Casting a Wider Net:

Fish Skin Grafts and the Future of Limb Salvage

Supported by an educational grant from Kerecis

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  New York, NY

Faculty Disclosures

- **Cyaandi Dove, DPM**
  Advisory Board: Solventum, Kerecis; Consultant: Mediwound, LLC, AOTI, Inc., Aurealis Therapeutics
- **Michael P. Ogilvie, MD, MBA, FACS**
  Nothing to disclose in relation to this activity
- **Alisha Oropallo, MD, PhD, FACS, FSVS, FABWMS**
  Nothing to disclose in relation to this activity

Disclosures

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Learning Objectives

- Describe the biological properties, mechanisms of action, and clinical evidence supporting the use of fish skin grafts (FSGs) in wound healing and limb salvage
- Analyze illustrative clinical cases demonstrating the use of fish skin grafts to support limb salvage

FSG = fish skin graft.

Omega-3-Rich Fish Skin for Chronic or Complex Wounds: Examining the Latest Publications and Clinical Applications

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New York, NY

Is Fish Skin an Important Piscine (Dermal-Derived) Extracellular Matrix (ECM)?

Structural and Regulatory Role of ECM

- Extracellular matrix (ECM) serves as supporting scaffold for invading cells
- Cell adhesion to ECM is a prerequisite for maximal bioactivity of growth factors
- ECM molecules and growth factors regulate cellular processes together during wound healing
- Fish skin is a xenograft (acellular graft, ADG) that retains the natural ECM structure of the fish dermis – high Omega-3 Fatty Acid profile

ECM = extracellular matrix; ADG = autogenous dentin graft.
Briquez PS, et al. *Adv Wound Care (New Rochelle).* 2015;4(8):479-489.

Fish Skin – Product Overview

- Fish skin for medical use is patented
  - Consists of cells embedded in a network of non-living tissue
  - CE-marked and FDA-cleared
  - Proteins and lipids in their natural state
  - Decellularized, non-allergenic, and biocompatible
  - Skin sourced from Icelandic cod



CE = conformité européenne; FDA = Food and Drug Administration.

Tissue Engineering

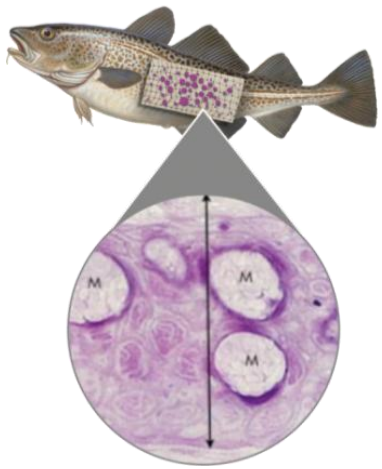
- Three Dimensionality
- Mechanical Properties
- Chemical Complexity
- Native Organization



Optimal tissue has removed cells, yielding a debris-free native structure that is not affected or altered by the applied treatment, retaining the overall lipid content, ECM biochemical composition, structure, and complexity.

Evangelatov A and Pankov R. Regenerative Medicine and Tissue Engineering; 2013.

Patented Processing



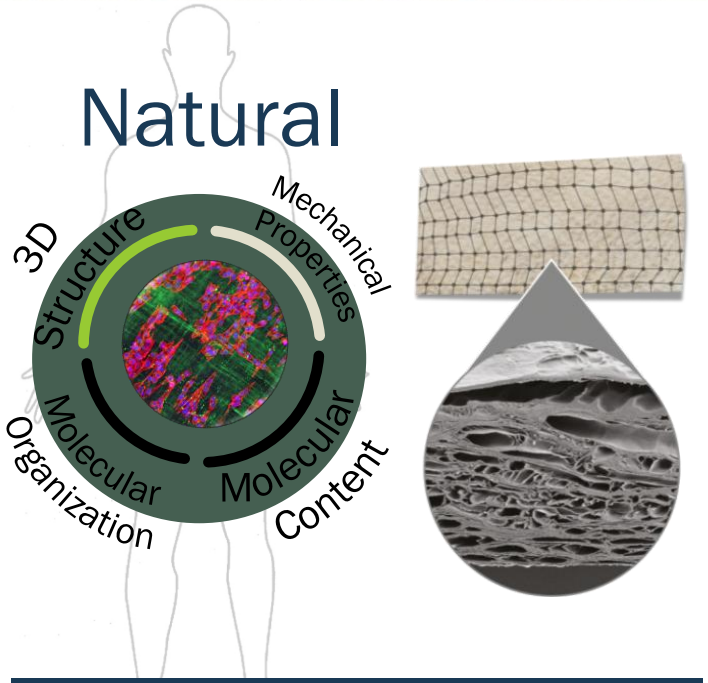
Fish Skin

- Apart from scales and the fish cell's DNA, fish skin is **identical** to human skin
- Viruses in **cold water fish** do not have utility in the human body
- Cells are removed from skin in a **gentle process**

7-Step Processing Method

Patented Process

- **Lack of viral transmission risk removes need for harsh viral inactivation phase**
  - No strong alcohols or detergents
  - No mechanical pressing or tampering
  - No crosslinking
- **Sustainable and environmentally friendly,** as it utilizes fish skin as a byproduct of commercial fisheries
- These factors create **the most cost-effective product on the market**



Omega-3-Rich

- All skin components **preserved**
  - Proteins, glycans, and fats (including Omega-3s)
- Graft is applied to human wounds
- Recruits **stem cells** and **regular cells**
- Facilitates **tissue regeneration**

Kerecis. Accessed September 23, 2026. https://www.kerecis.com/fish-skin-technology.

IFSG Regenerative Tissue Technology: Advantages

Product Category	Preserved Molecular Content	Intact Native Organization of Molecules	Skin-Like Natural Mechanical Properties	Skin-Like 3D Structure	Causes Second Wound	Summary
Allograft	✓	✓	✓	✓	✓	Graft failure can be a problem
Embryonic	✓	✓	✗	✗	✗	Dense barrier membrane, no cellular ingrowth
Tissue-Engineered	✓	✗	✗	✓	✗	Briefly living cells
Mammalian	✗	✓	✓	✓	✗	Some structural scaffolding, buffer proteases
Fish Skin	✓	✓	✓	✓	✗	**Biologically active structural tissue** Faster healing with guided tissue regeneration

Ganesan O, et al. *Front Surg.* 2025;12:1504563.

Dermal Scaffold Grafts: A Closer Look

Mechanism of Action

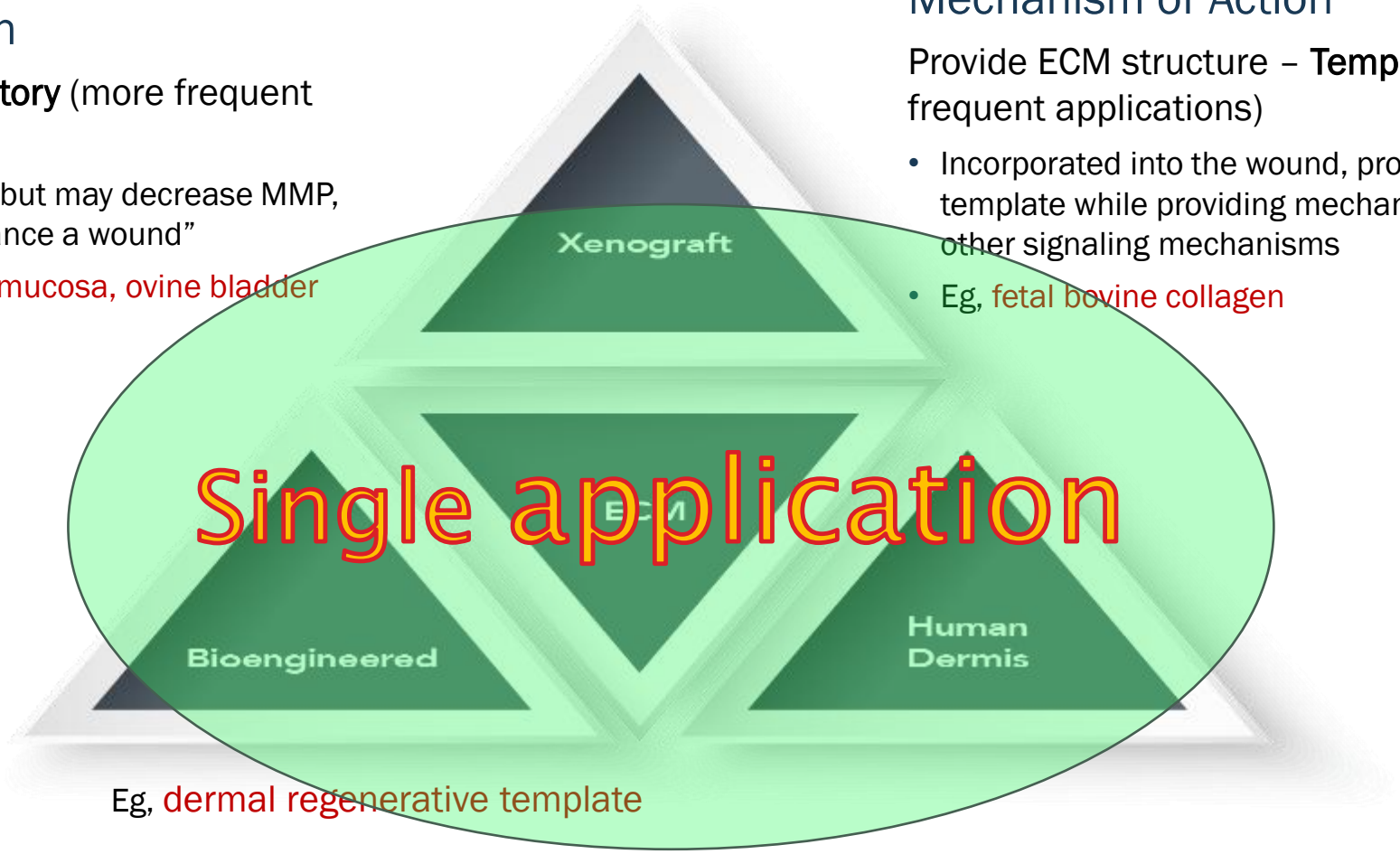
Provide signals – **Modulatory** (more frequent applications)

- Not so much incorporated but may decrease MMP, enhance signaling, “rebalance a wound”
- Eg, piscine skin; ovine submucosa, ovine bladder

Mechanism of Action

Provide ECM structure – **Template** (less frequent applications)

- Incorporated into the wound, provide a structural template while providing mechanical as well as other signaling mechanisms
- Eg, fetal bovine collagen



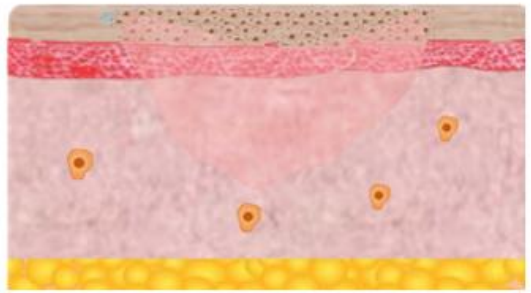
Eg, dermal regenerative template

Debels H, et al. *Plast Reconstr Surg Glob Open*. 2015;3(1):e284.

Four Hallmarks of IFSG Technology

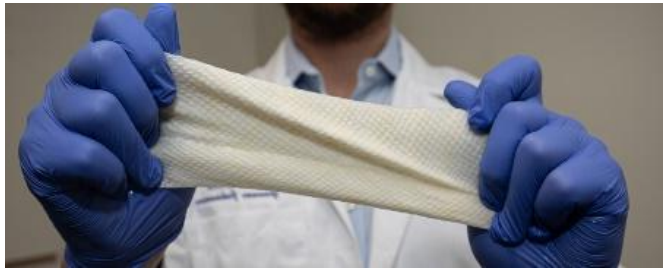
1. Natural 3D Structure

- Intact natural structure with its chemical complexity is inimitable by synthesis or even the most advanced engineering
- Natural structure to guide natural tissue regeneration
- The right pore size, chemicals, signals, fatty acid profile, and tensile strength



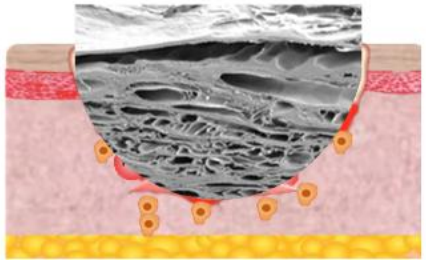
The intact structure provides a scaffold for guided tissue regeneration, limiting scarring

2. Natural Mechanical Properties

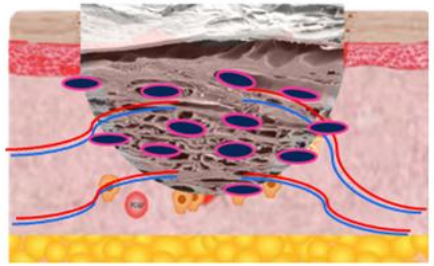


- Naturally strong
- Preserves superior handling characteristics
- **Handles like skin – pliable and easy to suture and staple**
- Surgeon favored for ease of use and efficacy

3. Natural Molecular Content



Lipid-rich biologic barrier protects against pathogens, limits irritation, and modulates tissue response



Chemical complexity of the fish skin promotes rapid cell ingrowth and neovascularization

4. Natural Molecular Organization



- Fish source allows for uniquely gentle processing
- Thousands of proteins, lipids, and glycans are **natively organized** and mimic natural tissue for ingrowth

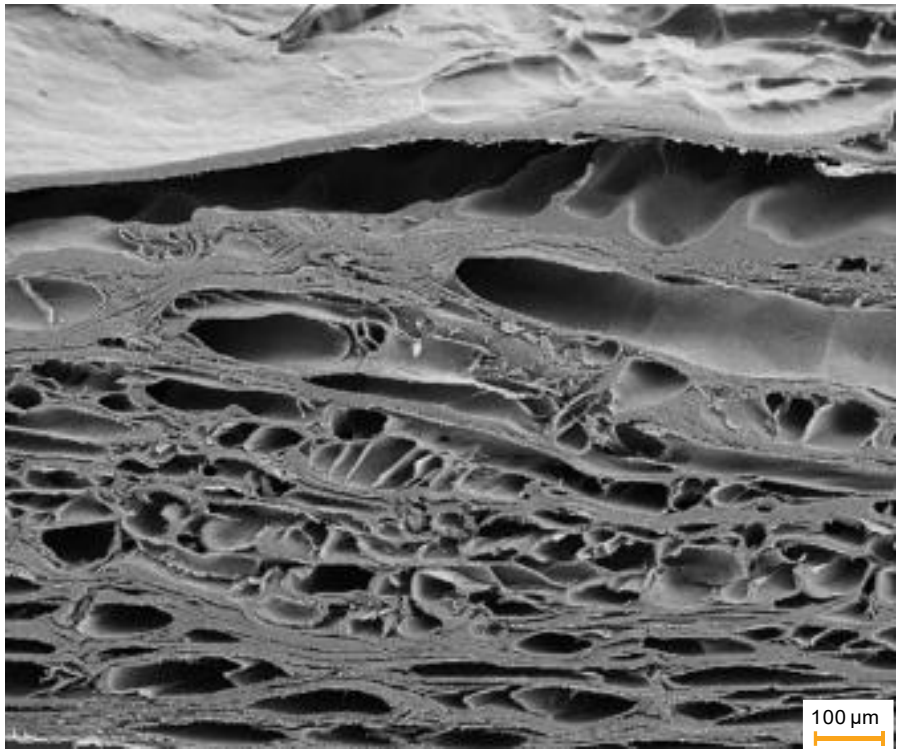
IFSG = intact fish skin graft.

Evangelatov A and Pankov R. Regenerative Medicine and Tissue Engineering; 2013.

1. Natural 3D Structure

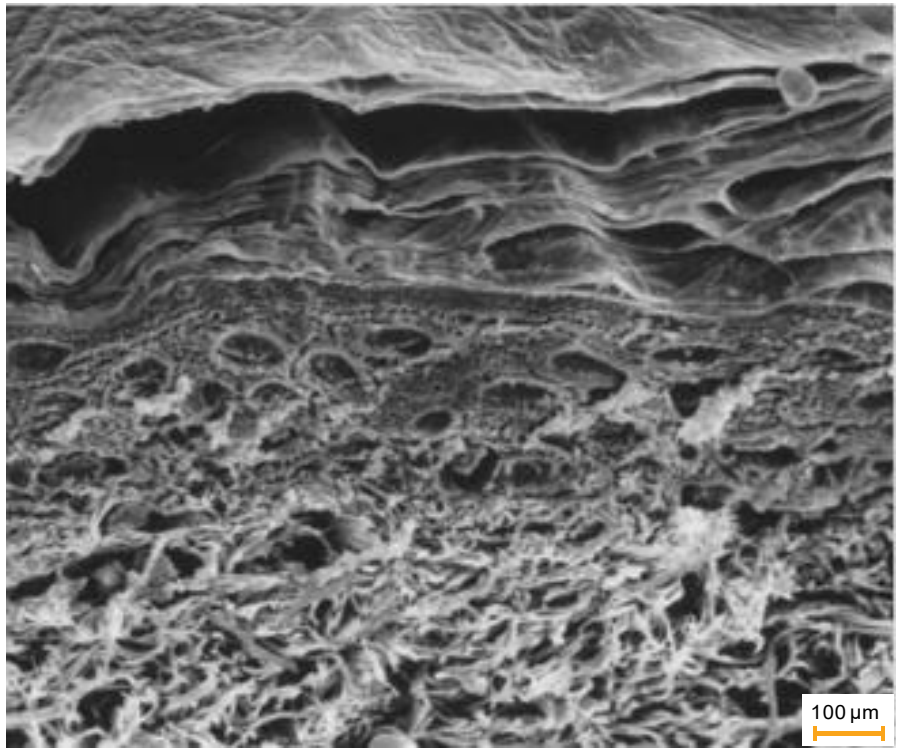
Fish skin: Full-thickness from epidermis to dermis

FISH SKIN for **HUMAN SKIN**



Epidermis

Dermis

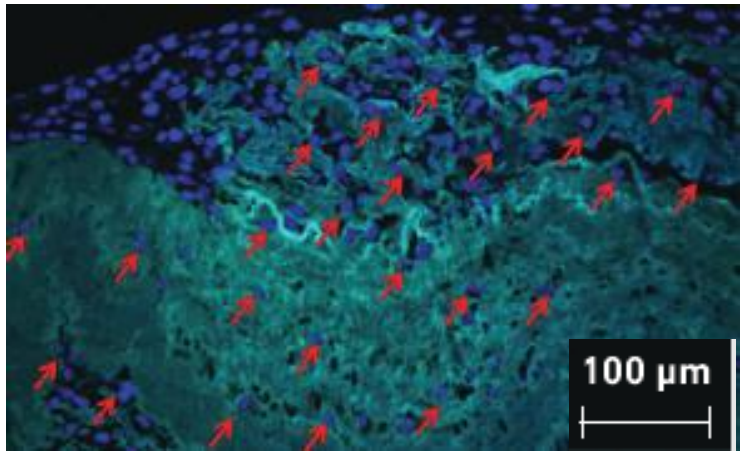


Magnusson S, et al. *Mil Med.* 2017;182(S1):383-388.

1. Natural 3D Structure

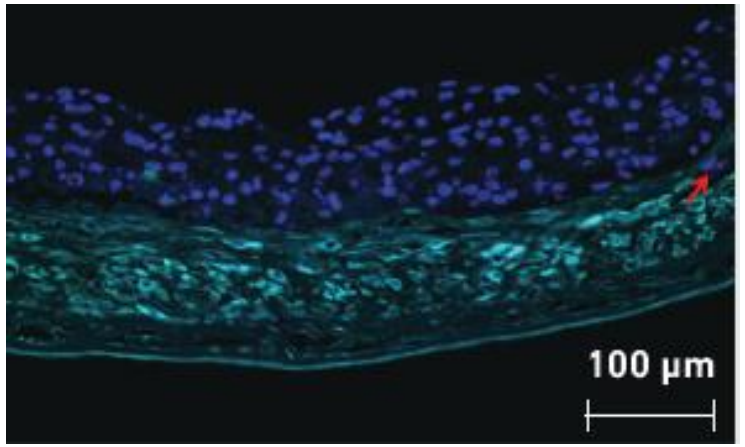
10x greater porosity – significantly more cell ingrowth

Omega-3 Fish Skin

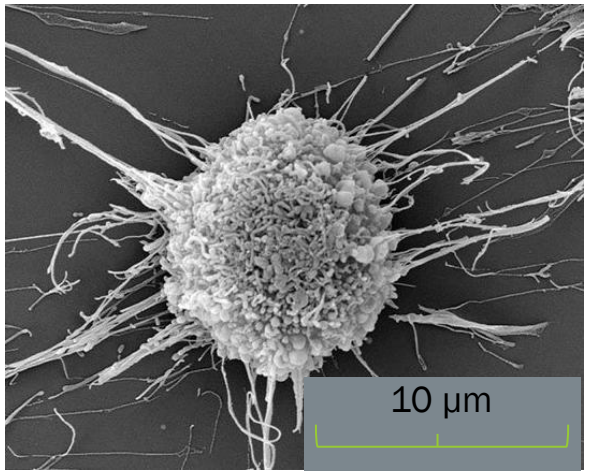




Amnion/ Chorion







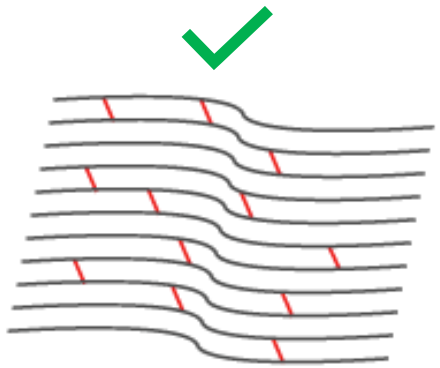
Human Fibroblast

Magnusson S, et al. *Mil Med*. 2017;182(S1):383-388.

2. Natural Mechanical Properties

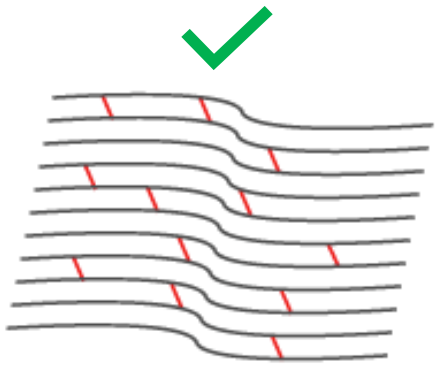
Artificial cross-linking leads to slower cellular ingrowth

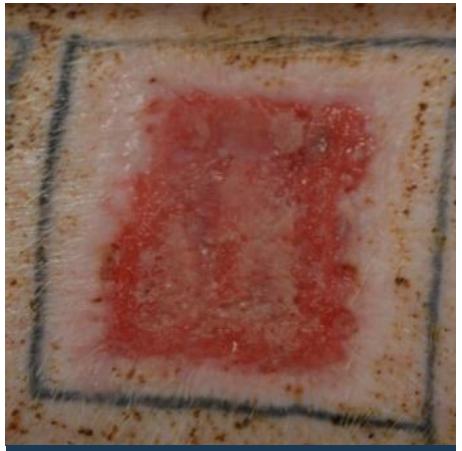
No Artificial Cross-Linking



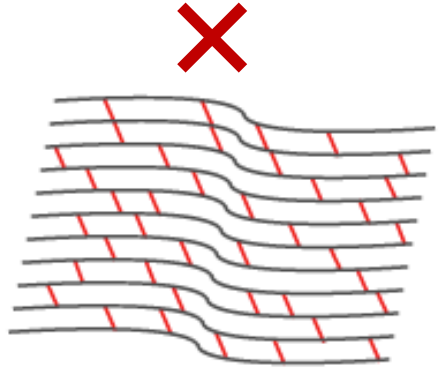


Human Skin





Fish Skin



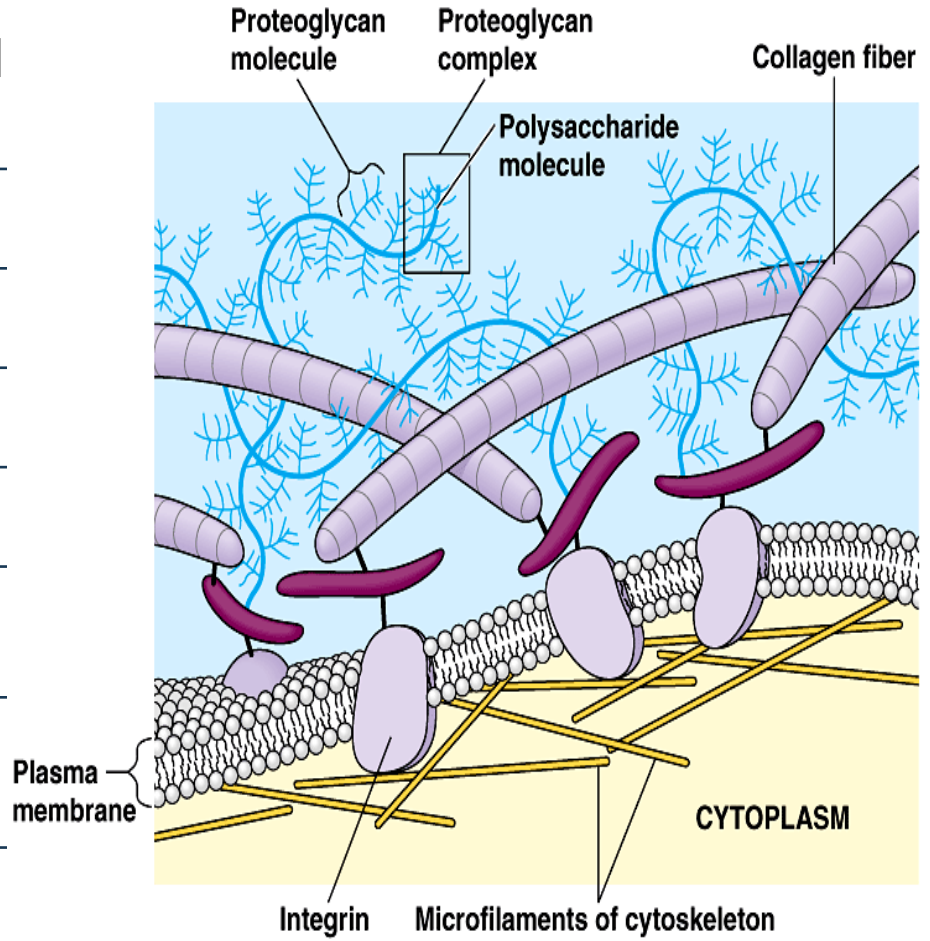


Fetal Bovine Tissue

Stone R 2nd, et al. *Int J Mol Sci*. 2021;22(4):1590.

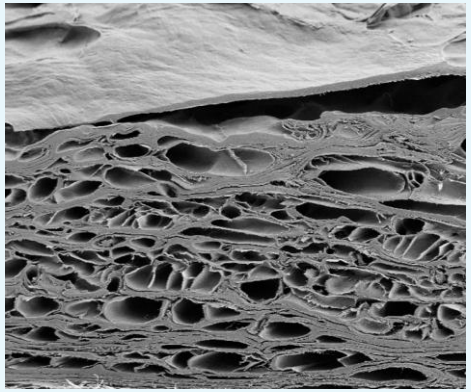
3. Natural Molecular Content: Comparison of Human Skin, Fish Skin, and Mammalian Tissue

	HUMAN SKIN	INTACT FISH SKIN	PROCESSED MAMMALIAN TISSUE
Collagen	✓	✓	✓
Elastin	✓	✓	✗
Laminin	✓	✓	✗
Fibronectin	✓	✓	✗
Proteoglycans	✓	✓	✓
Glycosamino-glycans	✓	✓	✓
Lipids *No Omega-3s*	✗	Includes Omega-3s	✗

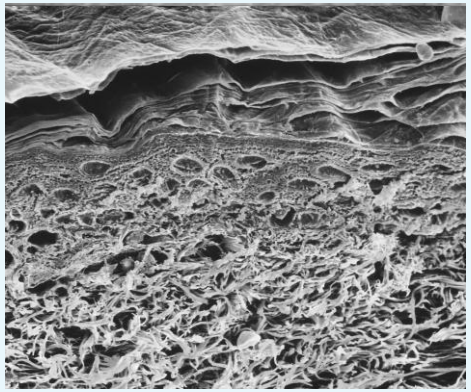


Kerecis. Accessed September 23, 2026. https://www.kerecis.com/fish-skin-technology.

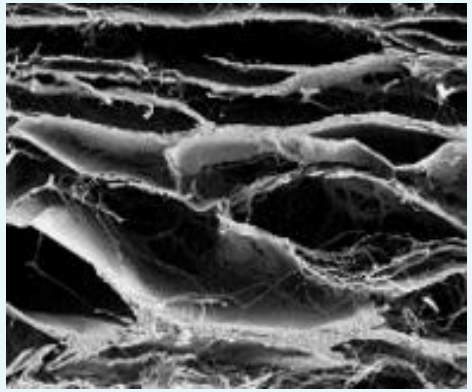
4. Natural Molecular Organization: Microstructure Comparison



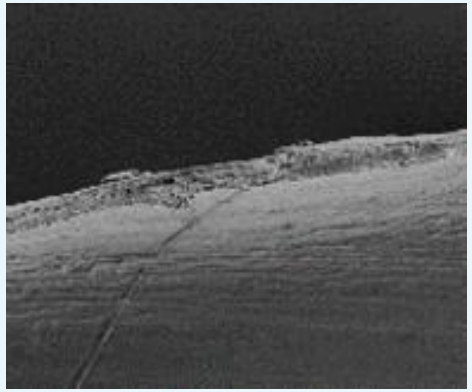
Fish Skin



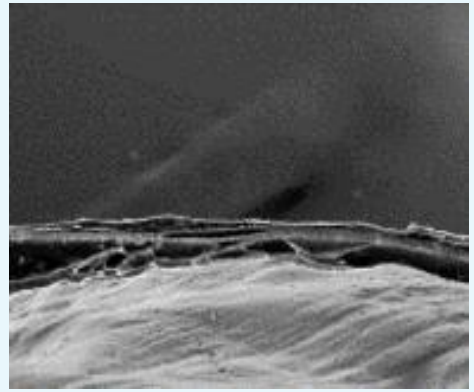
Human Skin



Porcine Urinary Bladder Matrix



Human Amnion/Chorion



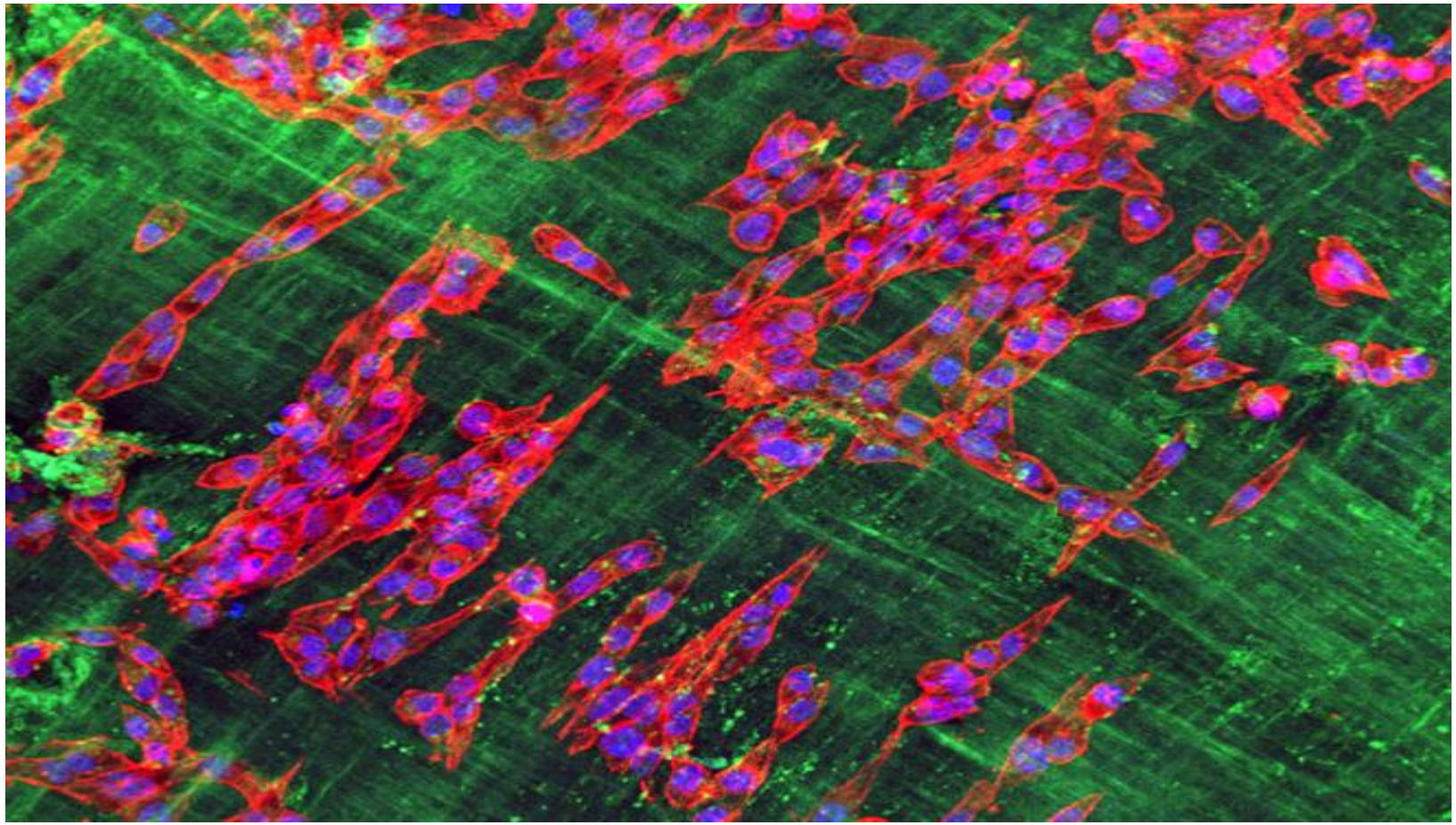
Porcine Small Intestinal Mucosa

Magnusson S, et al. *Mil Med.* 2017;182(S1):383-388.

The Four Hallmarks: Summary

Four Hallmarks

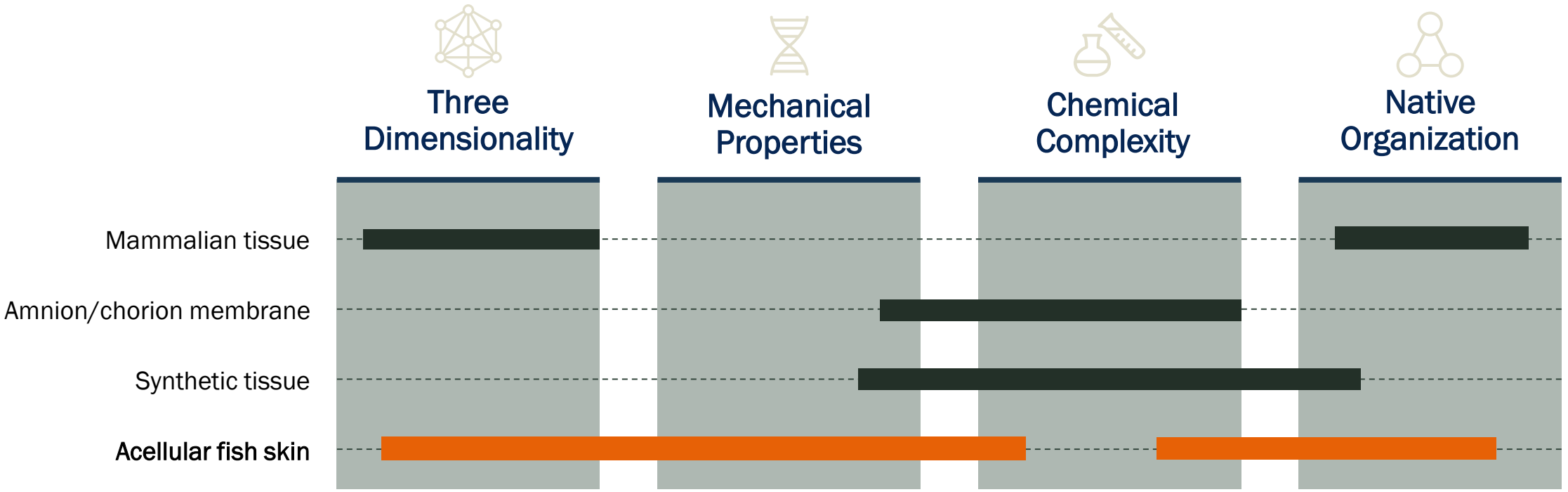
1. Natural 3D Structure
2. Natural Mechanical Properties
3. Natural Molecular Content
4. Natural Molecular Organization



Tissue regeneration starts at the cellular level. This confocal image shows fluorescently labeled fibroblast recognition, migration, and proliferation in fish skin

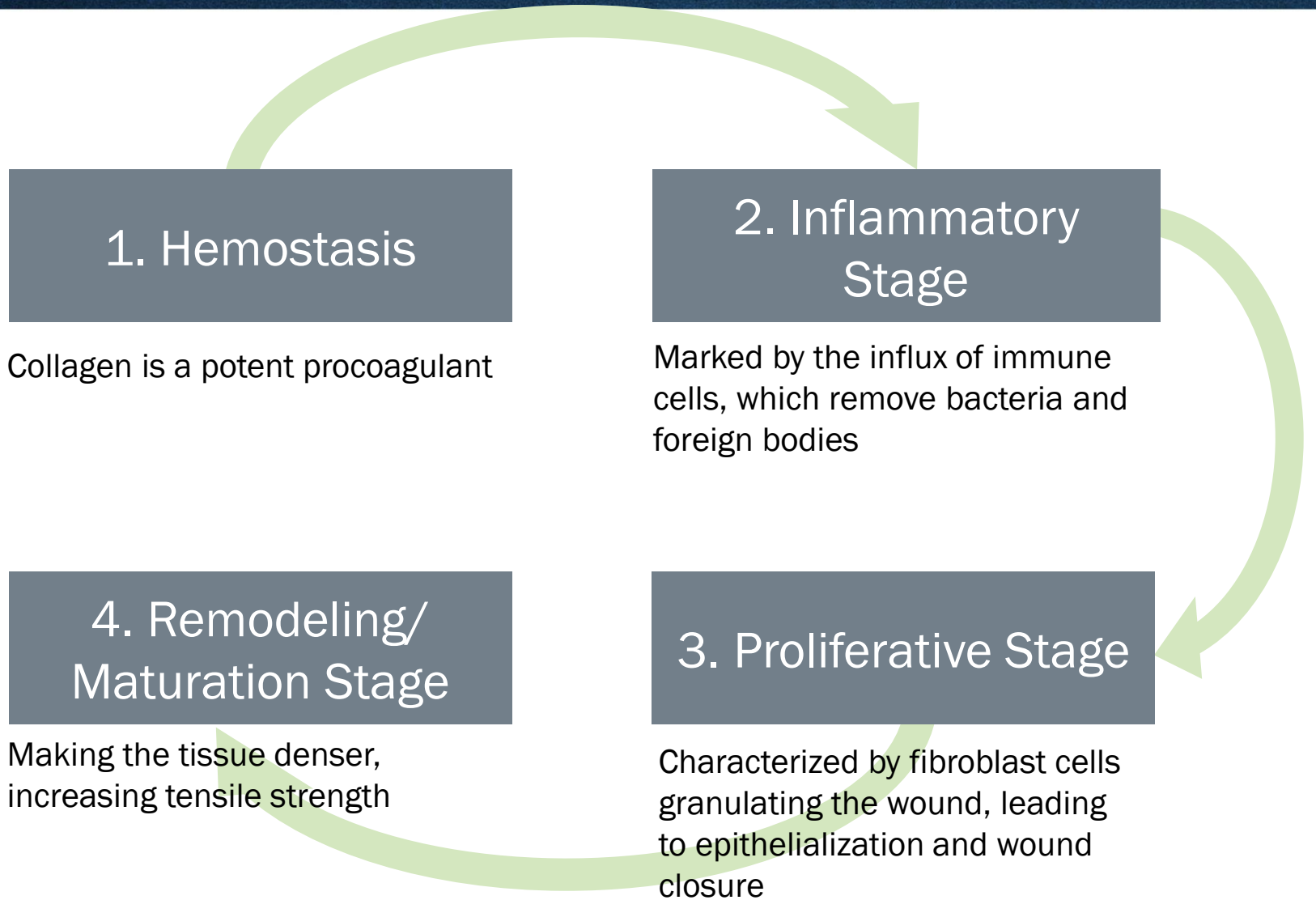
Kamolz LP, et al. *Eur Surg*. 2022;54:163-169.

Hallmarks of Tissue Engineering



Evangelatov A and Pankov R. Regenerative Medicine and Tissue Engineering; 2013.

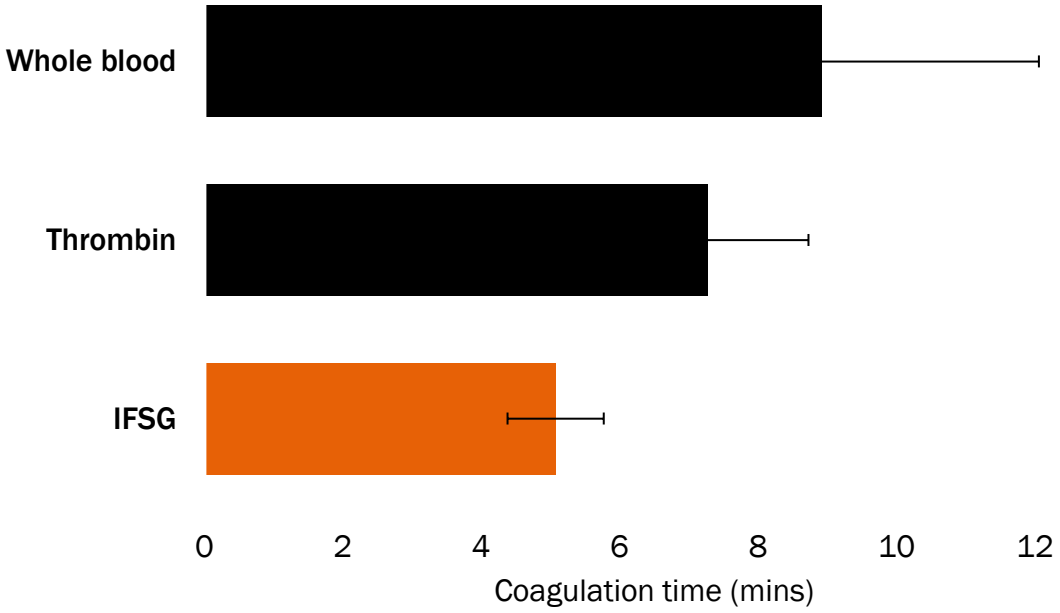
The Wound Healing Cascade

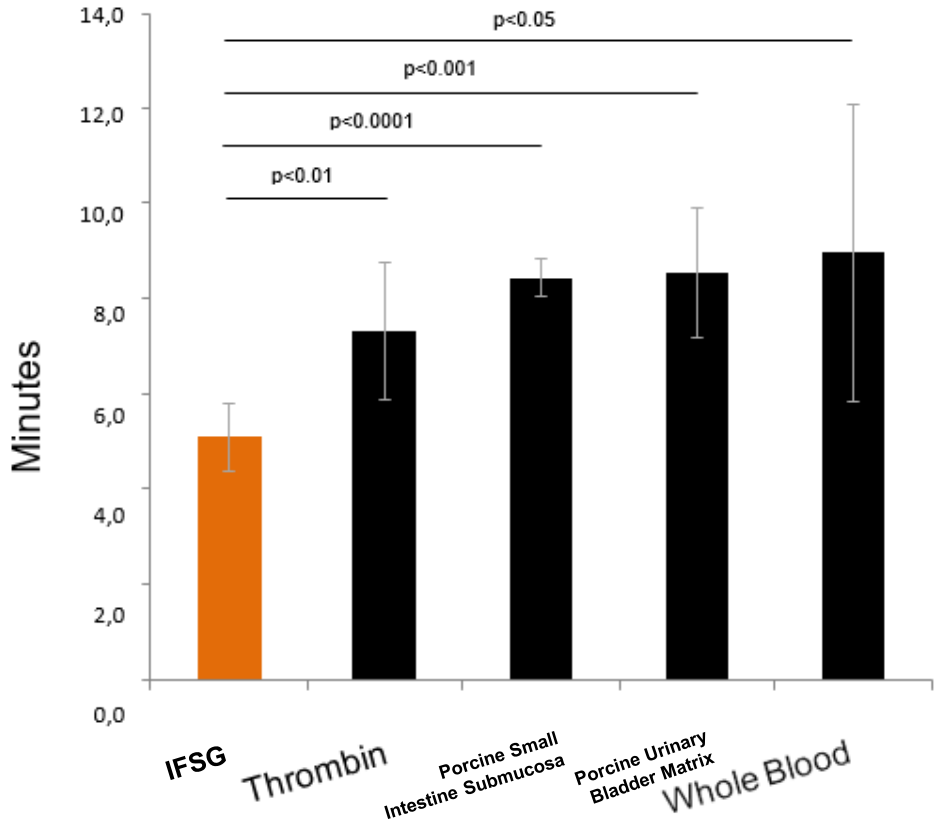


Fish skin has unique properties that aid in all stages of wound healing.

Wallace HA, Basehore BM, Zito PM. Wound Healing Phases. Updated June 12, 2023. In: StatPearls [Internet]. Treasure Island, Florida; StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK470443.

1. Hemostasis: Potent Procoagulants, Vital in Wound Healing

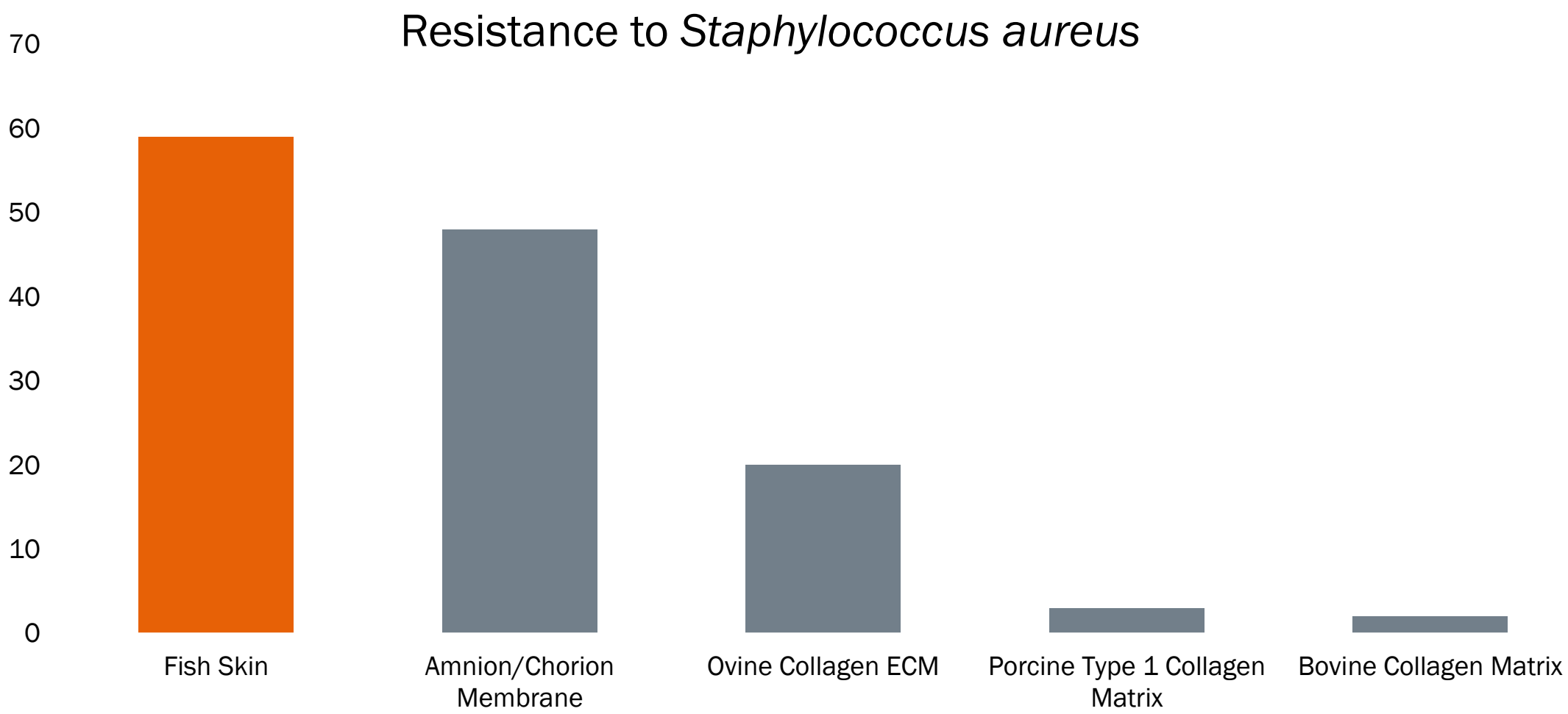




Lee-White coagulation assay comparing IFSG Omega-3-treated wounds with thrombin and whole blood in healthy volunteers.

Magnusson S, et al. *Mil Med*. 2017;182(Suppl 1):383-388.

2. Inflammatory/Chronic Infection Stage

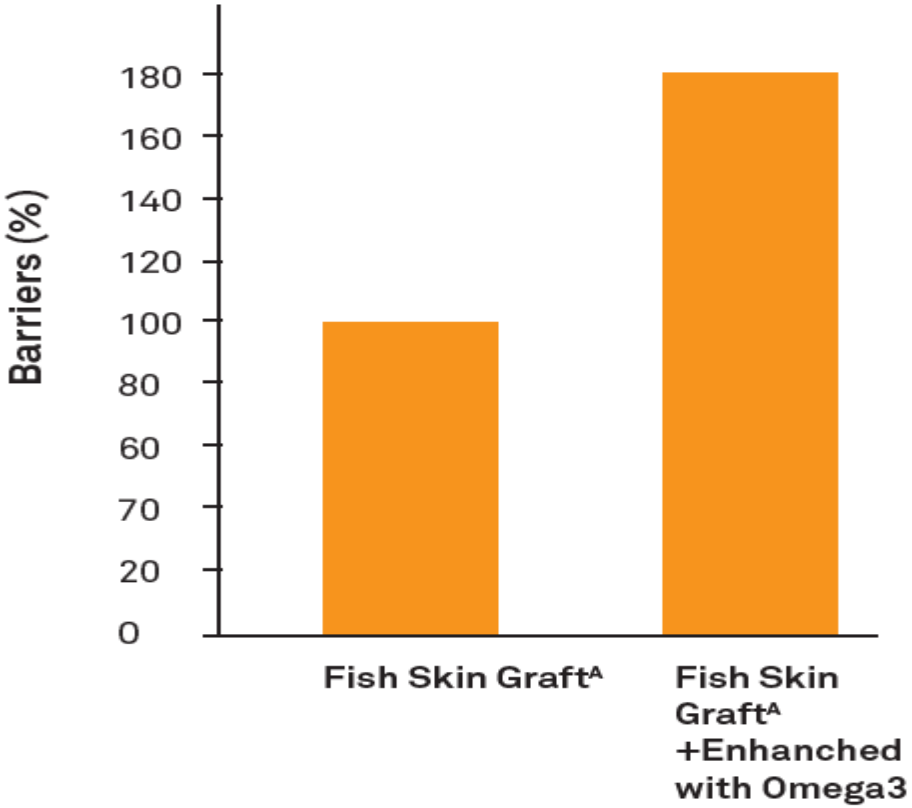


Magnusson S, et al. *Mil Med*. 2017;182(Suppl 1):383-388.

Two-Chamber *Staphylococcus Aureus* Model

- In the two-chamber assay, fish skin graft performed as a bacterial barrier for close to 60hrs compared to 5-45hrs for human amnion/chorion membrane products and several collagen matrix products

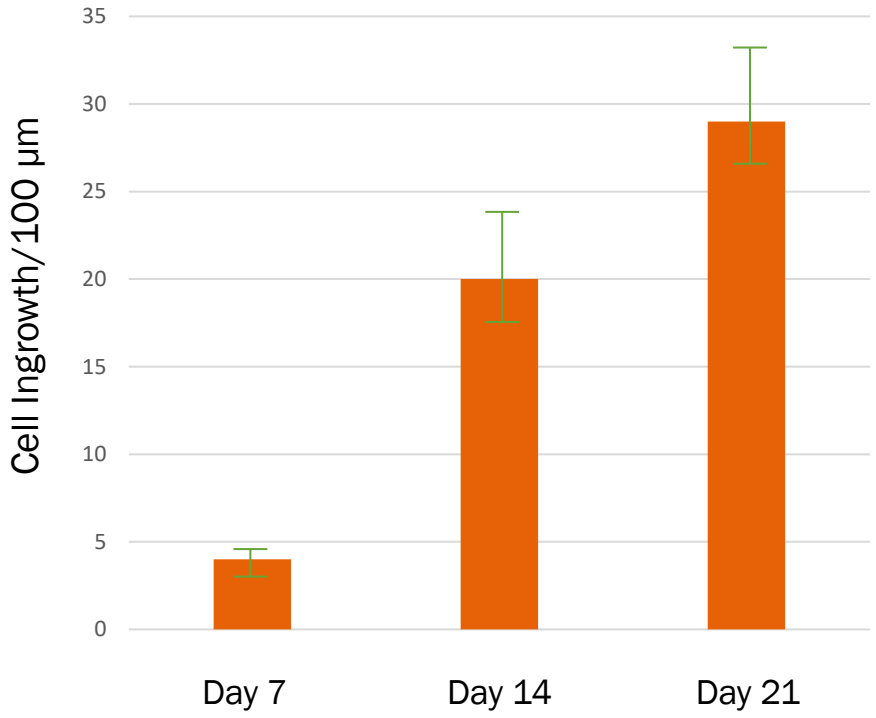
- Spiking (>10%) the fish skin with more Omega-3 fatty acids enhanced its bacterial barrier function by roughly 80%



Magnusson S, et al. *Mil Med*. 2017;182(Suppl 1):383-388.

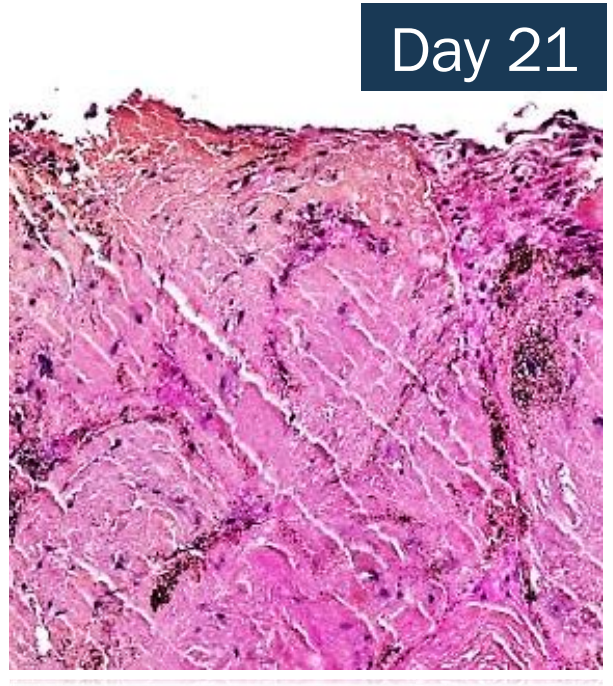
3. Proliferative Stage

IFSG Omega-3 supports the migration and proliferation of native human cells, including mesenchymal stem cells



ADSCs infiltration into fish skin increased gradually over a 3-wk period. Unseeded IFSG Omega-3 (negative control) did not contain any cells, as expected.

Adipose-Derived Stem Cells (ADSCs)



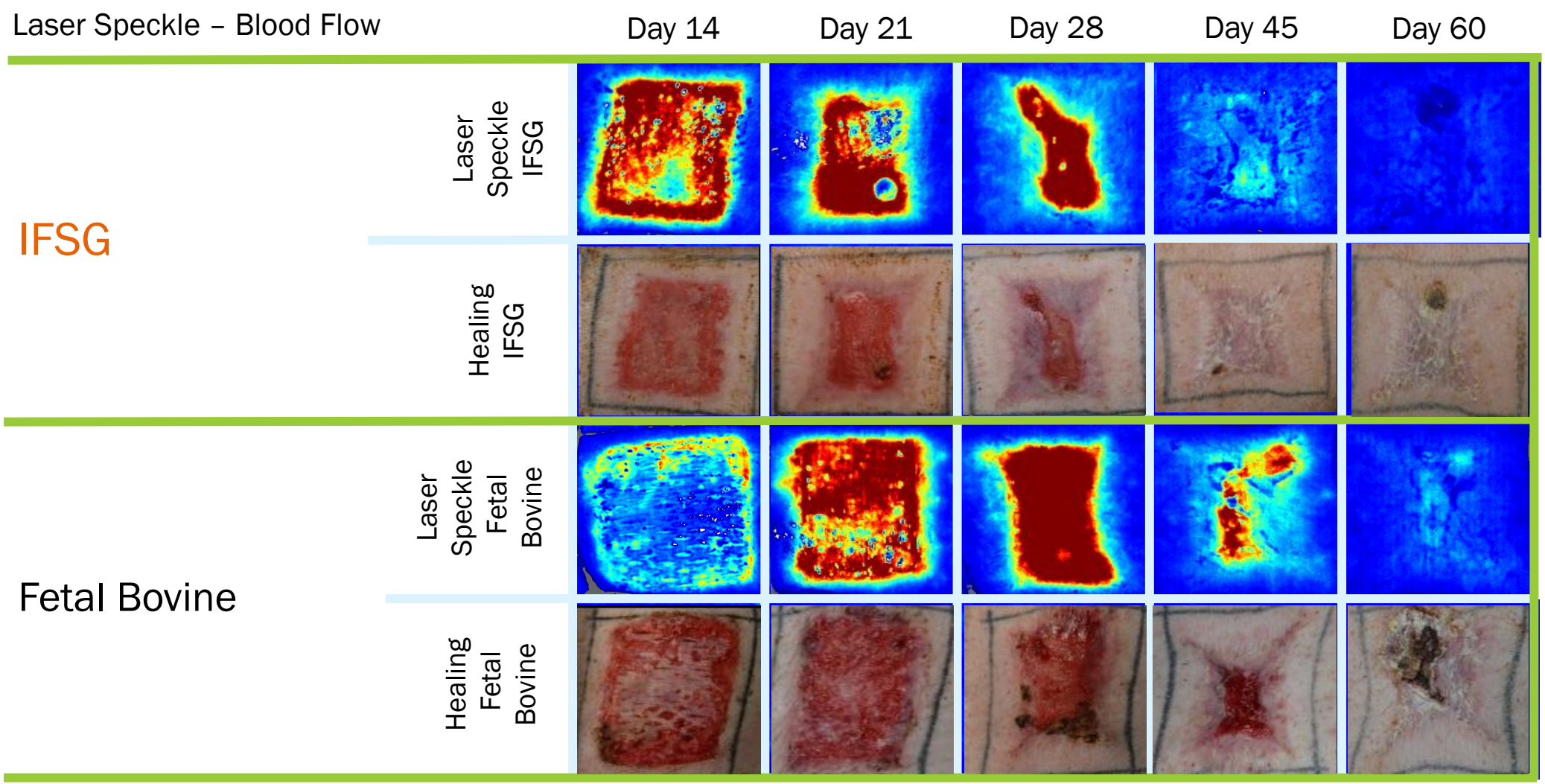
H&E staining of IFSG Omega-3 seeded with ADSCs. The blue dots are ADSC cells that have populated the graft.

ADSC = adipose-derived stem cell; H&E = hematoxylin and eosin.

Magnusson S, et al. *J Burn Care Res*. 2018;39(Suppl 1):S63.

3. Proliferative Stage

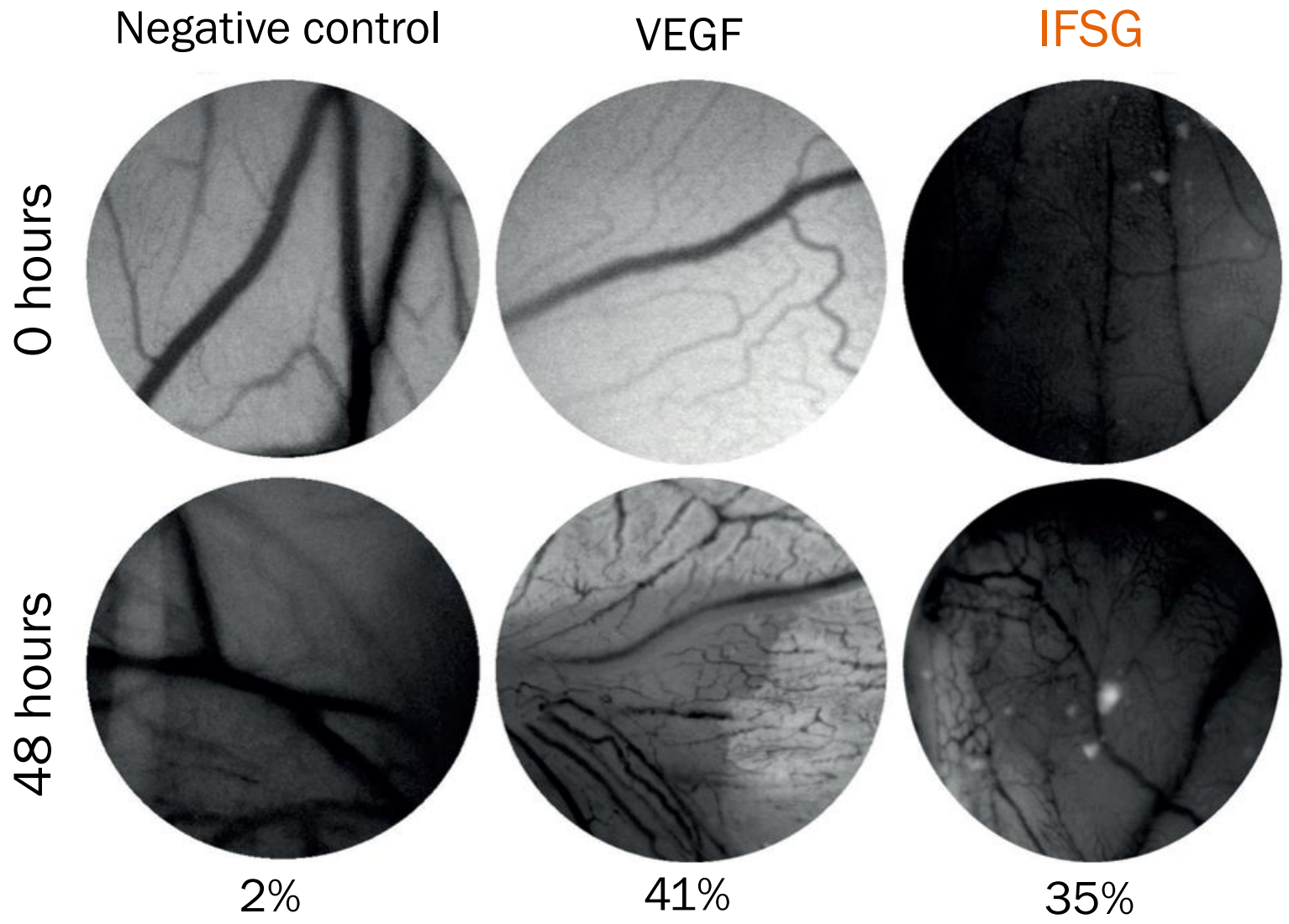
IFSG Omega-3 results in accelerated blood perfusion in wound bed



Stone R 2nd, et al. *Int J Mol Sci*. 2021;22(4):1590.

3. Proliferative Stage

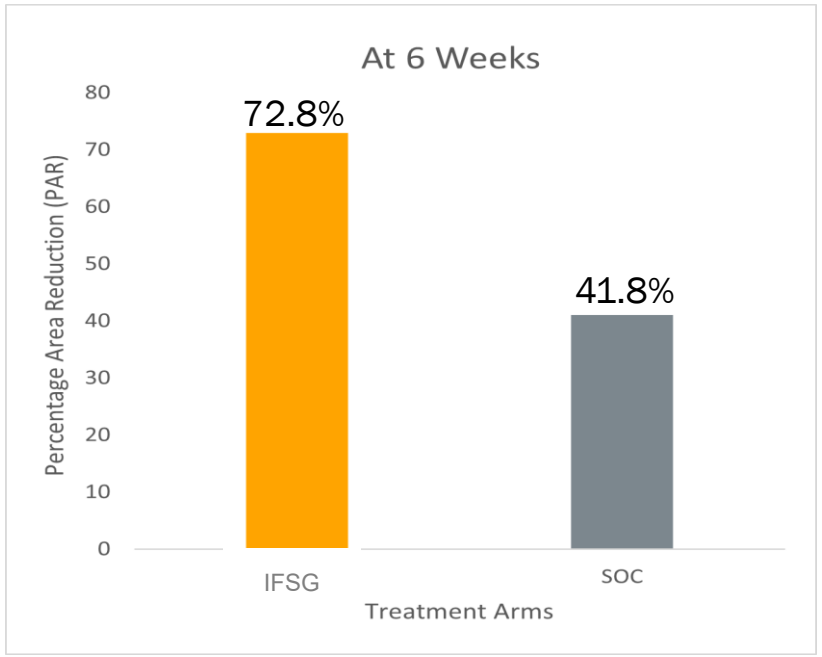
IFSG Omega-3 promotes the formation of new blood vessels

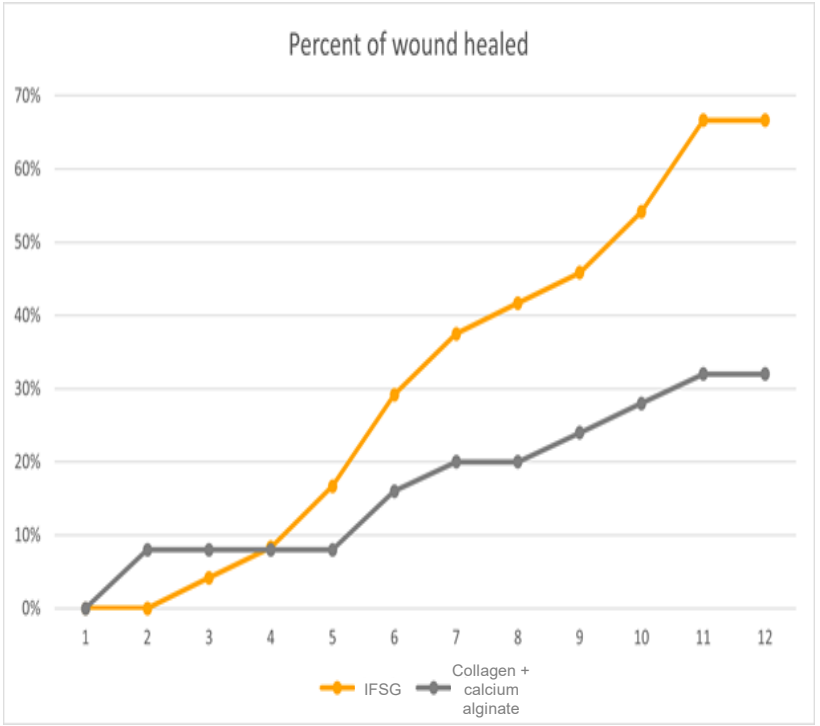


VEGF = vascular endothelial growth factor.
Magnusson S, et al. *Laeknabladid*. 2015;101(12):567-573.

IFSG Is Significantly More Effective Compared to Standard of Care for the Management of DFUs*

Single-blinded, multicenter, randomized-controlled clinical trial



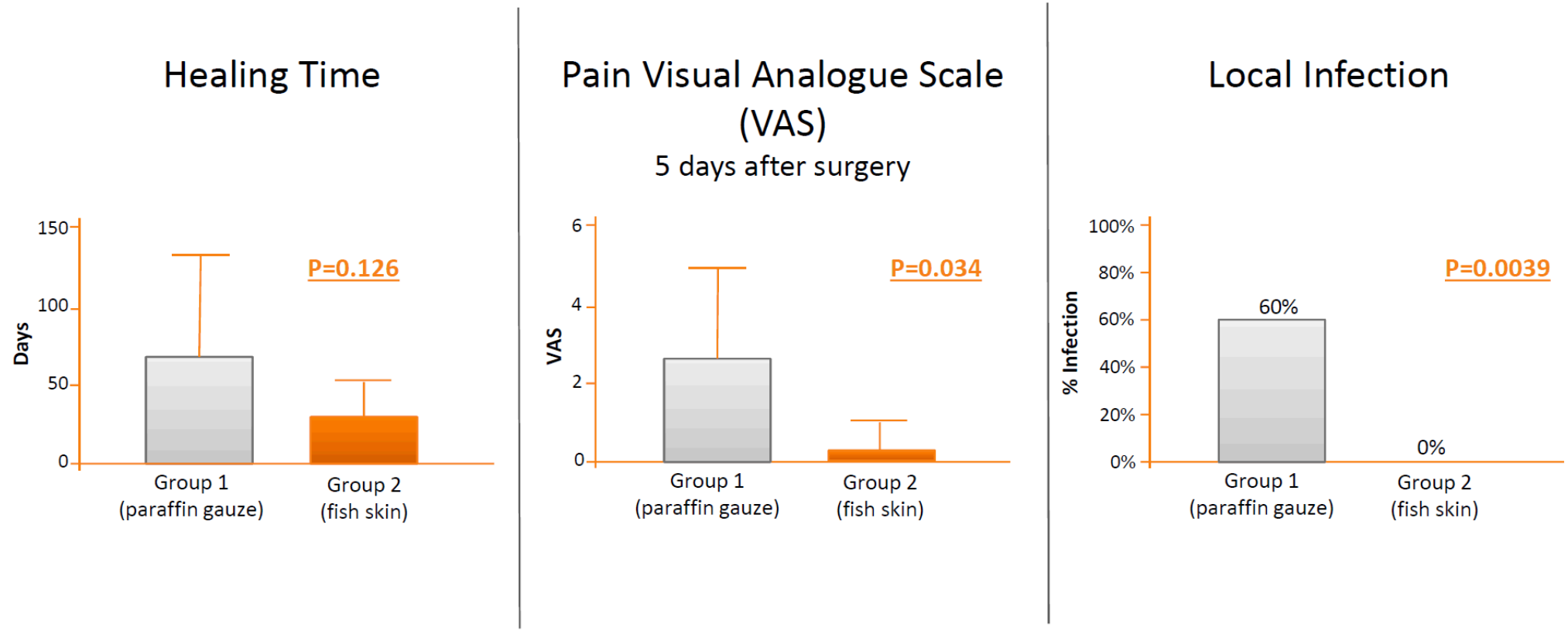


At 12wks, 67% of patients in the treatment arm had fully healed, compared to 32% in the SOC group (*P*<.047)

*Study shows clinical effectiveness of IFSG Omega-3 in improving wound outcomes when applied to non-healing DFUs, compared with SOC treatment alone.
DFU = diabetic foot ulcer; SOC = standard of care.
Lullove EJ, et al. Wounds. 2021;33(7):169-177.

Fish Skin for Donor Site Wounds vs SOC

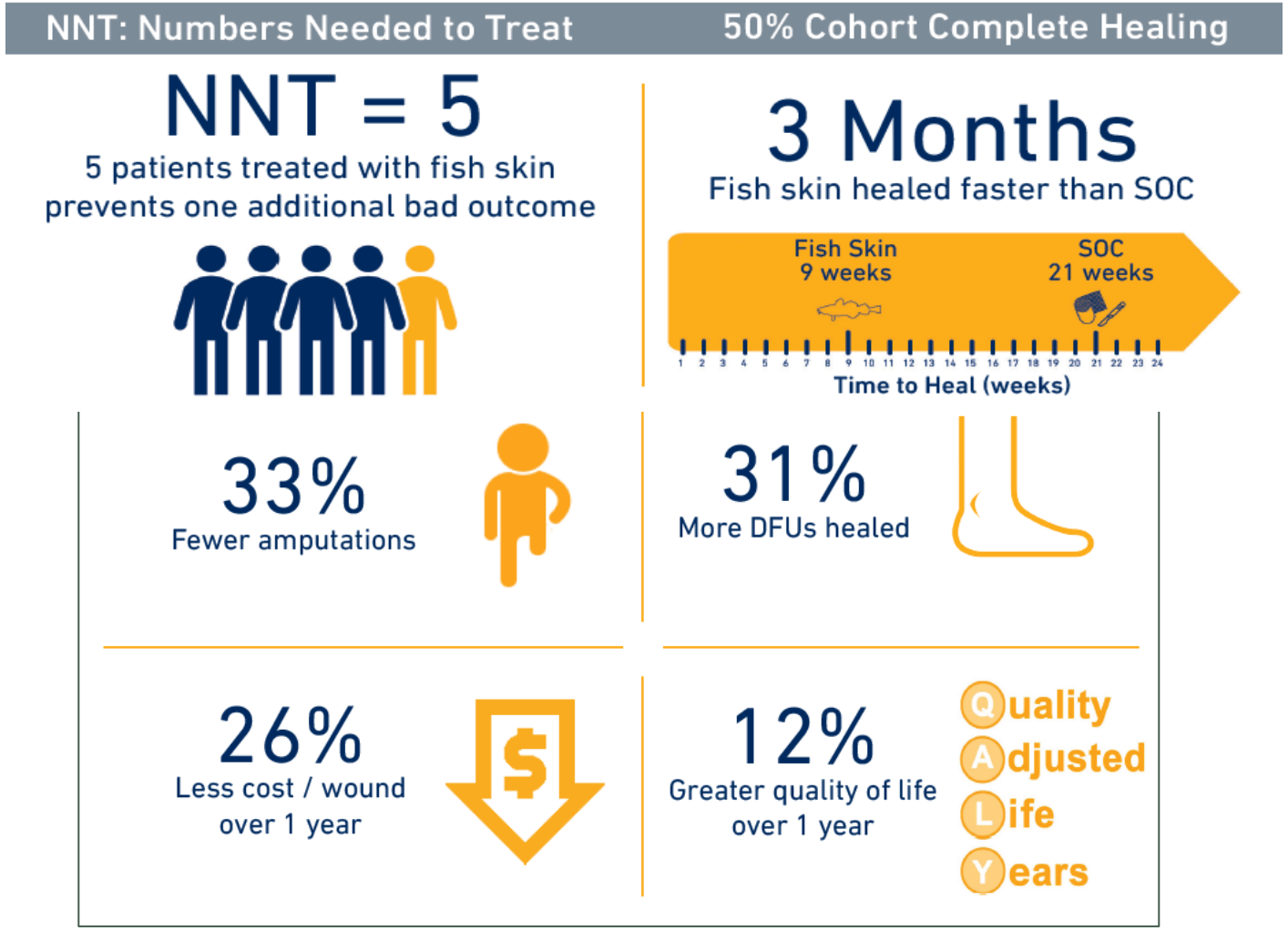
IFSG group healed 50% faster, experienced little pain, and had no infections



VAS = visual analog scale.

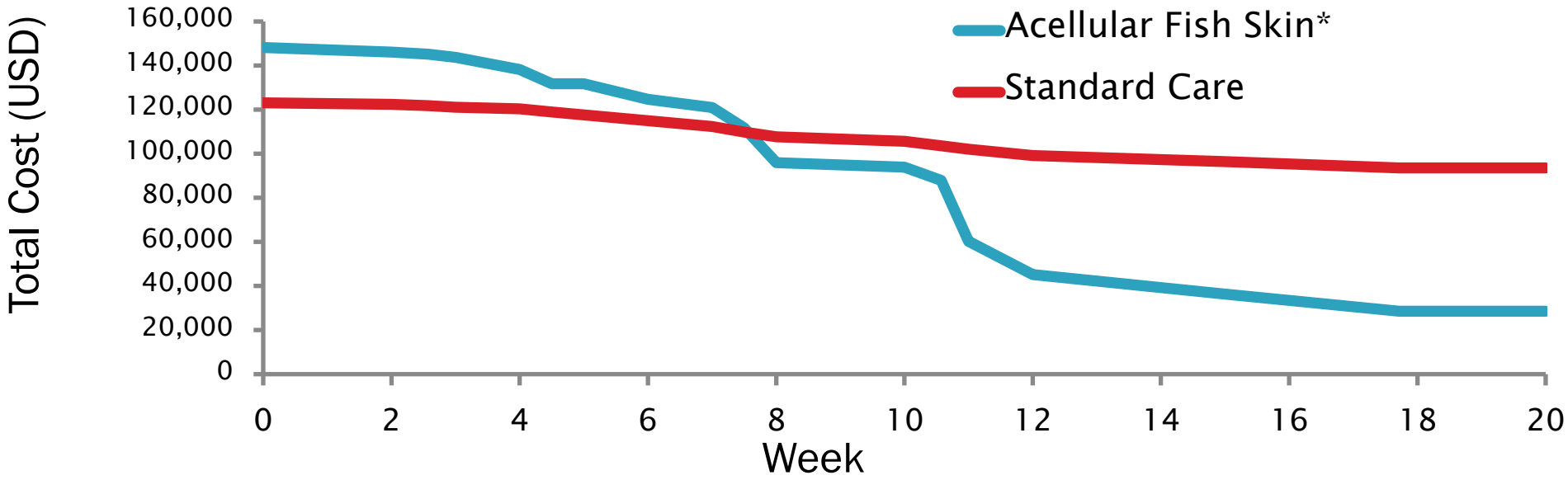
Badois N, et al. *J Wound Care*. 2019;28(9):624-628.

IFSG Is More Cost-Effective than SOC and Improves Patient Outcomes



NNT = numbers needed to treat; QALY = quality-adjusted life years.
Winters C, et al. *Wounds*. 2020;32(10):283-290.

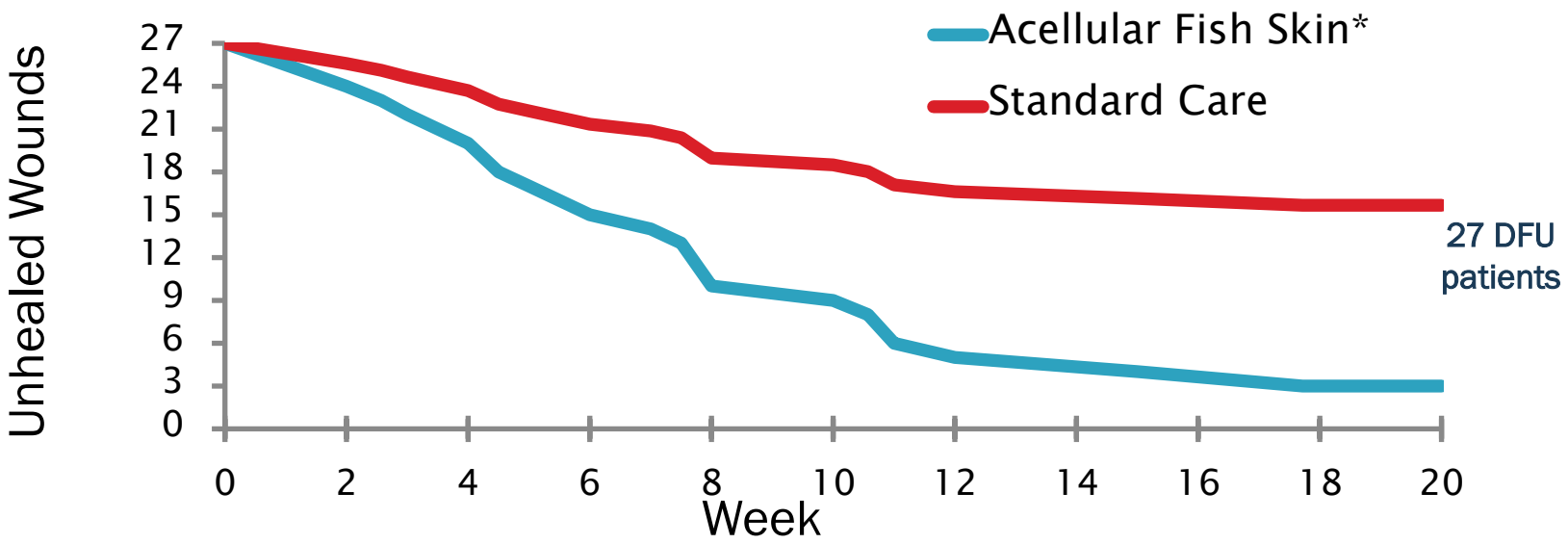
Model of Potential Cost Savings: Omega-3 Fish Skin vs Modeled Standard of Care



- **Cost per week** at 20wks was $28,576 for fish skin group compared to $93,575 for modeled SOC group
- Cost saved with the acellular fish skin graft **per healed wound was 62.5%**

*Only closed patients analyzed.
USD = U.S. dollar.
Patel M, Lantis JC 2nd. *Chronic Wound Care Manage Res*. 2019;6:59-70.

DFU Treated with Fish Skin vs Predictive Model



- Reduction in wounds with acellular fish skin compared to modeled SOC
- At 20wks, 24 acellular fish skin graft patients had healed compared to 11 patients with the modeled SOC group

Patel M, Lantis JC 2nd. *Chronic Wound Care Manage Res*. 2019;6:59-70.

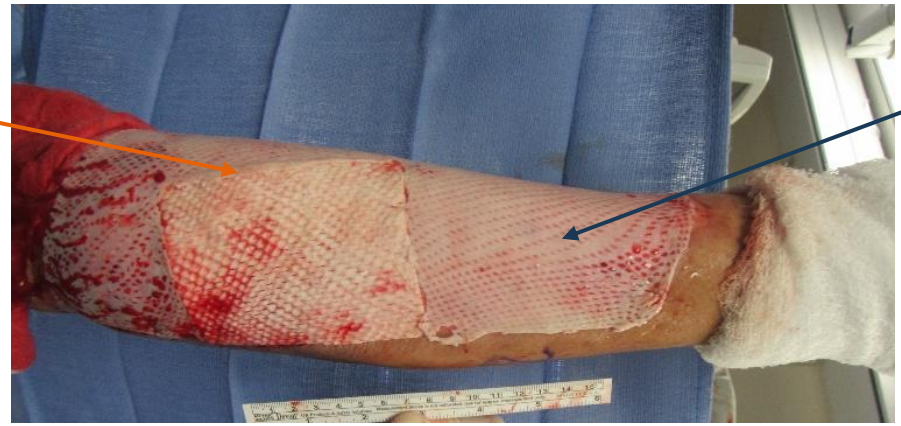
MedStar FDA IDE Study

Final phase of a U.S. military burn research program

- 5-patient, full-thickness burn trial governed by an FDA-approved Investigative Device Exemption (IDE)
- Split-thickness skin graft 7 days later
- Healing followed at 7, 14, 21, 90, and 365 days
- Vancouver Scar scale and Quality of Life at 90 and 365 days
- Shows trend toward better graft take, less scarring, and less pain

IFSG (area 1)

Adjacent areas **randomized** to early cover post-excision with cadaver skin or fish skin



Cadaver Skin (area 2)

IDE = Investigative Device Exemption.
Shupp JW, et al. Presented at: AMUS Annual Meeting; December 6, 2020; Virtual.

Evidence to Impact: Can We Deliver Real-World Limb Preservation with Fish Skin Grafts?

Cyaandi Dove, DPM
Director, Diabetes Foot Program
Division of Endocrinology, Diabetes, and Clinical Nutrition
Harold Schnitzer Diabetes Health Center, OHSU
Portland, OR

The Handoff: From “Why Believe?” to “How Do We Act?”

DR. OROPALLO

Evolution of the science

Biology + strength of evidence

DR. DOVE

Evidence to impact

Generalizability • ease of use • value • access • limb strategy

DR. OGILVIE

Proof at the bedside

Technique + complex cases

Thesis: The evidence matters most when it helps us treat the patient in front of us—earlier, more consistently, and with fewer barriers to limb salvage.

Real-World Impact Requires More than a Positive Trial

Evidence

Who healed? How fast? How certain?

→

Fit

Which wounds?
Which settings?
Which workflows?

→

Execution

Debridement, offloading, infection, and vascular control

→

Impact

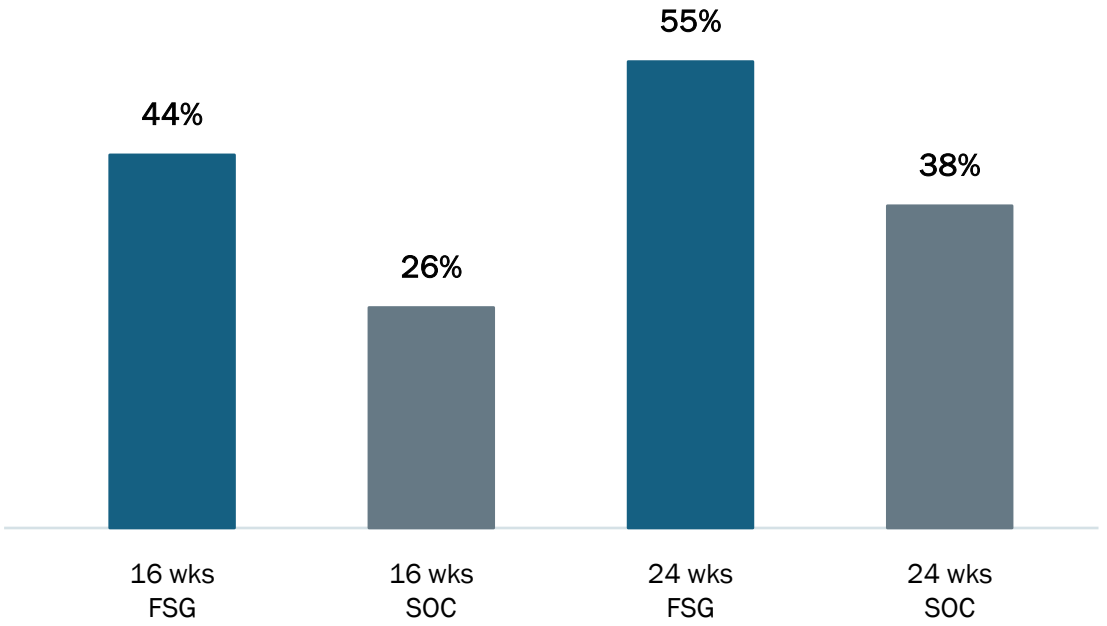
Closure, function, limb salvage, value

Clinical promise becomes a limb-preservation strategy only when these four pieces line up.

ODINN Gives Us a Strong Starting Point—Now We Need to Operationalize It

Deep DFUs/Exposed Structures | Clinical Translation

- The trial supports efficacy in high-risk deep DFUs
  - 255 patients randomized
  - 44% vs 26% at 16wks
  - 55% vs 38% at 24wks
  - HR 1.59
- Benefit was not limited to “easy” ulcers
- Real-world value depends on selecting and preparing wounds well



HR = hazard ratio.
Dardari D, et al. NEJM Evid. 2024;3(12):EVIDoa2400171.

Where Fish Skin Grafts May Matter Most: The Limb-Risk Patient

Wound complexity	Depth • Exposed tendon/bone • Stalled trajectory • High bioburden risk
Patient complexity	Diabetes • PAD • Neuropathy • Infection history • Social barriers
System complexity	Clinic access • OR access • Cost approvals • Dressing changes • Adherence

Impact is not simply “did the wound close?”
It is whether we reduce the cascade that leads to hospitalization, reconstruction, or amputation.

PAD = peripheral artery disease; OR = operating room.

The Product Does Not Replace Fundamentals, It Amplifies Them

1. **Debride**
   Remove nonviable tissue
2. **Perfuse**
   Confirm blood flow/ revascularize
3. **Control**
   Infection, edema, exudate
4. **Offload**
   Pressure control and adherence
5. **Reassess**
   Trajectory and escalation timing

Practical message:
Fish skin grafts fit best in a disciplined wound bed preparation pathway, not as a substitute for it.

Generalizability and Ease of Use: Where Can This Work outside of the Trial?

Trial conditions

- Protocolized visits
- Standardized endpoints
- Selected sites
- Structured follow-up

Real-world care

- Variable visit cadence
- Coverage constraints
- Home support differences
- Team variation

Adoption question

Can the same biology fit the workflow patients and teams can actually sustain?

The trial result is credible: Real-world impact depends on fit, access, and reliable execution.

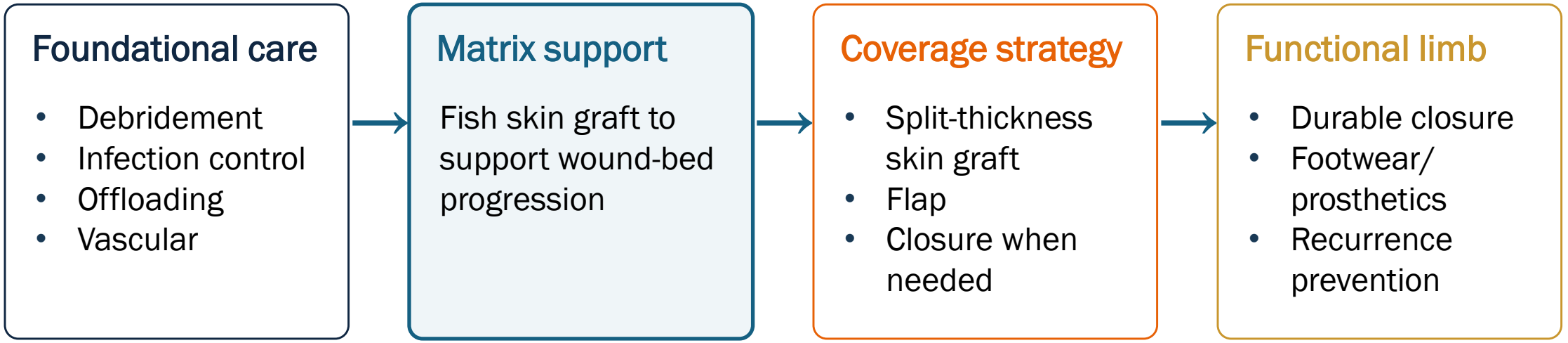
A Value Lens: Not Cheaper Care, Better-Timed Care

Clinical value	Shorter path to closure; fewer stalled wounds
Operational value	Less dependence on late-stage rescue procedures
Economic value	Avoid downstream utilization when healing is accelerated
Equity value	More patients can access advanced therapy before limb threat escalates

The value proposition is strongest when fish skin grafts prevent delay, drift, and late escalation.

Where Does It Sit in the Reconstructive Ladder?

Strategic placement is the point: Use biologic support early enough to change trajectory, but within a full reconstructive and limb preservation plan.



Use biologic support early enough to change trajectory, while preserving reconstructive options.

Closing Message: Evidence Should Widen Access

When evidence is strong and implementation is thoughtful, fish skin grafts can help us:

Treat earlier	Before wounds drift into rescue mode
Treat broader	Across settings with different resources
Treat smarter	As part of a limb-preservation pathway
Treat toward Function	Closure that supports mobility and quality of life

That is the real-world impact: Not just a healed ulcer—a preserved limb, a functional patient, and a system that can deliver advanced care consistently.

At the Bedside:
The Proof Is in the FISH Pudding

Michael P. Ogilvie, MD, MBA, FACS
Advocate Christ Medical Center
Oak Lawn, IL

About Me



- Double board-certified Plastic and Reconstructive Surgeon
- Education
  - Undergrad: Harvard University
  - Medical School: University of Chicago
  - Business School: University of Chicago
- Training
  - General Surgery: University of Miami
  - Trauma Research fellowship: University of Miami
  - Plastic Surgery: Duke University
- Attending surgeon at Advocate Christ Medical Center – 2017

Advocate Christ Medical Center

- Level 1 Trauma Center, Oak Lawn, IL
  - Traumatic wounds
  - Orthopedic
  - Cancer
  - Infectious
  - Pressure Sores

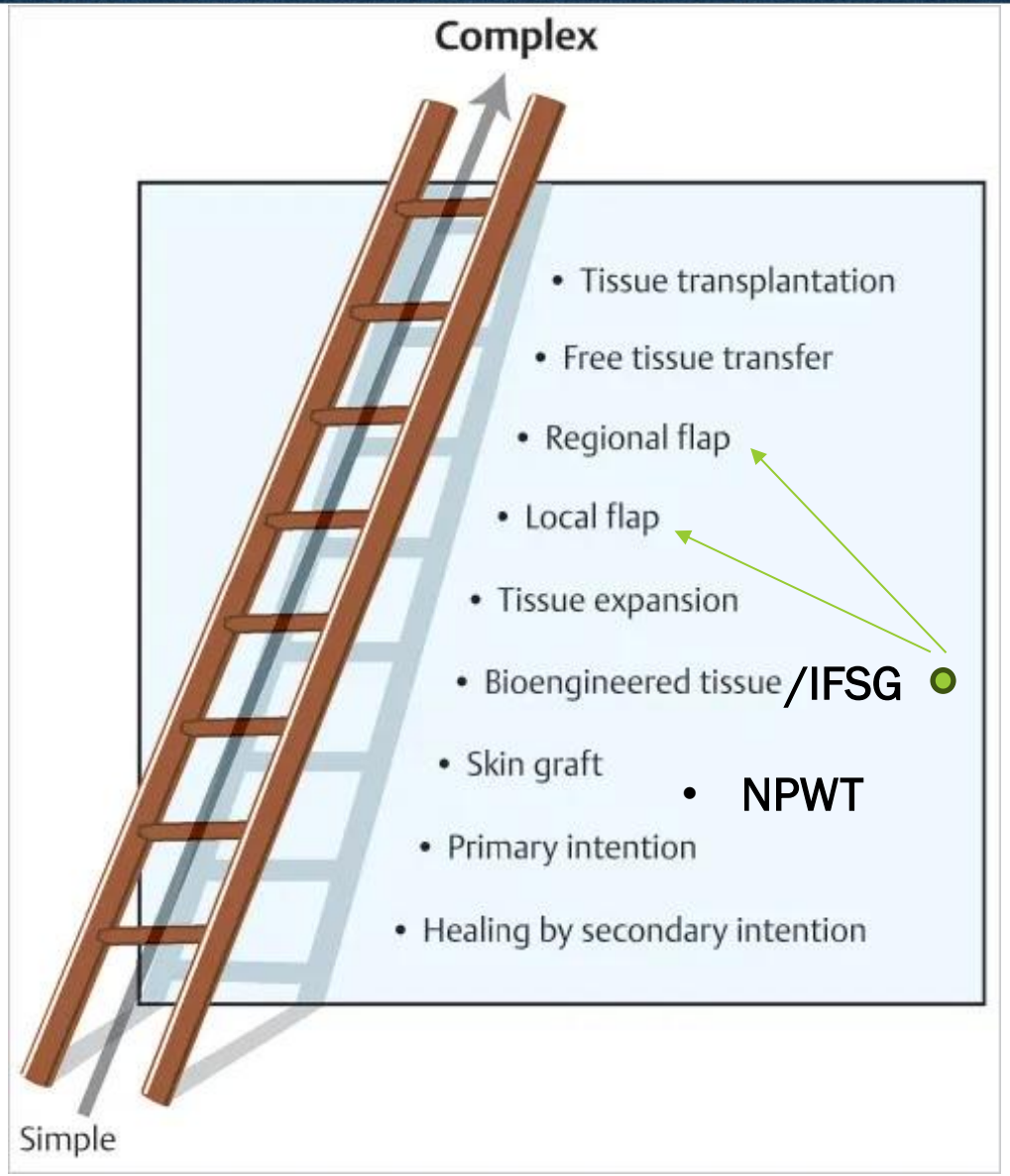








Reconstructive Ladder



Case 1

- 56yo RHD Male involved in MVC rollover with ejection
- Traumatic injury with mangled left upper extremity



RHD = right hand dominant; MVC = motor vehicle collision.

Case 1

Brachial artery ligation and completion amputation with spare parts fillet flap by Orthopedic Surgery





Case 1







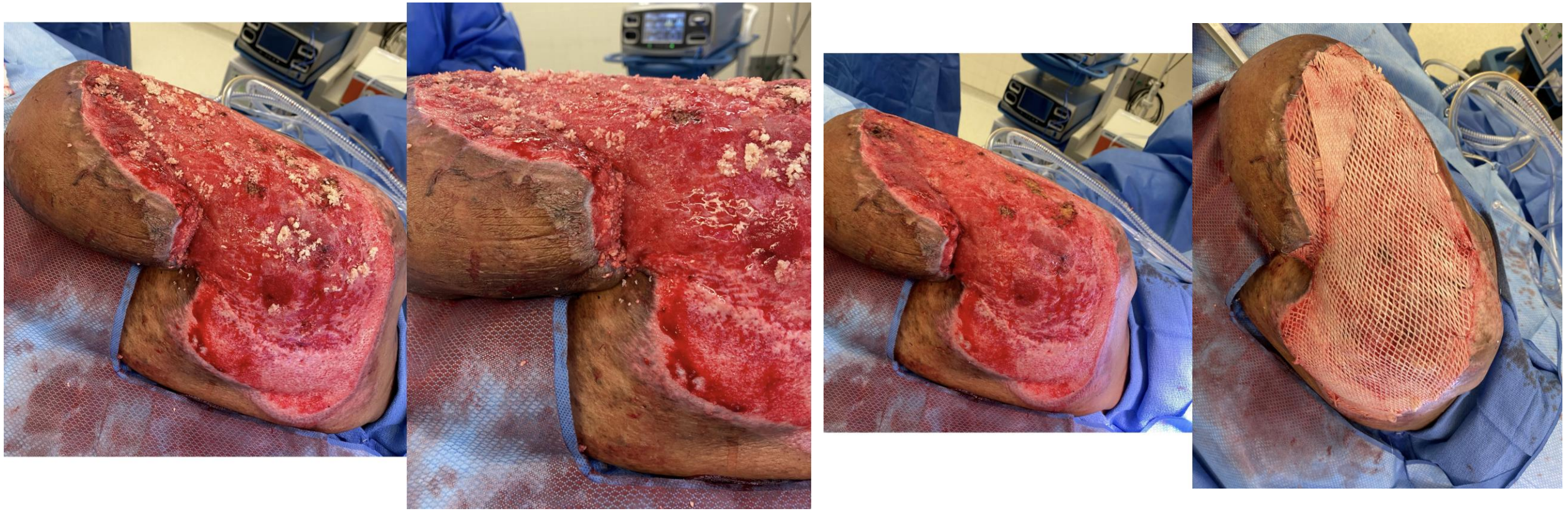
Case 1

Initial debridement with hydrosurgery system and wound vac placement



Case 1

Secondary debridement with IFSG meshed sheet, micro IFSG placement, and wound vac dressing



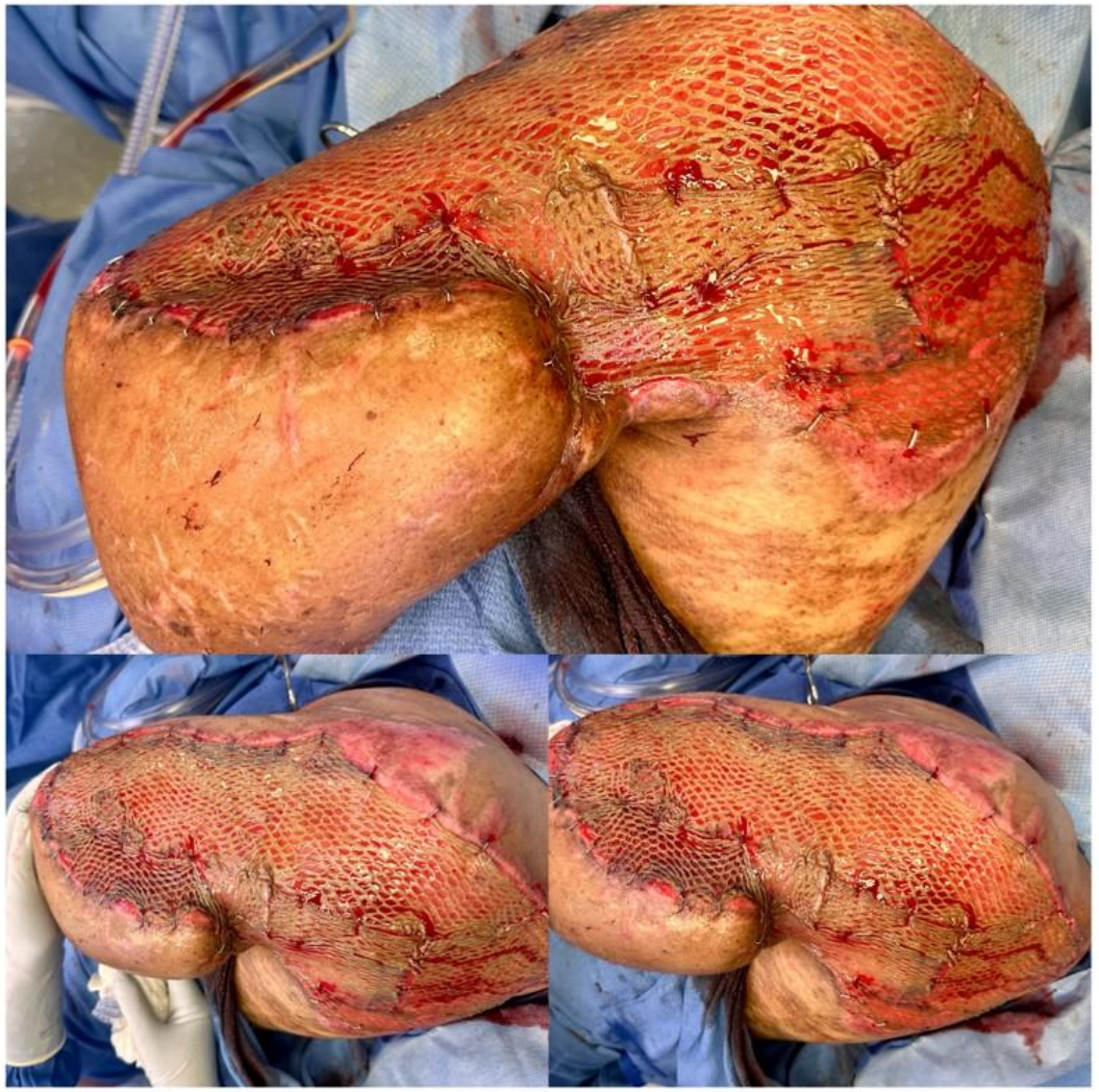
Case 1

Outpatient follow-up at 2wks



Case 1

Skin grafted at 3wks with just one application



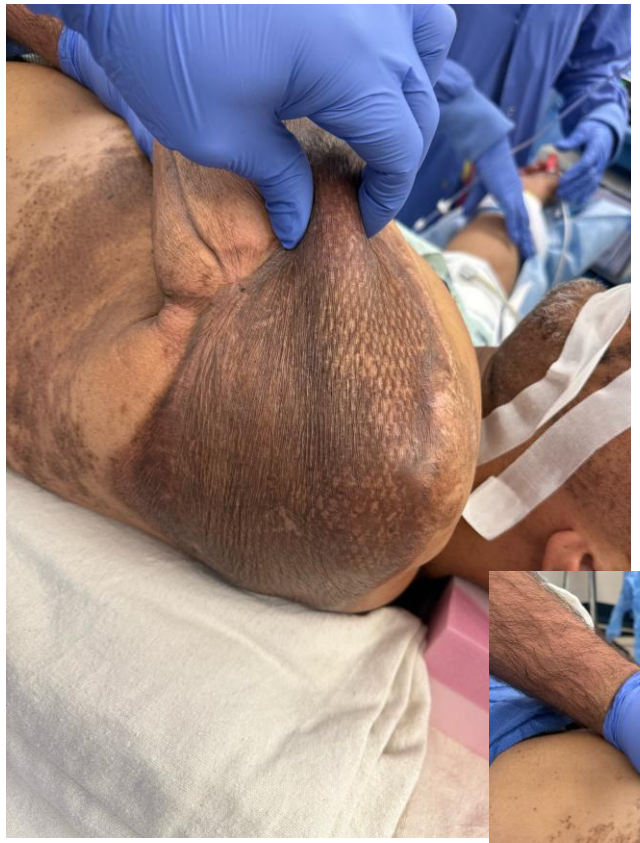
Case 1

3mo follow-up with excellent healing and contour, ready for prosthetic



Case 1

- At 1yr, patient developed a scar cord in axilla that we were able to release… as you can see, the skin graft is supple and able to be used for Z-plasty without compromise







Case 2

- 21yo Female with necrotizing fasciitis of left foot and lower leg s/p debridement and “wound closure” by Orthopedic Surgery



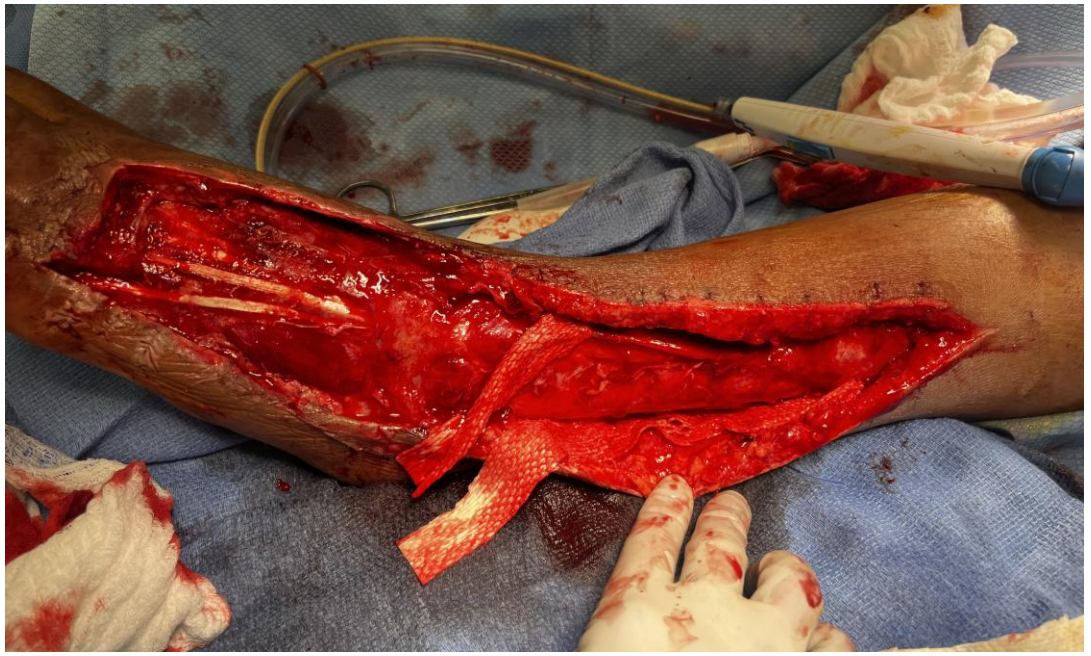
Case 2

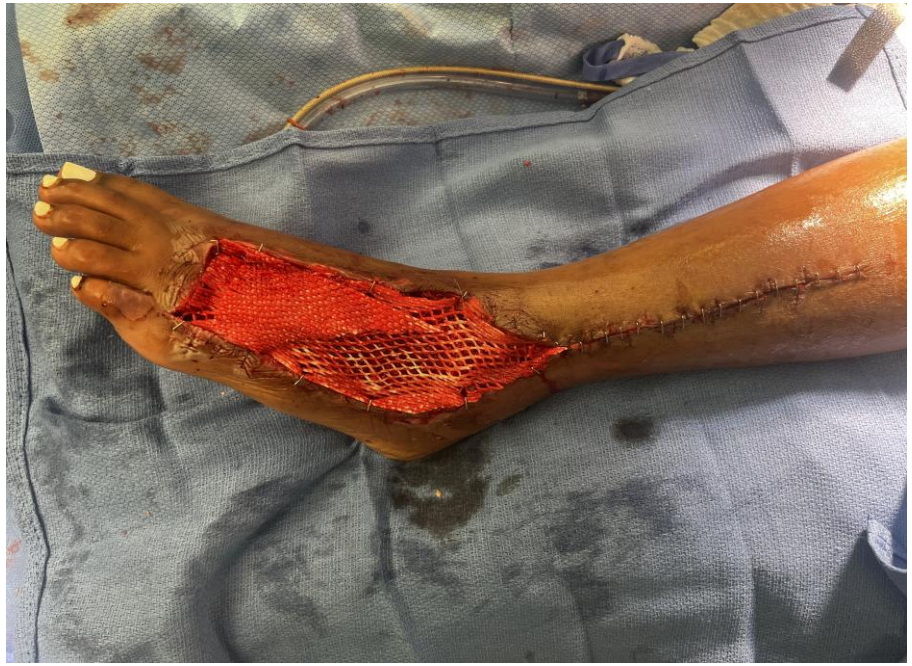
- Wound was reopened
- Further debridement of necrotic/non-viable tissue
- Significant tissue undermining noted

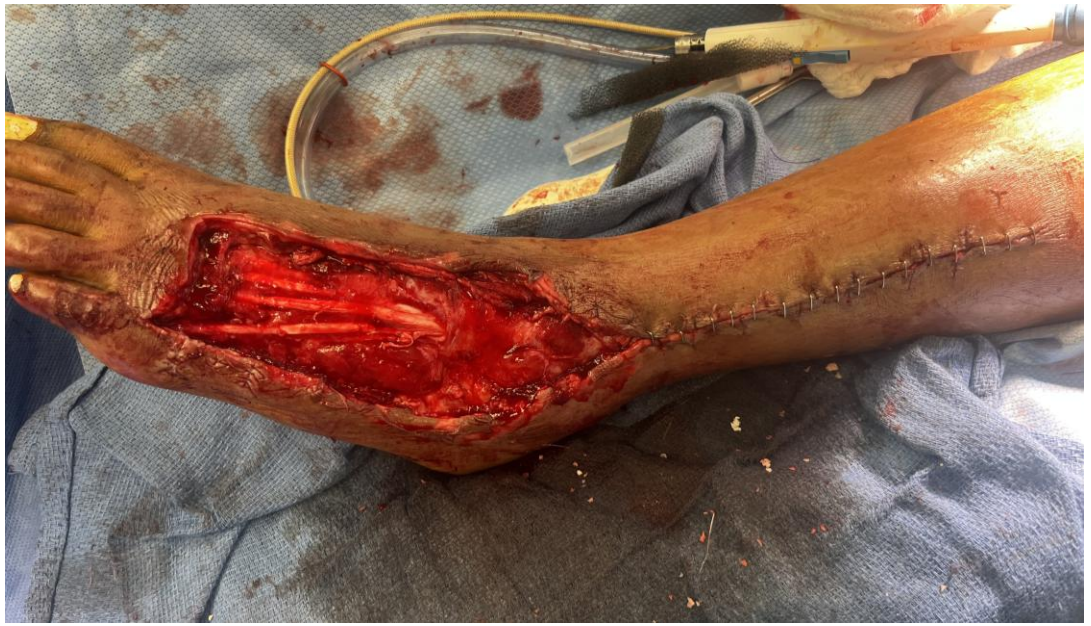


Case 2

- Wound debridement
- Tacking down of undermined tissue with IFSG meshed sheets and micro IFSG underlay
- Double-layer IFSG sheet of open wound for tendon coverage







Case 2

- 1wk with healthy granulation tissue, complete tendon coverage, and contour improvement
- Skin graft performed at wk 2



Case 3

- 79yo Female with multiple medical problems presented with long-standing (years) venous stasis ulcers of L leg that stalled with wound care
- Multiple lesions
- Very thin skin
- Concern for underlying bone exposure





Case 3

- Skin and bone eschar debrided
- Bone trephination
- 4 x 6 cm IFSG and wound vac placed





Case 3

3 days



3mos







Case 4

68yo Male with multiple medical problems

- Suffered a fall resulting in complicated RLE tib/fib fx with comminution
- Ortho originally treated with ex-fix followed by ORIF and plating
- Subsequently developed osteomyelitis and wound breakdown with exposed hardware*



*Off-label indication.
RLE = right lower extremity; ORIF = open reduction and internal fixation.

Case 4

OR: Wide debridement, fenestrated IFSG placement, and wound vac





Case 4

After a week of wound progression…

- Local muscle flap
- Fenestrated IFSG underlay
- Meshed IFSG overlay

- Went back for STSG at 2wks







STSG = split-thickness skin graft.

Case 4

4-mo follow-up…





Case 5

- 33yo Female, morbidly obese (300 lbs, BMI 47.5)
- Pinned under a guardrail
- Comminuted femur fracture, which was rodded by Ortho
- Significant degloving injury to RLE



BMI = body-mass index.

Case 5

1 week



Case 5

Over 1wk

- Serial debridement x 3
- Total wound 5600 cm^2 (50 x 112 cm)
- Wound vac changes









Case 5

Over 3wks

- Weekly IFSG (1500 cm^2) applications
- Weekly wound vac changes (could not tolerate bedside)









Case 5

- Underwent 3 rounds of STSGs
- Recently presented for her 6-mo follow-up
  - Fully healed
  - Out of rehab but working on knee and ankle range of motion
  - Walking with assistance







Clinical Pearls

- Good surgical decision-making and sound technique are key to success
- No wound can heal without adequate debridement
- Think outside the box when it comes to challenging wounds… IFSG truly is a game-changer

Questions?

Thank You!