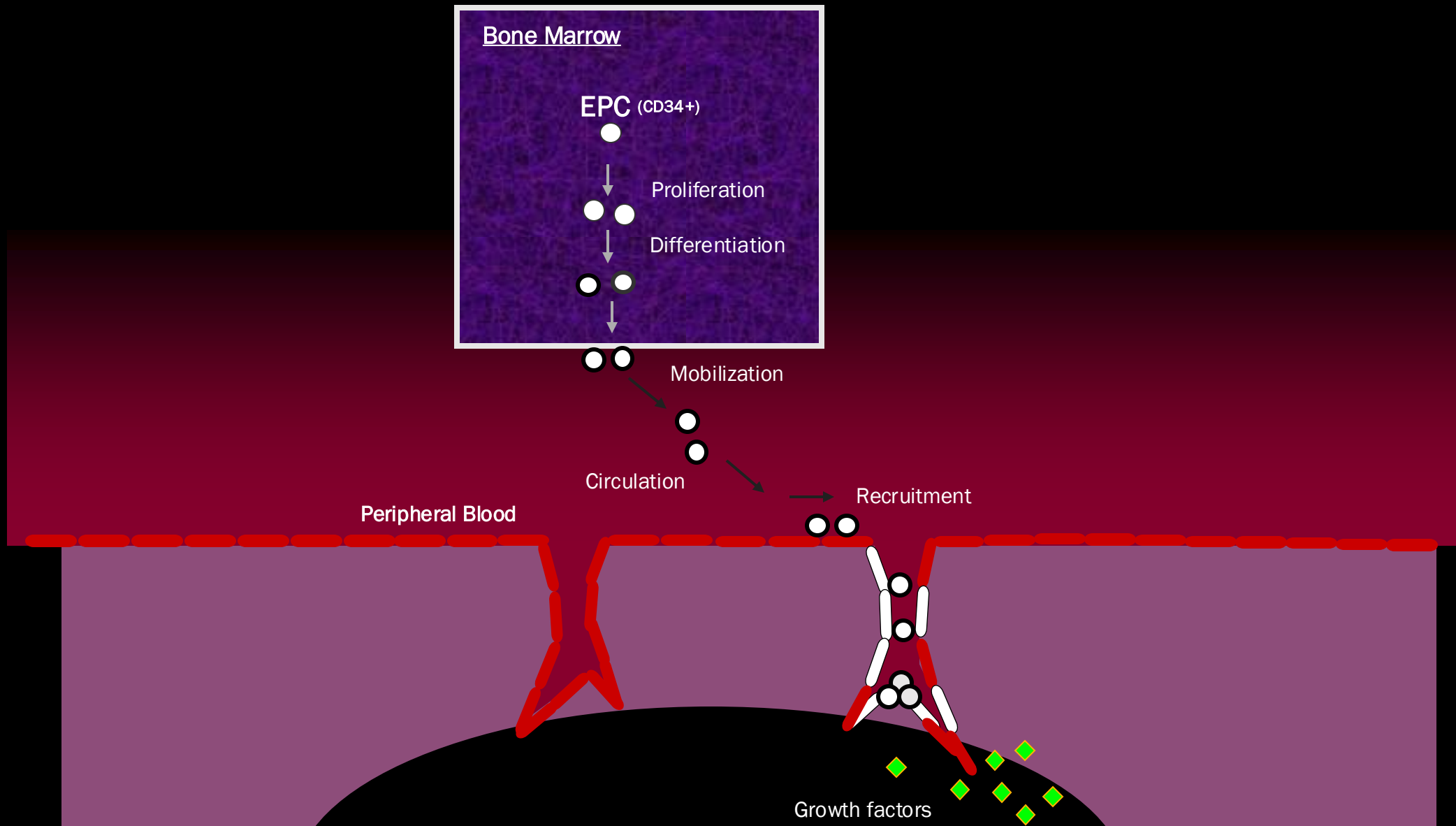
Angiogenesis Cascade



Endothelial Progenitor Stem Cells

- Bone marrow
- Peripheral circulation
- Adipose tissue

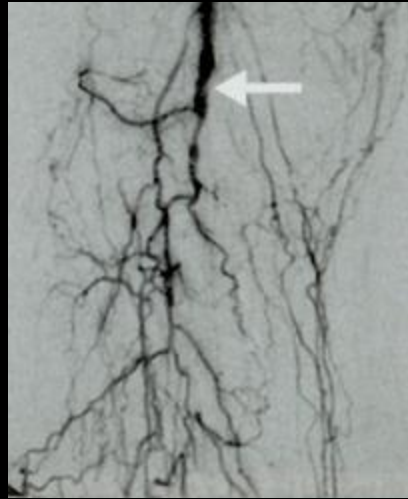
Endothelial Progenitor Cell Recruitment



Angiogenic Stem Cell-Based Therapy

Thigh

Before Treatment



24 Wks Post-Treatment



Harvest bone marrow-derived CD34⁺ / CD34⁻ cells



IM inject
2.8 X 10⁹ cells
into limb

Tibia



↑ ABI

↑ TcO₂

↓ Rest pain

Angiogenic Stem Cell-Based Therapy

Before Treatment



IM inject
 2.8×10^9 cells
→
Gastrocnemius

8 Wks Post-Treatment



At 24 wks, 15 of 20 (75%) patients
had salvage from toe amputation

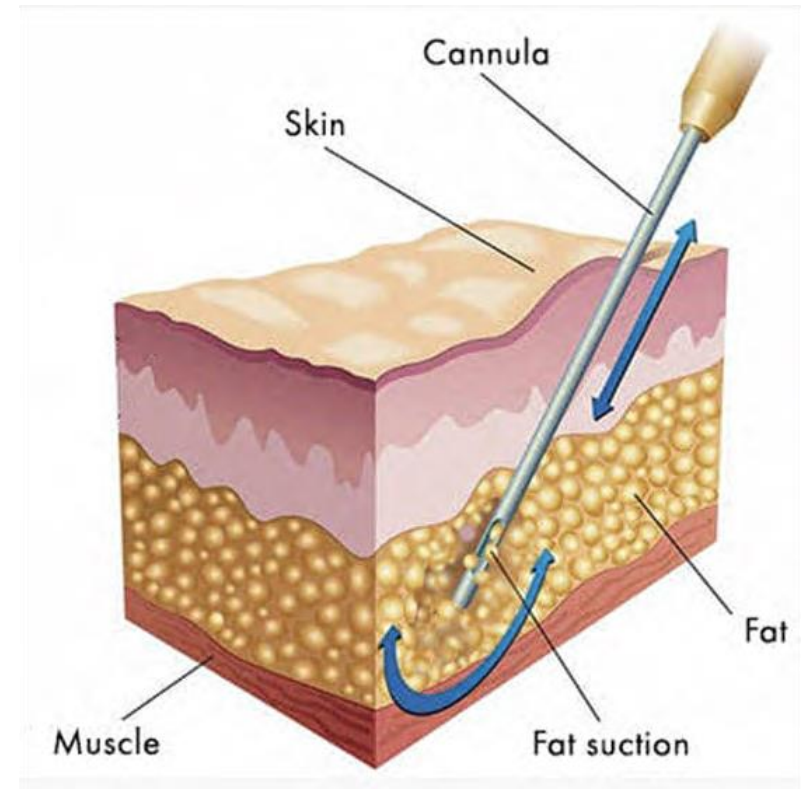
ADIPOSE TISSUE (FAT)



Abundant source of
angiogenic stem cells

Fat

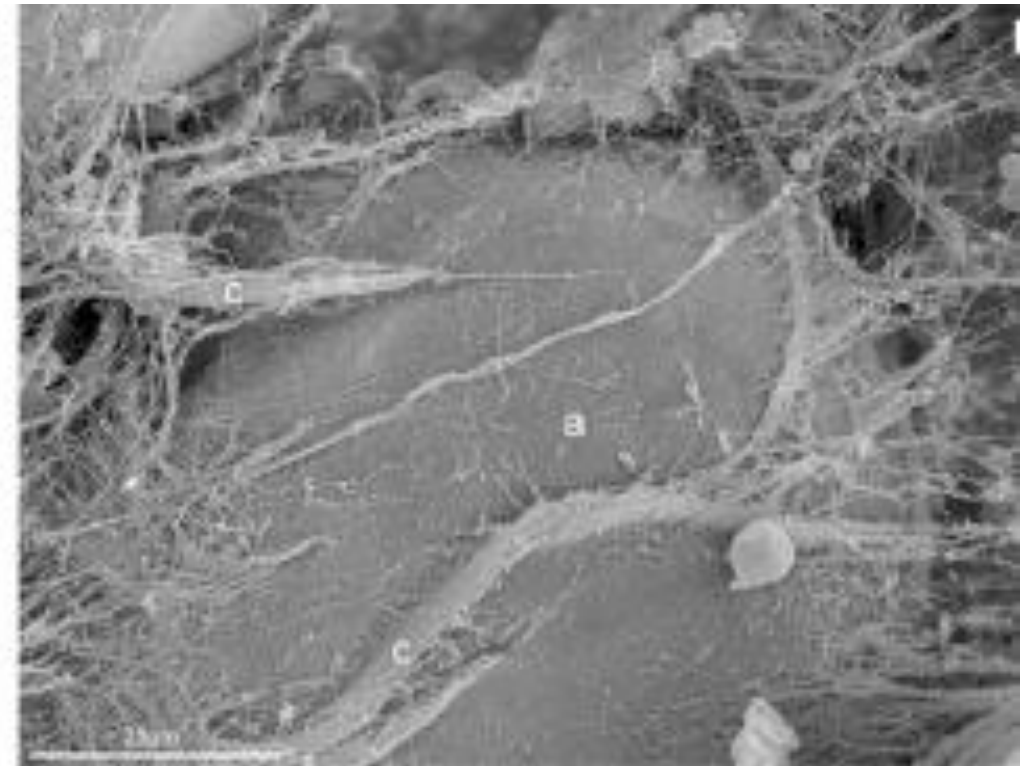
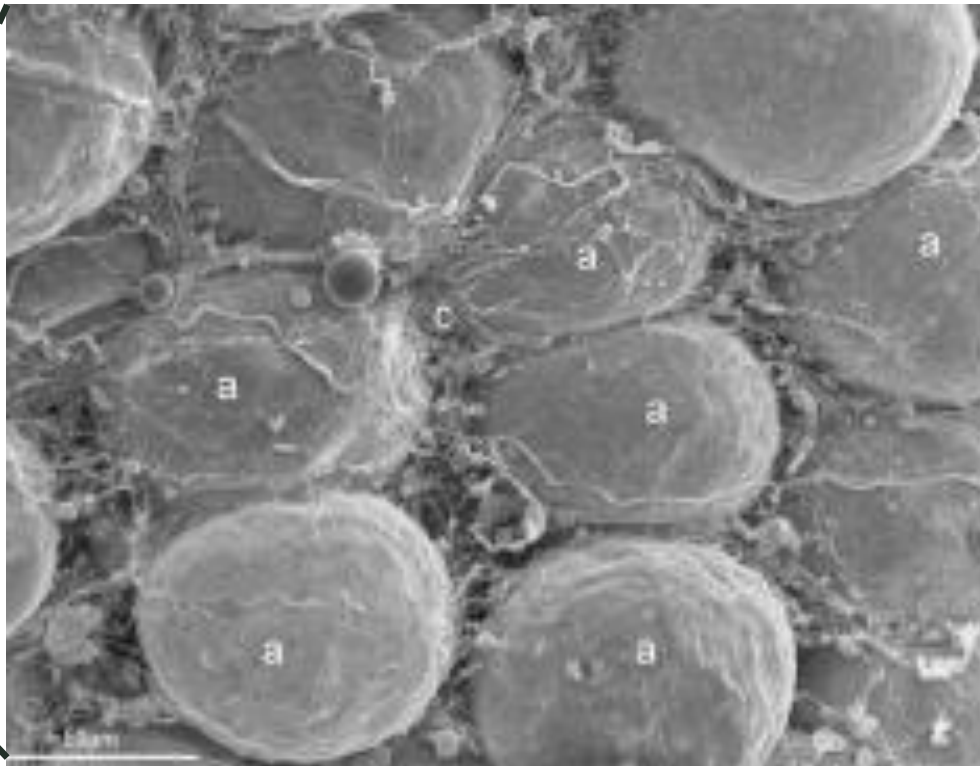
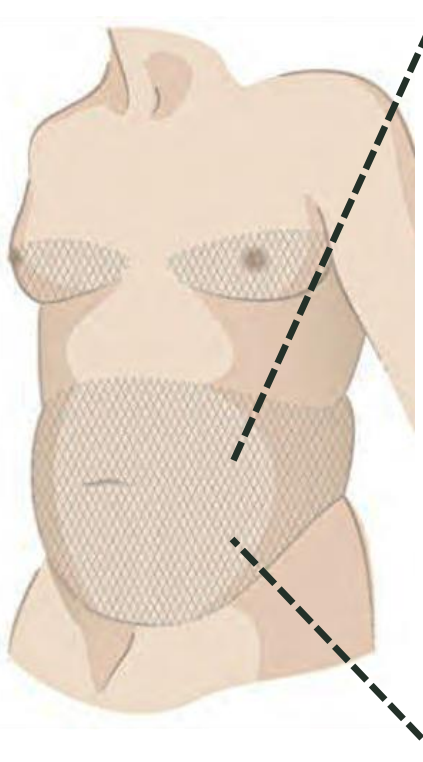
- Minimally invasive to harvest
- Most people have extra fat
- 100-500x more reparative cells than other tissues
- As a person ages, fat maintains reparative properties



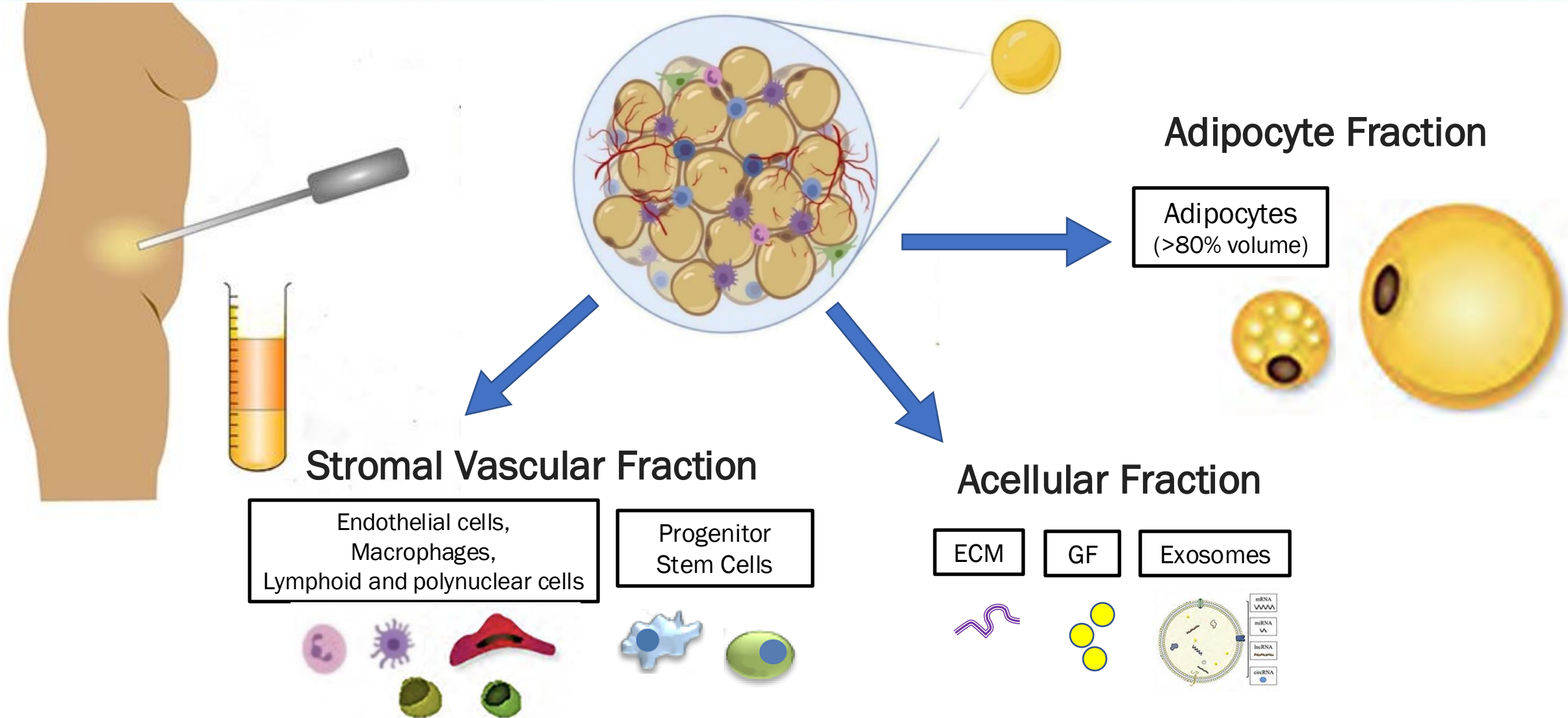
Age Effects on Stem Cell Senescence



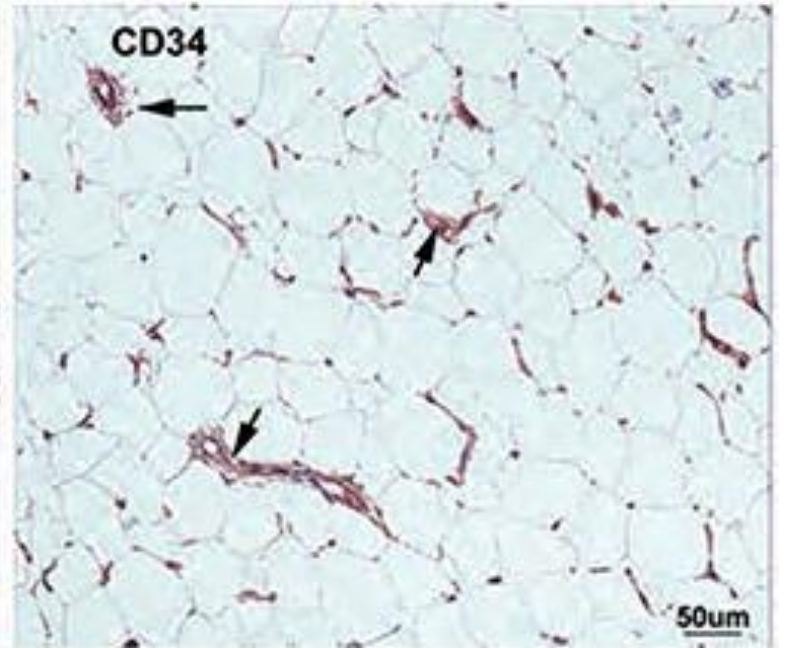
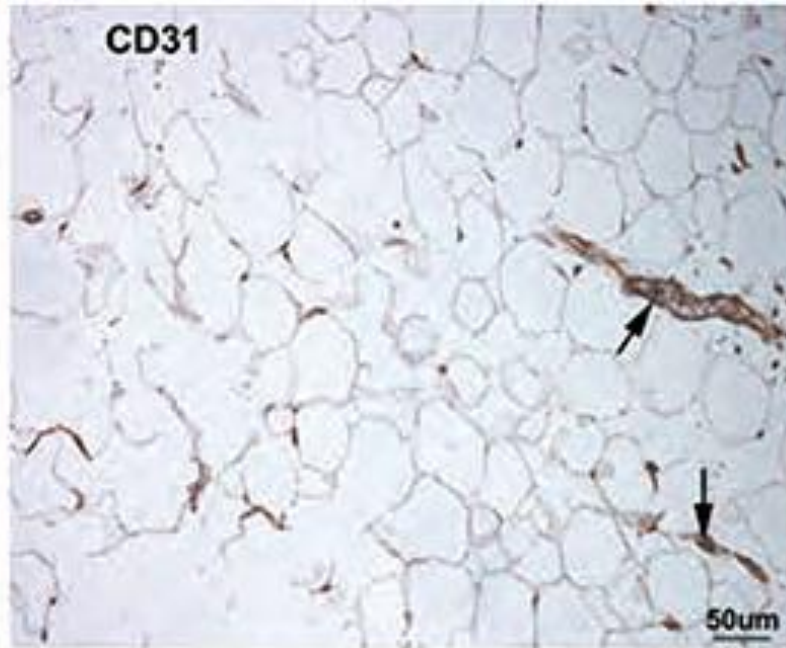
Abdominal White Abdominal Adipose Tissue



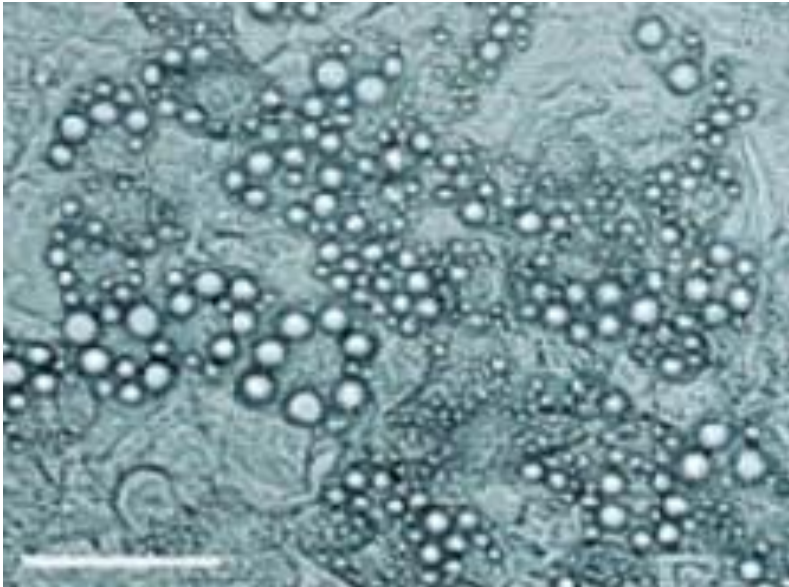
Architecture of Fat



Human Adipose Tissue Is Highly Vascularized and Contains Stem Cells



Human Adipose Tissue Contains Angiogenic Stem Cells



Adipose Tissue
From **Liposuction**

Digest in Collagenase
Centrifuge (10 min)



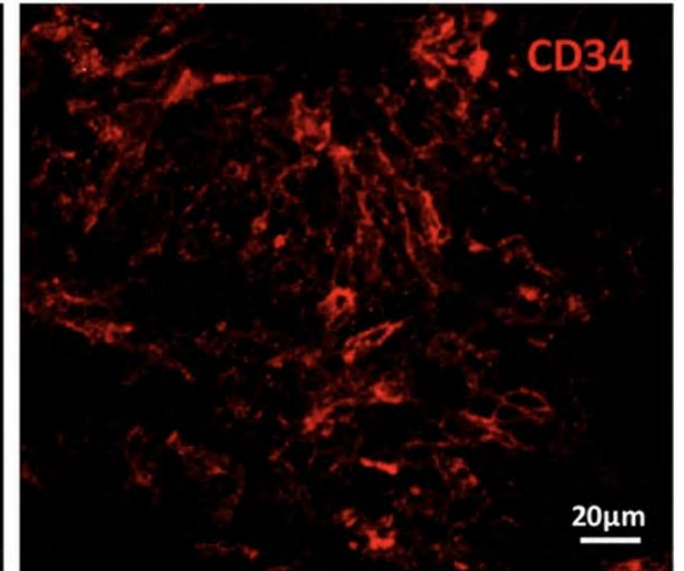
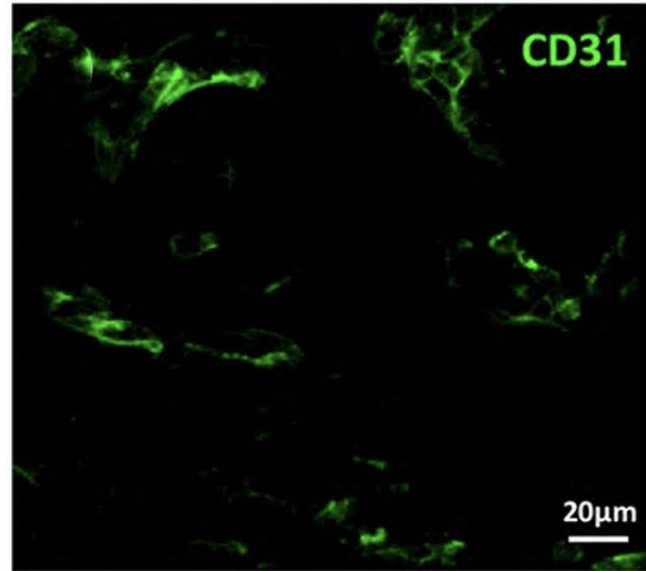
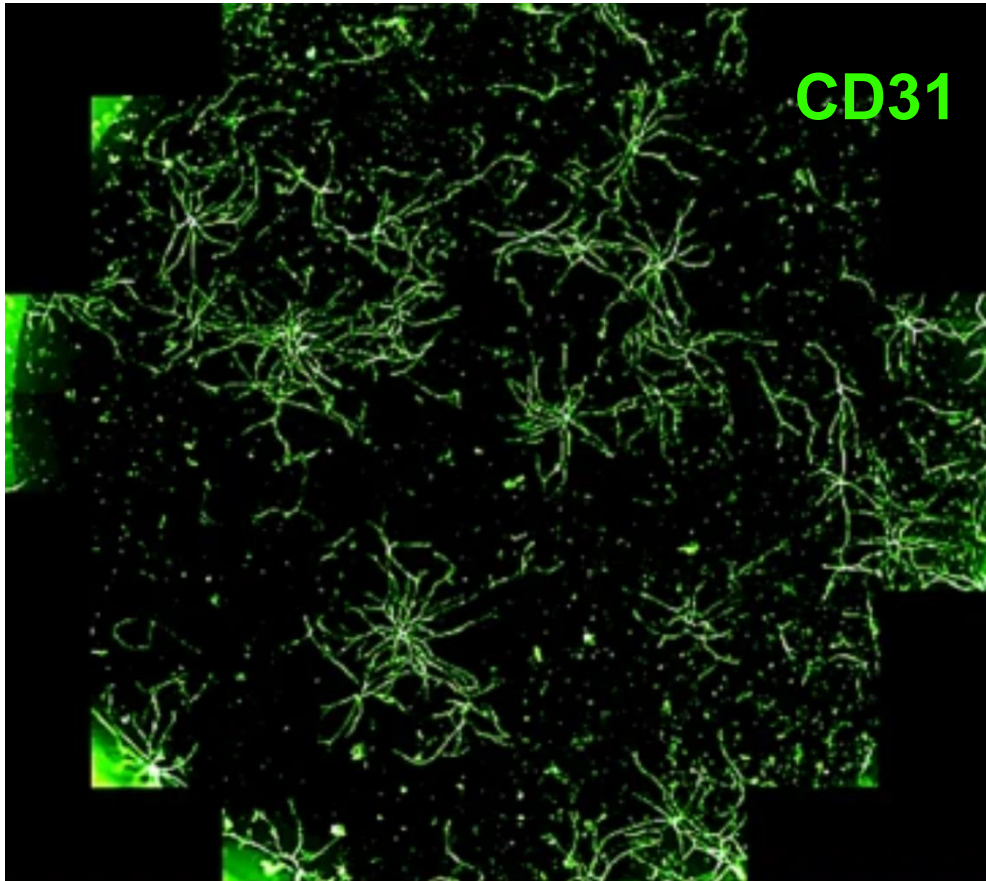
Endothelial Basal Medium-2



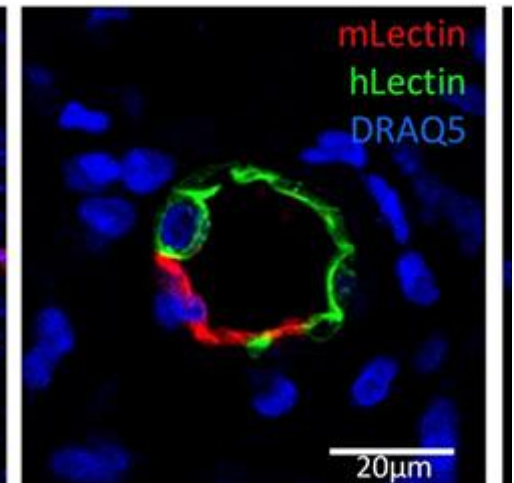
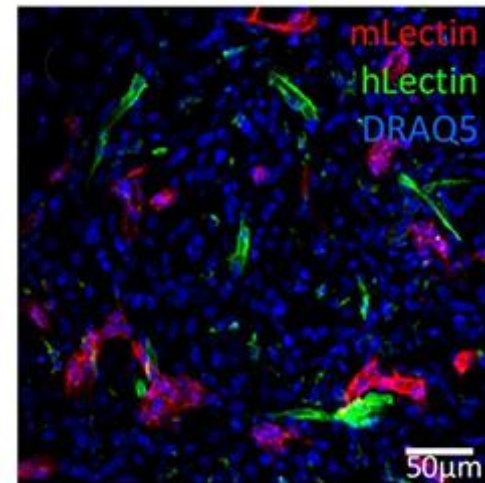
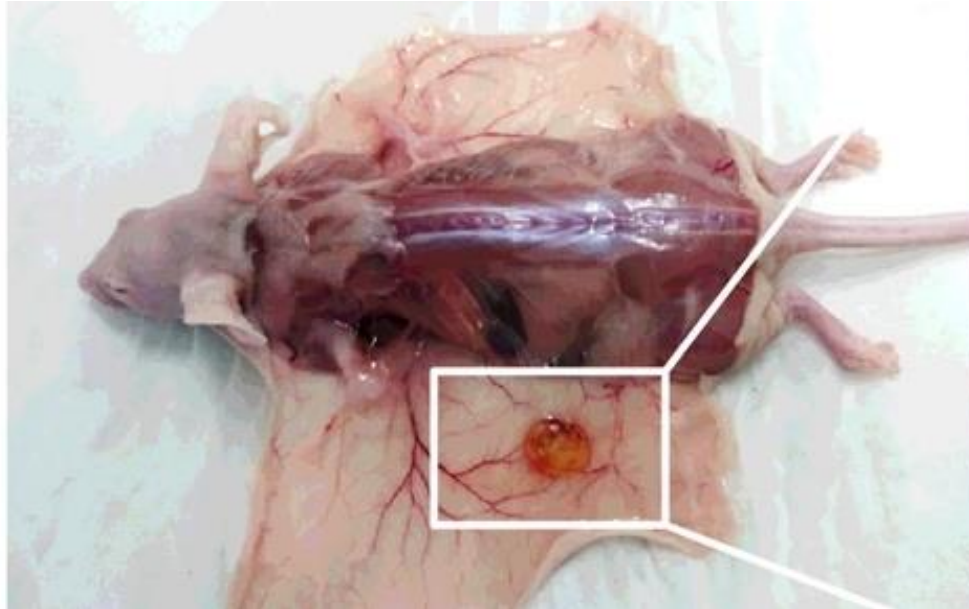
Angiogenic Adipose Stromal Cells (hASCs)
(80% CD34+)

↓
2-30 million cells (per 10-50 g fat)

Capillary Structures Formed in Vitro by Stromal-Vascular Fraction (SVF)-Derived Cells

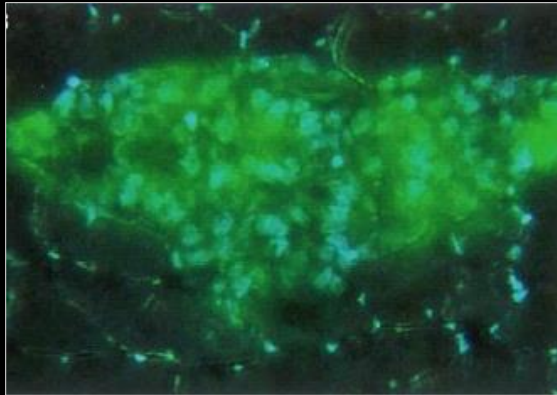


Engraftment of Human SVF-Derived Cells Generates Vascularized Tissue

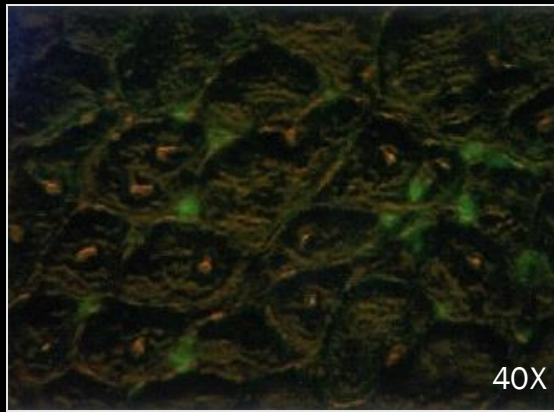


Injection of Human Adipocyte Stromal Cells Into Ischemic Hindlimb

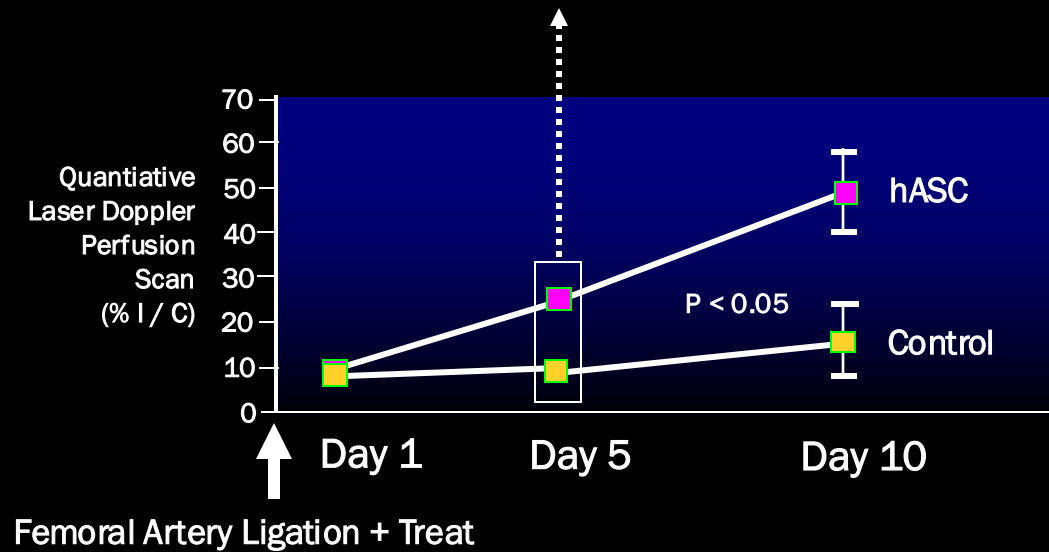
Inject cells into tibialis anterior muscle



1 wk later



28% hASCs Persistent





Lipoaspirate



Micronizing



4000 μ m

2400 μ m

600 μ m

200 μ m



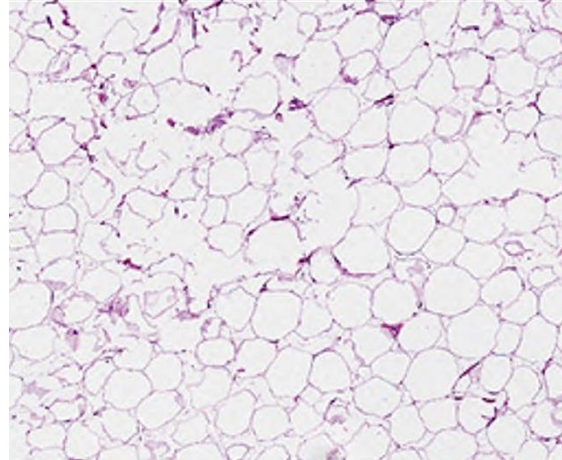
Saline Wash



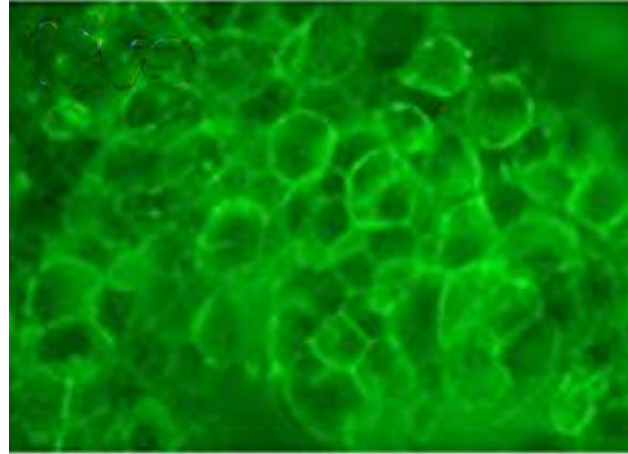
Invert 10-15 min

Cellular Viability

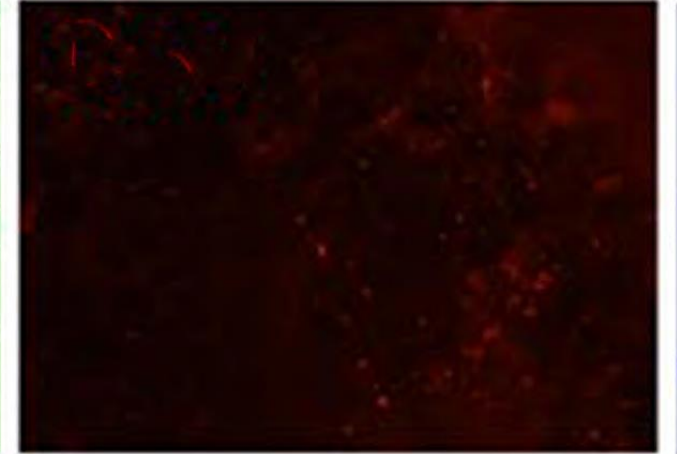
Lipoaspirate



LIVE



DEAD



Calcein AM

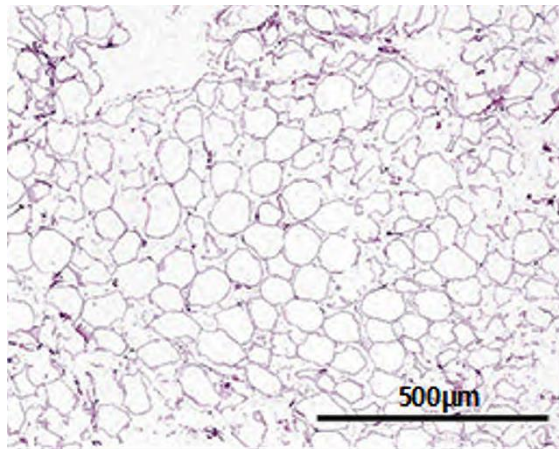
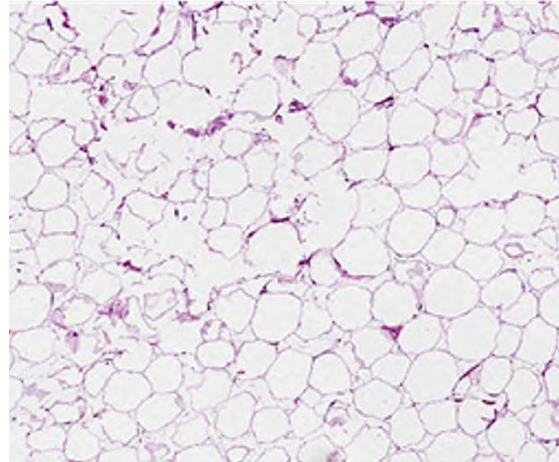
Ethidium homodimer

Cellular Viability

Lipoaspirate

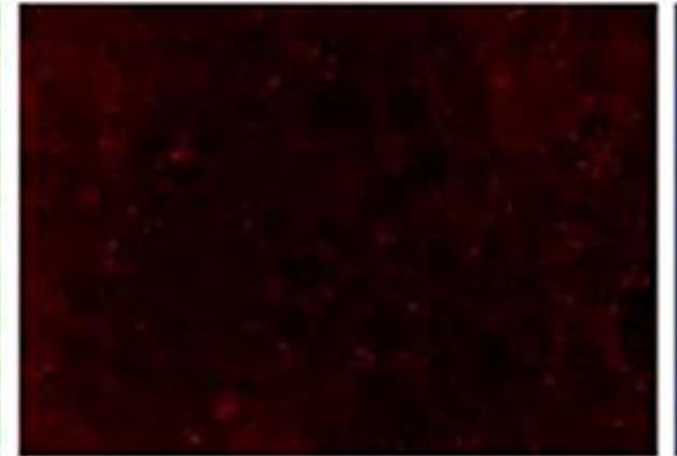
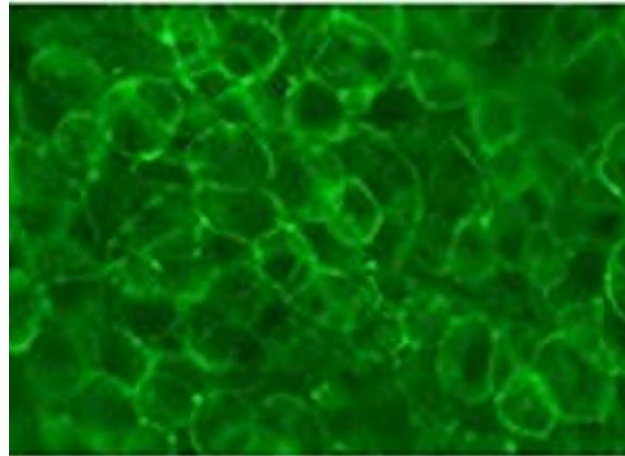
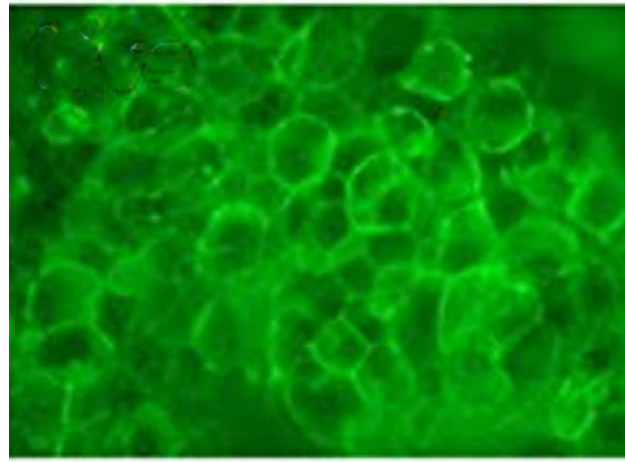


Micronized



LIVE

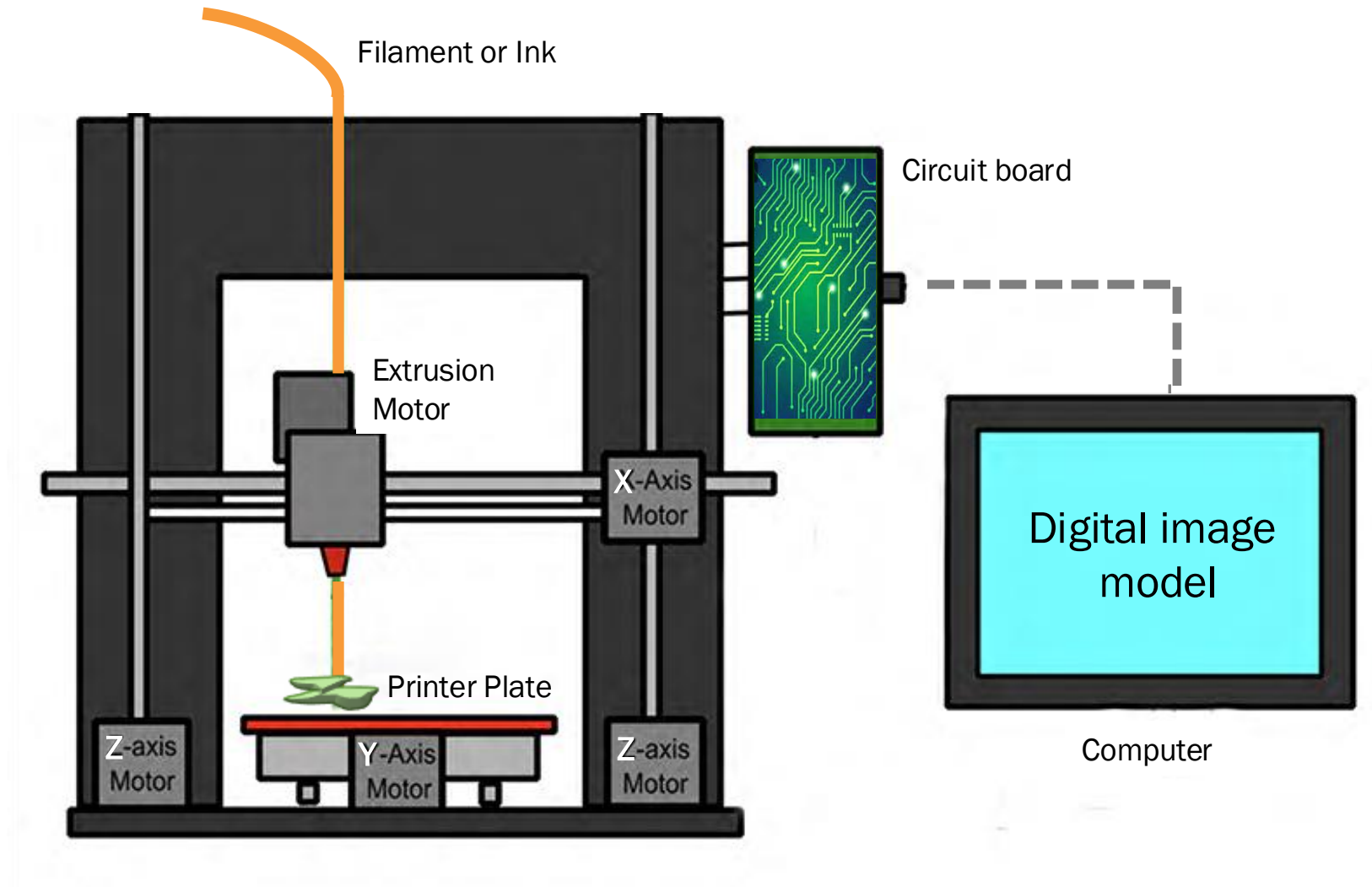
DEAD



Calcein AM

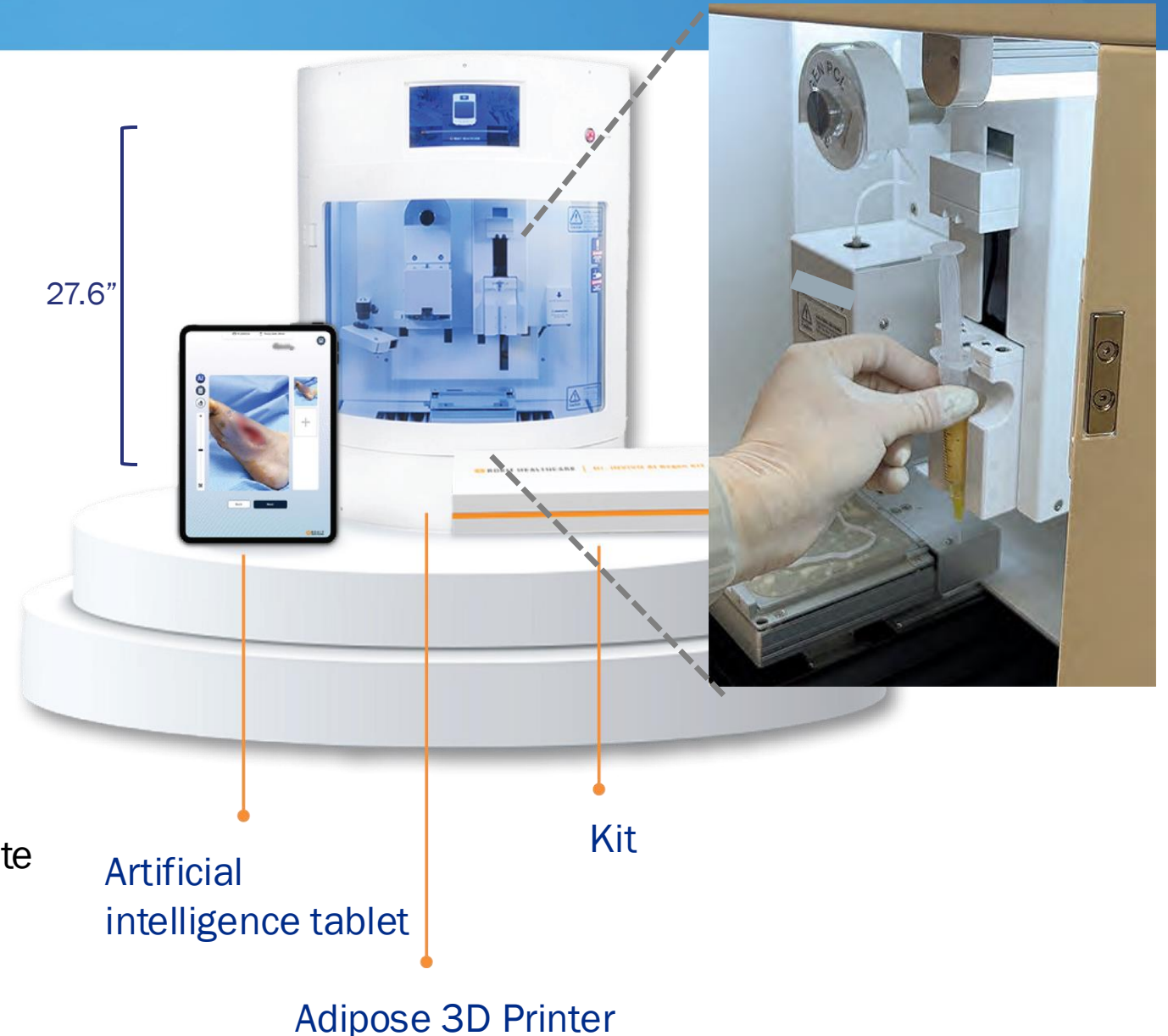
Ethidium homodimer

3D Printing



Adipose 3D Printer System

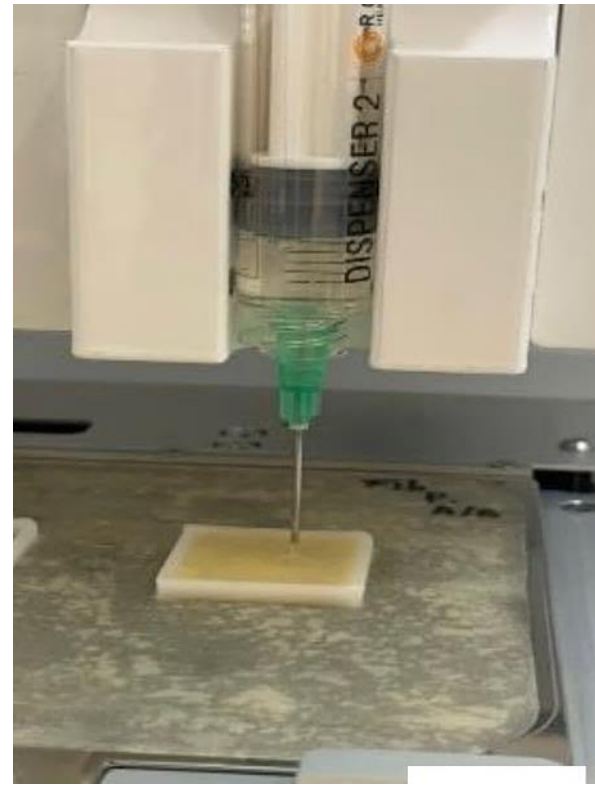
- 1 Artificial Intelligence tablet**
Integrated AI application with wound detection and 3D file generator
- 2 Adipose 3D Printer**
Adipose bioink 3D printer
- 3 Kit**
Single-use micronizers and printing accessories to process adipose and create PCL mold



Bioink Method 1: Low Temperature



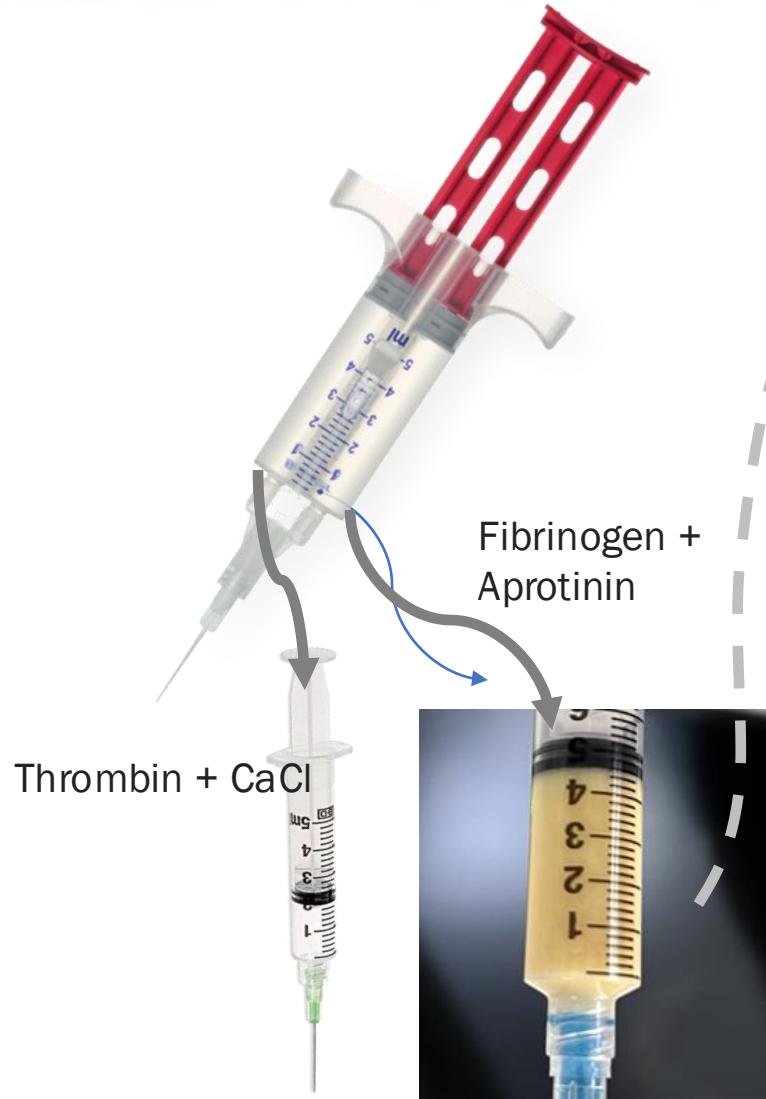
5cc syringe, 21G 1" needle



 -20 °C

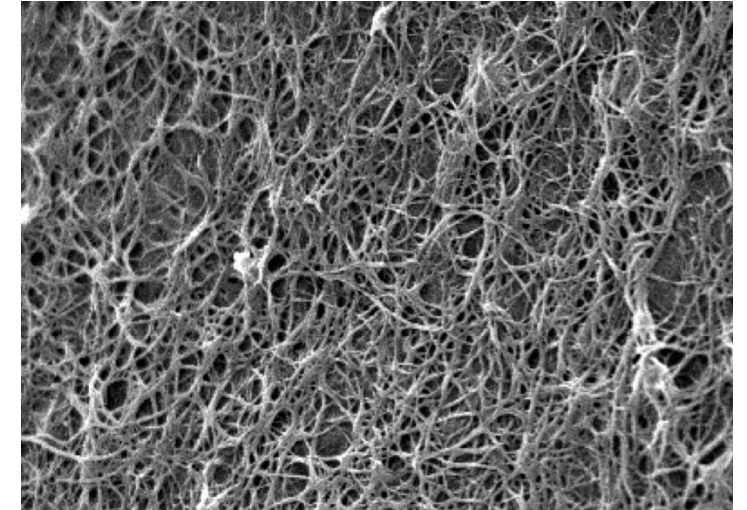
1. PCL mold in shape of wound is printed
2. Bioink extruded and frozen on same plate

Bioink Method 2: Fibrin



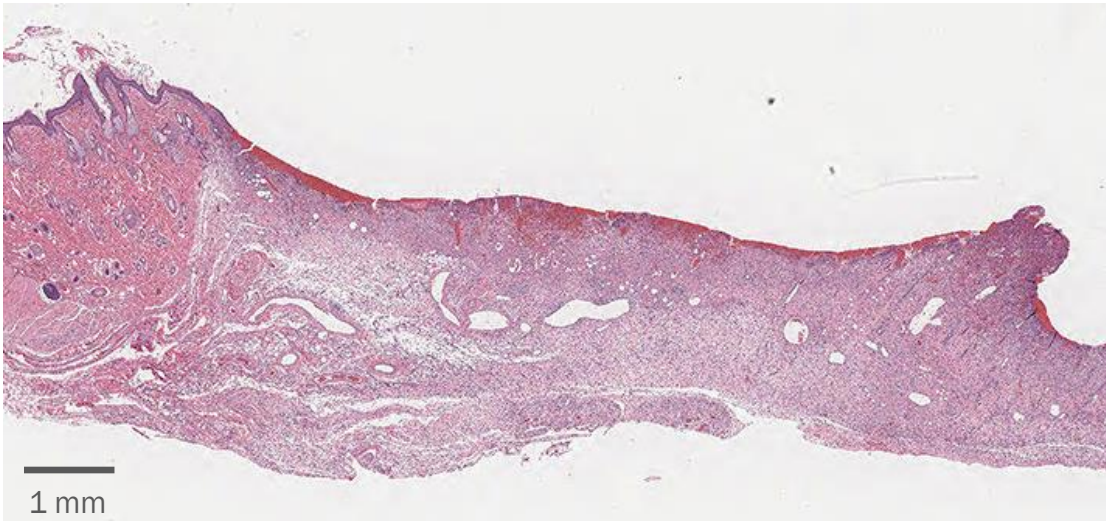
Fibrin glue kit - Fibrinogen
-Thrombin

1. Add fibrinogen to adipose mixture
2. Draw thrombin into separate tube

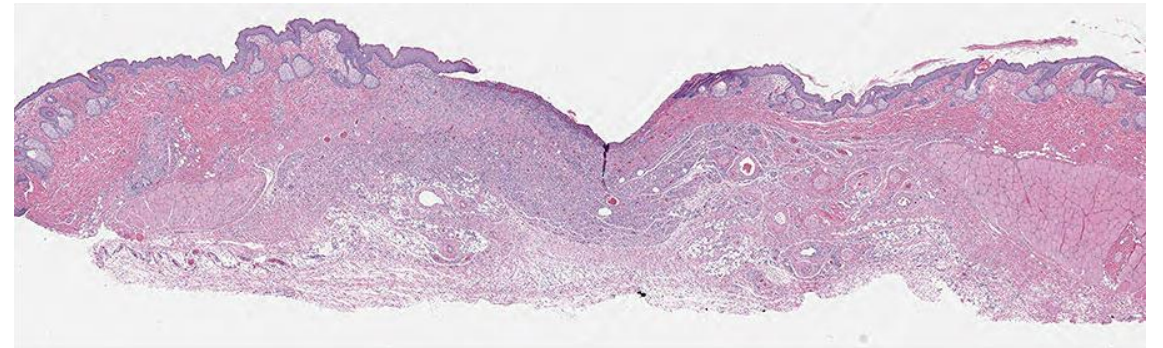




Human Adipose Bioink Treated Wounds in Vivo Murine Model



Day 7

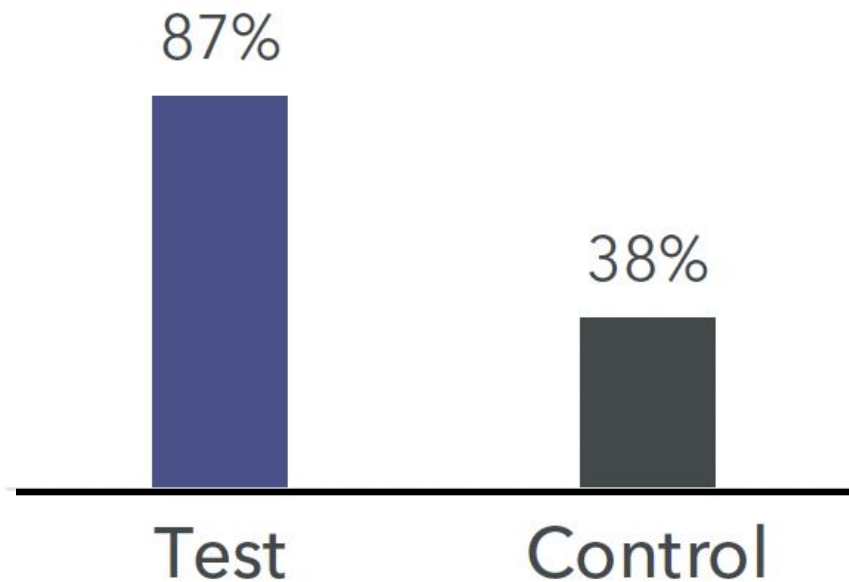


Day 21

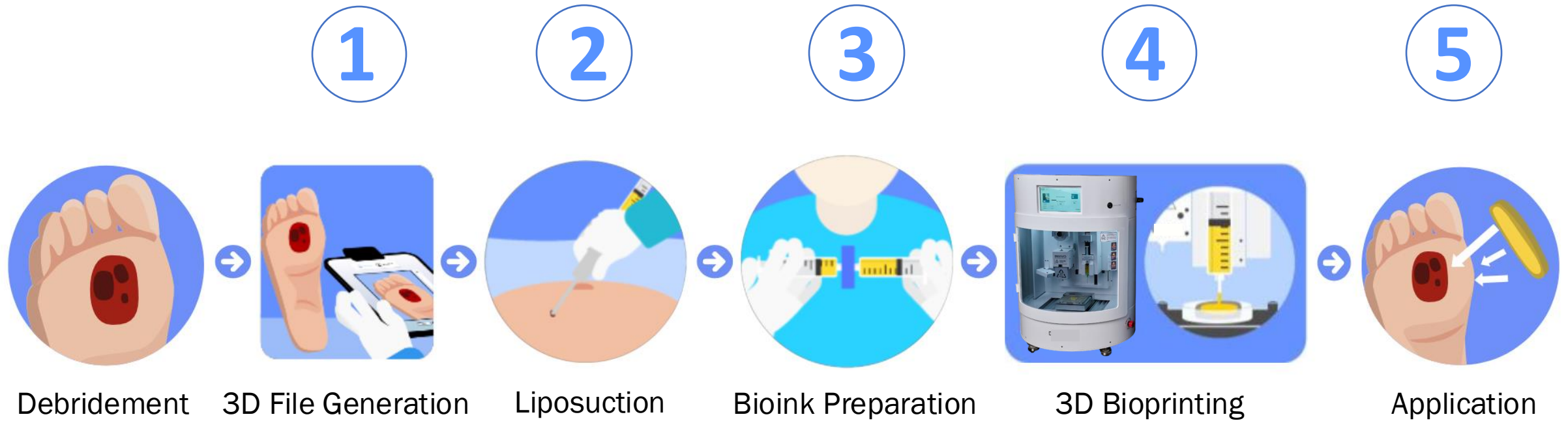
Initial Clinical Data

n=120 (U.S., India, Korea, Turkey, Malaysia) with 100 DFU, 20 Burns

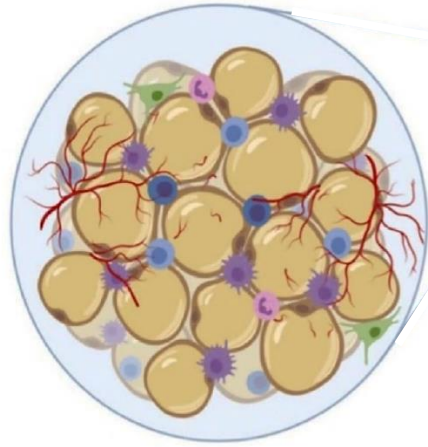
Wound Healing Rate
Week 12



Method



Why Process and Print Fat?



Adipocyte Fraction

Adipocytes
(>80% volume)



Stromal Vascular Fraction

Endothelial cells,
Macrophages,
Lymphoid and polynuclear cells



Progenitor
Stem Cells



Acellular Fraction

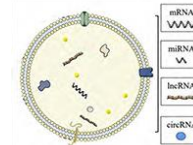
ECM



GF



Exosomes



High
Regenerative
Potential

Fat Processing Enriched Regenerative Potential

1000-5000 μm

Lipoaspirate

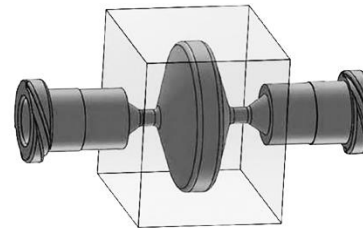
Primarily adipocytes



600-1000 μm

Micronized fat

Intact adipocytes, SVF cells preserved



<600 μm

Sub-Microfat

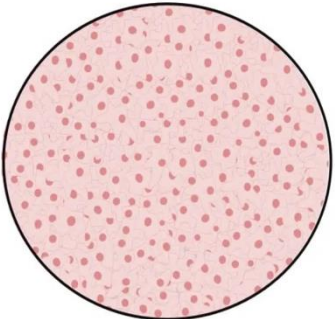
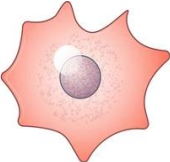
*Adipocytes lost
Enriched in SVF*

SVF-enriched fat bioink



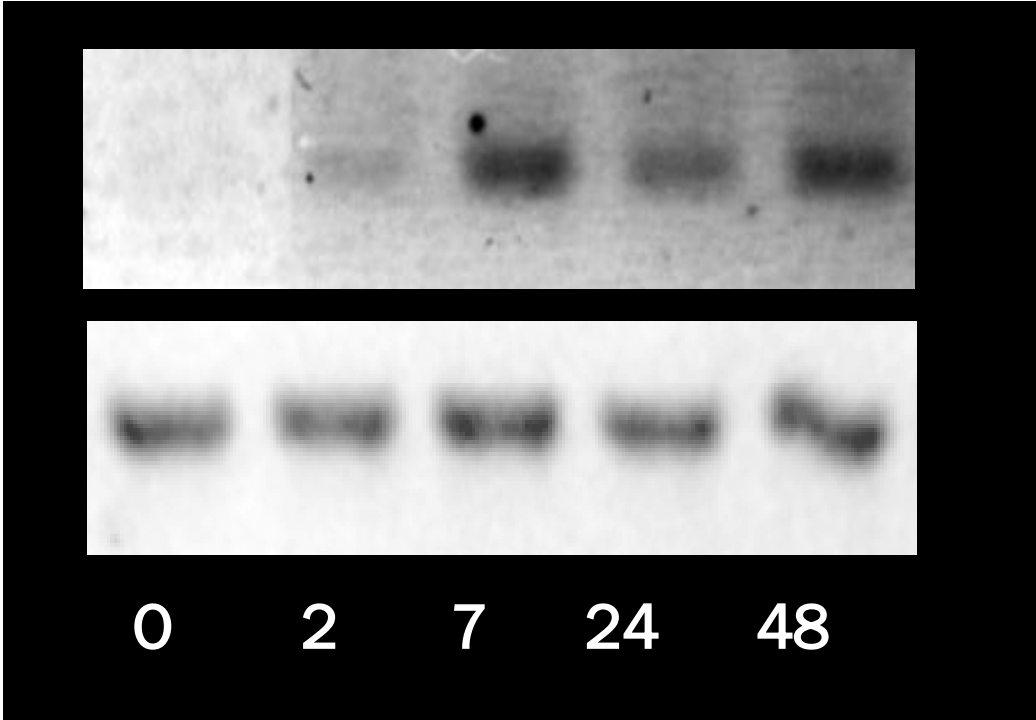
Cells Respond to Injury (Mechanical Processing) Bilayered Skin Construct

Fibroblasts

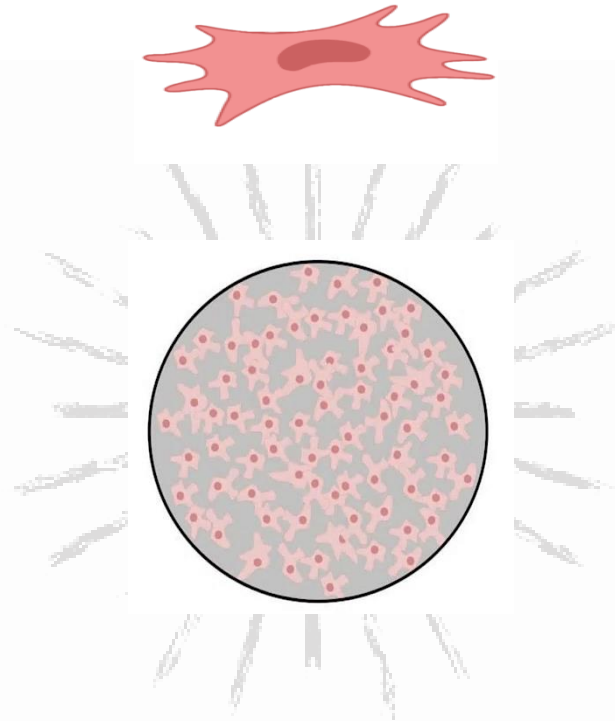


TGF-β2

G3PDH

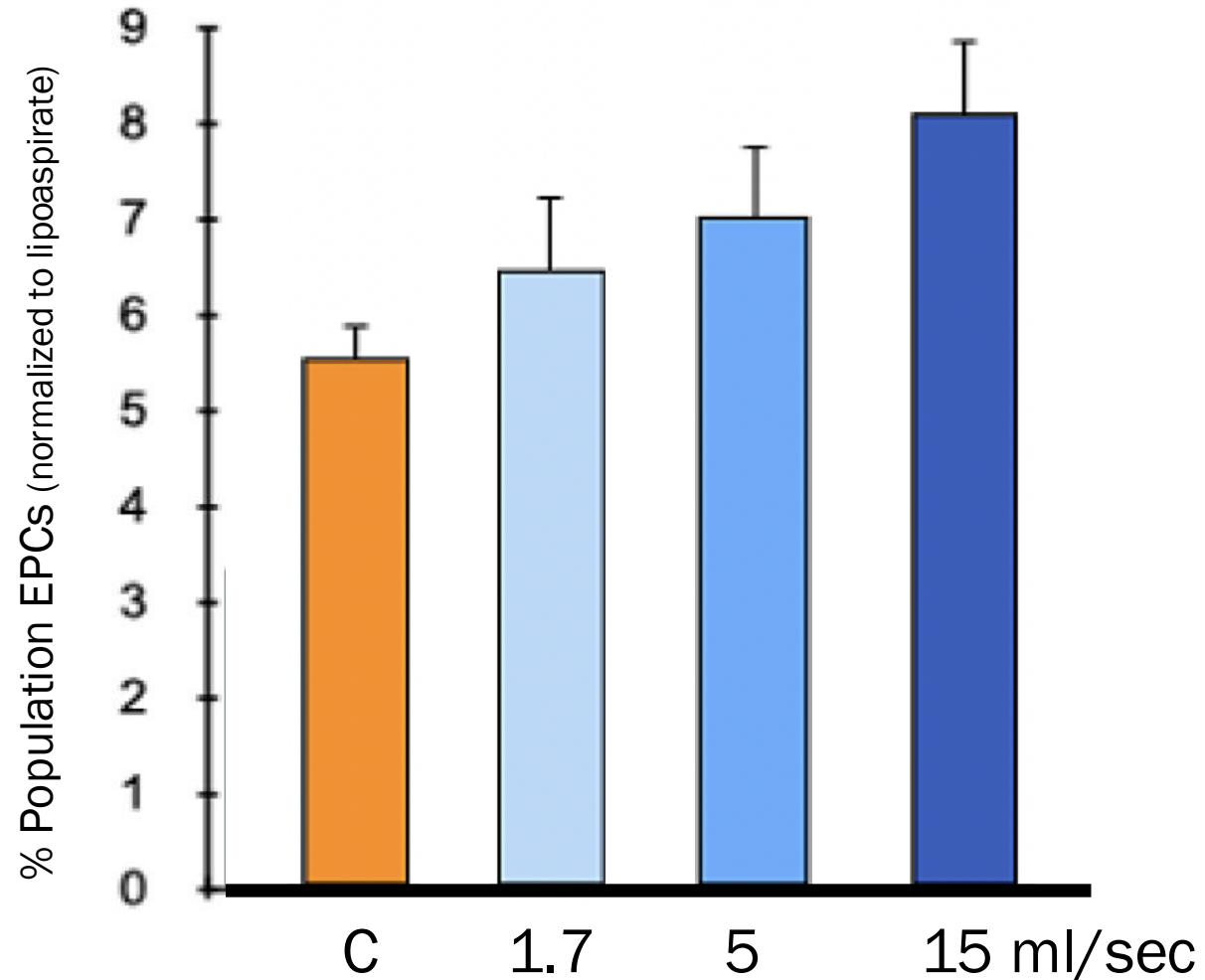


Hours Post-Injury

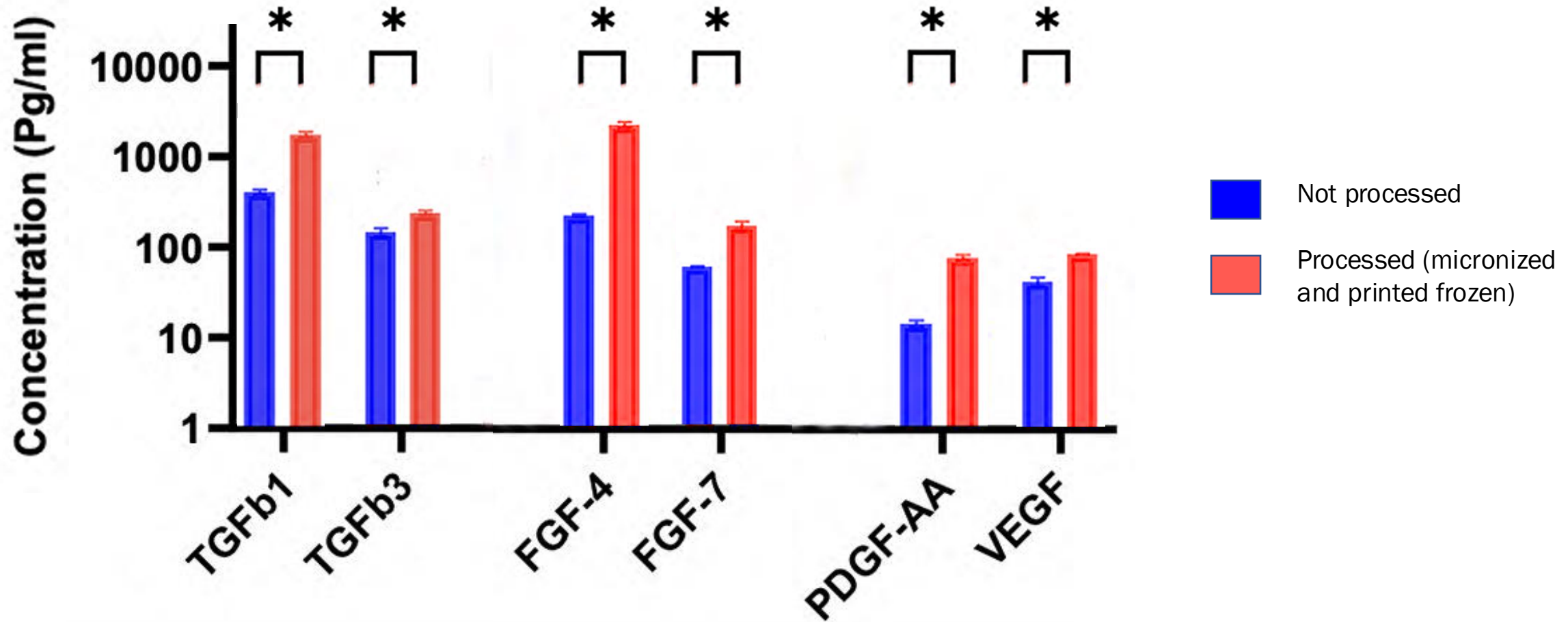


Shear Stress (Flow Speed) Increases EPCs

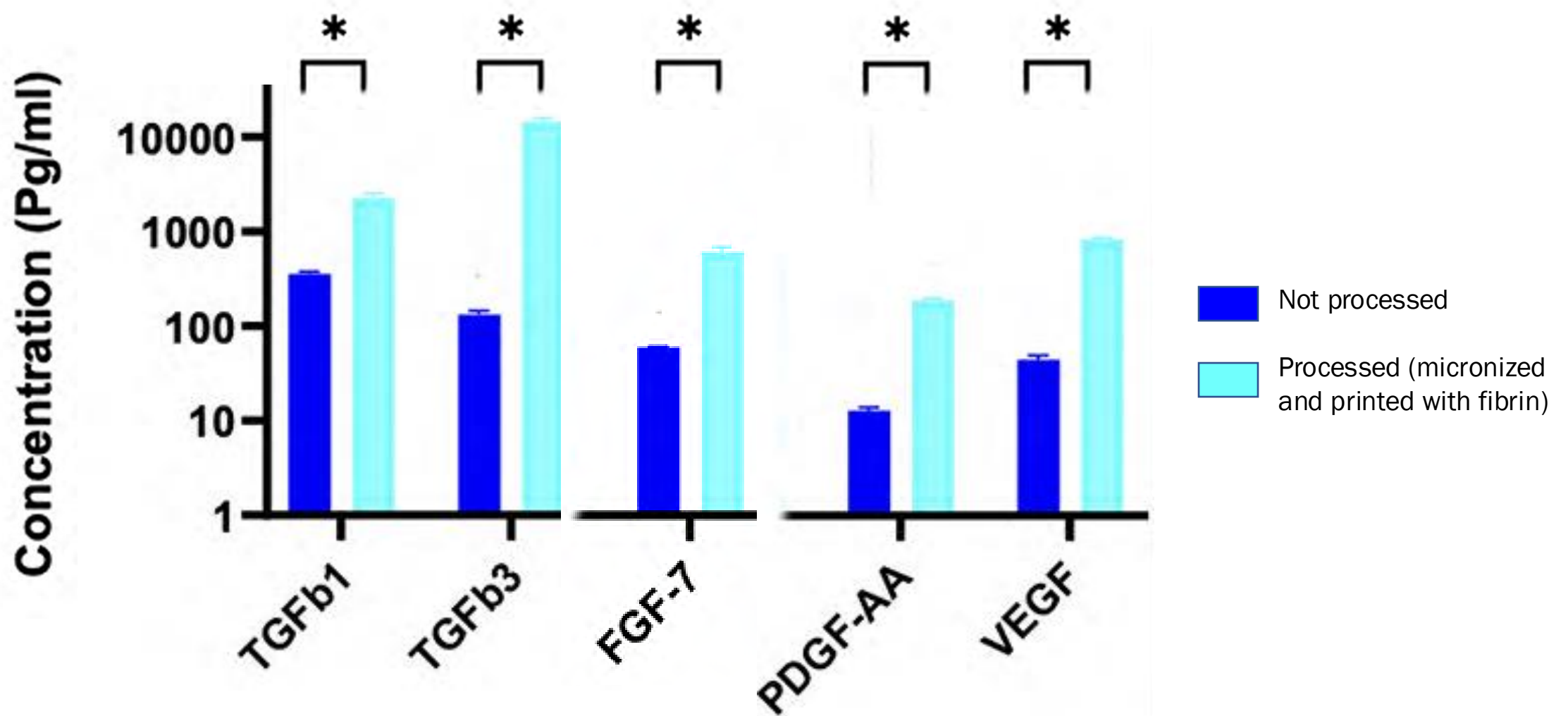
Human lipoaspirate analyzed by flow cytometry



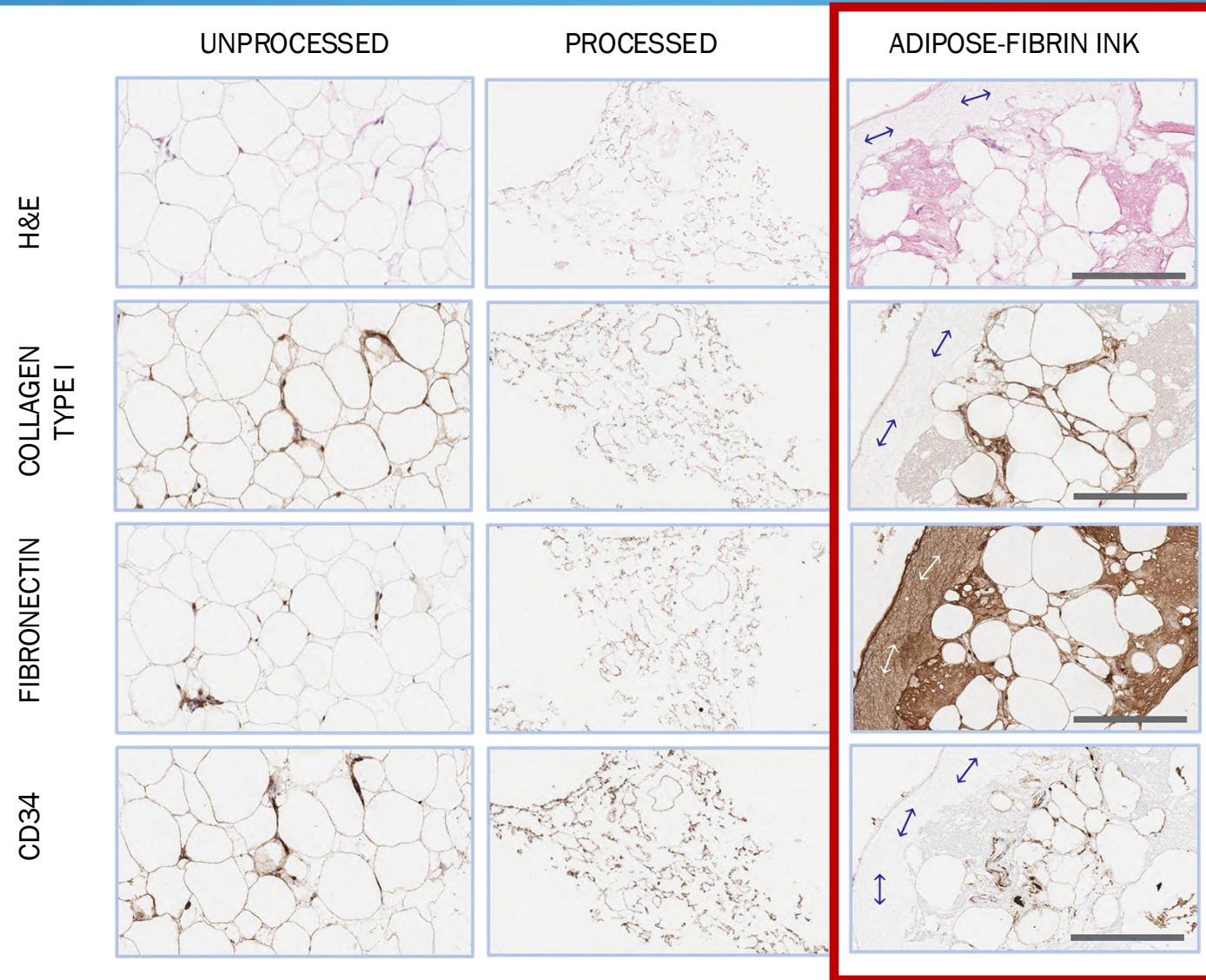
Processing Improves Growth Factor Profile



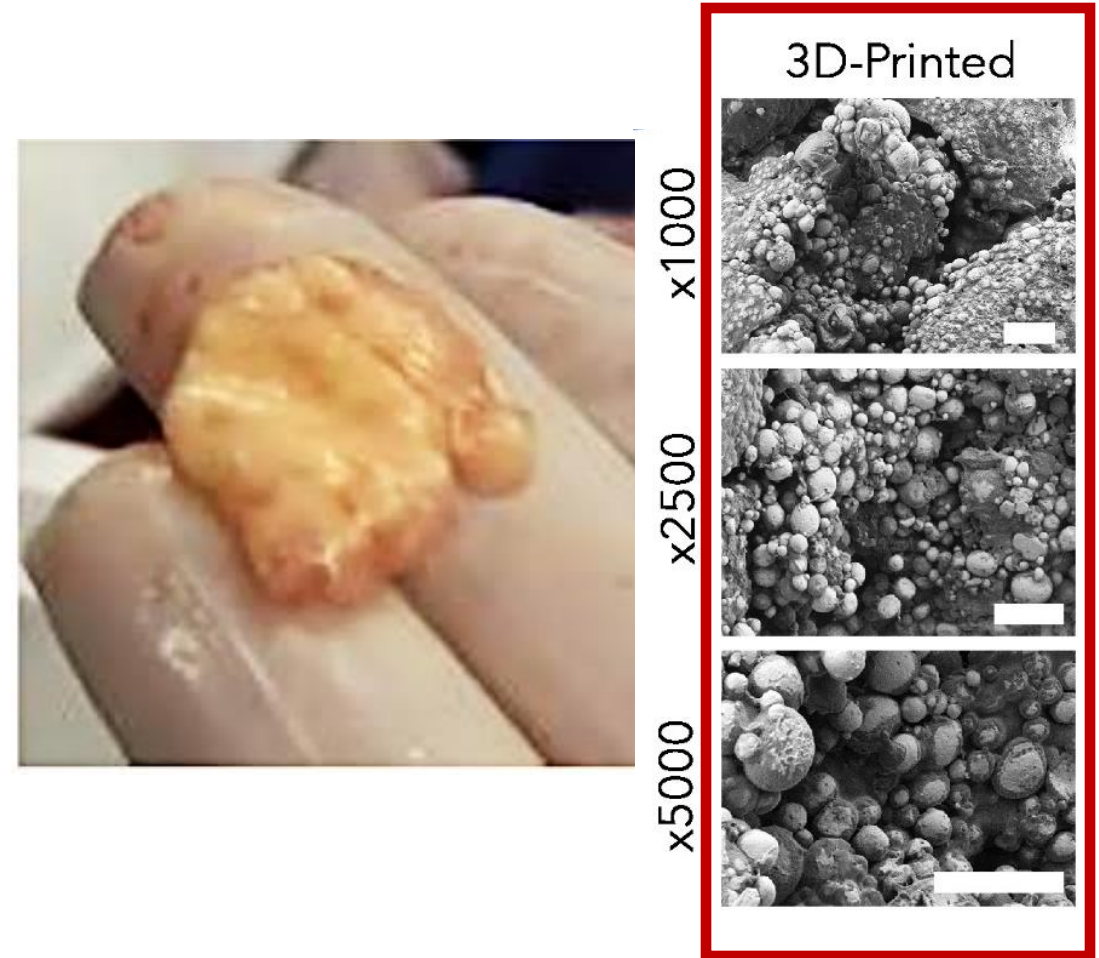
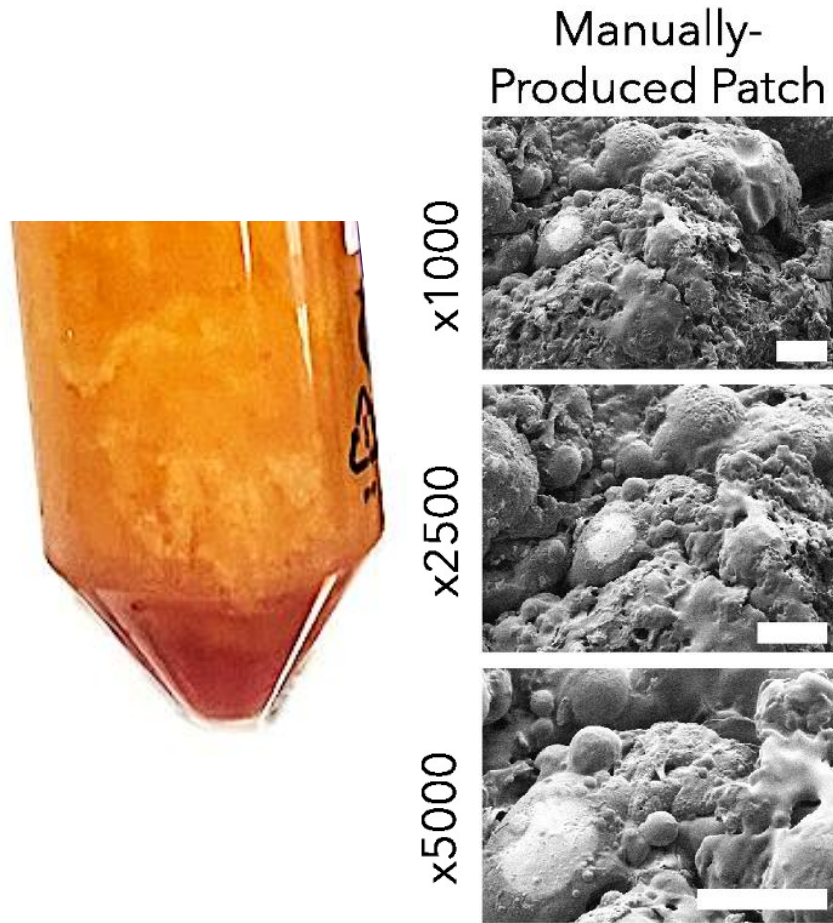
Processing Improves Growth Factor Profile



Adipose Fibrin Bioink Creates Organizing Scaffold

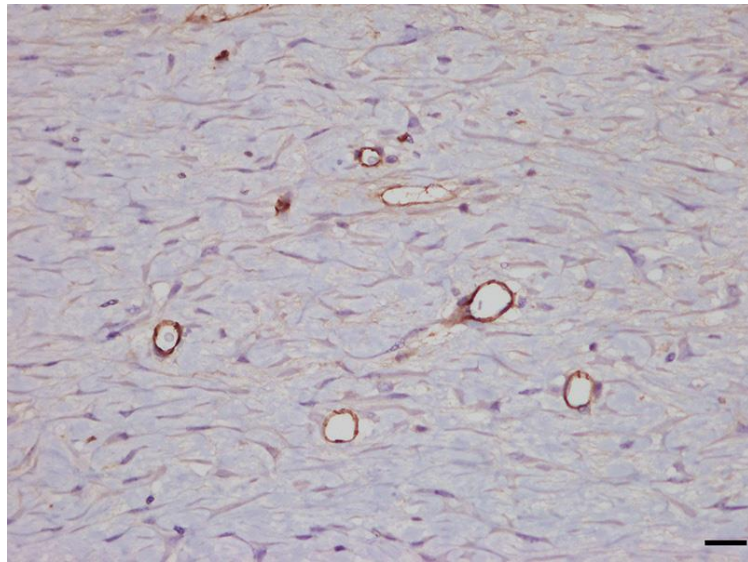


3D Printed Adipose Fibrin Bioink Has Improved Capture of Lipid Droplets and Uniform Distribution

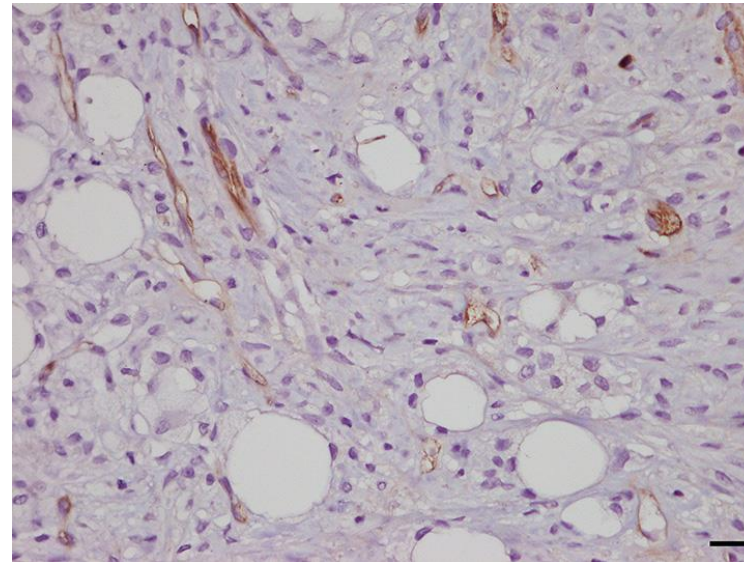


Neovascularization

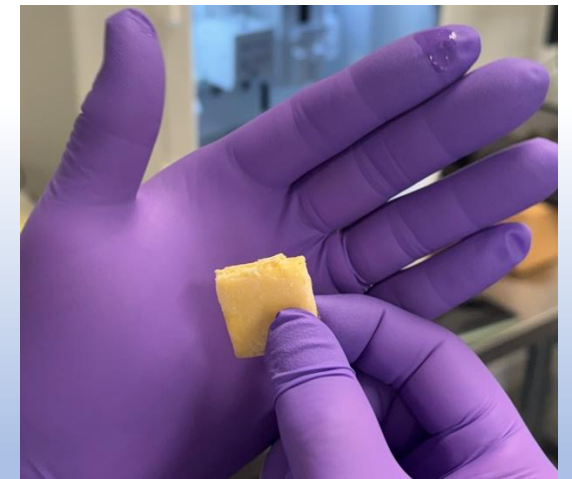
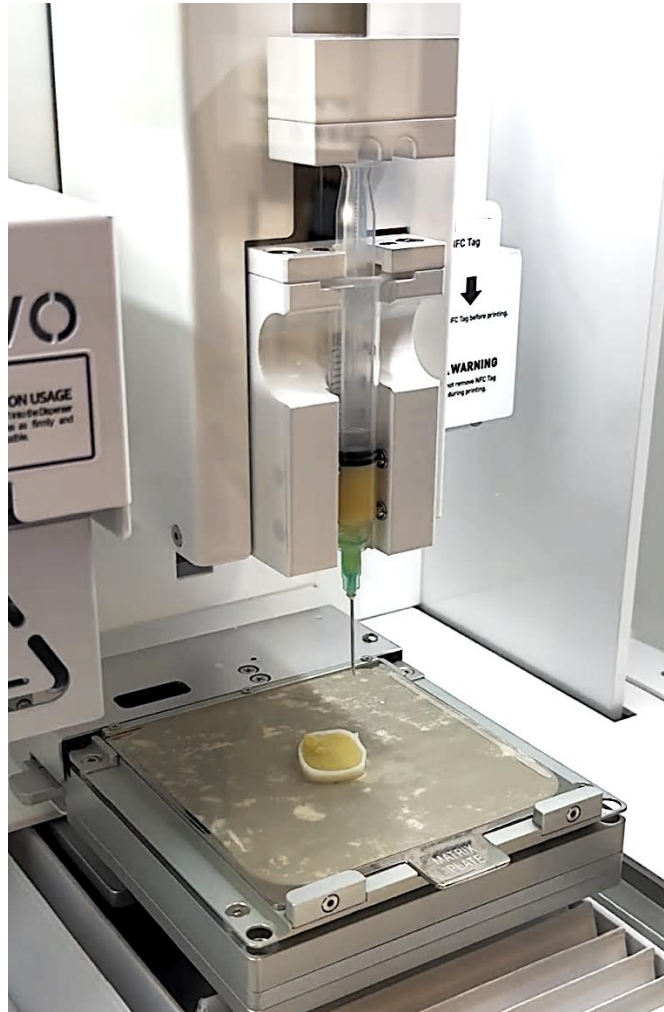
Control Wound



Adipose-Fibrin Bioink



Personalized Medicine



Clinical Pearls

- Adipose tissue is an easily accessible **autologous source** of **angiogenesis stimulation** and regeneration
- Adipose can be easily processed to yield “**bioink**”
- Studies show sub-micronized adipose tissue has biologically **active cellular and molecular elements** that promote wound healing
- The process matters: adipose-derived **SVF-enriched bioink** is more regenerative
- 3D printing of adipose bioink provides a flexible adaptable “**PLATFORM**” that allows the clinician to create **personalized treatment**

Complex Vascular and Wound Cases: Autologous Fat Grafting

Munier Nazzal, MD, MBA, M Ed, FRCS, FACS, DFSV, FACCCWS

Professor, Chief Division, Vascular, Endovascular and Wound Surgery

Department of Surgery and Department of Medical Education

University of Toledo

Toledo, OH

Case 1

- JB, 75y, squamous cell carcinoma (SCC) post excision by derm with subsequent chemo and radiation, 1 yr care by dermatology
- Present with radiation necrosis of the right leg anterior, ulcer, pain (9/10), pain x3 mos
- Edema, serosanguinous drainage
- US venous reflux, treated by ablation
- Mechanical drainage done at the first day
- Hyperbaric oxygen therapy (HBOT), compression (non-adherent)

Case 1: Soft Tissue Radio Necrosis



Key Outcome: Improved pain with compression — decongestion!
Shortened course of corticosteroids.

Case 1: 3D Fat Graft

5/16/25



Case 1



5/29/2025

Case 1



5/23/2025



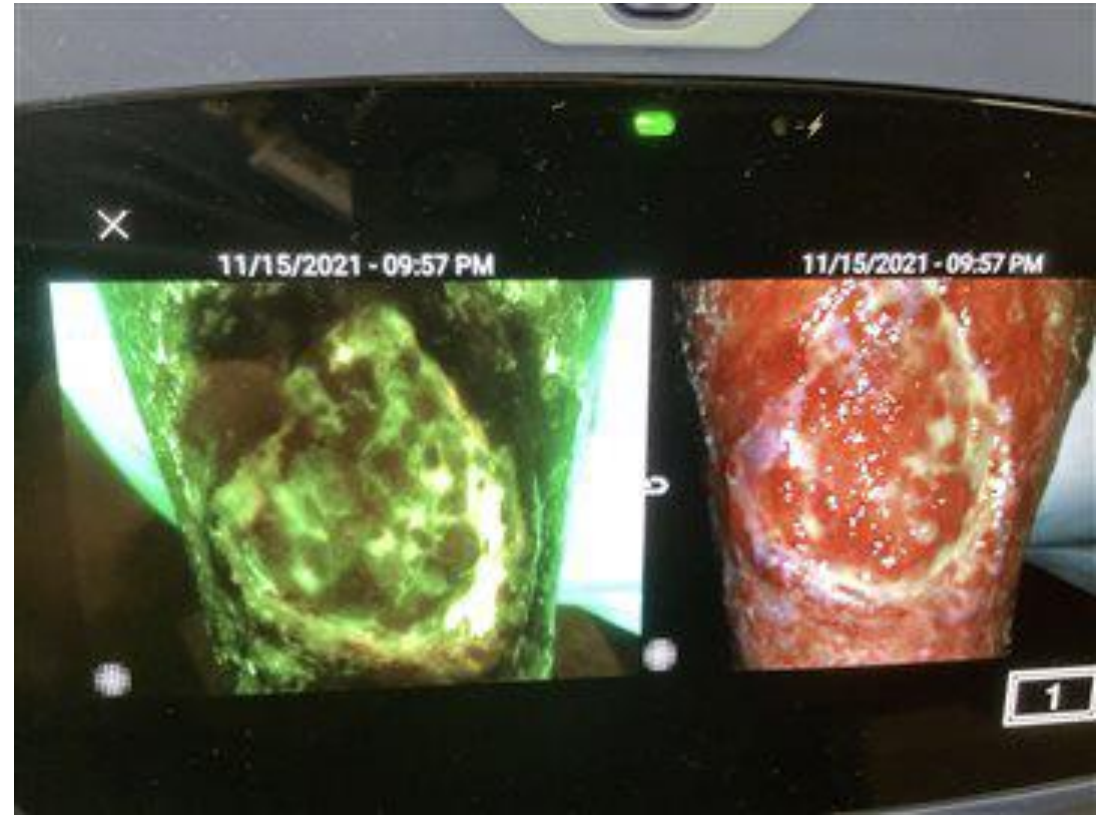
6/13/2025



5/23/2025

Case 1

8/1/2025



Case 2

- JS, 74y
- BMI 37.66
- Right lower extremity venous ulcer, 7cm x 7.2cm x 0.8cm
- Edema, pain for 3 mos
- ABI: 0.67
- Onset: 7/11/2023, treated with collagen, APD, 2-layer wrap
- Venous reflux done, angio and intervention done
- CTP certified

Case 2: Procedures

- 8/28/2023: RF ablation of the great saphenous vein (GSV)
- 10/6/2023: Angiogram and intervention
 - Balloon angioplasty (BA) of the tibio-peroneal
 - BA peroneal arteries
 - Directional atherectomy (DCA) of the right superficial femoral artery (SFA) popliteal arteries
- 12/11/2023: Right leg excisional debridement
- 5/24/2024: Excisional debridement of ulcer and great toe
- 5/28/2024: Great toe amputation

Case 2: Modify Wrapping Technique Based on Progress



Case 2: Venous Leg Ulcer (VLU) with Exposed Tendon

- PMH: Right lower extremity deep vein thrombosis (RLE DVT) with post-thrombotic syndrome (PTS), anti-phospholipid syndrome, peripheral arterial occlusive disease (PAOD), diabetes mellitus (DM), gout, chronic kidney disease (CKD), hypertension (HTN)
- Multi-modal therapy
 1. Angiogram with drug-coated balloon (DCB) angioplasty of the anterior tibial artery (ATA) and percutaneous transluminal angioplasty (PTA)
 2. GSV radiofrequency ablation (RFA)
 3. CTP
 4. Glycemic control
 5. Anticoagulation
 6. Multi-disciplinary with hematology, ID, nephrology; ortho said NO
 7. **Key Point: Original VLU closing nicely- distal ulcer with spontaneous worsening 2/2 poor compression application**



Case 2: VLU with Exposed Tendon

1/10/2024



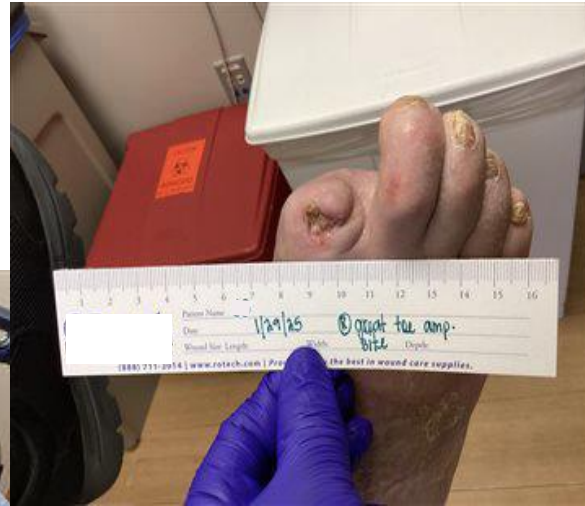
12/31/2024



Case 2: VLU with Exposed Tendon



1/29/2025



2/12/2025



Case 2: VLU with Exposed Tendon

3/13/2025



4/09/2025



4/23/2025

Case 2: Debridement with APLICOR 3D™ (3D Printed Adipose Tissue Matrix Graft)

4/28/2025

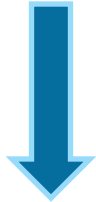


6/13/2025



Case 2: Debridement with 3D Printed Adipose Tissue Matrix Graft

5/07/2025



Surgery 5/16/2025



5/23/2025



Case 2: Debridement with 3D Printed Adipose Tissue Matrix Graft

7/02/2025



Splint: Get Creative (with Caution)



Case 3

- LS, 51y Female patient
- DM, HTN, hyperlipidemia (HLD), coronary artery disease (CAD), hypothyroidism, obesity
- Referred from Orthopedics for a dehisced surgical site of her right first metatarsophalangeal (MTP) fusion and second hammertoe correction surgeries, which were done on 2/25
- Hardware exposed

Amputation??



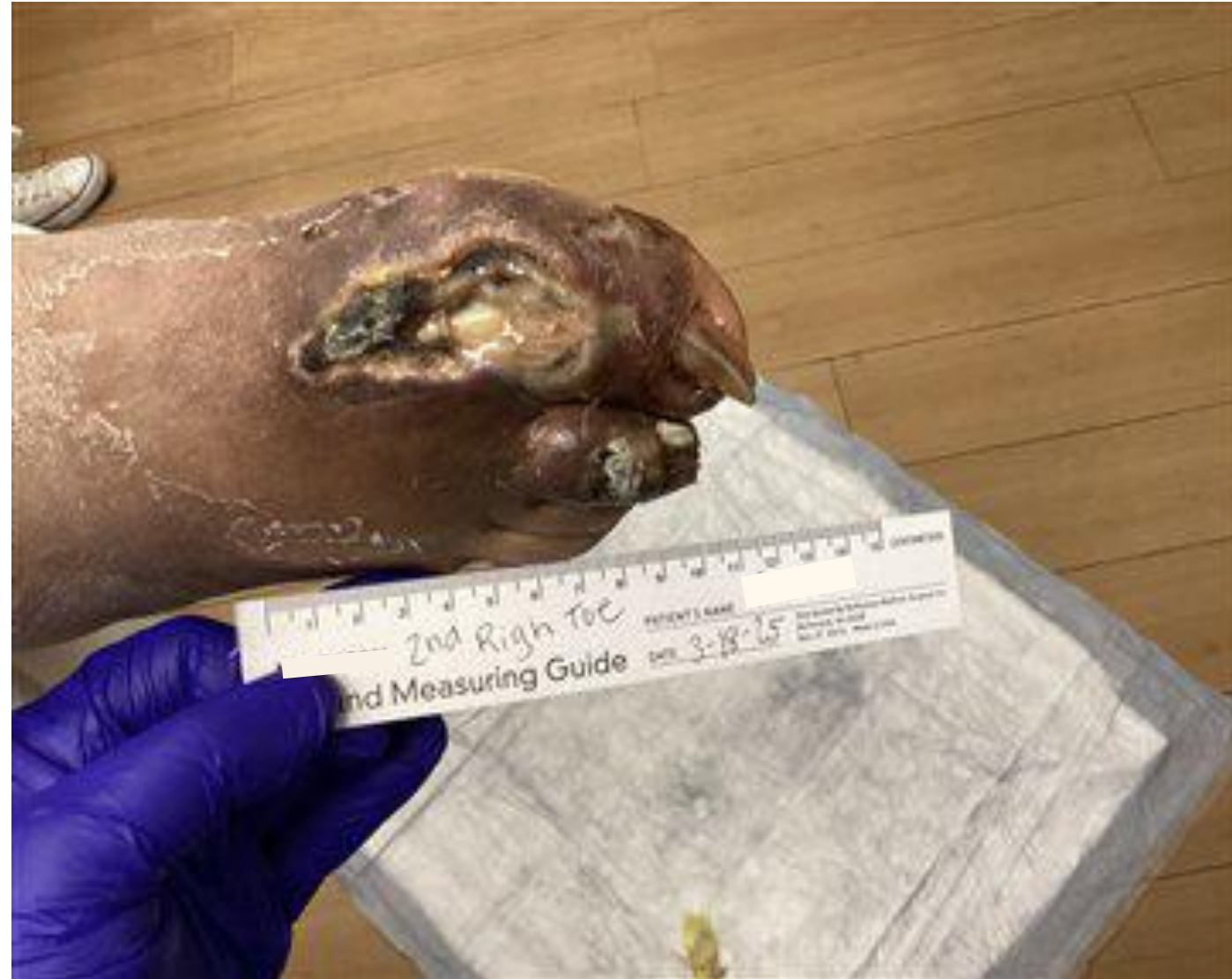
3/11/2025

Case 3

- 3/28/2025: Right leg angiogram, drug-coated balloon of superficial femoral artery (SFA), popliteal; BA of all calf arteries; excisional debridement and CTP
- 4/25/2025: Excisional debridement and 3D printed adipose tissue matrix graft

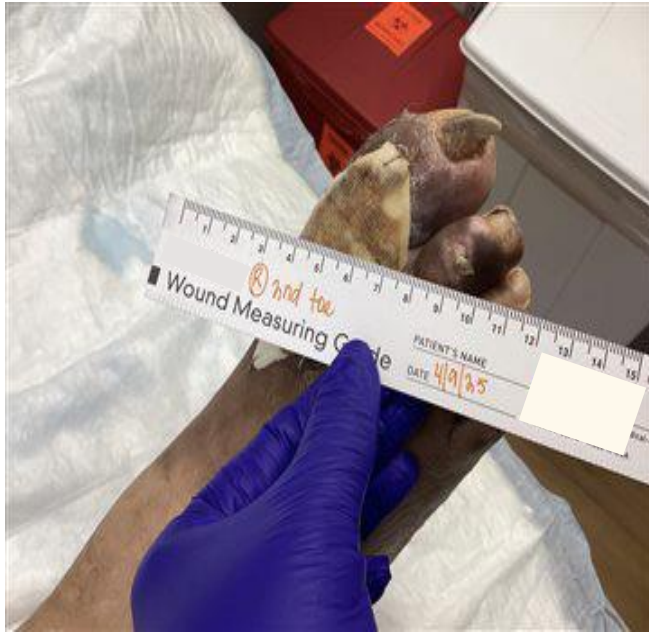
Case 3

3/18/2025



Case 3: 3D Printed Adipose Tissue Matrix Graft

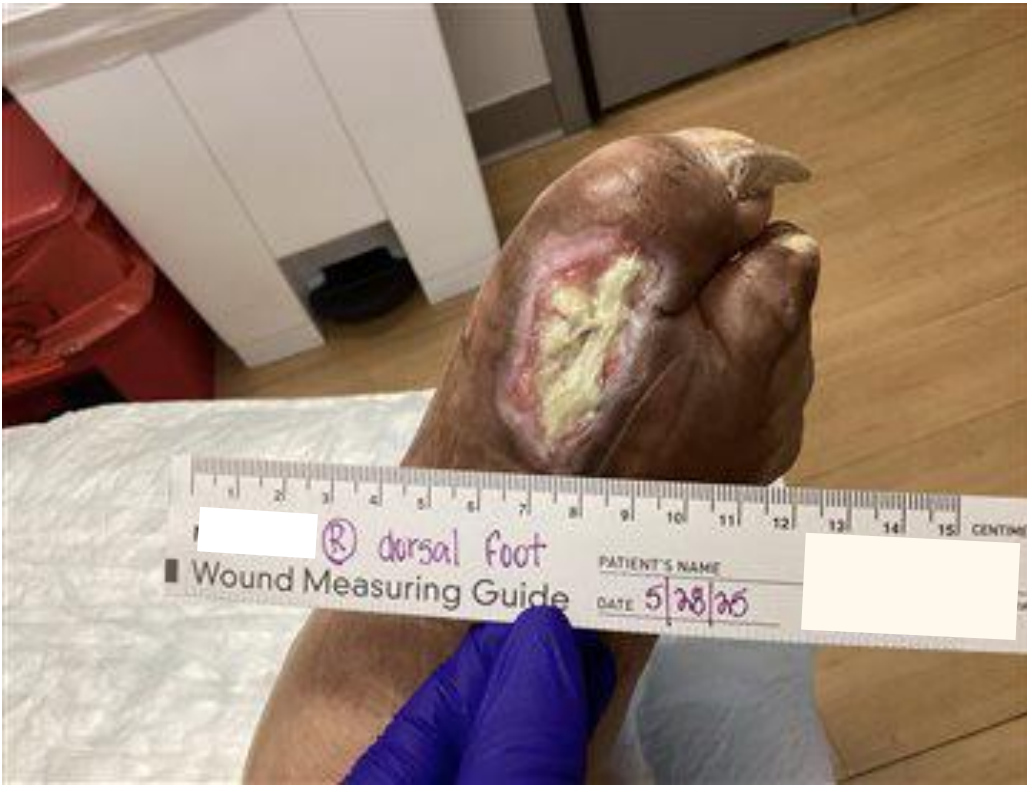
4/9/2025



5/13/2025

Case 3

5/28/2025



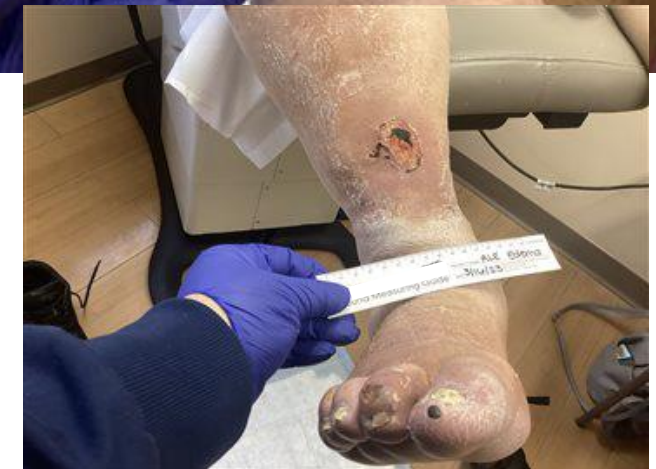
7/25/2025



Case 4

- PJ, 70y White Male
- DM, gout
- 2/22/2023, has RLE VLU from trauma
- RLE VLU, LE edema, left heel pressure ulcer (PU) stage 3, right 2nd toe diabetic foot ulcer (DFU)

3/16/2023



Case 4: Procedure

- 3/25/2025: Right GSV ablation
- 4/8/2025: Right small saphenous vein (SSV) ablation
- 5/16/2025: Debridement and 3D printed adipose tissue matrix graft

Case 4

3/4/2025



3/10/2025



3/13/2025



Case 4



3/27/2025



4/17/2025



Case 4: Procedure

- 5/16/2025: 3D printed adipose tissue matrix graft

Case 4



5/23/2025



6/13/2025



Case 4

7/3/2025



7/14/2025



7/25/2025



Case 4

7/25/2025



Case 5

- 47y
- Chronic venous ulcer first noticed 10/20/2022
- Edema
- Had open reduction internal fixation on 5/9 for trimalleolar ankle fracture with external fixator removal, and she was admitted earlier in April to our facility due to right ankle fracture status post external fixator application
- Treated: antibiotics, compression

10/20/2022



Case 5: Procedure

- 6/23/2023: Excisional debridement and CTP
- 8/14/2023: Excisional debridement and CTP
- 1/27/2025: Angiogram, ATA occlusion around the ortho procedure
- 5/16/2025: Right leg debridement and 3D printed adipose tissue matrix graft

Case 5

10/24/2024



10/17/2023



Case 5

12/09/2024

12/12/2023

VS



Case 5

1/22/2025



4/18/2025



2/26/2025

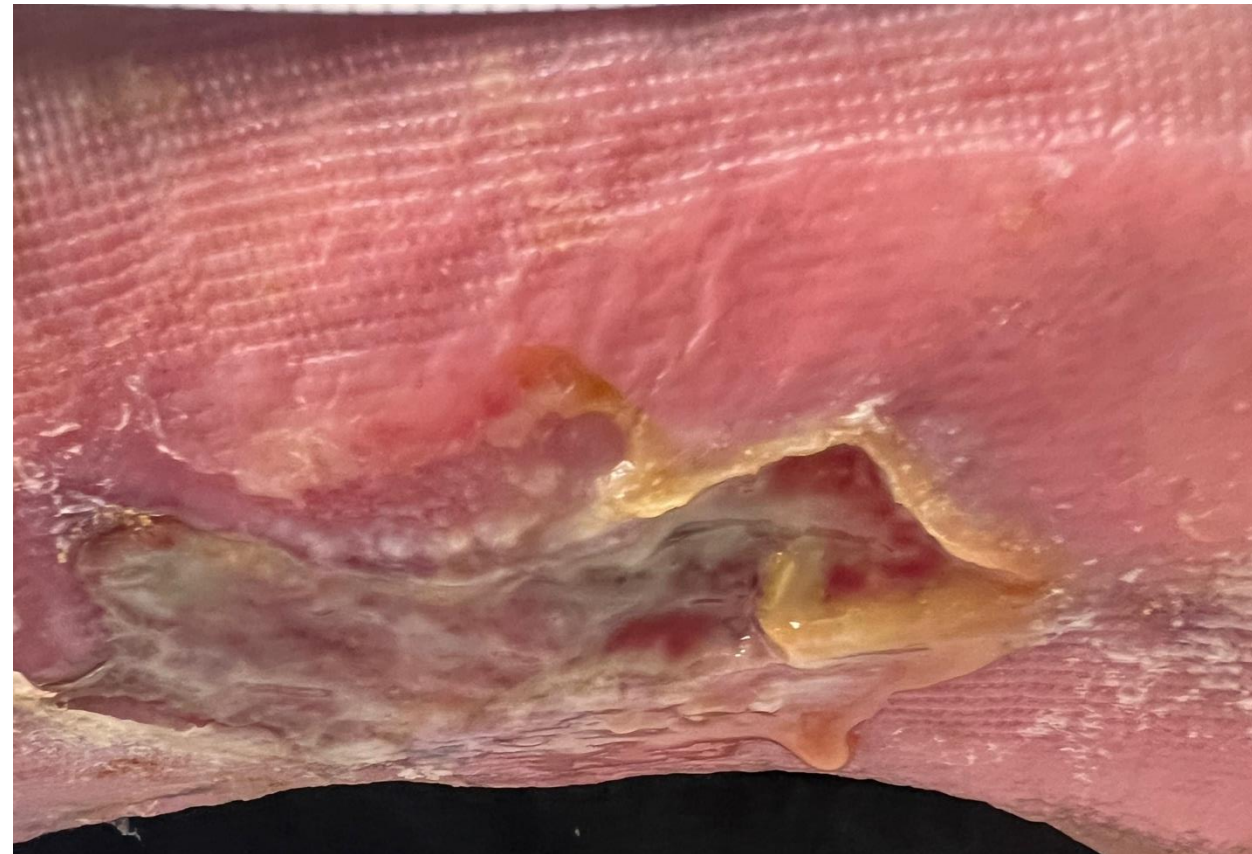
5/14/2025



Case 5



5/16/2025 surgery



5/23/2025

Case 5



5/30/2025



6/13/2025



7/29/2025

Cases: Application of Adipose Tissue Grafting Techniques

Michael N. Desvigne, MD, FACS, CWS, FACCWS, MAPWCA
Plastic & Reconstructive Surgery, Wound Care & Hyperbaric Medicine
Abrazo Arrowhead Hospital & Wound Clinic
Glendale, AZ

What Is the Adipose 3D Printer System?

1. Artificial intelligence tablet
 - Integrated AI application with wound detection and 3D file generator
2. Adipose 3D printer
 - Adipose bioink printer
3. Kit
 - Single-use micronizers and printing accessories to process adipose and create PCL mold



Cytokines and Wound Healing

- Adipose graft provides all necessary cytokines for wound healing

Cytokine	Role in Wound Healing
TGF- β 1	Stimulates collagen production, strengthens the wound
TGF- β 3	Reduces scarring by balancing collagen deposition
TGF- β 2	Controls inflammation, preventing excessive scar tissue
PDGF-R β	Promotes blood vessel growth, ensuring oxygen and nutrients for healing
FGF-4	Encourages skin and connective tissue cell growth
FGF-7	Helps new skin form by promoting epithelial cell multiplication
ANG-2	Works with other growth factors to form new blood vessels
ANG-1	Strengthens newly formed blood vessels
PDGF-AA	Recruits fibroblasts to rebuild tissue
VEGF	Stimulates new blood vessel growth, ensuring oxygen delivery

46y Female with Double Lung Transplant Sustains IV Infiltration

- 7/29: Injury
- 9/3: Excision
- 10/1: Dermal bilayer
- 10/9: Bilayer removed



10/25



46y Female with Double Lung Transplant Sustains IV Infiltration

- 11/25: s/p Codfish skin micronized
- On prednisone 10 mg, mycophenolate, cyclosporine



46y Female with Double Lung Transplant Sustains IV Infiltration

- 12/23: Operative debridement, synthetic mini matrix and umbilical cord placed
- 12/26: First dressing change, silicone non-adherent, ABD, sterile gauze, and elastic compression bandage



46y Female with Double Lung Transplant Sustains IV Infiltration

- 1/7: 3D fat grafting
- “Fatsicle”
- Dressing: Non-adherent



46y Female with Double Lung Transplant Sustains IV Infiltration



46y Female with Double Lung Transplant Sustains IV Infiltration

- 2/10: Negative pressure wound therapy
- 2/13: Intraoperative prior to full-thickness skin graft
- 2/17: First dressing change



46y Female with Double Lung Transplant Sustains IV Infiltration

3/25



46y Female with Double Lung Transplant Sustains IV Infiltration

10/25



03/26



Other Indications for Adipose 3D Printing System

Case Summary: Recurrent Pressure Ulcer

- 64y Male with paraplegia for 30 yrs presents with recurrent pressure ulcer right hip, deemed poor candidate for additional surgery
- Surgical History: Multiple procedures for pressure injury
- Medical History: CAD, HTN, smoker
- Treatment: Trial of adipose 3D printing using freezing method

Recurrent Pressure Ulcer: Day 1



Recurrent Pressure Ulcer: Day 1



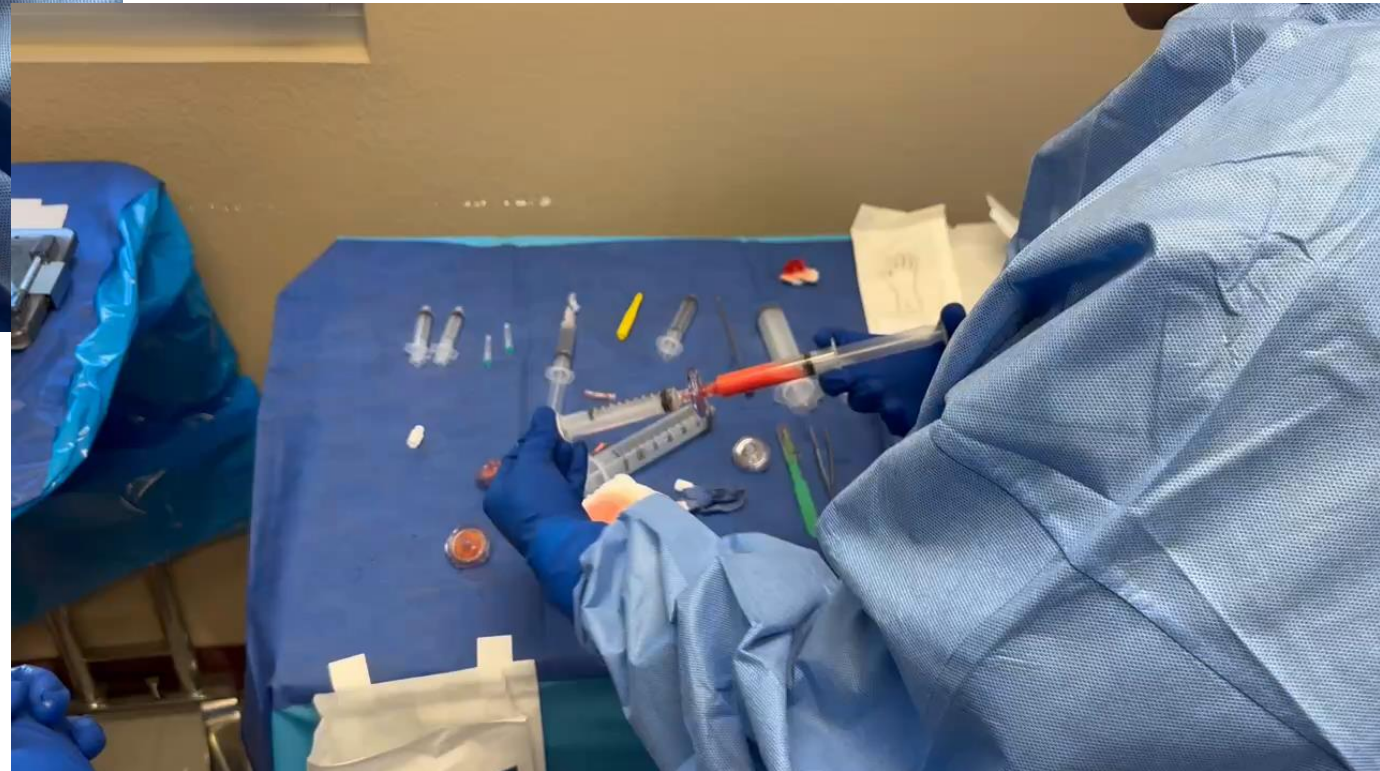
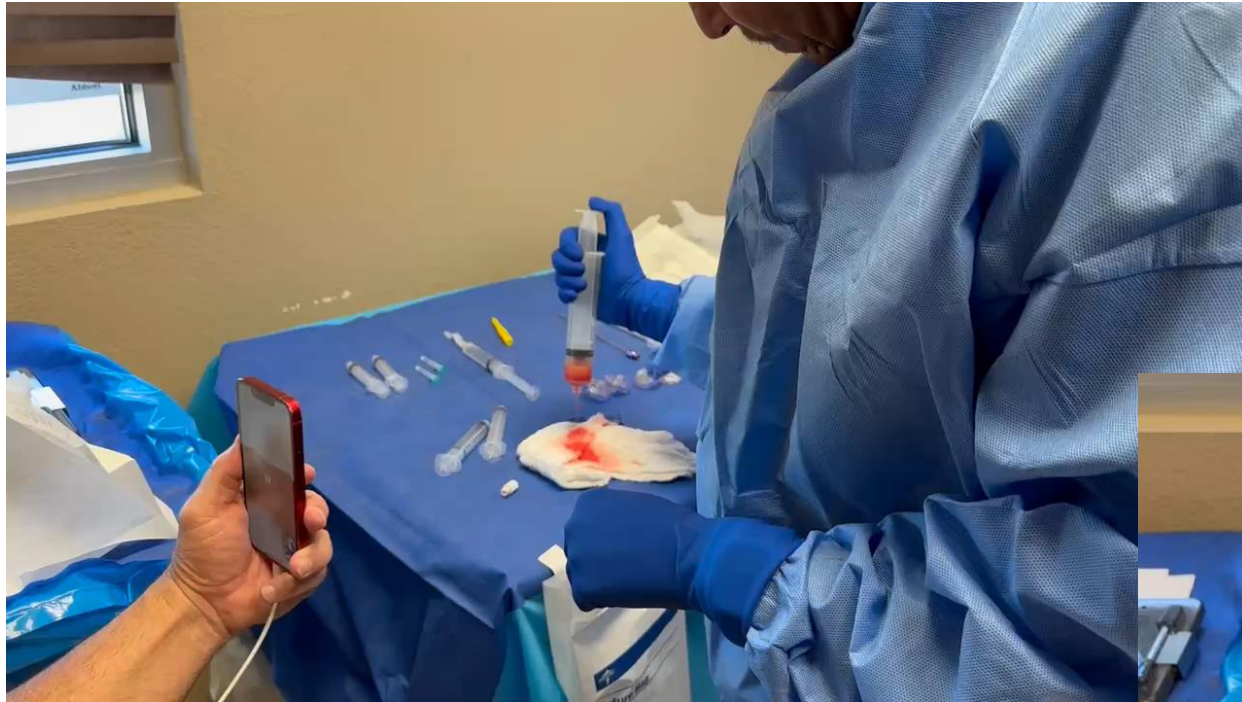
Recurrent Pressure Ulcer: Day 1



Recurrent Pressure Ulcer: Day 1



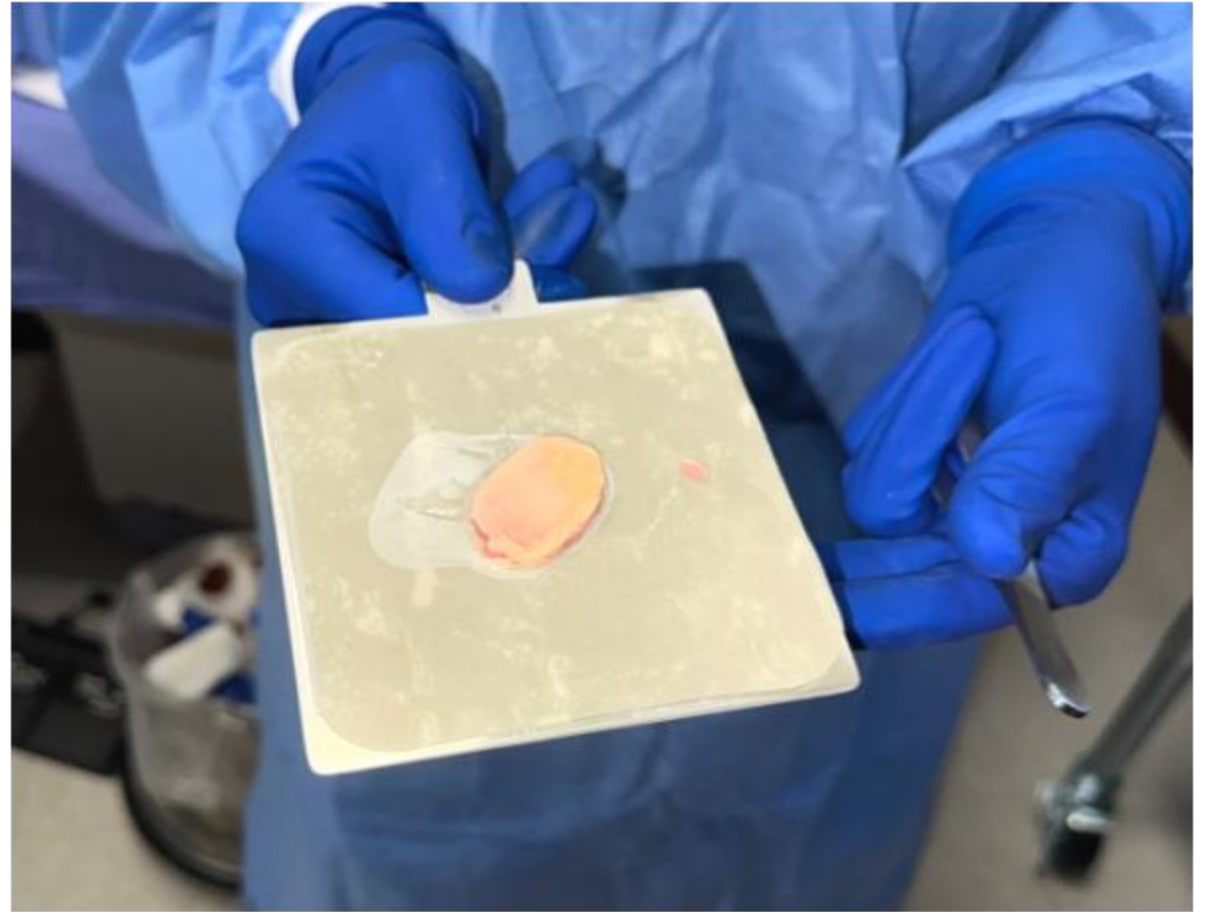
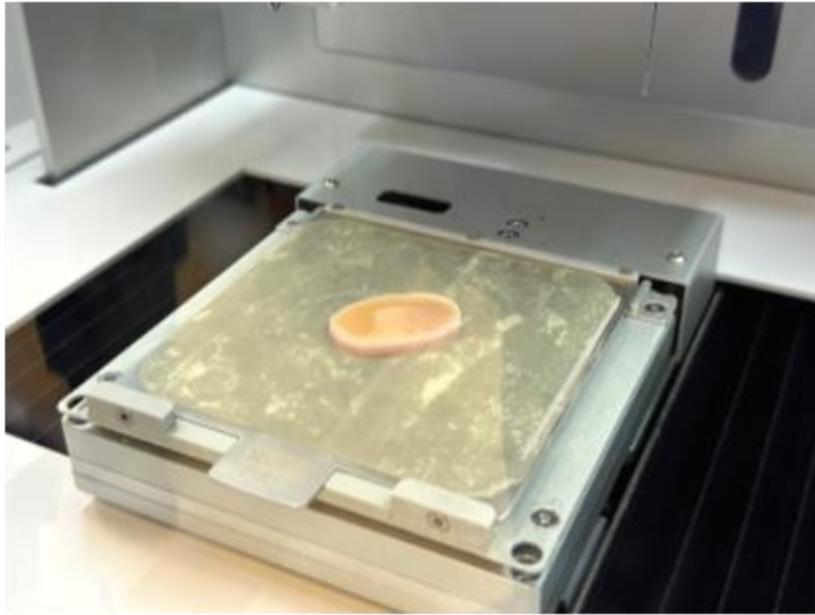
Recurrent Pressure Ulcer: Day 1



Recurrent Pressure Ulcer: Day 1



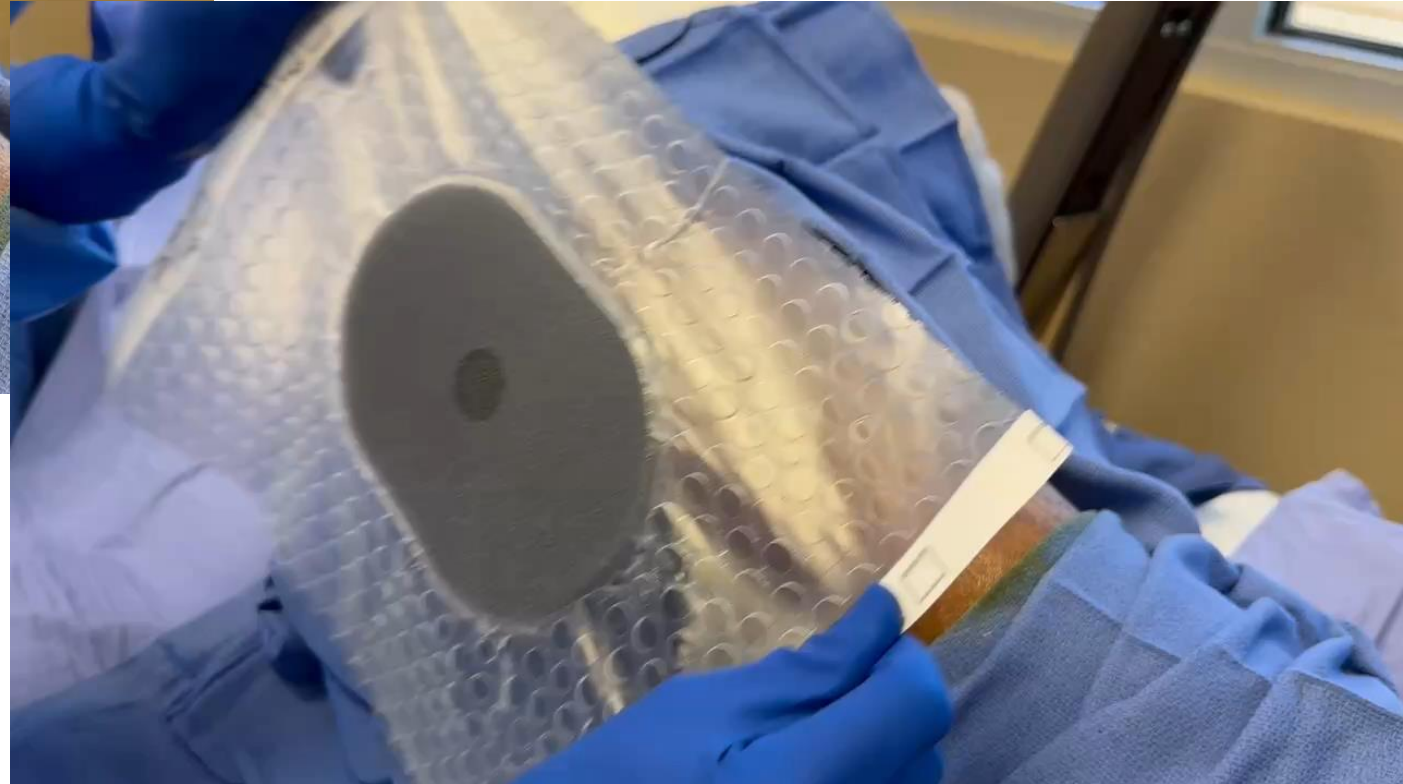
Recurrent Pressure Ulcer: Day 1



Recurrent Pressure Ulcer: Day 1



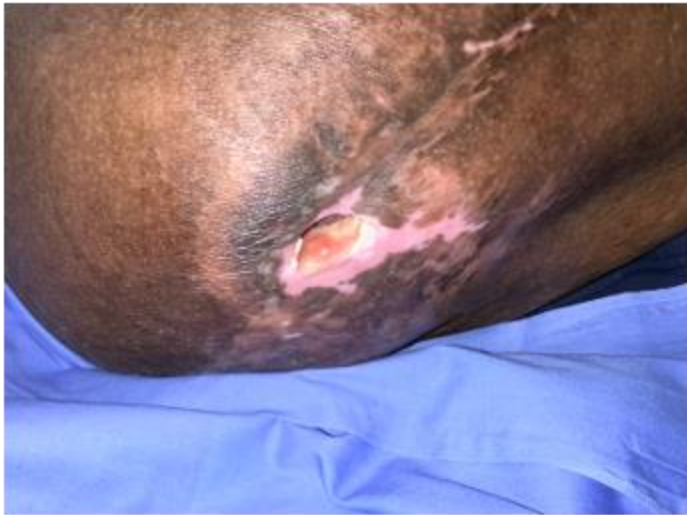
Recurrent Pressure Ulcer: Day 1



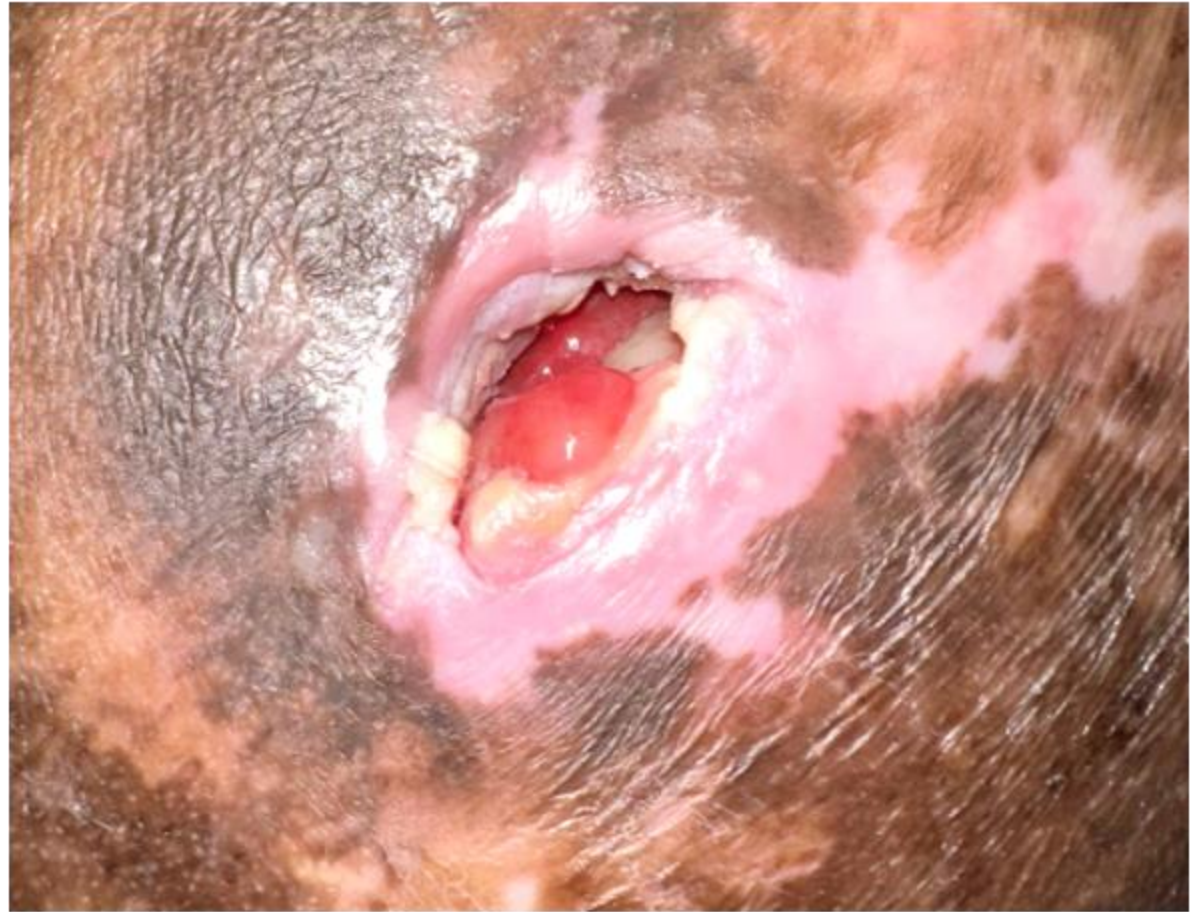
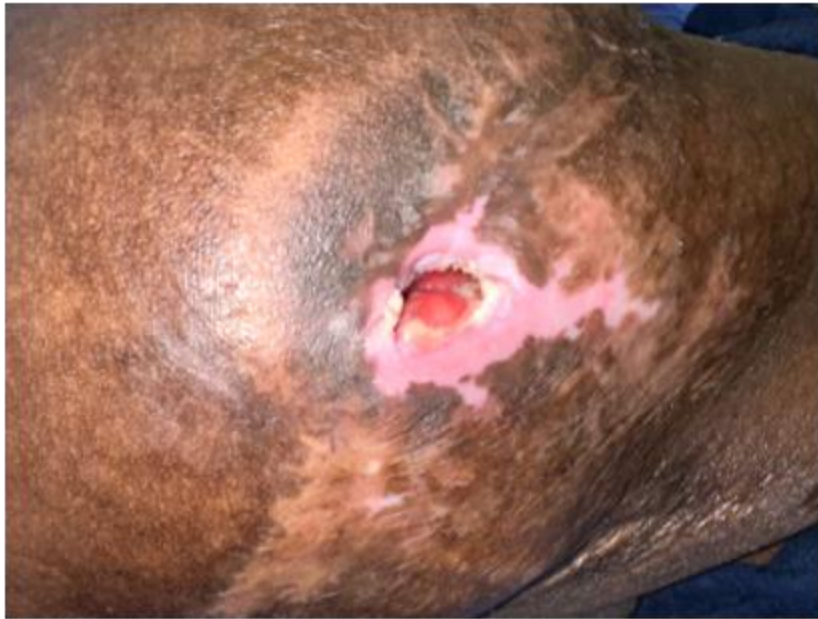
Recurrent Pressure Ulcer: Day 14



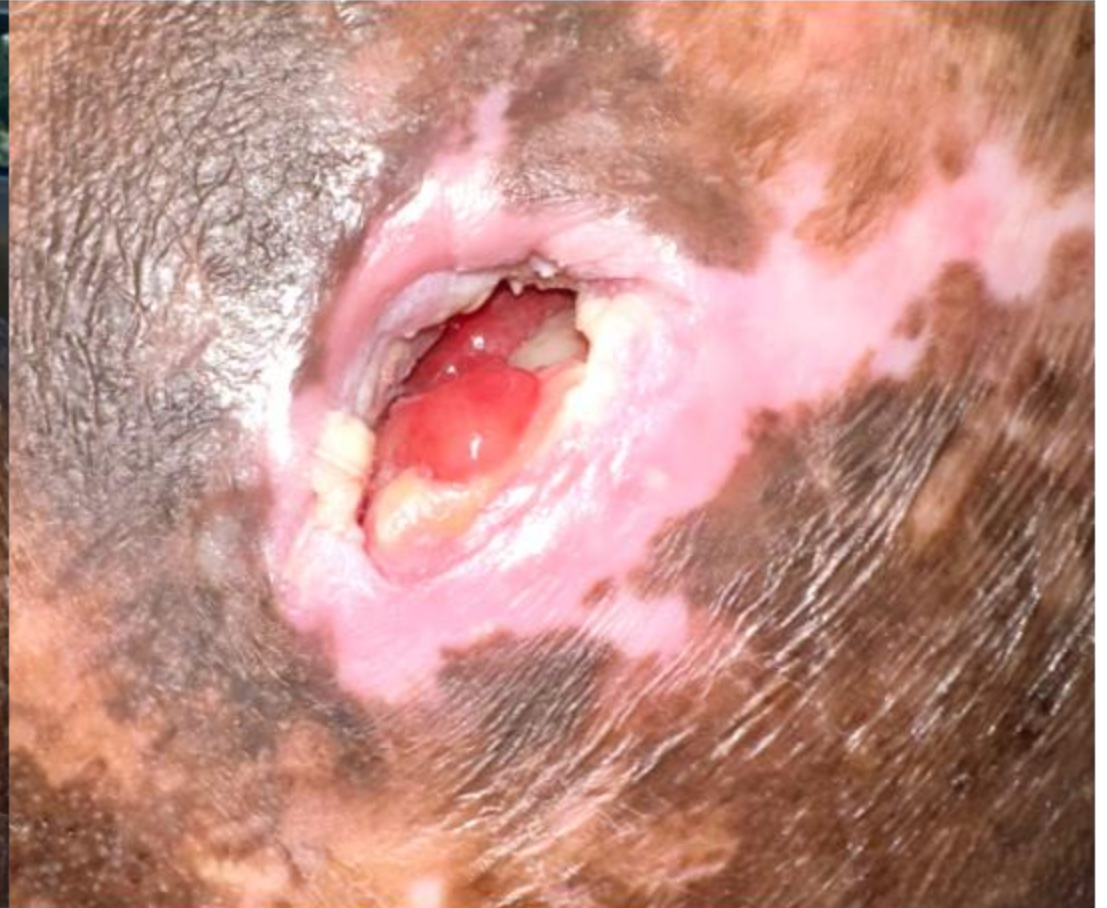
Recurrent Pressure Ulcer: 4 Wks



Recurrent Pressure Ulcer: 6 Wks



Recurrent Pressure Ulcer: 1, 6 Wks



Case Summary:

Right Hip Ulcer, Stage 4

- 77y Female with spina bifida who is ambulatory with a walker presents with right hip ulcer from soft tissue trauma; patient prefers nonsurgical intervention
- Medical History: No CAD, DM, HTN
- Social History: Lives with her husband at home
- Treatment: Excisional debridement performed with negatively charged dense fiber dressings changed 2-3 times wkly; trial of adipose 3D printing using fibrin method

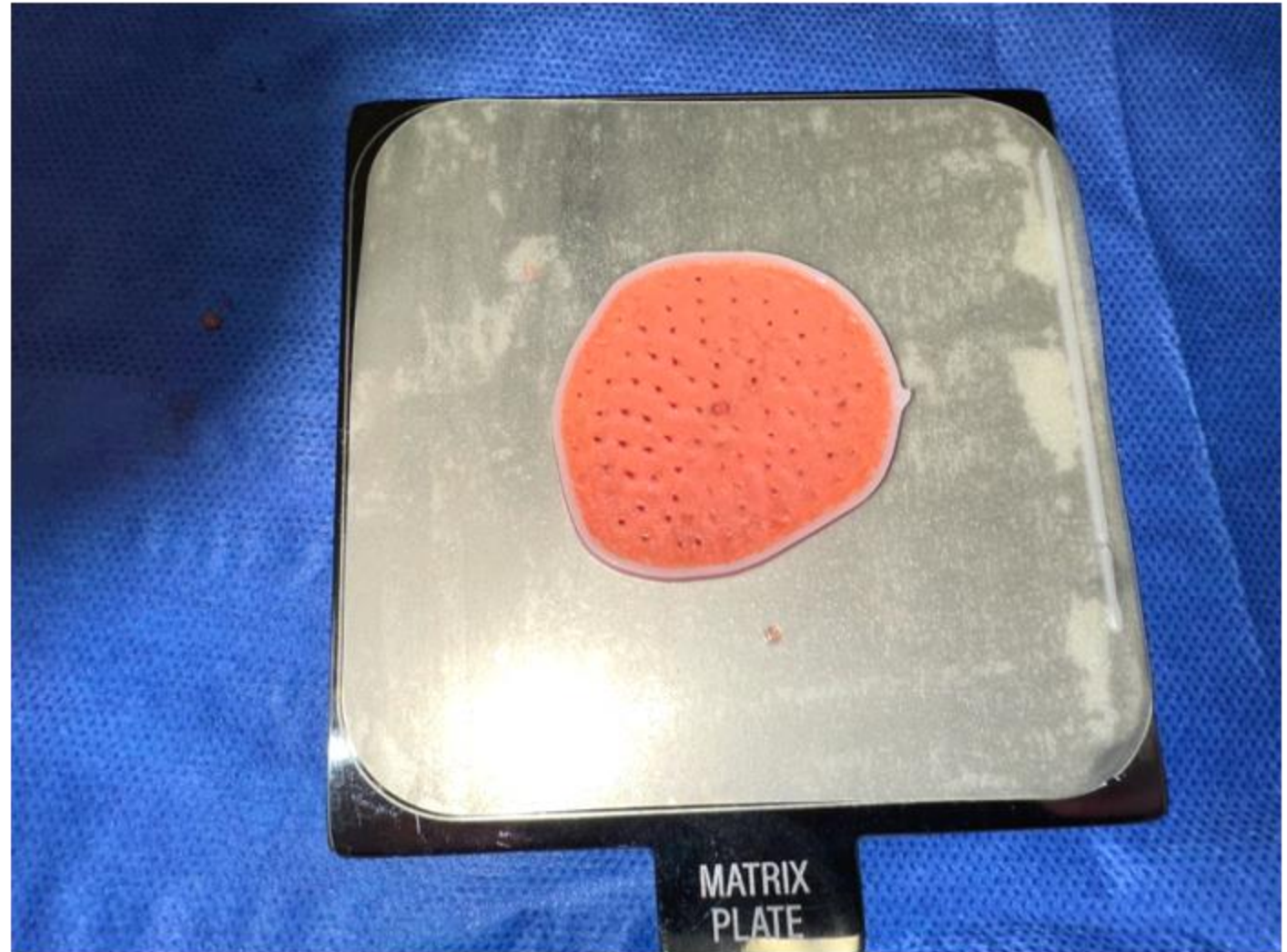
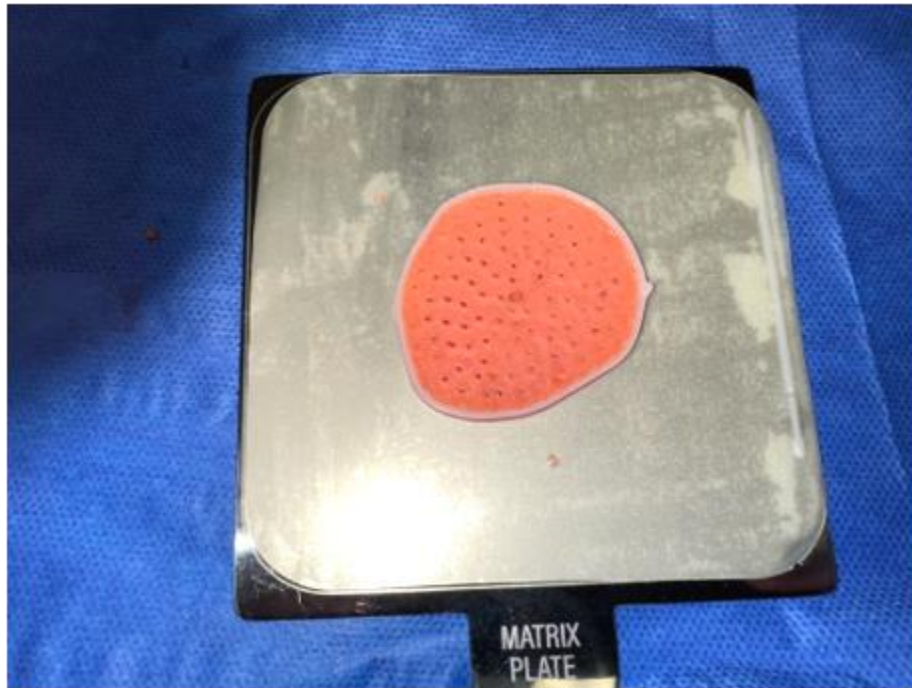
Right Hip Ulcer, Stage 4: Day 1



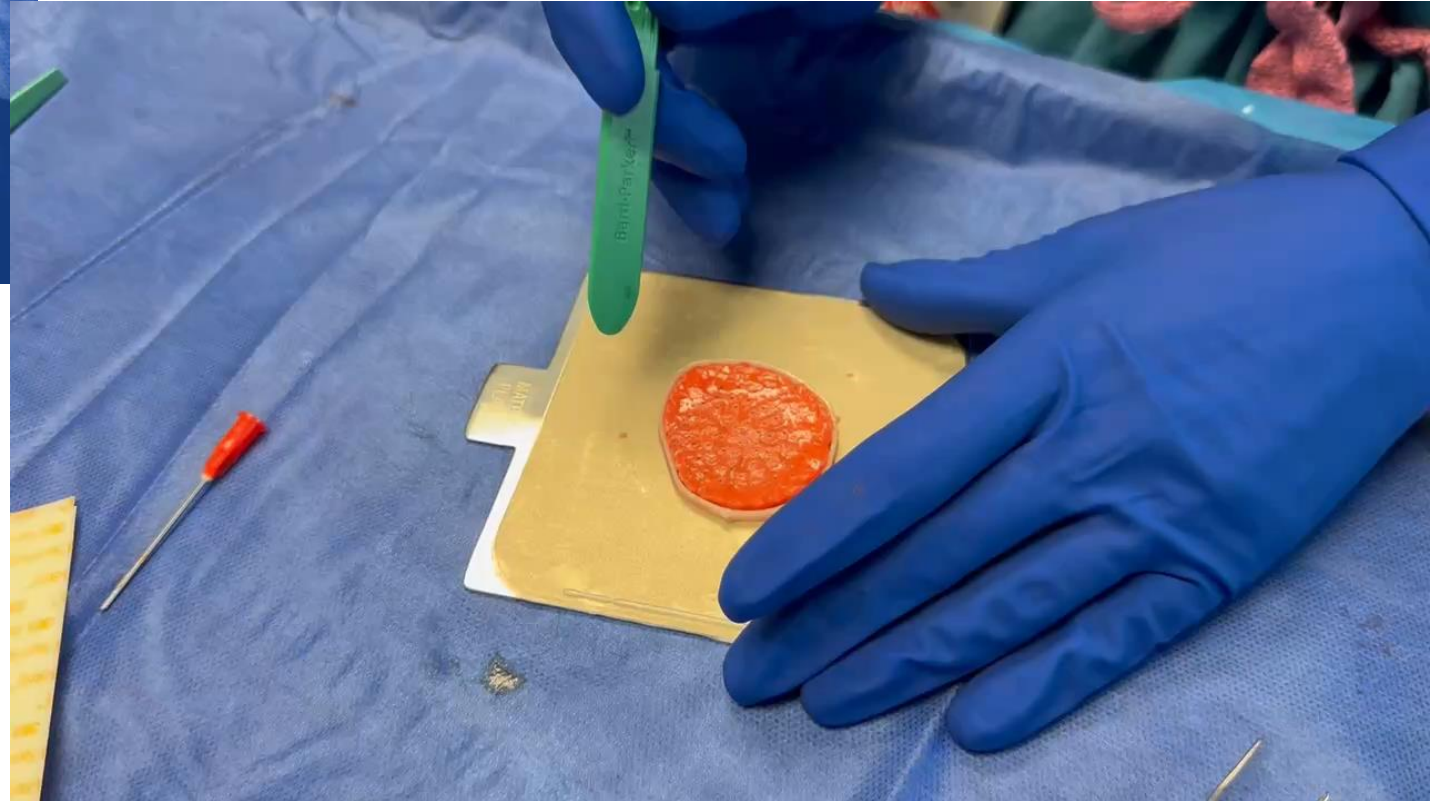
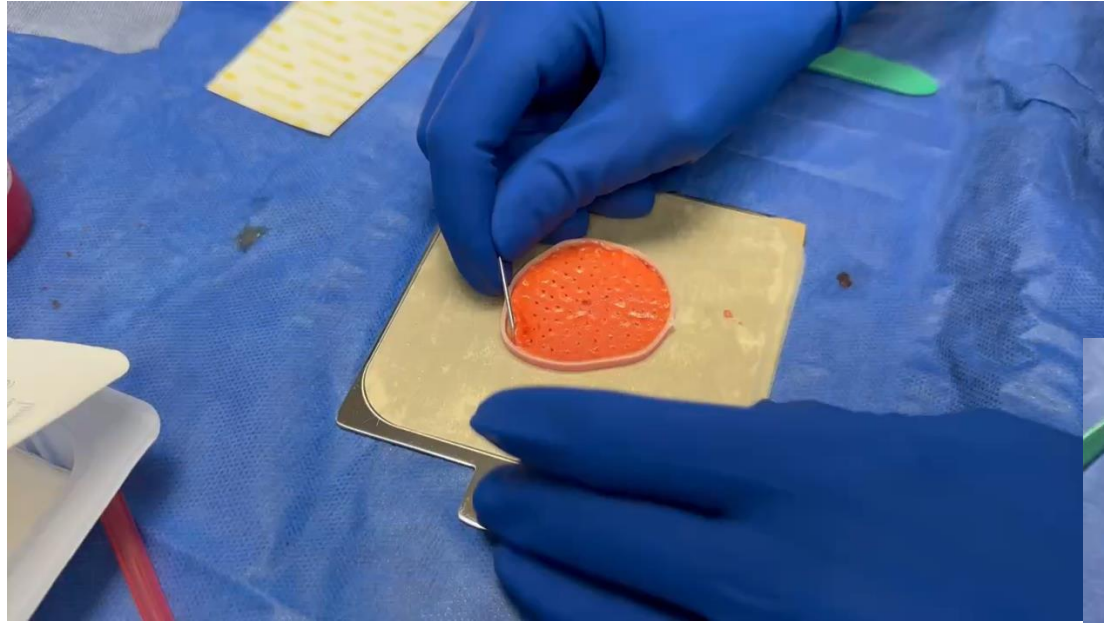
Right Hip Ulcer, Stage 4: Day 1



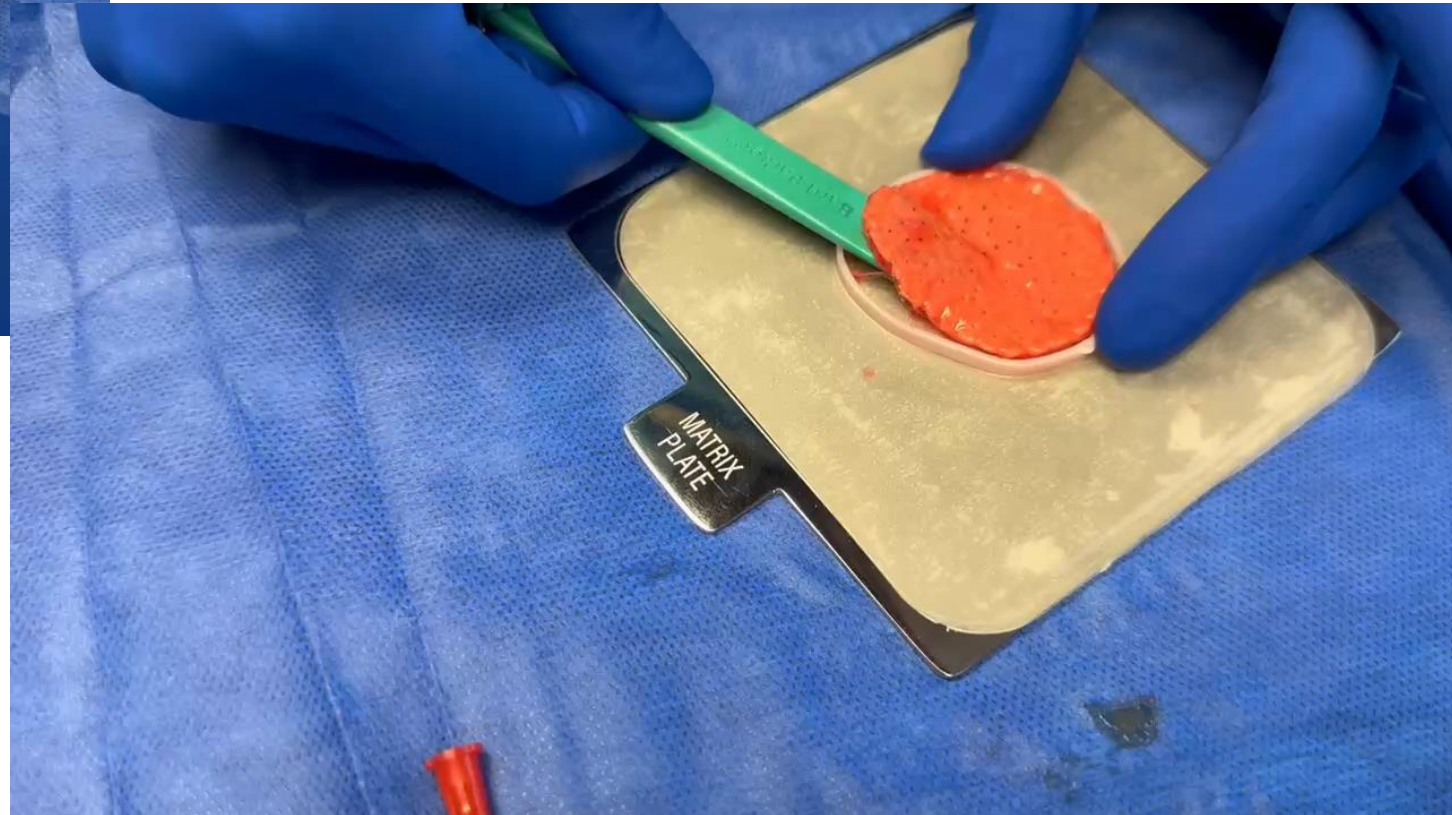
Right Hip Ulcer, Stage 4: Day 1



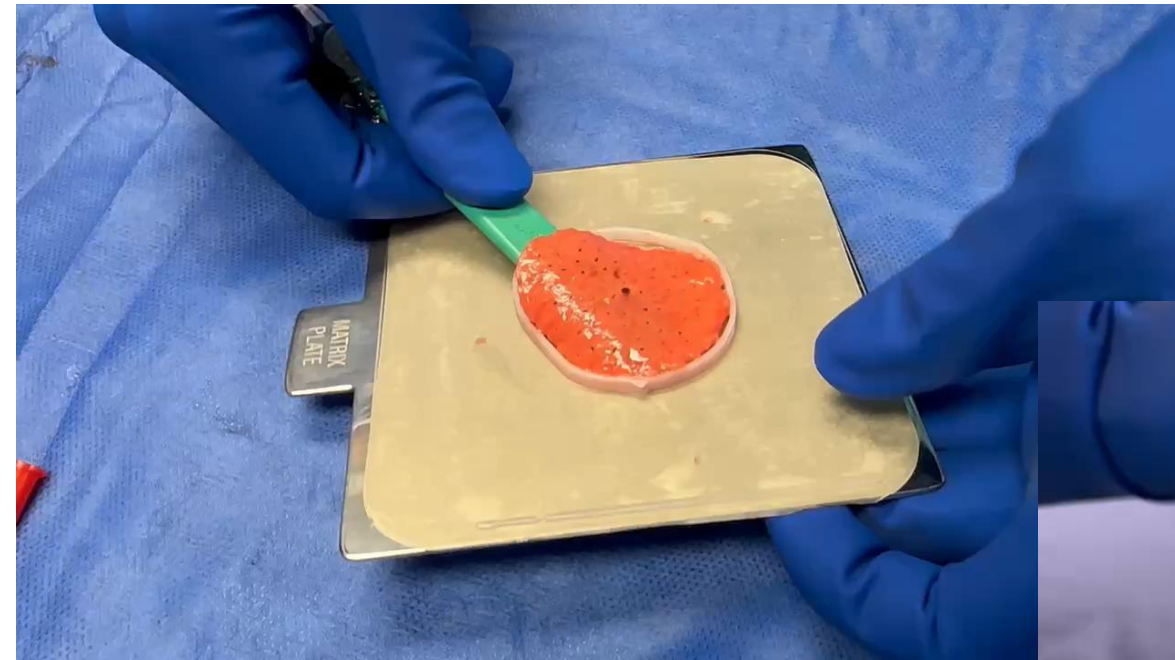
Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1



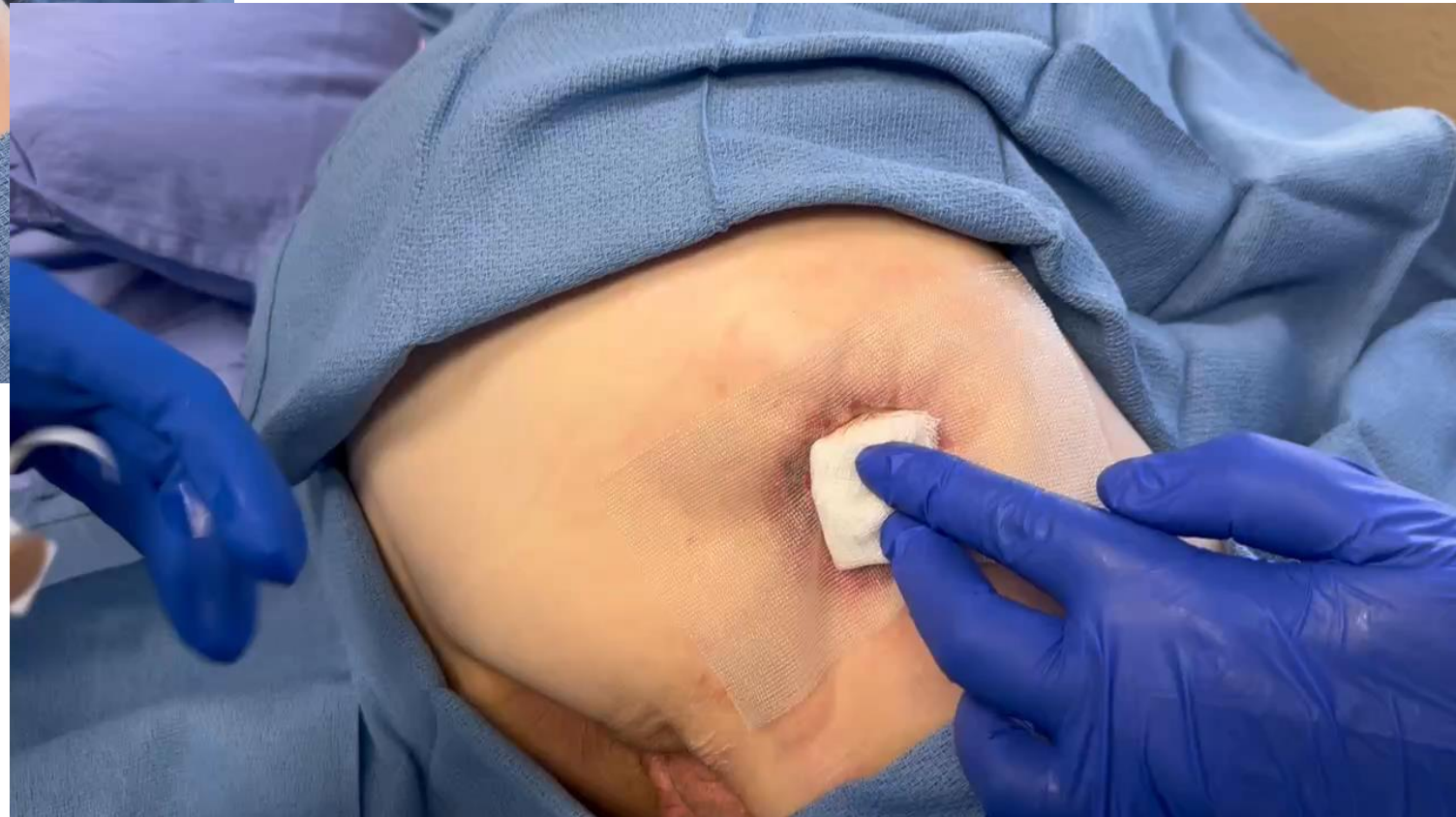
Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1



Right Hip Ulcer, Stage 4: Day 1, 14



Right Hip Ulcer, Stage 4: Day 14



Clinical Pearls

- Adipose bioprinting is a novel approach to wound management but not a novel approach to regenerative tissue engineering
- Adipose bioprinting allows for personalized point-of-care delivery
- The technique is evolving, and the learning curve is steep
- The use of bioinks and adipose grafting may provide an option for patients with soft tissue deficits requiring tissue support for wound bed preparation and or complete healing
- I believe the level of innovation challenges us, the clinicians, to think outside the box

Thank You