

The Promise of Cell Therapy



Armed Forces Institute of Regenerative Medicine (AFIRM):
A Proven National Capability for Battlefield Trauma

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Regenerative Medicine in 1995

Human Embryonic Stem cells not yet described

Dolly, the sheep, had not yet been cloned

Most normal primary human cells could not be grown and expanded outside the body

No cell therapies yet in front of the FDA

Term “Regenerative Medicine” not coined- Science Fiction?

1990 - 1999

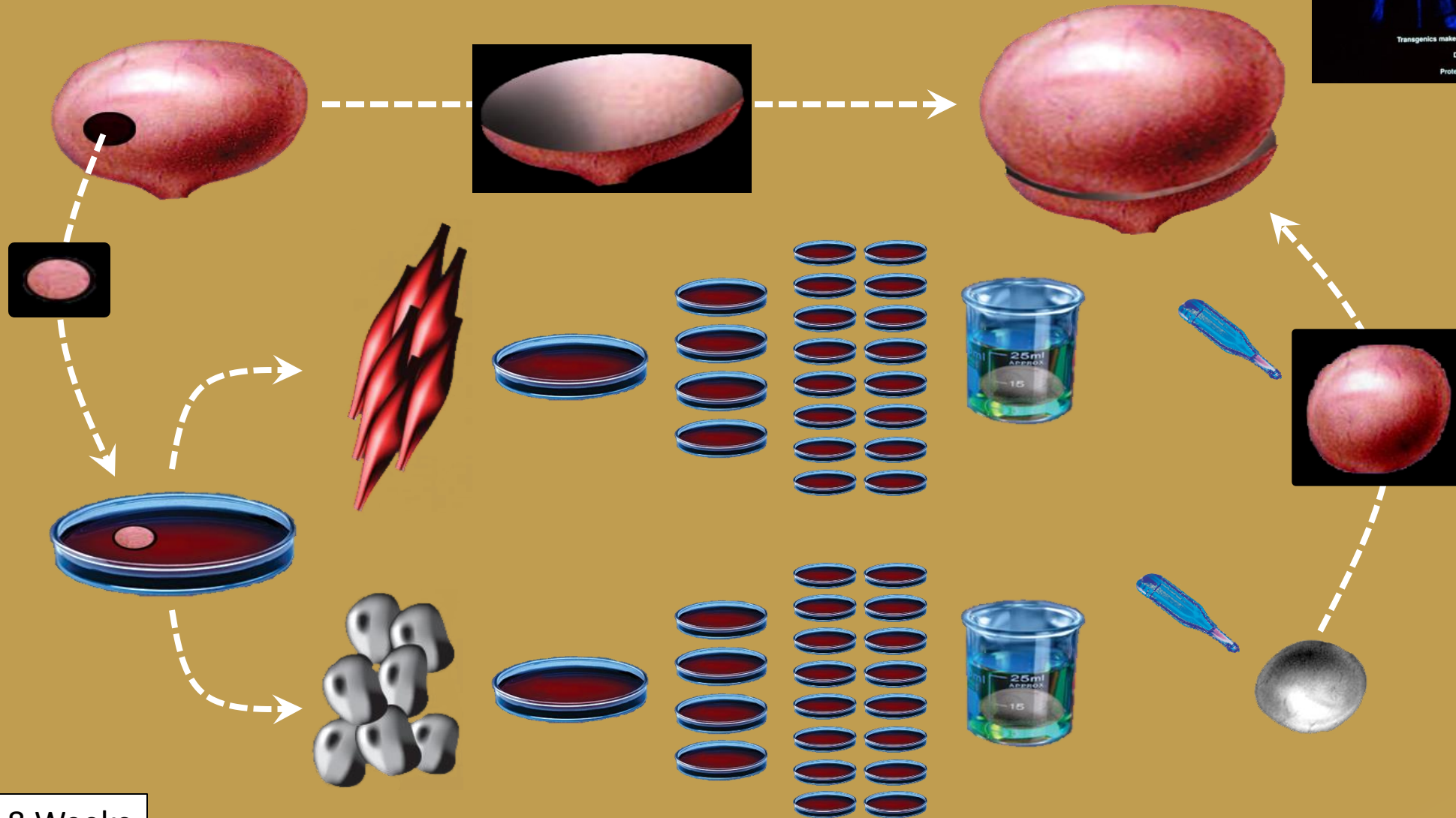
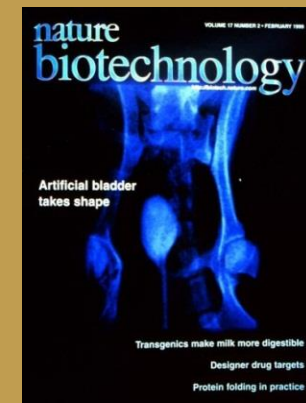
Growth factor & molecular biology

Cell differentiation

Angiogenesis and vascularization

Biomaterial sciences

Creation of First Engineered Organ Experimentally: Bladder



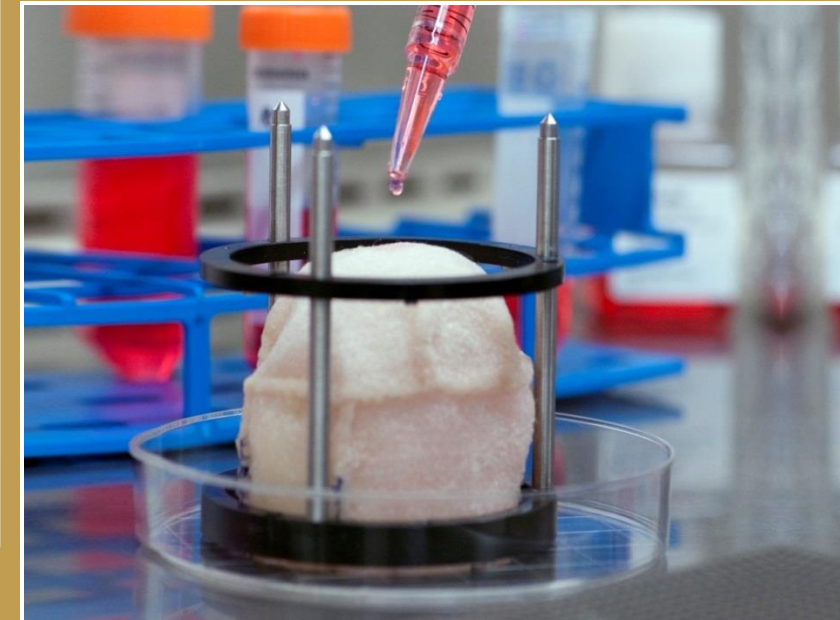
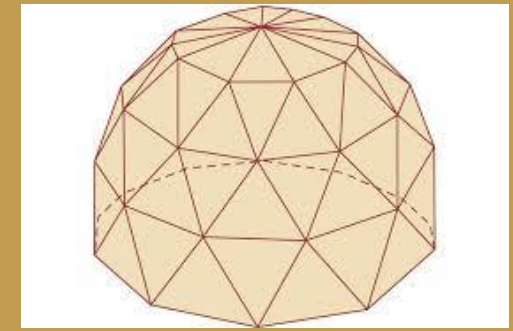
First Engineered Organ for Permanent Implantation in Humans: Bladder



THE LANCET.

“Tissue-engineered autologous bladders for patients needing cystoplasty”

April 2006



Efforts Launched 2006-08:

Col. Robert Vandre

General Lester Martinez-Lopez

General Eric Schoomaker

Subsequent Oversight 2008-2023:

General George Weightman

General James Gilman

General Joseph Carvalho

General Brian Lein

General Barbara Holcomb

General Michael Talley

General Anthony McQueen

January 2024- DHA via MTEC

Dr. Terry Rauch

Dr. David Smith

Capt. Travis Polk

Dr. Jennifer Ojeda

Dr. Therese West & Lt. Col Angela Phillips

2006

Soldier Treatment
and Regeneration
Program



DoD-led program to
advance regenerative
medicine solutions
for wounded, ill,
and injured
Service members

2008

AFIRM
established



Formal launch of
AFIRM to accelerate
regenerative medicine
for Service Members

Mission and Vision of the AFIRM

FROM DISCOVERY TO DEPLOYMENT



DISCOVER

Identify and develop
promising regenerative
medicine solutions



DEVELOP

Optimize and advance
therapies through rigorous
pre-clinical evaluations



TRANSLATE

Conduct clinical studies
to establish safety
and efficacy



DELIVER

Make effective therapies
available to wounded
warriors



HEAL

Restore health,
enhance recovery,
and improve quality of life

AFIRM-Delivered Results

96

Projects across more than 20 states

30+

Human clinical trials initiated across AFIRM

20+

Commercial partnerships driving products to practice

3-4X

Leveraged investment from NIH, VA, academia, and industry

Currently, AFIRM is running 21 active projects with 10 clinical trials open for enrollment.

Success Story: Burn Care

RECELL®

ReCell®

- First FDA-approved cell-based therapy for burn wounds and full-thickness skin defects (2018)
- Label expanded in 2023 for repigmentation of stable depigmented vitiligo lesions
- RECELL GO mini (2024) broadens point-of-care adoption



Success Story: Burn Care

STRATAGRAFT®

- First FDA-approved cell-based therapy for deep partial-thickness burns (2021)
- Label expanded in 2024 for adult deep partial-thickness burns



Success Story: Symvess™

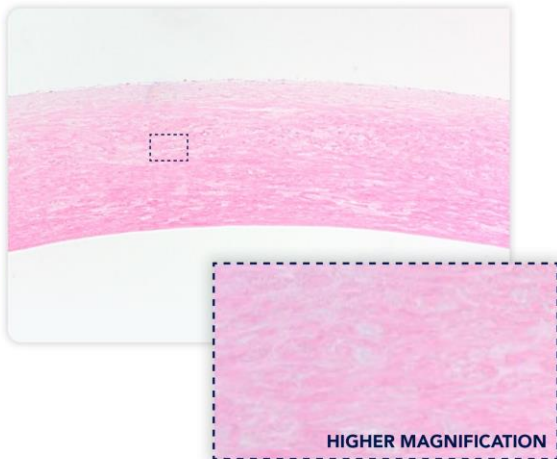
EXTREMITY TRAUMA: ACELLULAR VASCULAR GRAFT

- Humacyte's human acellular vascular graft: first approved for extremity vascular trauma repair
- FDA approved December 19, 2024; commercial launch announced February 2025

RETAIN

Retains ECM structure and mechanical and biological activity¹⁻³

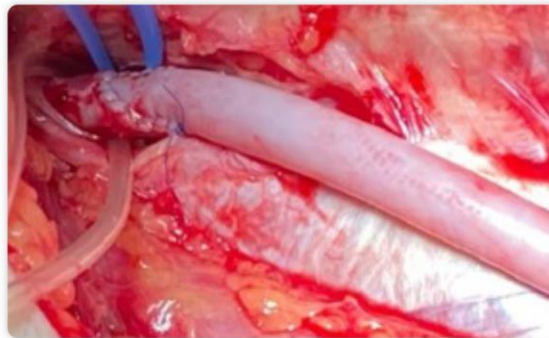
PRE-IMPLANTATION*



RESTORE

Restores blood flow upon implantation¹⁻³

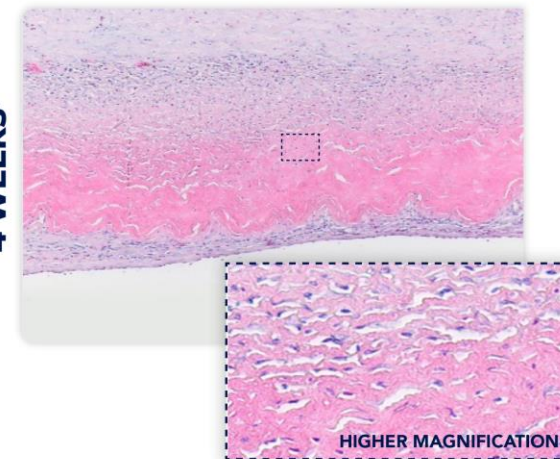
IMPLANTATION**



REPOPULATE

Repopulates with the patient's cells¹⁻³

4 WEEKS†



Success Story: Embrace®

WOUND HEALING: SCAR THERAPY

- Only FDA-cleared scar therapy that relieves tension around surgical incisions (Neodyne dressing)
- Works by inhibiting a FAK-mediated signaling pathway that drives scar-forming MMP9 activity

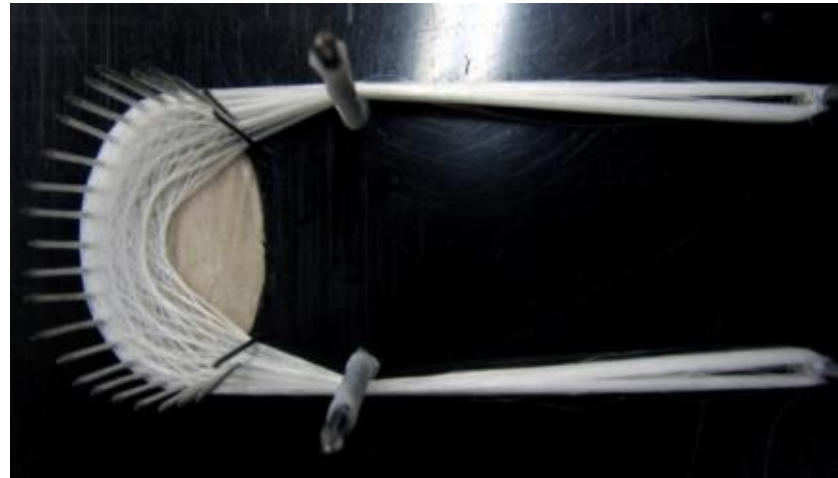
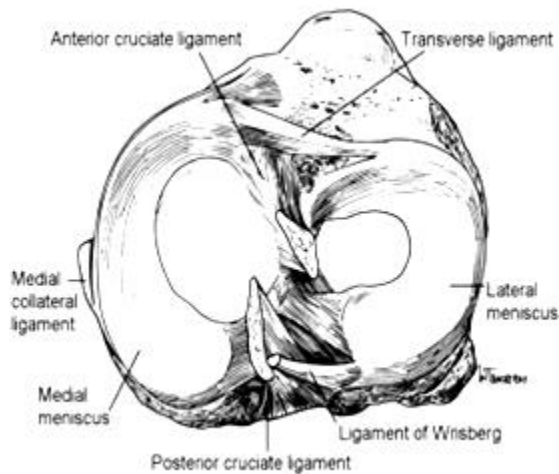


MeniscoFix™

Meniscus scaffold - Recognized by the FDA as a “Breakthrough device”

>1.5 million meniscus tears each year

MeniscoFix™ represents a new strategy to completely replace damaged meniscal tissue



Expanding Promise of Regenerative Therapies

Initial AFIRM- Rehabilitation

Current AFIRM- Treatments close to the point of injury

From undifferentiated stem cells to specialized cells

Blood

Neural

Complex extremity reconstruction

Fully functional organs

From scaffolds to regenerative promoters

Exosomes

Secretomes

Lyophilization for austere operational environments

The AFIRM Consortium Model- Investment that Multiplies Itself

Conventional DoW Research Portfolio

AFIRM Consortium DoW Portfolio

Individual investigators funded in isolation



AFIRM promotes national collaborations, ideas sharing and co-development

Infrastructure duplicated across institutions



AFIRM provides shared infrastructure across a coordinated national network

Findings often stall before reaching a product



Accelerates interactions/partnerships driving products to the clinic

DoW carries full cost and risk



Venture and industry co-investment reducing long-term DoW exposure

DoW oversight & peer accountability and guidance

Building a Regen Med Support Ecosystem: REGENERAT//OR



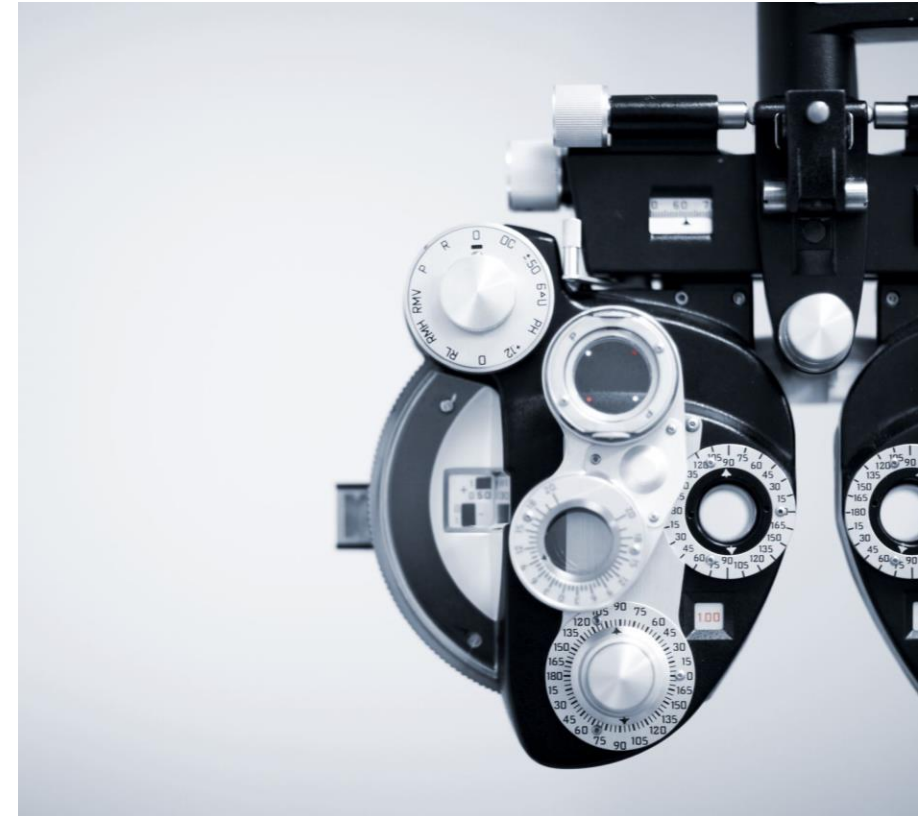
Part 1: Workforce Development: 2019

Part 2: Test Bed for New Technologies: 2021

Part 3: Innovation Accelerator: 2021

Part 4: Clinical Trial Catalyst: 2023

Part 5: Regulatory Navigator: 2024



REGENERATOR TEST BED

Assists regen med start-ups and growth companies with new and emerging technologies

Funded with major investments from emerging manufacturing support industries

Regen med entities have free access to the test bed and all its equipment to support product development and prototyping



Regulatory Navigator



The regulatory navigator advises entities on the best regulatory strategies

Directed and supported by highly experienced ex-FDA staff :

Dr. Steve Bauer, 30-year history at the FDA, 16 as Branch Chief for Cell and Tissue Therapies & Dr. Stephen Sawyer

Regenerator Clinical Trial Catalyst

 Advocate
Health Care



Access to 70 hospitals and >1000 outpatient facilities through a single IRB and contract approval process

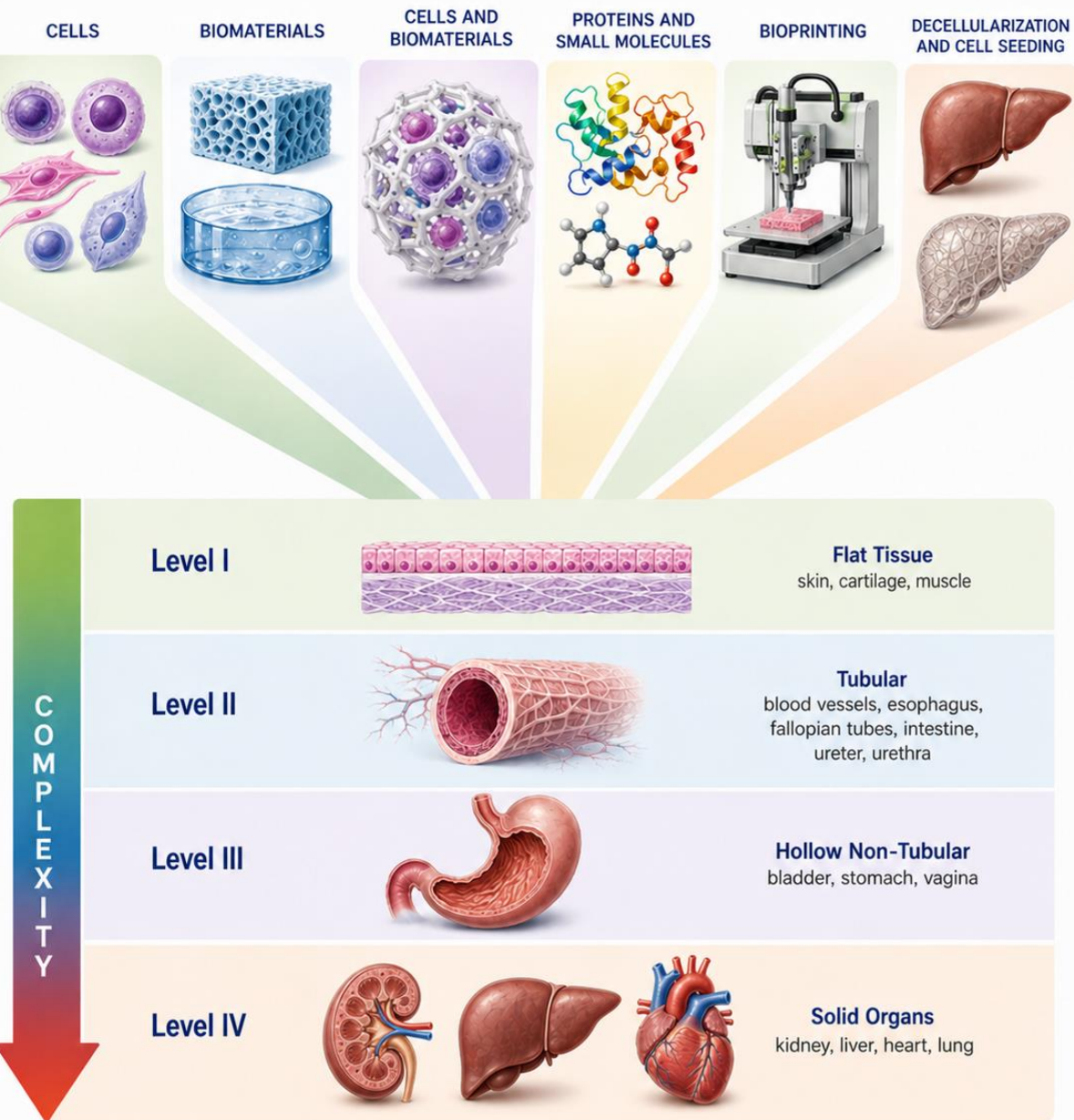
Launched January 2023 with first clinical trial for Panasonic Health



News

Epredia Receives U.S. FDA 510(K) Clearance for the Epredia E1000 Dx™ Digital Solution Designed to Improve Tissue Diagnostics

Cell, Tissue and Organ Engineering



Wake Forest Institute for Regenerative Medicine

(WFIRM) - Current Pipeline

Working on >40 different tissues and organs

Stem cells

Bioreactors

Bioprinting

Small Molecules

Body-on-a-Chip Technologies

Drug development

Physiological modelling

Diagnostics

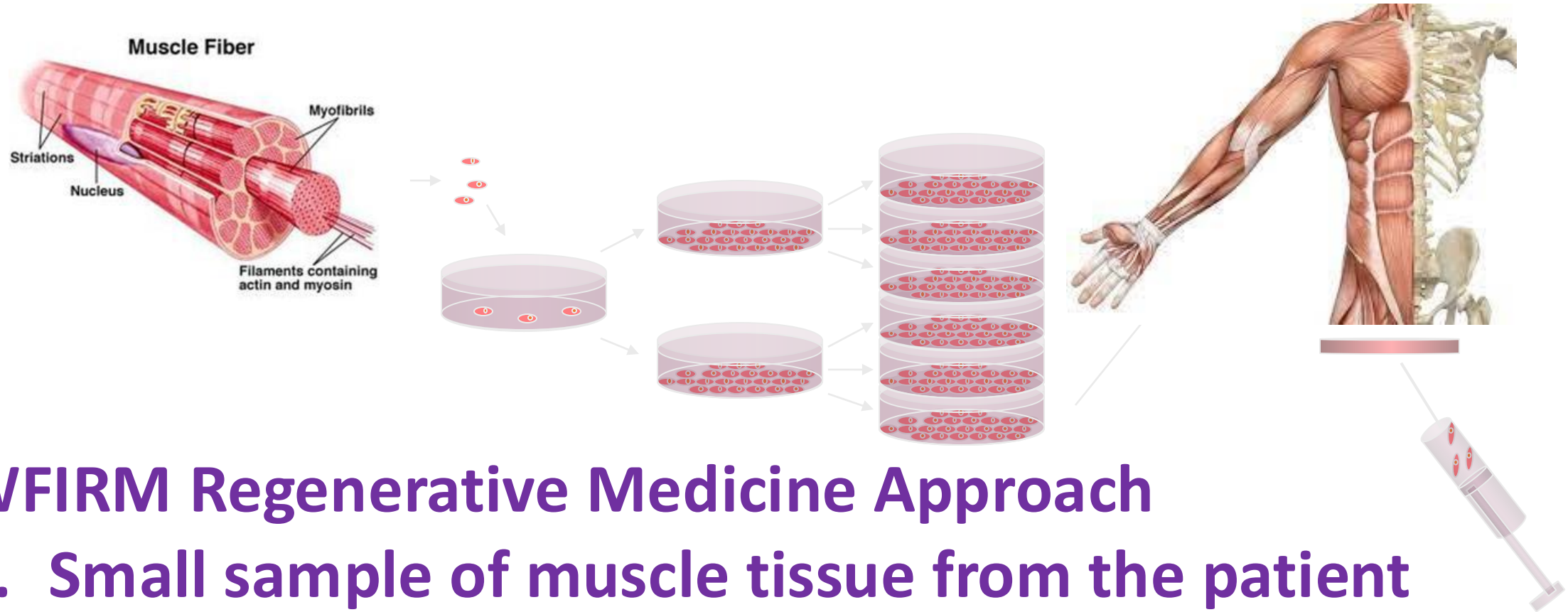
Personalized medicine

Cancer treatment prediction

18 applications of technologies developed by WFIRM scientists are in human patients to date

Skeletal Muscle Injury / Disease

Orthopedic, Urologic, Gastroenterology...

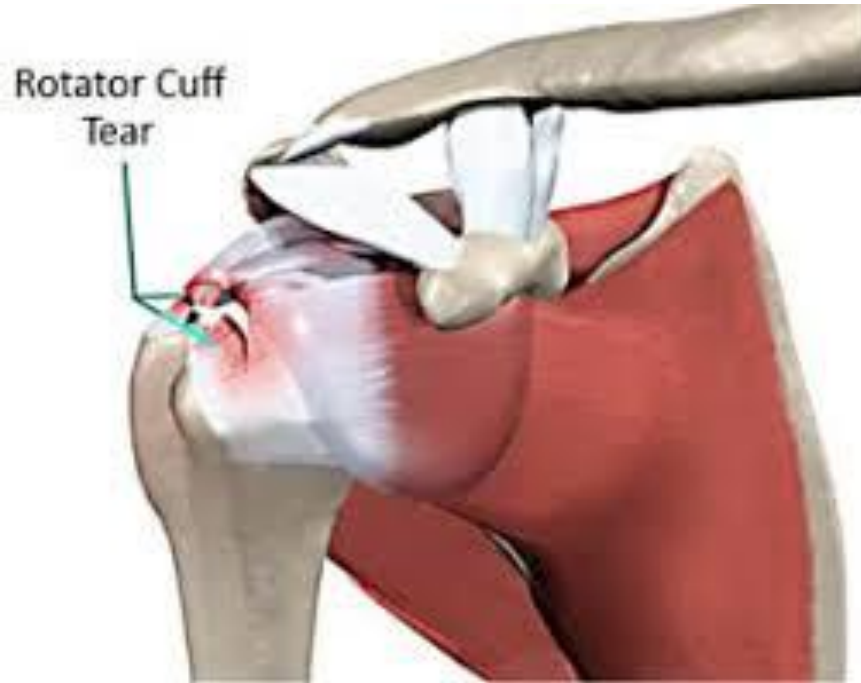


WFIRM Regenerative Medicine Approach

1. Small sample of muscle tissue from the patient
2. Expand cells in tissue culture
3. Inject cells in damaged area in the same patient

Shoulder Rotator Cuff Injury: Current Human Trials

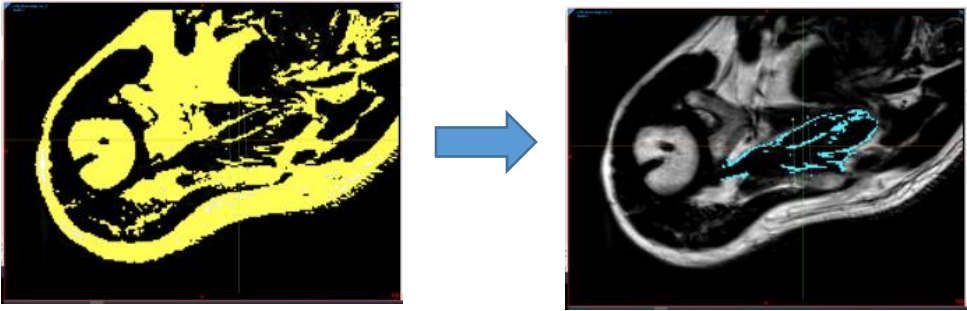
- Patient selection
 - 40-80 year of age
- Muscle biopsy and processing
- Rotator cuff surgical repair
- Muscle therapy injection
- Outcomes: safety, increased muscle tissue, increased muscle strength



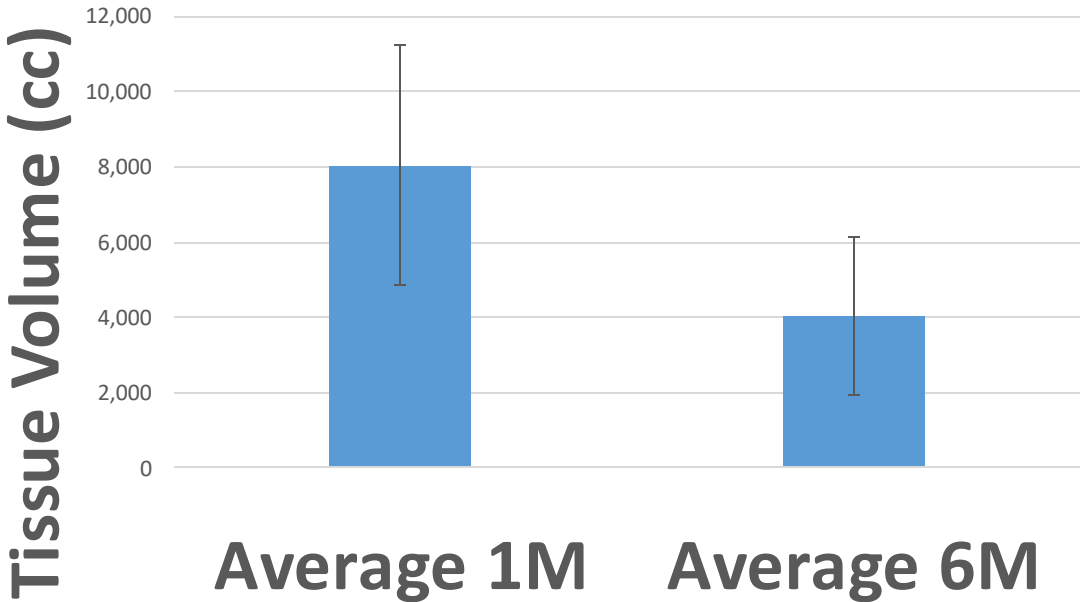
ASES: Shoulder Function

Time	#1	#2	#3	#4	#5	Avg
Baseline	36	28.3	8.35	34.9	61.6	33.83
3 Mos	80	88.32	18.33	70	79.99	67.33
6 Mos	97	86.69	fail	98.33	93.32	93.84

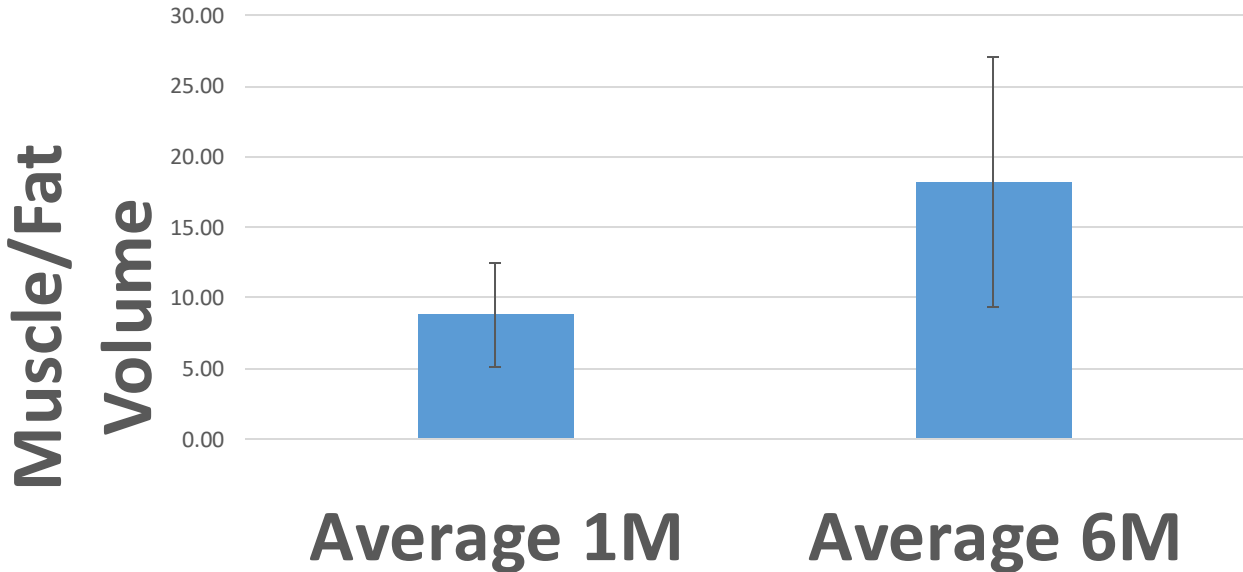
MRI Muscle:Fat
Studies



Fatty Infiltration

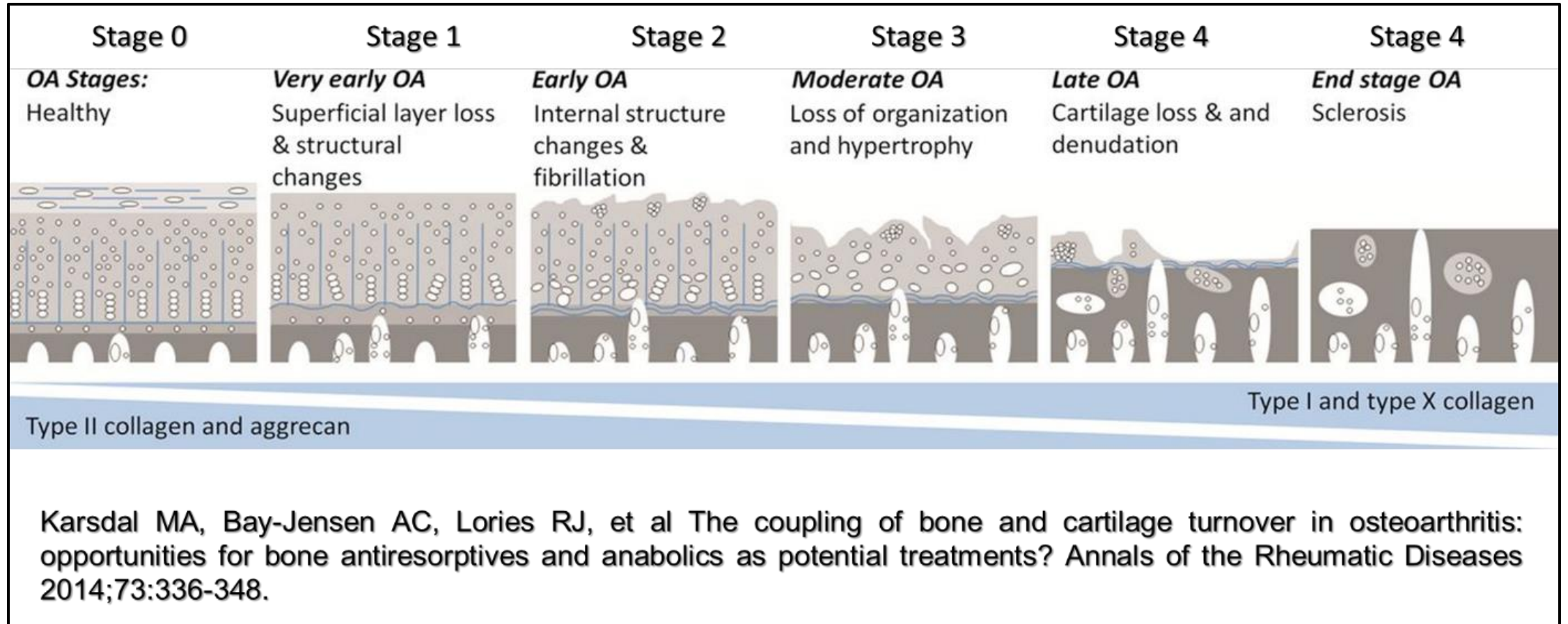


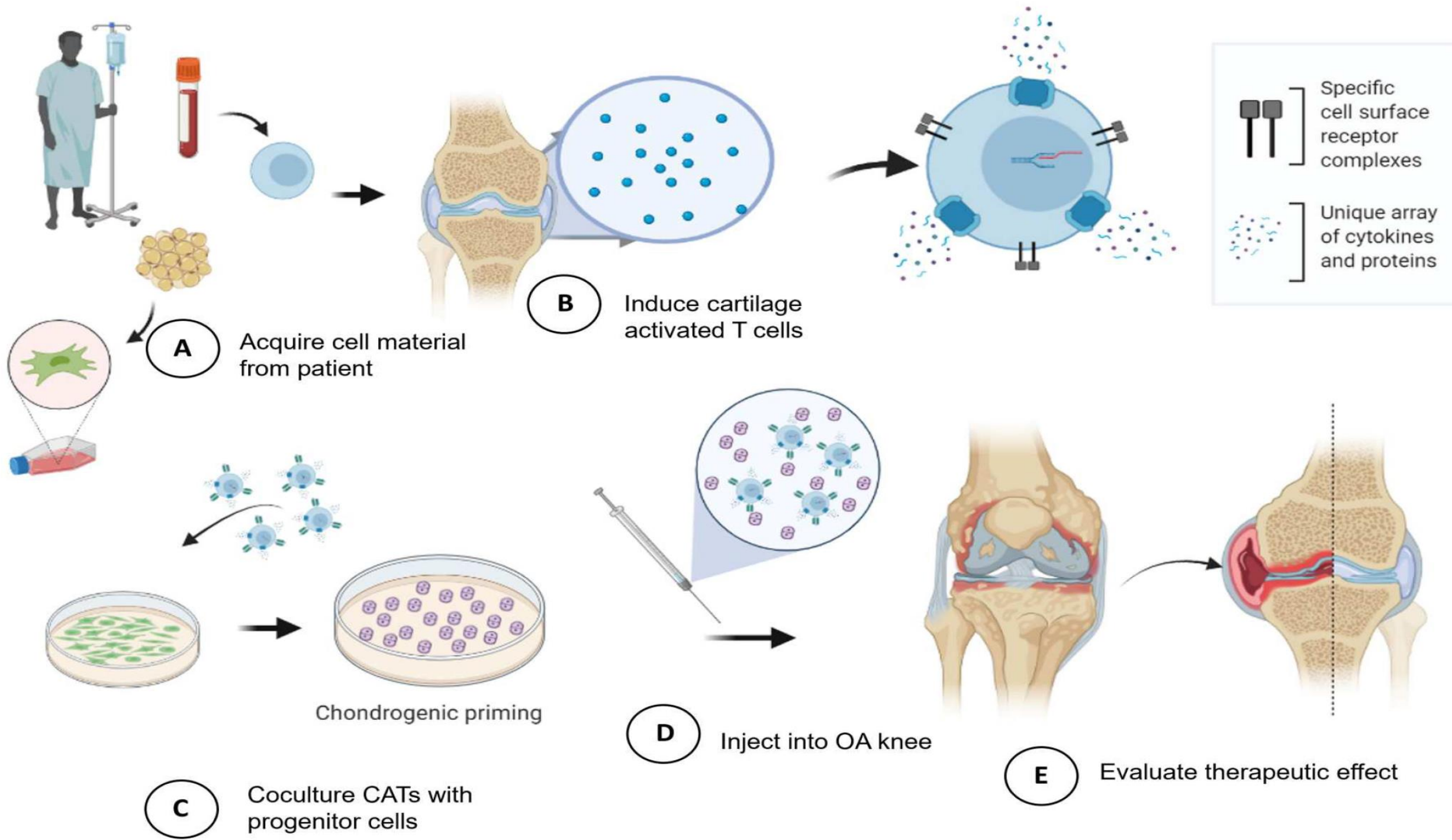
Muscle to Fat Ratio



Cartilage Regeneration Human Clinical Trials

Osteoarthritis (traumatic and degenerative)

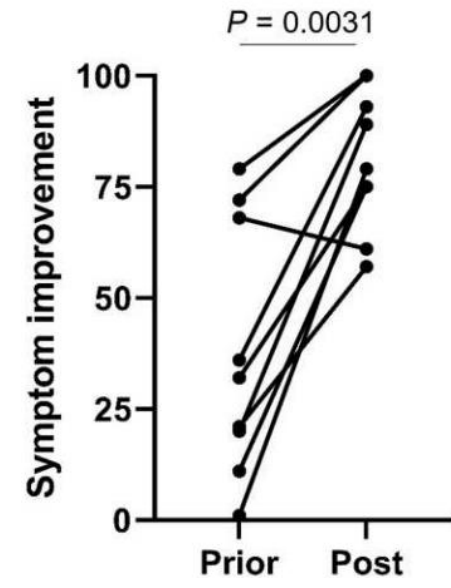
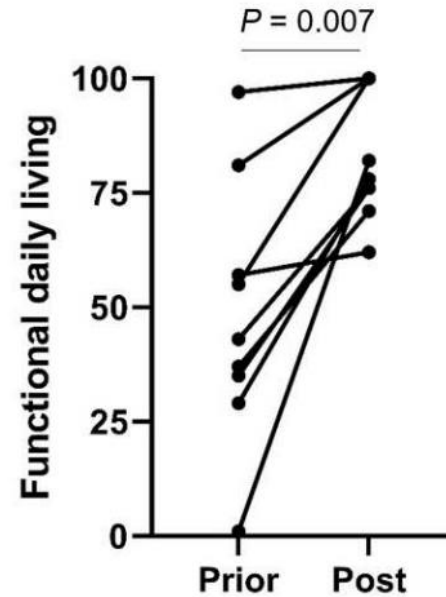
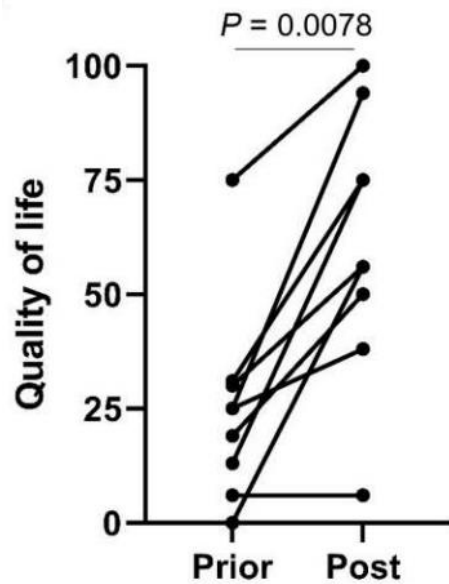
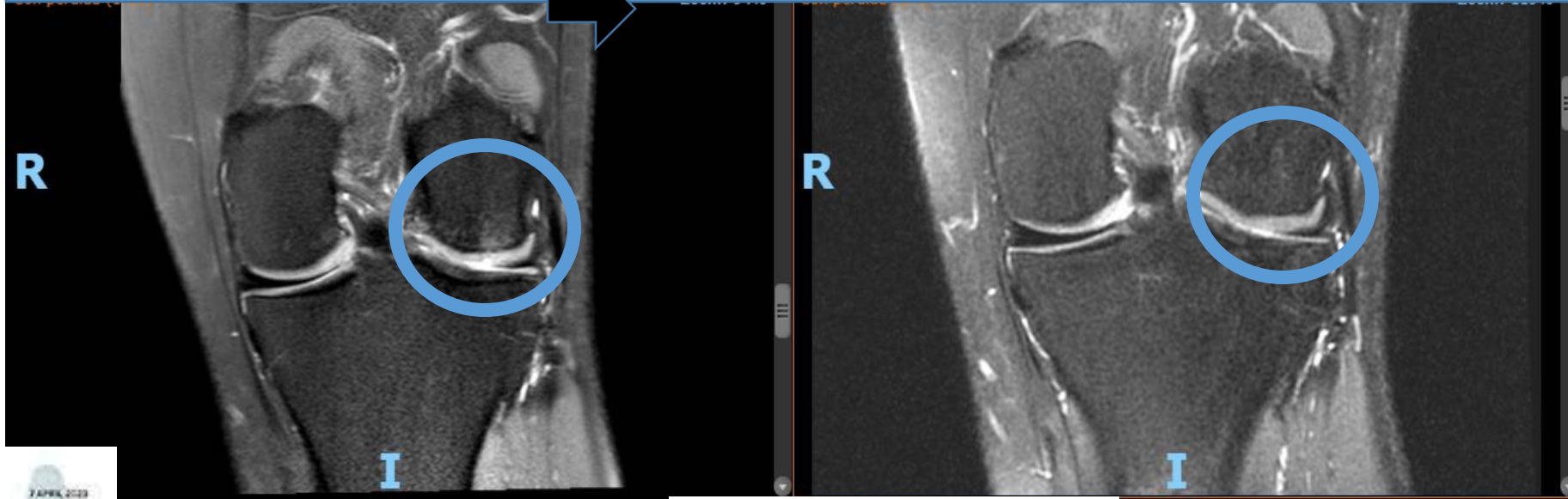




Knee MRI Before and After Cartilage Differentiated Cell Injection

Pre-Treatment

13 months post-Treatment



Moviglia et al

Kidney needle biopsy

Normal kidney cells
expanded outside the body

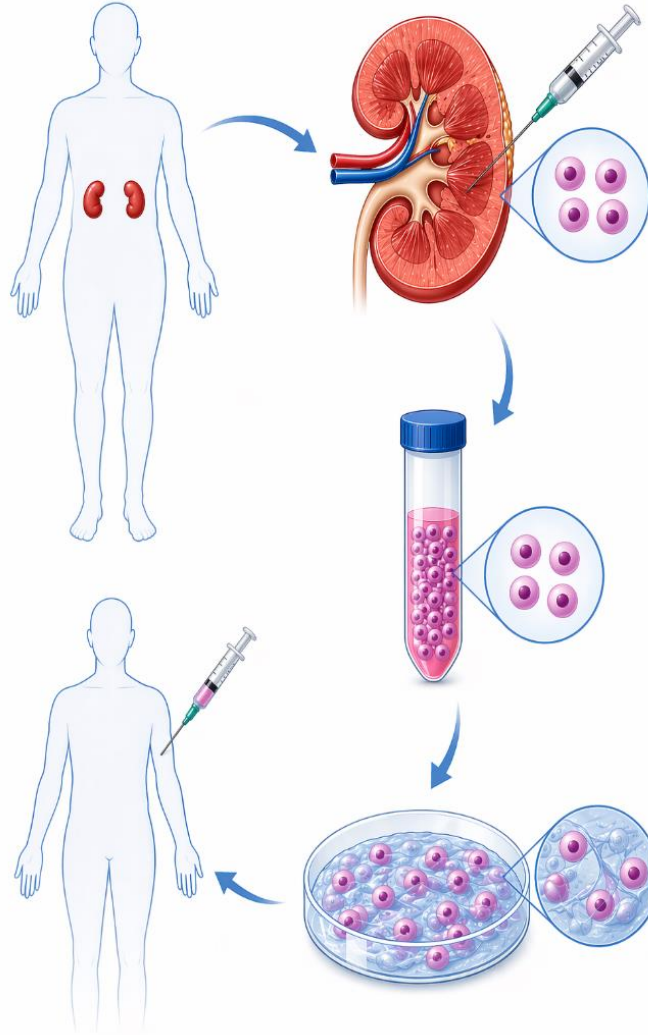
Kidney cells inserted back into
the diseased kidney

Completed FDA Phase I and II
Human Trials

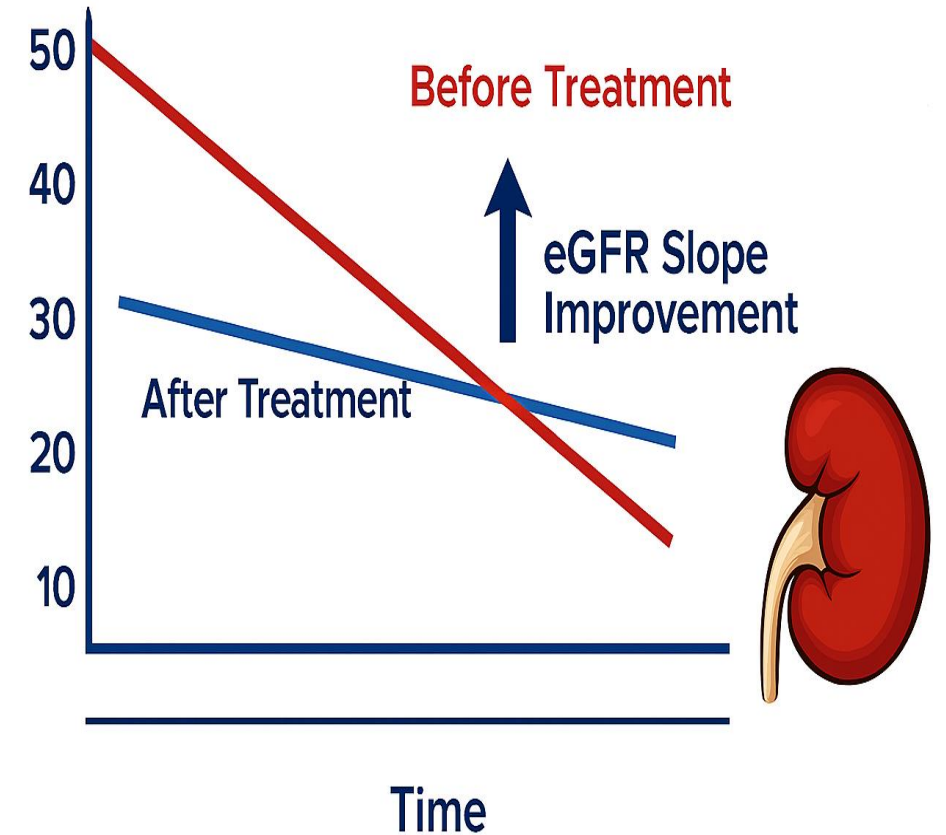
Phase III trials in progress in >
70 sites in the US and globally

Initial outcomes: Over 120
patients > 3 years, overall
prevention of dialysis

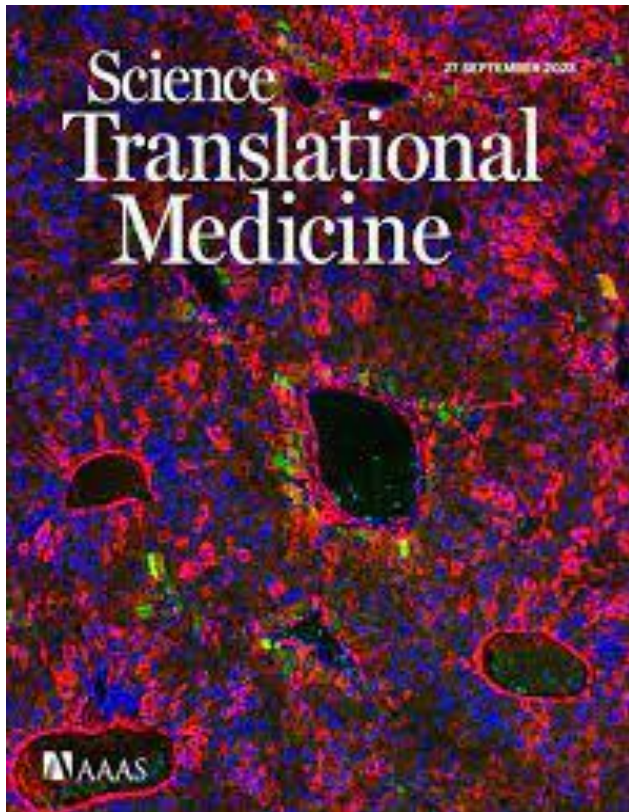
No rejection (autologous cells)



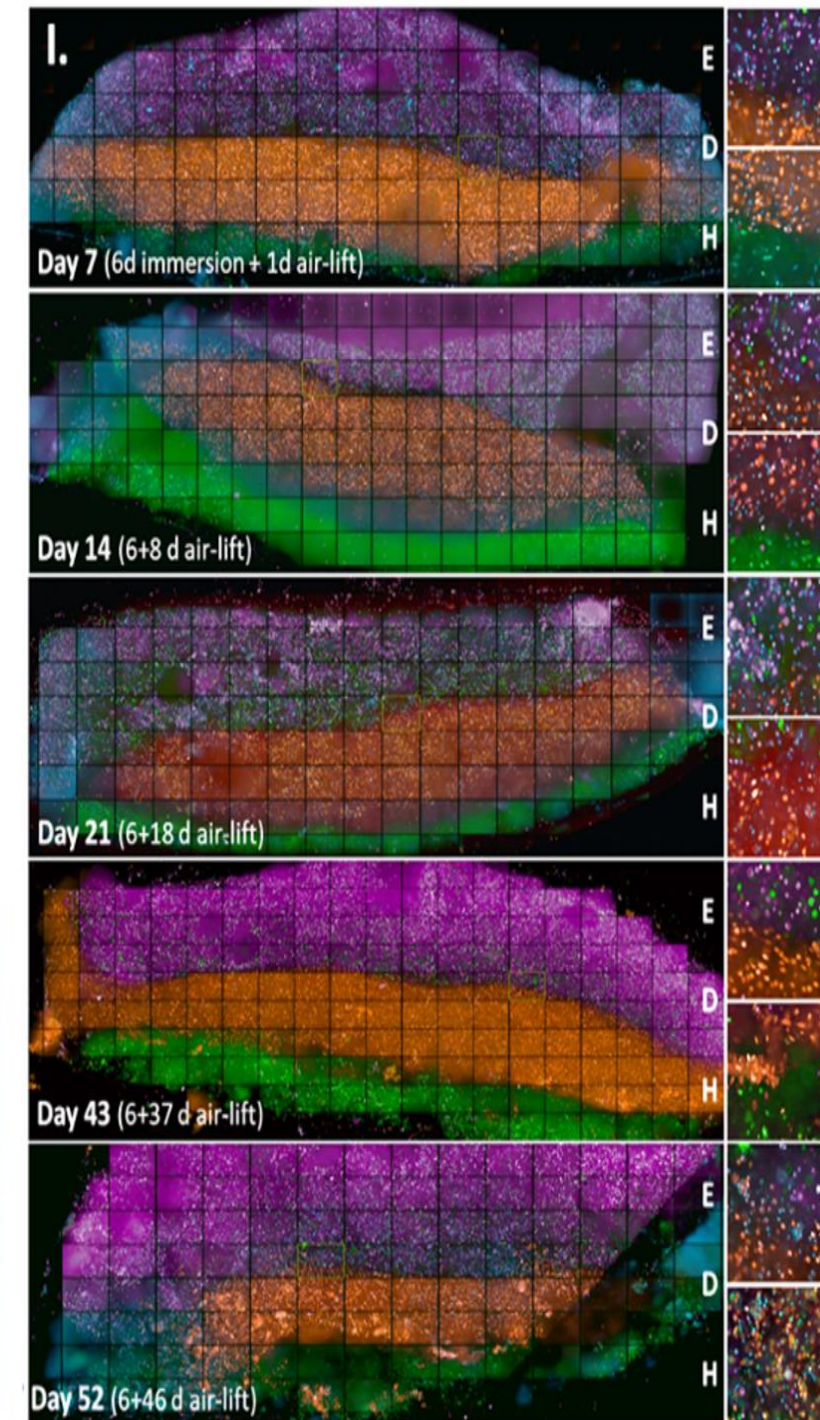
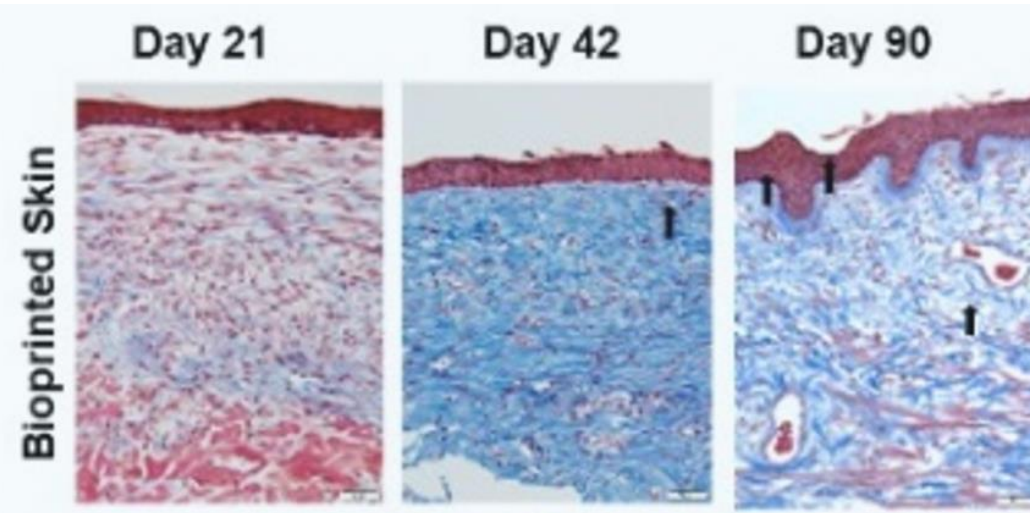
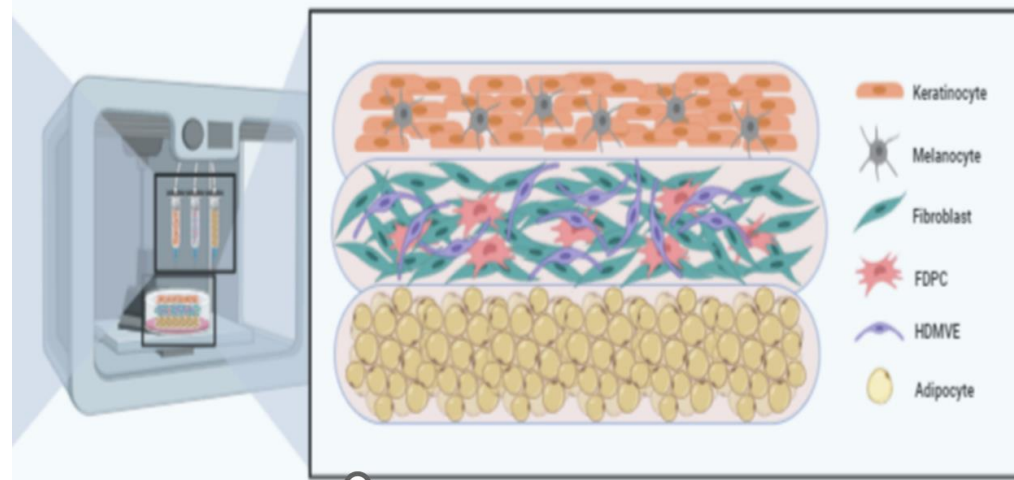
Outcome



3D Printed Full Thickness Human Skin Equivalent- 3 layers/6 cell types



Sept 2023



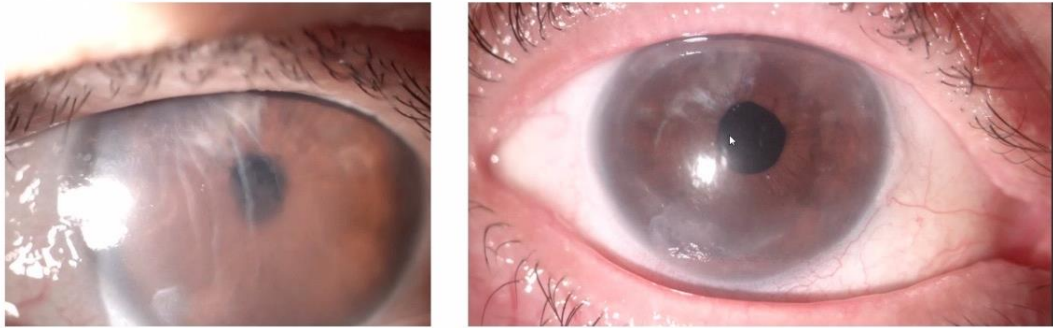
70 year old female patient with pseudophakic bullous keratopathy
Severe corneal edema (CCT 710 μm)
Prior cataract surgery and iridotomy
Legally blind for 14 years



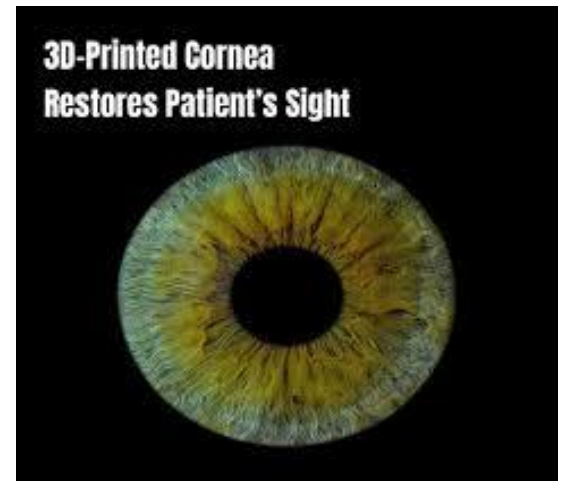
Visual acuity 20/400 (legally blind)

70 year old female patient with pseudophakic bullous keratopathy
Severe corneal edema (CCT 710 μm)
Prior cataract surgery and iridotomy
Legally blind for 14 years

3D Printed Cornea



Visual acuity 20/400 (legally blind)
to 20/23 over ~5 months



WFIRM - Partial List of over 500 Faculty and Staff

Abdelgawad, Essam	Calafiore, Rebecca	Goel, Sandeep	Kulkarni, Gauri	Morrison, Hannah	Romero, Michaela	Tripathi, Ratnakar
Abdulkhuseynova, Salomat	Campagna, Courtney	Gorantla, Vjay	Kumar, Ashmitha	Moviglia, Gustavo	Roscoe, Robbie	Trivett, Frank
Acoff, Eboni	Campbell, Justin	Gore, Robyn	Ladd, Mitchell	Murphy, Sean	Roseboro, Makayla	Tucker, Donna
Adams, Karri	Carstens, Michael	Gorkun, Anastasiya	Leach, Timothy	Mutkus, Lysette	Ruetten, Hannah	Van Acker, Cindy
Aguiayo, Caleb	Cayea, Steven	Gregg, Brieana	Lee, Chul Ho	NickKholgh, Bitia	Ruley, Ainsley	Vaughan, Bill
Aguilar Meza, Antonio	Chae, Minsuk	Gregg, Emily	Lee, Jae Seok	Nie, Wei	Sadri, Hooman	Vyong, Vy
Ahmad, Sarfaraz	Chalasani, Roopa	Gugliani, Anchala	Lee, Po-Feng	Nikmehr, Banafsheh	Salinas, Alejandro	Wachtman, Sarah
Albertson, Sarah	Chandra, Prafulla	Gupta, Rohan	Lee, Sang Jin	Nix-Denmark, Sarah	Sanabria, Juan	Wajih, Nadeem
Albertson, Steven	Cheng, Joshua	Gyabaah, Ken	Li, Claire	Nyul-Toth, Adam	Santiago, Nicole	Wall, Gresham
Aliftiras, Elisabeth	Chwiakowski, Shannon	Hampson, Robert	Li, Qingqi	O'Brien, Sean	Sawyer, Stephen	Walling, Stefanie
Almeida-Porada, Graca	Clark, Caroline	Han, Xu	Liaskonis, Vasilios	Oliver, Karla	Sazoglu, Bedreddin	Walker, Steve
Anthony, Christel	Clayton, Bert	Hann, Ronald	Libby, Kara	Opala, Emmanuel	Schaaf, Cecilia	Wan, Meimei
Arafa Mohamed, Walaa	Cleary, Jacob	Heathershaw, Caleb	Lim, Grace	Orlando, Giuseppe	Schanck, Joan	Wang, Donghai
Asthana, Amish	Clemensen, Olivia	Heydarian, Parichehr	Lindert, Kevin	Ots, Heather	Schwartz, Marshall	Watson, Julie
Atala, Anthony	Congress, Zachary	Hua, Liang	Liu, TieFu	Pandolfi, Guinevere	Seeds, Michael	Watts, Shannon
Babatunde, Oluwaseun	Contag, Max	Hutchins, Damian	Lizanets, Dariya	Park, Sang Hyug	Shakeri-Astani, Kiarash	Weaver, Matthew
Barlow, Jo	Criswell, Tracy	Inniss, Sharina	Long, David	Parsons, Emma	Shankle, Douglas	Weis, Jared
Barnes, Karen	Cutie, Stephen	Jackson, John	Lookbill, Emie	Pathak, Sharvari	Sharma, Akanksha	Weis, Victoria
Bauer, Steven	Dadhania, Gia	Jacobson, Alan	Lu, Baisong	Paul, Amber	Shirdel, Abolfazl	Wentz, Travis
Beatson, Bryce	Davis, Anna Belle	Jalboush, Sara	Makris, Leo	Peatross, Kaylah	Shirley, Molly	Whitaker, Emily
Becker, Brent	Day, Mary-Clare	Jankelow, Aaron	Manyonga, Kundai	Pendino, Alexandria	Shirling, Pamela	Willard, Elizabeth
Beiner, Daniella	Demir, Fatma	Jena, Satarupa	Marahwa, Pamela	Perez, Alfredo	Short, Samantha	Williams, Jada
Benson, Katie	Demir, Zeynep	Jennings, Bridget	Marcet, Paul	Pettengill, Mary	Shraga, Ava	Williams, Michelle
Benton, Allie	Diaz, Jonathan	Jeong, Jin-Oh	Marini, Frank	Peveri, Emma	Shupe, Tom	Wilson, Kathryn
Bergman, Chris	Dilber, Betul	Jeong, Wonwoo	Markert, Chad	Poddar, Suruchi	Siahmazgi, Zohreh	Wilson, Thomas
Bertram, Ken	Dirican, Omer	Jiang, Cuili	Marrotte, Eric	Porada, Christopher	Sides, Rachel	Winkler, Lisa
Bertram, Tim	Dobroski, Timothy	Jiao, Yan	Martin, Tanya	Potter, Dejanae	Sierra-Sanchez, Alvaro	Woehr, Andrew
Bibby, Maddi	Doby, Kathryn	Johnson, Lillian	Mashanov, Vladimir	Prokopiou, Nicos	Simon, Trang Le	Wolfe, Will
Billman, Erika	Doney, Aaron	Jones, Tara	Mason, Linda	Qi, Grace	Sivanandane, Sittadjody	Wright, Timothy
Bishop, Colin	Edenhoffer, Nicholas	Ju, Young Min	Mateo, Beatriz	Rains, Brandon	Smith, Jennie	Wu, Fan
Bissette, Randall	Edminister, John	Kabasakal, Abdulkadir	Maxwell, Joshua	Rahman, Sharifur	Soker, Shay	Xie, Rongyuan
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Bowen, Terri	Ferrara, Kaylee	Kasten, Jared	Merritt, Danyelle	Rebman, Alisha	Stumpf, Kristina	Young, Tracey
Bowlby, Joshua	Fearby, Lynn	Kelly, Geneva	Michael Forshaw, Olivia	Reeves, Kimberly	Sun, Susan	Zaho, Tarek
Brennen, Bailey	Figuereo, Yosauri	Kengla, Carlos	Miller, Brendyn	Reeves, Tony	Surendran, Vikram	Zakkam, Hema
Brigham, Kaitlyn	Folk, Marissa	Khader, Balqees	Miller, Kyla	Refaquat, Noor	Sutter, Alton	Zayas, Norma
Broughton, Jimmy	Frost, Haddie	Kim, Jeong Beom	Mock, Sarah	Rengaraj, Arunkumar	Sweeper, Donald	Zhang, Y uanyuan
Bruno-Garcia, Michelle	Garrison, Alex	Kim, JiHyun	Montgomery, Cindy	Renteria, Eric	Taylor, Dale	Zhao, Weixin
Burnett, Lisa	Gartner, Anna	King, Elsa	Moore, Jillian	Rezapour, Mostafa	Thanappazham, Hemanth Raj	Zhou, Yu "Joy"
Butterbaugh, Cindy	Gaser, Ola	Koch, Amber	Morgan, Ted	Rice, Jim	Thomas, Karma	Zimmernan, Cindy
Byers, Lori	Gaviña, Catalina	Krishnan, Anisha	Morris, Andrea	Richards, Celeste	Thornburg, Jesse	
Byrne, Shannon	George, Sunil	Kulahci, Yalcin	Morris, Lauren	Rodriguez, Martin		

The AFIRM: Fulfilling Promises

- **Supporting Warfighters with FDA-approved products, clinical trials, and commercial partnerships**
- **Delivering at a fraction of the cost of equivalent private-sector development**
- **Restoring function**
- **Improving lives**



SCIENCE
INNOVATION



CLINICAL
TRANSLATION



AFFORDABLE
SOLUTIONS



RESTORING
FUNCTION



IMPROVING
LIVES



According to the US Department of Health and Human Services report



**“Regenerative medicine will be the
standard of care for replacing
tissue/organ systems in the human
body”**