ADVANCED BIOTECH PRODUCTS (P) LTD.

INFORMATIONAL MATERIAL PACKAGE ON

SURGICOLL-MESH®

IMPLANTABLE, BIORESORBABLE, TISSUE REGENERATIVE
STERILE, TYPE-I COLLAGEN MATRIX
A Patented American Technology

Manufacturing Address:
PL. 111 to 114 SIDCO Pharma Estate, Alathur 603 110.

Sales & Marketing Office:
#77, 1st Cross St, Ragavan Colony
Chennai - 600 083. TN, INDIA. Phone: 044 – 24744650
E-mail: info@advanced-biotech.com
Website: www.advanced-biotech.com

Under the technology from:

ENCOLL

Fremont, CA, USA.

Advanced Biotech Products (P) Ltd.

Head Office : 77, First Cross Street, Ragavan Colony, Ashok Nagar, Chennai, TN - 600083, India.
Factory : PL.111 to 114, SIDCO Pharma Estate, Alathur, TN - 603110, India.

PROPRIETARY ARTICLE CERTIFICATE (PAC)

(To be submitted by the indenter along with the indent)

Certified that to the best of our knowledge, the items indented vide indent No..... Dated..... for **Surgicoll-Mesh** tissue regenerative innovative biological device products that are manufactured only by **M/s. Advanced Biotech Products P Ltd**. There is no other option of the Facility except to Purchase this item(s) as it is having unique features. (Please see the patented product features attached)

Further it is essential for the high quality R&D and Clinical treatments that cannot be met through any other similar tissue regenerative biological products currently available. Also the product is Proprietary through its US patents.

I/we shall be held responsible in case the certificate is found to be incorrect.

Signature of Indenting Officer / Project Leader

S. Gnanasekaran

Advanced Biotech Products (P) Ltd. Chennai

Designation: Scientist and Managing Director / ~~Project Leader~~

Date: 24 Feb. 2020

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UNIQUE FEATURES OF
SURGICOLL-MESH®

Surgicoll-Mesh, an innovative, high purity Type-I collagen has the following description and unique features:

1. High functional efficiency.
2. Its bioactivity is further enhanced by phosphorylation.
3. High degree of wound healing and tissue regenerative features.
4. Evidenced by equivalent Product approved in the US market.
5. US Patented for its purity and clinical efficacy[1,2].
6. Prepared using USP/IP, WHO GMP standards with ISO 13485:2016 regulations for quality compliances

Indications of Surgicoll-Mesh:

- Soft Tissue & Muscle Flap Reinforcement - As a patch to reinforce soft tissues repaired by suture or suture anchors, suture line reinforcement, muscle supplement with sling, repair and anchorage of tendon damage, and Transverse Rectus Abdominis Muscle (TRAM) flap procedures.
- Cartilage Regeneration.
- Hernia repair including abdominal, inguinal, femoral, diaphragmatic, scrotal, umbilical, and incisional hernias.
- Neurosurgical - As a substitute for dura repair and nerve wrap.
- Orthopedic Surgery - Osteochondral resurfacing, synovial tissue implant, repair of rotator cuff, patellar, Achilles, biceps, quadriceps and other tendons.
- Cardio-vascular - Atrial, ventricular and arterial patch repair, suture line buttress, intra-cardiac patch, thoracic wall etc.
- Intra Oral Surgical - Post-operative mucosal defect in oral cancer and pre-cancerous lesions, dental/OMF applications.
- Diabetic ulcer treatment.
- Colo-rectal, urethral & vaginal prolapse.
- Pelvic floor reconstruction, sacro-colposuspension and urethral sling.
- Third-Degree Burn to accommodate the Skin Graft needs

Advantage of using Surgicoll-Mesh:

- **High purity Type-I Collagen:** Surgicoll-Mesh consists of native un-crosslinked pure Type-I collagen (>97% pure) free of immunogenic proteins, lipids, and elastin[3,4].
- **Faster Healing:** Collagen phosphorylation attracts cells, regenerates tissue, and stimulates blood capillaries/granulation within 4 to 5 days[5].
- **Innovative Technology:** Better than intact tissue-based membranes which contain at least 15% elastin and other immunogenic molecules.
- **Easy Application:** No washing needed prior to use. Can be Sutured and/or Stapled.
- **Pain Control:** Effectively reduces pain
- **Various Sizes:** Choose from our available wide range of standard sizes. For more details, see Brochure.
- **Cost-Effective:** Accelerated wound healing and tissue remodeling with minimal applications.
- **Long Shelf Life:** Remains clinically usable for 3 years when stored in room temperature conditions

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CLINICAL EVIDENCE OF
SURGICOLL-MESH®

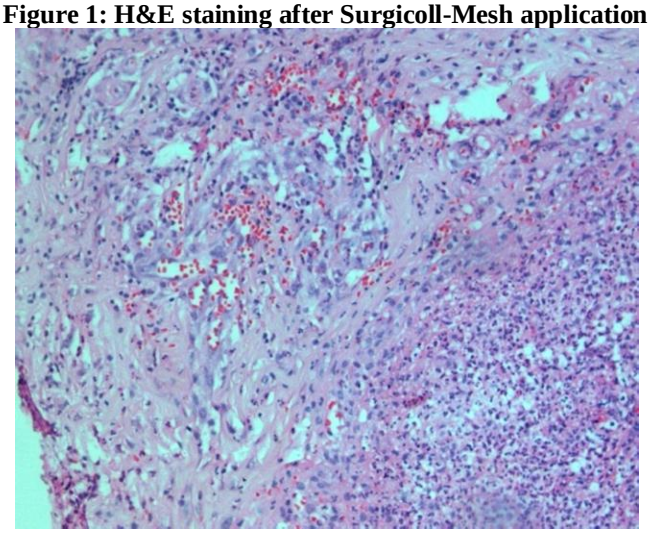
Surgicoll-Mesh has been subjected to the following clinical studies and the results are shown as below:

General Disclaimer:
Surgicoll-Mesh product is equivalent to that of US-FDA approved Helicoll of Encoll Corporation in USA. Some of the clinical efficacy of Surgicoll-Mesh are taken from that of Helicoll which will be referred as "Surgicoll-Mesh Equi"

Wound Healing Process

A bioactive collagen dressing, such as Surgicoll-Mesh, induces platelet aggregation. Inflammatory cells, neutrophils and macrophages invade the clotting area. After 4 days of wound healing, there is a complete connective tissue bridge covering the wound. The site fills with neutrophils and macrophages. At seven days, the inflammatory process recedes and the repair process (proliferative phase) begins with the fibroblastic synthesis and deposition of the extracellular matrix and collagen. Matured skin tissue develops consisting of bricks of fibroblast cells that are mortared by the collagen produced by fibroblasts (see Figure below). A combination of cells and collagen provides a secure bridge over the interrupted skin tissue.[6]

Figure 1: H&E staining after Surgicoll-Mesh application



After **Surgicoll-Mesh** application the acute inflammatory cells, fibroblasts and blood vessels proliferate into the collagen matrix. (50x). Absence of Lymphocytes indicates the non-immunogenic property of the collagen in **Surgicoll-Mesh**. [6]

SURGICOLL-MESH PRESENTATION

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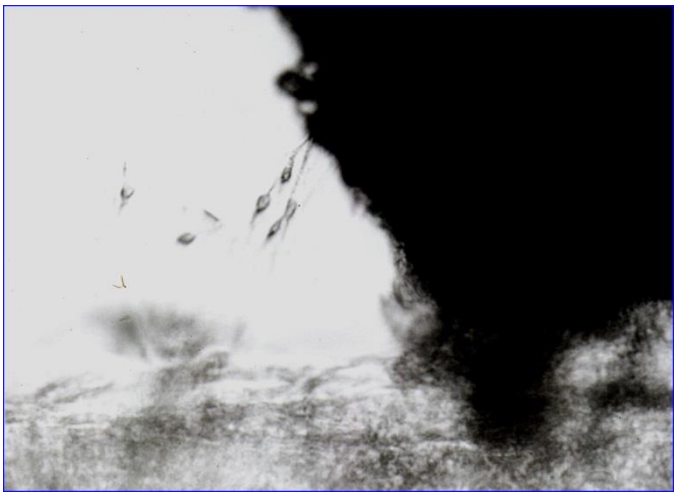
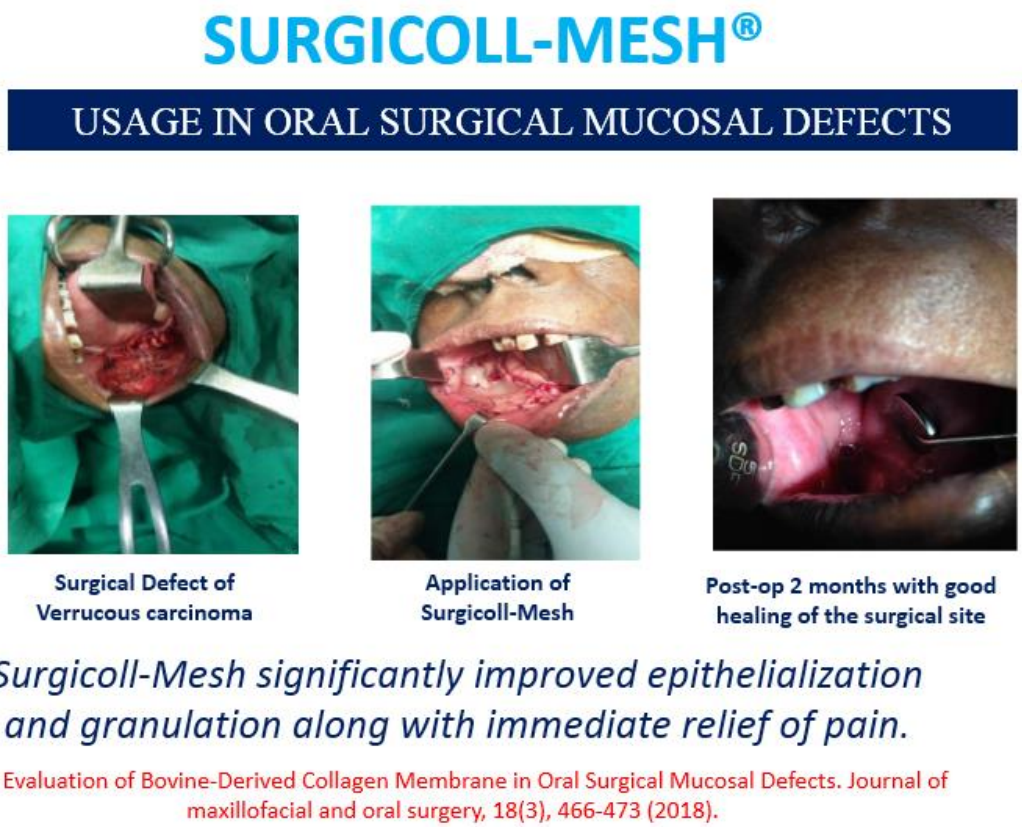
Figure 2: Bio Effects of Purified & modified EnColl COLLAGEN

EnColl's Patented Charge Modified (Phosphorylated) Type-I Collagen Attracts the Neuronal Cells Under Cell-Culture Experiments documented at Stanford University, California, USA





Surgicoll-Mesh has been clinically tested for oral cancerous lesions and the results have shown significant improvement in the aspects of hemostasis, stimulating epithelialization and formation of granulation tissue, as well as reliving the pain resulting in better functional outcome[7].

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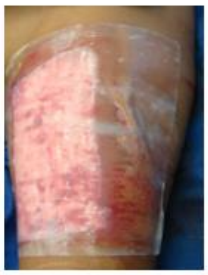
SURGICOLL-MESH® equi

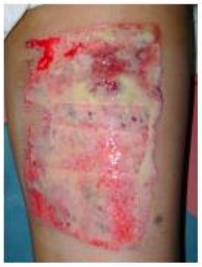
FAST SKIN REPAIR & REMODELING



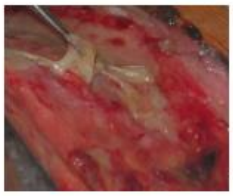
Day 1

Day 1

Day 2



Day 3



Day 4 & 5

FAST NEO-VASCULARIZATION

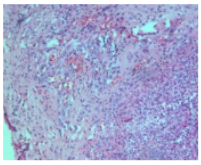
Evidenced by incorporation of "Surgicoll-Mesh Equi" into the surgical defective tissue on day 4 & 5

These results also assessed by histology & electron microscopy

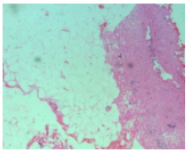
SURGICOLL-MESH®

CLINICAL EVIDENCE OF FAST NEO-VASCULARIZATION

Histology: After Surgicoll-Mesh application- acute inflammatory cells, & proliferating blood vessels (indicative of early tissue regeneration on day 4 and 5)

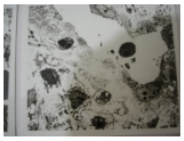


Control Histology: Before Surgicoll-Mesh application, only fibroadipose tissue is seen



Electron microscopy of tissue after Surgicoll-Mesh application

Scattered macrophages, monocytes, neutrophils fibroblasts & capillaries on day 4 and 5



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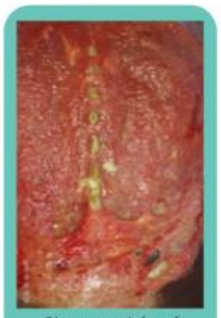
SURGICOLL-MESH®

TREATMENT OF SEVERE BURN/BED ULCER

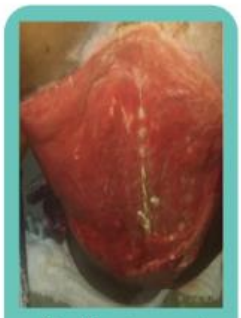
Electric Burn victim with bedsore resulting in chronic ulcer. (Day-0)

Ulcer wound debrided & cleaned. (Day-1)

Biological, Biocompatible Collagen product applied. (Day-1)



Shows uplift of healthy granulation soft tissue around vertebral spinous processes. (Day-4)



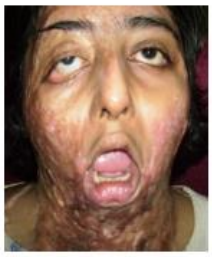
Significant wound healing is shown here. (Day-7)

Surgicoll-Mesh allowed rapid formation of granulation tissue & relieved pain upon application. Patient recovered within a week.

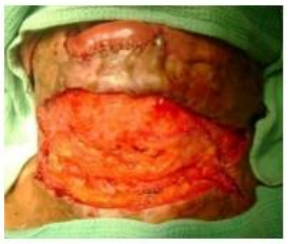
Courtesy of Dr. V. RamaDevi, Head, Department of Plastic & Burn Surgery, Kilpauk Medical College and Hospital, Chennai, India.

SURGICOLL-MESH® equi

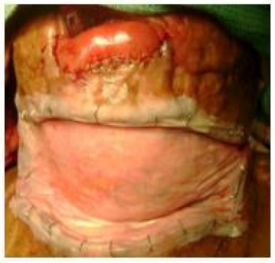
BURN RECONSTRUCTION



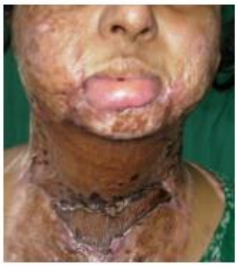
Day-0



Surgical Opening



Day-1: Surgicoll-Mesh Equi applied and stapled



21 days upon Skin-graft application over Surgicoll-Mesh Equi on day 5

Good Graft take, Firm adherence & early recovery

Ref: A Clinical Breakthrough in Wound Cover "Bioengineered Collagen" - A Cost Effective and Expeditious Permanent Skin Substitute International Society for Burn Injuries, Switzerland, 2010

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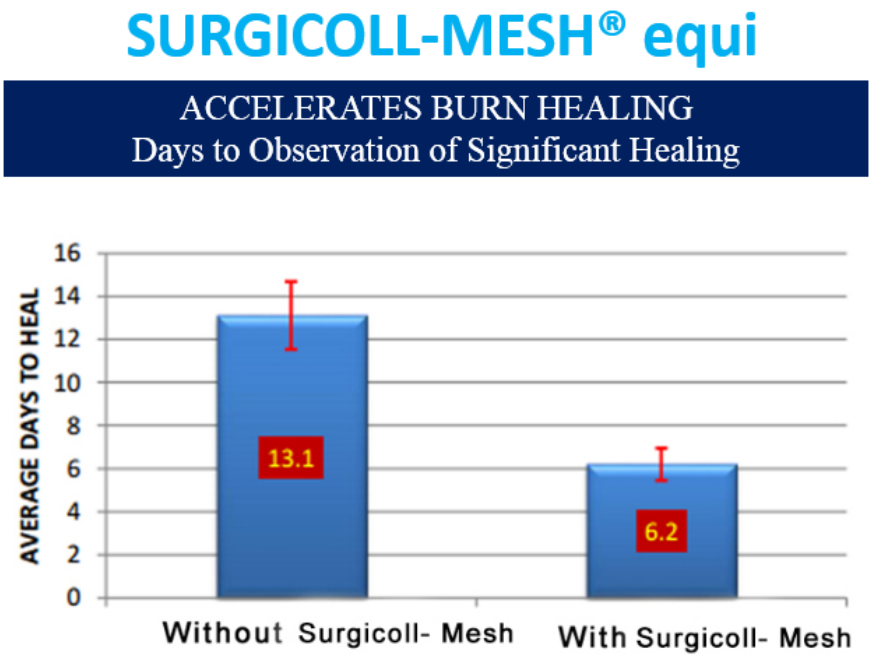

Ref: A Clinical Breakthrough in Wound Cover "Bioengineered Collagen" - A Cost Effective and Expeditious Permanent Skin Substitute International Society for Burn Injuries, Switzerland, 2010

Surgicoll-Mesh, in the clinical setting[6] significantly reduced burn healing time, provided rapid pain relief at the wound site, achieved 99.9% skin graft retention and reduced scarring, as well as return of native skin color to the patient after several months.

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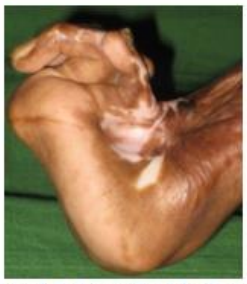
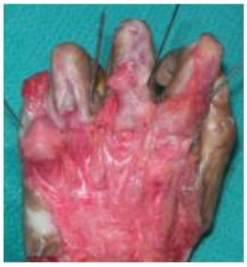
SURGICOLL-MESH® equi

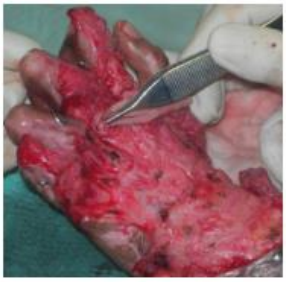
EXPOSED JOINTS - FILLS JOINT SPACES IN HAND



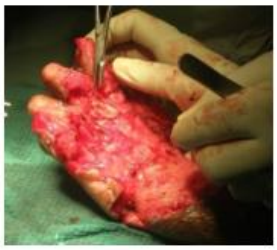
Hand deformation before surgery



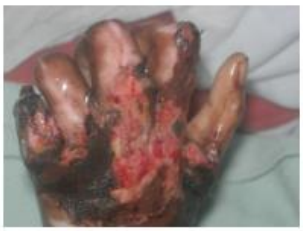
Surgical procedure day 1



Surgical procedure day 3



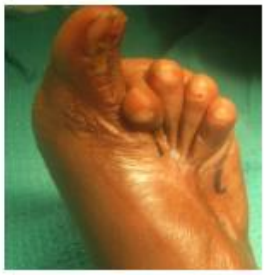
Surgical procedure day 5



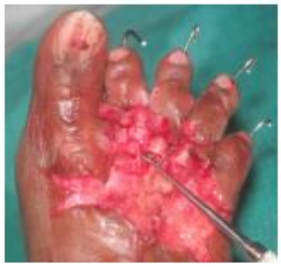
Day 9 after Surgicoll-Mesh equi application

SURGICOLL-MESH® equi

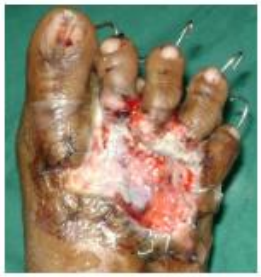
EXPOSED BONE & JOINTS IN THE LEG
(Need of a Flap Cover is Circumvented)



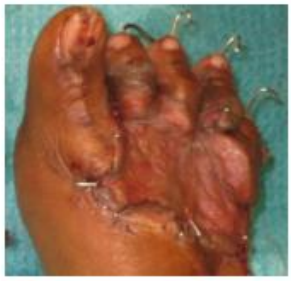
Before Surgery



Surgical intervention Day 1 with Surgicoll-Mesh equi



Day 7, a gel like substance covering the bare bones



Good graft take & healing, Day 25

Provides excellent coverage over exposed bone, tendon, cartilage and joints

Ref: Acta Medica International, 3(1), 146 (2016)

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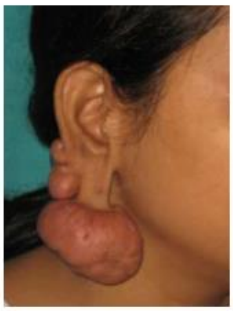
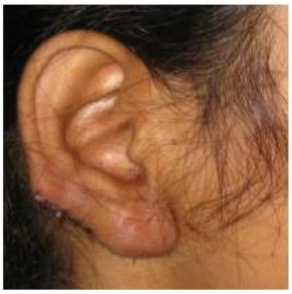
SURGICOLL-MESH® equi

KELOID EXCISION AND CLOSURE

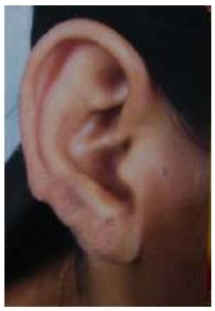


Day- 0

Day- 1: Insertion of Surgicoll-Mesh equi into the wound



Day- 15

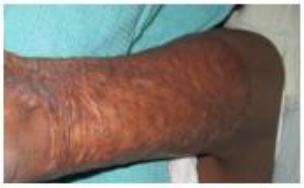


5 years- No Recurrence

Postulate that Surgicoll-Mesh equi acts to interrupt abundant collagen deposition and thus prevent hypertrophic scars and keloids

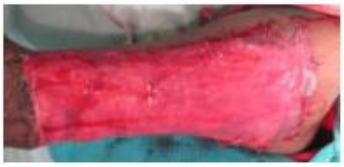
SURGICOLL-MESH®

HYPERTROPHIC SCAR



Day-0

Day-1 surgical excision of scar



Day-1, Surgicoll-Mesh

Day 12

Day-21

After 10 months

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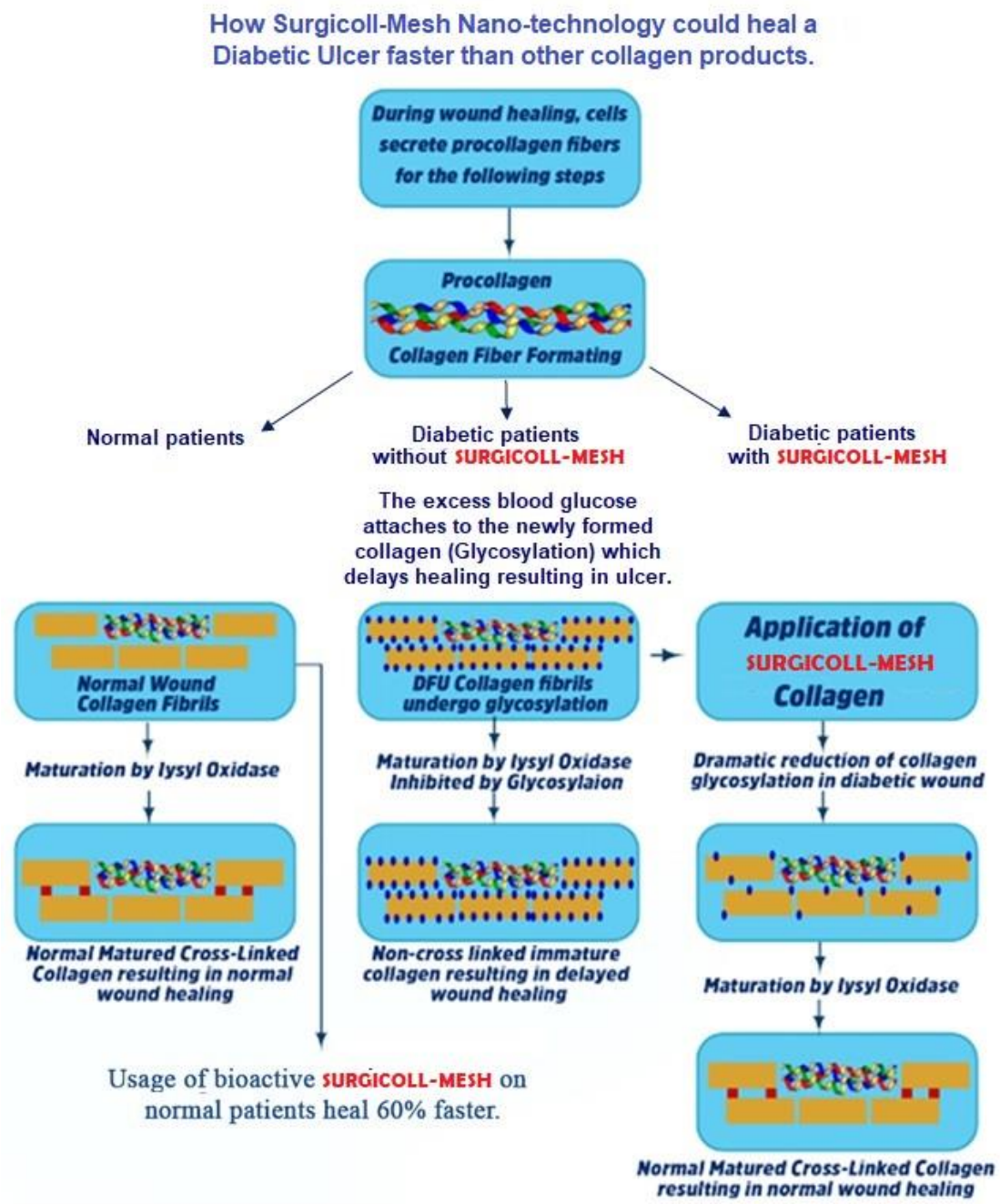
SURGICOLL-MESH®

WHY IT WORKS BEST FOR DIABETIC FOOT ULCERS?



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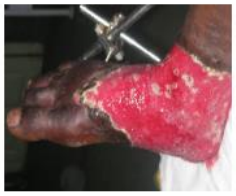
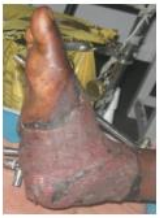
SURGICOLL-MESH® equi

LEG ULCERS

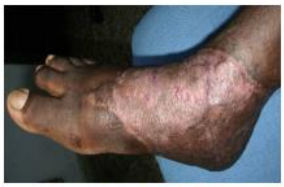


Full loss of initial graft

After Surgicoll-Mesh equi application



Upon graft application on Day 9 , by Day 21 shows 100% graft take

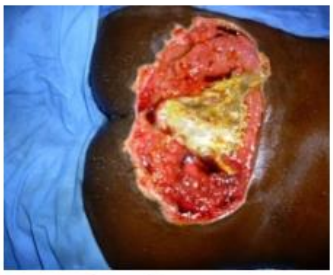


Stable & pliable graft at 3 months follow up

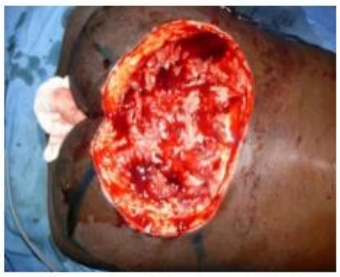
Surgicoll-Mesh equi allows neo-vascularization which facilitates 100% skin graft take when the skin graft is applied on 9th post op day.

SURGICOLL-MESH® equi

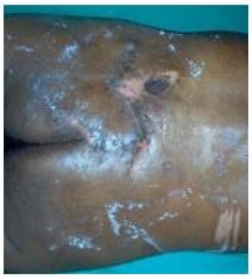
SACRAL PRESSURE SORE



Stage 4 pressure sore



10 Days Post "Surgicoll-Mesh Equi" application



Completely healed using "Surgicoll-Mesh Equi"

Complete Recovery in 6 weeks

Courtesy: Dr. Vinoth Philip , MD, DNB, Plastic Surgeon, Tirunelveli

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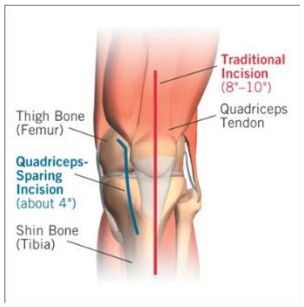
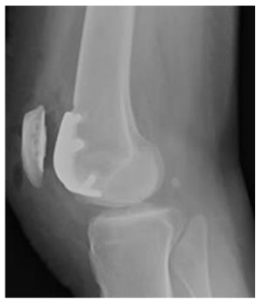
SURGICOLL-MESH®

ORTHOPEDIC APPLICATIONS
Knee Joint Cartilage Repair Using a Minimally Invasive Surgery





To treat injuries to bones, cartilage, ligaments, muscles and tendons.

The damaged cartilage parts can be repaired by inserting Surgicoll-Mesh or can be removed altogether and replaced with Surgicoll-Mesh.

Arthroscopic Meniscus Repair of Knee PreOp URL: http://www.youtube.com/watch?v=Gc8LtPUQ13E
Competing product info URL: http://www.geistlich-surgery.com/chondro-gide.html

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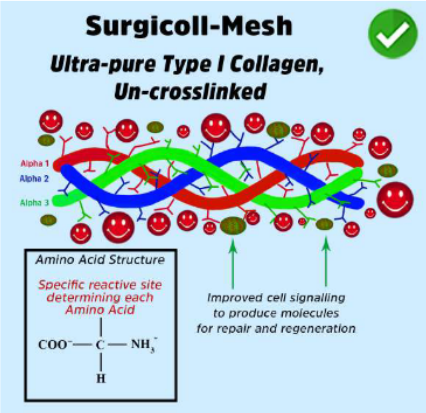
SURGICOLL-MESH®

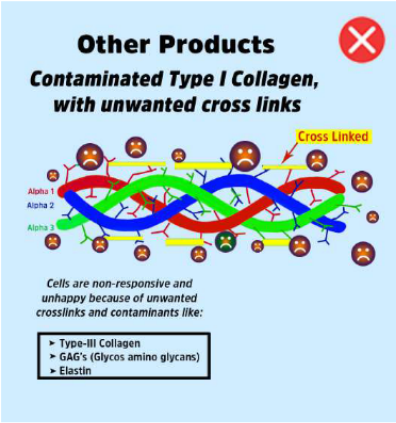
BIOCHEMICAL ADVANTAGES



- Surgicoll-Mesh is a bioengineered bio-resorbable high purity Type-I collagen (> 97% pure and free of lipids, elastin and other immunogenic proteins) membrane.
- It is further bio-activated by phosphorylation results in unique cell-signaling capabilities.
- As a result, Surgicoll-Mesh has clinically proven to form granulation tissue and invite new blood capillaries within 4 to 5 days after application.

SURGICOLL-MESH®

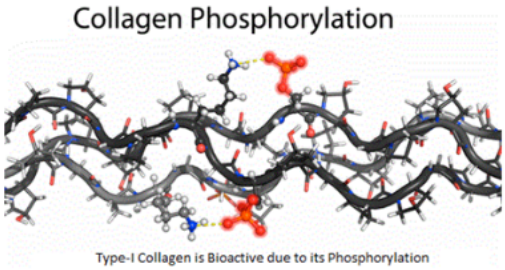
BIOCHEMICAL COMPARISON OF OTHER COLLAGENS



- Many of the available competitor skin-substitute products are derived from intact tissues (like amnion, intestinal wall, pericardium, skin etc.) of allograft or xenograft tissues.
- They incorporate all naturally immunogenic components (like Elastin, Type-III Collagen and other allergenic tissue components to the host tissue).
- Thereby, such products have to be cross-linked in order to reduce their immunogenicity.
- This process restrains the bio-effectivity of the useful Type-I collagen and its biological regenerative use in the host tissue.

SURGICOLL-MESH®

COLLAGEN PHOSPHORYLATION AND BIOACTIVITY



- The patented process yields high purity Type-I Collagen for maximum biocompatibility.
- Such collagen when phosphorylated results in cell signal transduction.
- Exceptional bioactivity of Surgicoll-Mesh collagen is derived due to its phosphorylation

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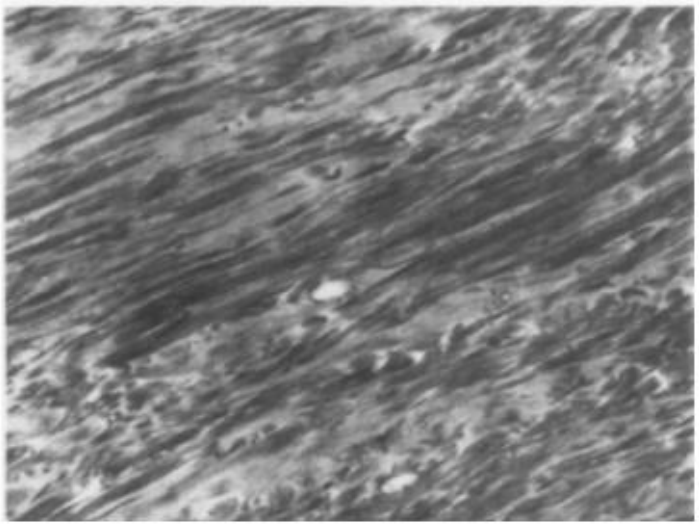
SURGICOLL-MESH®

ELECTRON MICROSCOPY OF THE SHEET

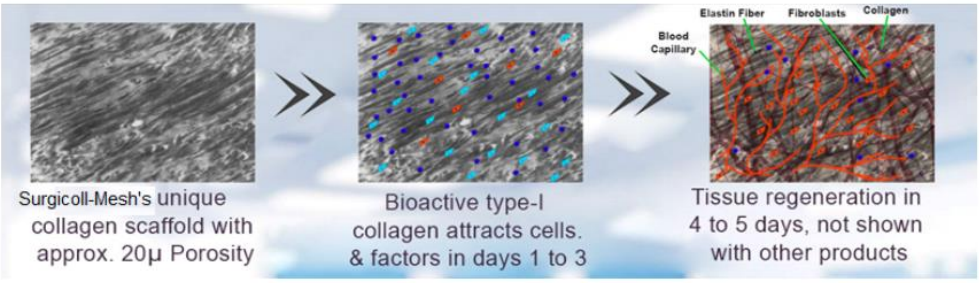
Shows meshwork of collagen fibrils in the Product

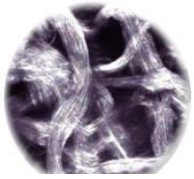


SURGICOLL-MESH®

HOW IT DIFFERS FROM OTHER EXTRACTED COLLAGEN PRODUCTS?

STRUCTURAL ADVANTAGE OF SURGICOLL-MESH COLLAGEN COMPARED TO OTHERS





Other collagen preparations (ex. Surgimend, Alloderm, Permacol) **as a result of lyophilization, yield random structural configuration that is non-native with avg. porosity > 800µ which is non-conducive for cell infiltration. Its bioactivity stays behind the bioactivity of sedimental preparation of SURGICOLL-MESH type-I collagen that yields native parallel fibrils with porosity of approx. 20µ to attract more cells/regenerative factors. Additionally, Surgicoll-Mesh is EtO gas sterilized that does not denature the protein unlike gamma sterilization which is used by most other collagen preparations.**

Ref.: Collagen structure affected by production method impacts clinical outcome, SAWC Fall 2020

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	SURGICOLL-MESH COMPARISION WITH OTHER PRIME PRODUCTS							
PRODUCT	**SURGICOLL-MESH®**	**SURGIMEND®**	**XENMATRIX™ SURGICAL GRAFT**	**PERMACOL™**	**FLEXHD® STRUCTURAL**	**ALLODERM SELECT™**	**PERI-GUARD®**	**REGENETEN™ BIOINDUCTIVE IMPLANT**
Manufacturer	**Advanced Biotech Products P Ltd**	**Integra LifeSciences**	**C.R. Bard**	**Medtronic**	**MTFBiologics**	**LifeCell Corporation**	**Synovis Surgical Innovations**	**Smith & Nephew**
Matrix	Patented high purity bovine Type-I collagen	Fetal and neonatal bovine dermal collagen	Non-cross-linked, regenerative porcine dermis collagen	Cross-linked acellular porcine dermis	Pre-shaped human dermis	Non-crosslinked cadaveric donor human dermis	Bovine pericardium cross-linked with glutaraldehyde	Highly purified bovine Achilles tendon
Native structural integrity	Fibrils are organized in parallel like in-vivo with native 20µ porosity.	Random, non-native fibrils	Random, non-native fibrils	Random, non-native fibrils	Non-native cross-linked fibrils	Random, non-native fibrils	Non-native cross-linked fibrils	Highly-porous, Random, non-native fibrils
Large presence of immunogenic elastin or adverse biomolecules	No	Yes (significant amnt of type-III collagen)	Yes (approx 15% elastin and Type III Collagen presence)	Yes (approx 15% elastin and Type III Collagen presence)	Yes (approx 15% elastin and Type III Collagen presence)	Yes (approx 15% elastin and Type III Collagen presence)	Yes (approx 15% elastin and Type III Collagen presence)	Yes (unwanted cross-linked type-I collagen)
Cell Infiltration Rate	Begins at 4 to 5 days. Cell signaling induces tissue regen to compromise strength	Cell infiltrates after 4 weeks post-implantation	Cell infiltrates after 2 weeks post-implantation	Moderate infiltration after 2 weeks due to cross-links	No vasculature even after 6 weeks	Cell infiltrates after 2 weeks post-implantation	Relatively slow infiltration due to cross-links	Cell infiltration can be expected after 5 weeks post-op
Bioactivity expressed via neo-vascularization & granulation enhanced by phosphorylation	Within 4 to 5 days after application (Clinically proven)	No vascular ingrowth up to 3 weeks	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days	No report indicates lesser than 9 days
Control of hyper glycosylation in tissue repair and regeneration	Yes	No	No	No	No	No	No	No
Sterilization	Terminal sterilization	Terminal sterilization	Terminal sterilization	Terminal sterilization	Aseptically processed	Aseptically processed	Terminal sterilization using ethanol	Terminal sterilization
Total Advantages of the product	**7 of 7**	**1 of 7**	**1 of 7**	**1 of 7**	**0 of 7**	**0 of 7**	**1 of 7**	**1 of 7**

Note: Intact tissue based membrane products (like PERI-GUARD®, SURGIMEND®, XENMATRIX™) naturally contain at least 15% of high immunogenic compound namely Elastin, besides other allergenic biological molecules like glycosaminoglycans and certain types of collagen other than Type-I collagen.

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