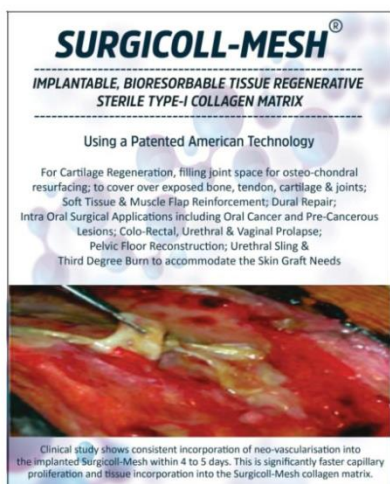




INFORMATIONAL MATERIAL PACKAGE ON

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:



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



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:

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

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 days⁵.
- **Innovative Technology:** Better than intact tissue-based membranes which contain > 49% 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



SURGICOLL-MESH® FOR INTRA ORAL SURGICAL DEFECTS

SURGICOLL-MESH®

USAGE IN ORAL SURGICAL MUCOSAL DEFECTS



**Surgical Defect of
Verrucous carcinoma**



**Application of
Surgicoll-Mesh**



**Post-op 2 months with good
healing of the surgical site**

*Surgicoll-Mesh significantly improved epithelialization
and granulation along with immediate relief of pain.*

Ref: Evaluation of Bovine-Derived Collagen Membrane in Oral Surgical Mucosal Defects. Journal of maxillofacial and oral surgery, 18(3), 466-473 (2018).

For full research article, visit

[https://www.advanced-biotech.com/img/Evaluation_of_Bovine_Derived_Collagen_of_ENCOLL_technology_\(2018\).pdf](https://www.advanced-biotech.com/img/Evaluation_of_Bovine_Derived_Collagen_of_ENCOLL_technology_(2018).pdf)

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 relieving the pain resulting in better functional outcome⁶.



SURGICOLL-MESH® FOR BREAST RECONSTRUCTION

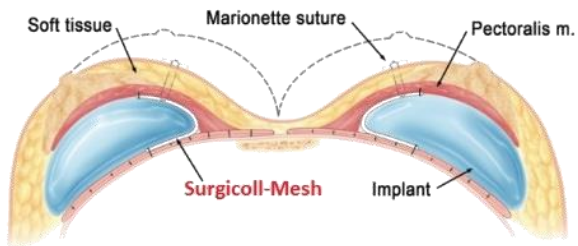
In breast reconstructive surgery, to facilitate the expansion of the submuscular pocket for direct-to-implant breast reconstruction and two-stage breast reconstruction, Surgicoll-Mesh can be used as a sling, interposed between the lateral pectoral edge and the thoracic wall. Following capsular elevation, Surgicoll-Mesh can be placed in-between tissues and frequently fixed with marionette sutures (ref 1).

It can also be used for:

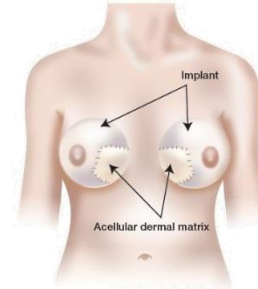
- ✓ Symmastia correction
- ✓ Mask rippling and Camouflage surface irregularities
- ✓ Inframammary fold malposition or bottoming out correction
- ✓ TRAM flap procedure

Symmastia correction

Symmastia is an implant displacement problem that occurs when the skin and muscle between the breasts over the sternum (breastbone) detaches and the two pockets of tissue that hold the breast implants come together to form one pocket.

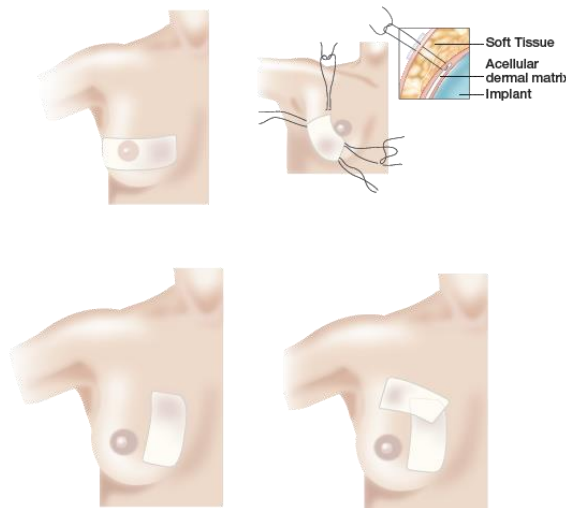


Placement of Surgicoll-Mesh to correct symmastia



Medial placement of Surgicoll-Mesh

Placement of a sling of Surgicoll-Mesh in the subpectoral position, between the lateral and inferior borders of the pectoralis major and the chest wall, to complete the inferior lateral part of the implant pocket, with either a tissue expander or a permanent breast implant (ref 2).

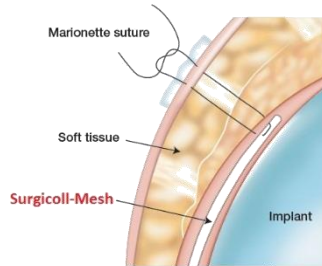


Different placement of the Surgicoll-Mesh: (a) centre, (b) lower lateral, (c) medial and (d) upper medial areas.



Breast Rippling

Rippling occurs when the breast implant shows visible folds or wrinkles underneath your skin. Using During the rippling revision procedure, Surgicoll-Mesh can be placed at the bottom of the breast to reinforce weak or inadequate tissue. This can help position the breasts in the desired location and reduce the presence of wrinkles and ripples on the skin surface (ref 3).

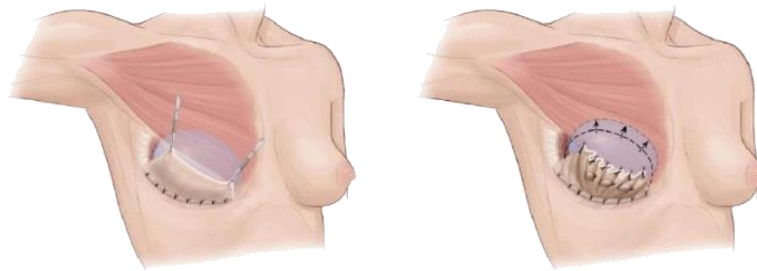


Placement of Surgicoll-Mesh to correct rippling

Correction of Inframammary Fold

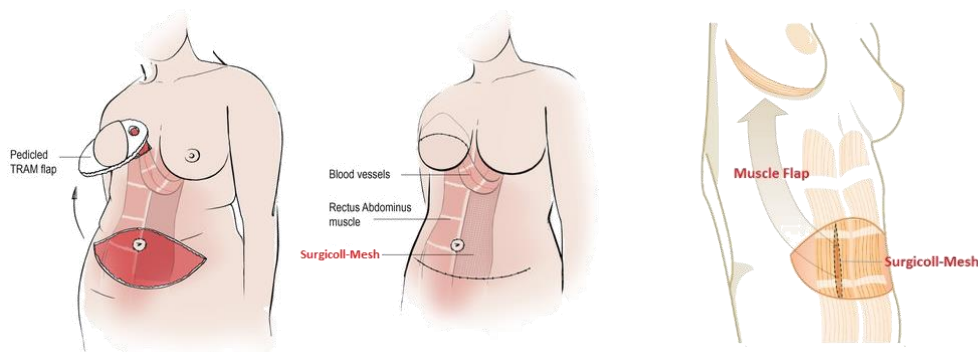
Surgicoll-Mesh sutured to the infra-mammary fold and draped over the implant with the superior edge approximating the inferolateral margin of the pectoralis major (Fig on left).

Suture plication of the Surgicoll-Mesh to help maintain a higher position of the implant on the chest wall (Fig on right). This includes plication of the Surgicoll-Mesh as needed, not only at the periphery but within the central areas (ref 4).



TRAM Flap Procedure

In TRAM Flap procedure for breast reconstruction, Surgicoll-Mesh can be used to achieve reinforcement of the entire abdominal wall (ref 5).



References:

1. Macadam, S. A. et. al (2012). Acellular dermal matrices: use in reconstructive and aesthetic breast surgery. Canad. J. of Plast. Surg., 20(2), 75-89.
2. www.ncbi.nlm.nih.gov/pmc/articles/PMC6378261/
3. www.ncbi.nlm.nih.gov/pmc/articles/PMC4290364/
4. <https://jmedicalcasereports.biomedcentral.com/articles/10.1186/1752-1947-7-275>
5. https://journals.lww.com/prsgo/Fulltext/2016/09000/Abdominal_Closure_after_TRAM_Flap_Breast.27.aspx



SURGICOLL-MESH® & HEMOCOLL® FOR USE IN CANCER

Treatment options for cancer

1. Existing anti-neoplastic and anti-angiogenics to treat cancer:

The following drugs (ref 1) are clinically approved for use either through local drug delivery or in combination for treating cancer: 5-fluorouracil (localized drug delivery in combination with estradiol (ref 2)), Cyclophosphamide, Epirubicin, Gemcitabine, Methotrexate, Vinorelbine, and Anti-Vascular Endothelial Growth Factor (VEGF).

2. Radiation therapy

3. Surgical therapy

Management of post-surgical complication of cancer

Surgicoll-Mesh can be used for the treatment following the removal of tumor in cases of intestinal, colo-rectal, breast cancer, skin cancer (see image), oral mucosal cancer (refer to pg 4), vaginal cancer, vulvar cancer, etc. The internal wound after the excision of cancerous growth, normally lead into non-healing ulceration. Accordingly, post-surgical handling of the wound is extremely critical.

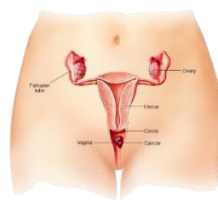
It is important to note that mortality associated with non-healing internal wounds and ulceration following the tumor removal is quite high. This includes post-operative infection, profuse bleeding, adverse cell-matrix interactions etc. Treating the post excision complications of cancer needs an effective, clinically viable selection of a bio-resorbable matrix. The use of an Implantable, Bioresorbable Tissue Regenerative, bioactive, non-immunogenic, and biocompatible product made of Sterile Type -I Collagen Matrix, **Surgicoll-Mesh**, seems to be clinically viable to successfully manage the healing of ulcerating/fungating wounds. In addition, **Hemocoll**, an effective high purity, surgical grade, bio-active Type-I collagen fibers intended for semi - occlusive and wound-adhering healing maybe used in conjunction in with **Surgicoll-Mesh**.



Good clinical outcome following Malignant melanoma wide excision treatment with Surgicoll-Mesh graft.

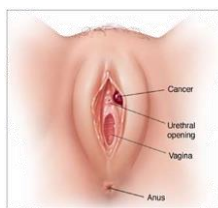
Vaginal Cancer:

In cases of vaginal cancer, Surgicoll-Mesh can be used to reconstruct the vagina following vaginectomy (surgery to remove all or part of the vagina) (ref 3).



Vulvar Cancer:

Surgicoll-Mesh can also be used to cover the area after skinning of the top layer of vulvar skin (skinning vulvectomy) in vaginal intraepithelial neoplasia (ref 4).



Why use Surgicoll-Mesh:

1. Effective healing of tumorectomy defects
2. Possibility of local delivery of anti-neoplastic and/or antibiotics drugs
3. Also act as an Hemostatic agent

Why Use Hemocoll:

1. Hemostatic agent, effectively controls bleeding
2. Accommodable for deep tunneling wounds
3. Shown effective in cardio-vascular applications
4. Decrease hospital length of stay

References:

1. www.cancer.gov/about-cancer/treatment/drugs/breast
2. www.ncbi.nlm.nih.gov/pmc/articles/PMC5576701/
3. www.cancer.gov/types/vaginal/patient/vaginal-treatment-pdq
4. www.cancer.gov/types/vulvar/patient/vulvar-treatment-pdq

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® 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



Post – op Day 12

Day-21



After 10
months



SURGICOLL-MESH® & HEMOCOLL® FOR USE IN DIABETIC FOOT ULCERS (DFU)

Introduction:

Diabetes is a growing challenge in India with estimated 8.7% diabetic population in the age group of 20 and 70 years¹. The overall perception of the delayed diabetic wound healing is neuropathy resulting in poor arterial blood supply and venous circulation.

However, high levels of blood glucose not only affect the nerves but also impedes the natural maturation of the healing/granulation tissue. This is a biochemical phenomenon called glycosylation of structural proteins.

We need to consider all the causes of Diabetic Ulcers at this point as shown below:

Understanding of the causes for Diabetic Foot Ulcers

Commonly recognized concepts of DFU

1. Nerve Damage

Damage to the nerve by increased level of glucose in blood may result in loss of sensation and the inability to feel any pain or pressure.

2. Poor Circulation

High blood glucose levels thicken the arteries and narrow its blood vessels, restricting the delivery of the blood and oxygen needed to support the body's natural healing abilities.

3. Infection

Suppressed immune system may facilitate pathogen proliferation eventually leading to an infection like non-healing diabetic ulcer.

4. Immune Suppression

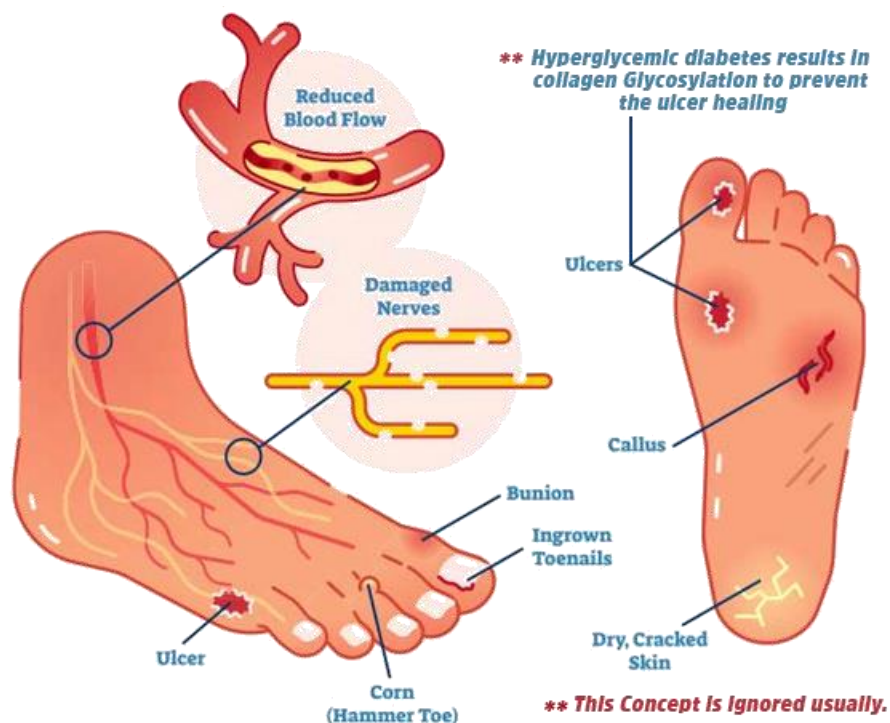
Diabetes may suppress the immune system that could impair the body's ability to fight-off an infection.

Unrecognized concept of DFU

5. Glycosylation of wound bed collagen

In hyperglycemic patients, Glycosylation of the newly formed wound bed collagen hinders the normal enzymatic (lysyl oxidase) maturation leading to non-healing. The hyperglycemic glucose may be absorbed by Surgicoll-Mesh for faster healing of the ulcer wound.





Diagrammatic representation of Hyperglycemic Diabetology

Treatment options for DFU:

Normal materials that are used to cover an ulcer:

1. Non-biological synthetic polymeric sheets and sponges
2. Cotton gauze
3. Vaseline

All such materials are able to protect wound as a wound cover and may absorb the secreted fluid (exudate). Upon usage of such non-biological scaffold materials, cells may not feel comfortable when they come in contact. Accordingly, this would un-necessarily delay the wound healing process because the exudation will continue until the cells are comfortable with the surrounding environment.

On the other hand, **Surgicoll-Mesh** biological dressing may provide a better result. However, all biological materials are not the same. Using an advanced biological skin substitute like **Surgicoll-Mesh** will not disturb the cells on the surface of the wound involved in the tissue granulation process.

All biological skin substitutes may NOT be ideal biocompatible matrices:

Two main categories of Biological matrices:

1. **Reconstituted Collagen membranes:** This includes products made from collagen extracted from animal tissues. Only a few such products are highly biocompatible and bioactive. **Surgicoll Mesh** happens to be one such unique product.
2. **Intact tissue membrane derived products:** These products are made from intact tissue membranes of amnion, pericardium, intestinal wall, urinary bladder etc. These membranes are contaminated with approximately 10 to 49% elastin, type-III collagen, lipids and other proteoglycans which are all highly immunogenic. They have to be cross-linked to minimize their immunogenicity and on the other hand loses the bioactivity and wound healing abilities if the material is not chemically modified or cross-linked, it can effectively be used in tissue regeneration and in the granulation process.



Etiology of Diabetic Ulcers:

- High levels of blood glucose leads to slow healing of DFU
- High levels of blood glucose makes collagen Glycosylated
- Glycosylation is the covalent addition of the excess blood glucose to collagen

Impact of Glycosylation:

- Glycosylation prevents the normal collagen maturation of healing wounds
- Glycosylation inhibits lysyl oxidase that matures collagen to heal the wound (Fig. 1 below)
- This is the reason why the diabetic patient's foot ulcer doesn't heal easily.
- How an innovative, patented, **SURGICOLL-MESH** collagen helps

Surgicoll-Mesh's NANOTECHNOLOGY could help heal DFU faster!

- **Surgicoll-Mesh**, as an uncross-linked biocompatible collagen, when tightly applied over the wound, it would osmotically absorb glucose.
- Such glucose pulling of **Surgicoll-Mesh** collagen would reduce the glycosylation of the collagen produced in the wound-bed.
- When the collagen in the wound is relieved from glycosylation, it matures and the Diabetic wound heal faster.
- This provides a scientific explanation for the successful use of **SURGICOLL-MESH** to treat the non-healing **DIABETIC FOOT ULCERS**.

Treatment of Diabetic Foot Ulcer



**One-month
post traumatic ulcer
with gangrene of 4th toe**



**Application of
Surgicoll-Mesh**



**31 Days Post
Application**

Indications of Hemocoll:

Hemocoll is intended for the surgical procedures as an adjunct to hemostasis when control of bleeding by ligature or conventional procedures is ineffective or impractical includes:

- Cardiovascular surgery
- Neurosurgery
- Uro-surgery
- General surgery
- Trauma surgery
- Intracranial bleeding, and
- Control post-surgical.

Why Use Hemocoll:

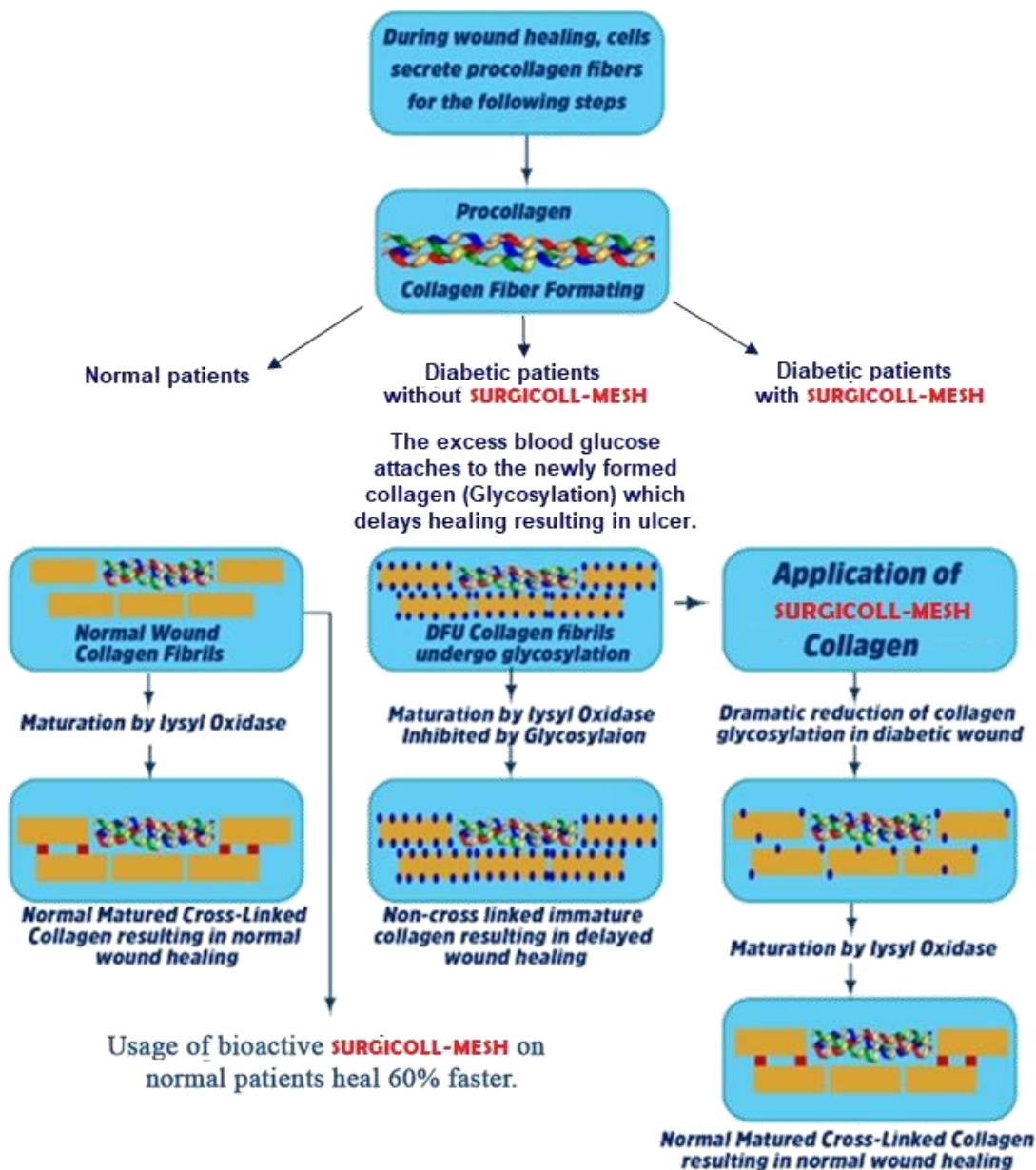
1. Hemostatic agent, effectively controls bleeding
2. Accommodable for deep tunneling wounds
3. Decrease hospital length of stay



SURGICOLL-MESH®

WHY IT WORKS BEST FOR DIABETIC FOOT ULCERS?

How Surgicoll-Mesh Nano-technology could heal a Diabetic Ulcer faster than other collagen products.



References:

<https://www.who.int/india/events/world-diabetes-day>



SURGICOLL-MESH®

TREATMENT OF SEVERE BURN/BED ULCER



Electric Burn victim with bed sore 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

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®

POST-TRAUMATIC ULCER



Post traumatic ulcer
before treatment



Placement of Surgicoll-Mesh



Completely healed ulcer – Day 7



Complete Recovery in 7 days

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



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

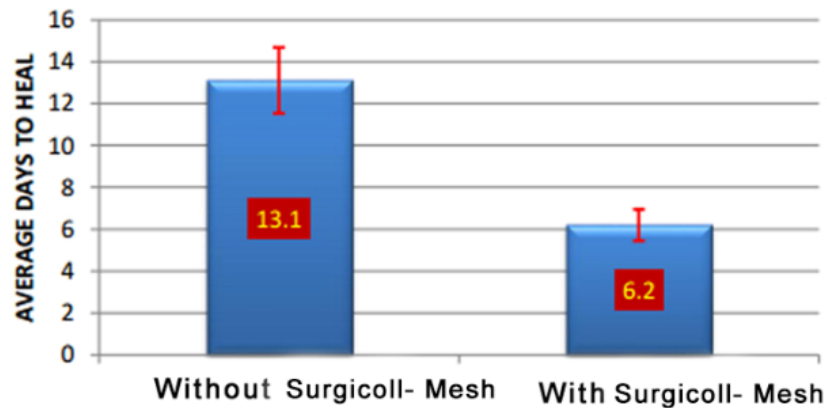
Good Graft take, Firm adherence & early recovery

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



SURGICOLL-MESH® equi

ACCELERATES BURN HEALING
Days to Observation of Significant Healing



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 setting⁶ 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.



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 injecting **Surgicoll-Mesh** or can be removed altogether and replaced with **Surgicoll-Mesh**.

<http://www.shc.org/Medical+Services/Minimally+Invasive+Surgery/Orthopedic+Joint+Replacement/>
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>



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

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

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)



SURGICOLL-MESH® FOR PELVIC FLOOR RECONSTRUCTION SURGERIES

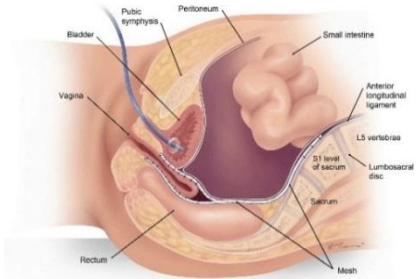
Types of Pelvic Organ Prolapses (ref 1):

- ✓ **Vaginal prolapse:** This is a prolapse of the vagina.
- ✓ **Urethrocele:** This is a prolapse of the urethra (the tube that carries urine).
- ✓ **Cystocele:** This is a prolapse of the bladder into the vagina, the most common condition.
- ✓ **Uterine prolapse:** uterus descends toward or into the vagina
- ✓ **Enterocoele:** This is a small bowel prolapse.
- ✓ **Rectocele:** This is a rectum prolapse.

✓ **Vaginal Prolapse:**

Weak muscles and ligaments supporting the pelvic organs may fall out of place and bulge down in the vagina. To treat POP, **Surgicoll-Mesh®** can be implanted to reinforce the weakened vaginal wall. Surgery can be done through the abdomen using mesh (ref 2).

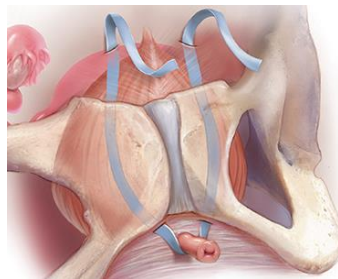
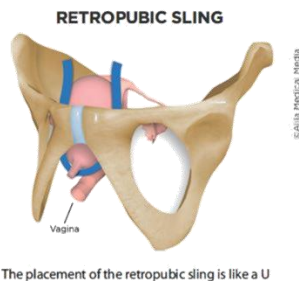
The length of the mesh should represent the length of the vagina, and the breadth should represent the wideness. The vagina is approximately 3 cm wide distally and up to 10 cm proximally between the ischial spines (ref 4).



✓ **Urethrocele (Urethra Prolapse):**

A urethrocele occurs when the tissues surrounding the urethra sag downward into the vagina (ref 5). **Surgicoll-Mesh®** urethral slings can be implanted through the vagina to support the bladder neck or the tube that carries urine from the body (urethra). This is known as a **midurethral sling or a mesh sling procedure**.

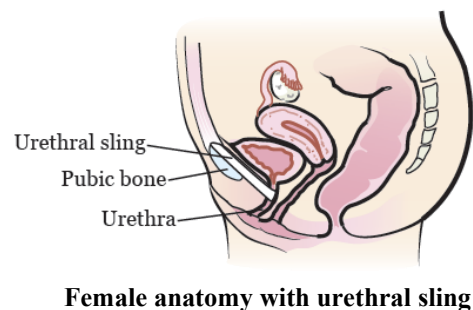
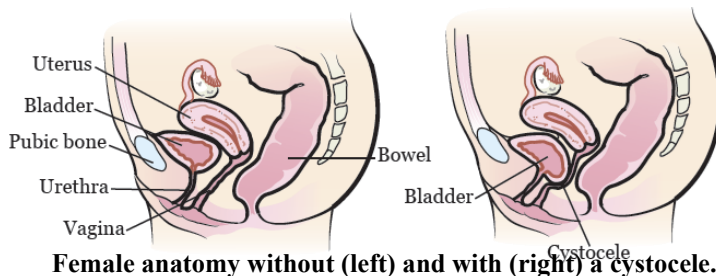
Incorporation of mesh in Sacrocolpopexy (ref 3)



Urethral Sling Procedure

✓ **Cystocele (Bladder Prolapse):**

A cystocele occurs when the wall of the bladder presses against and moves the wall of the vagina (ref 5). **Surgicoll-Mesh®** urethral sling holds your urethra in its correct position. The sling is looped around your urethra and the ends are attached to the pubic bone.



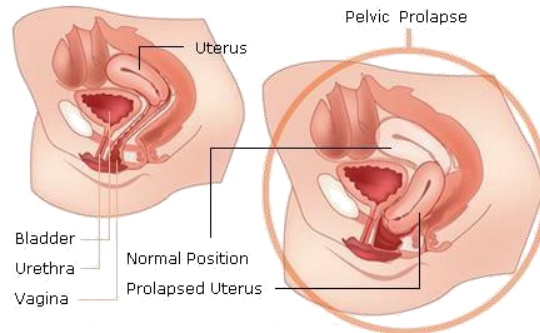
✓ **Uterine Prolapse:**

A uterine prolapse is when the uterus descends toward or into the vagina. It happens when the pelvic floor muscles and ligaments become weak and are no longer able to support the uterus (ref 6).

Uterus is supported in its natural position by attaching a piece of **Surgicoll-Mesh®** to connect the uterus to the vertebral spinal bone (ref 7).

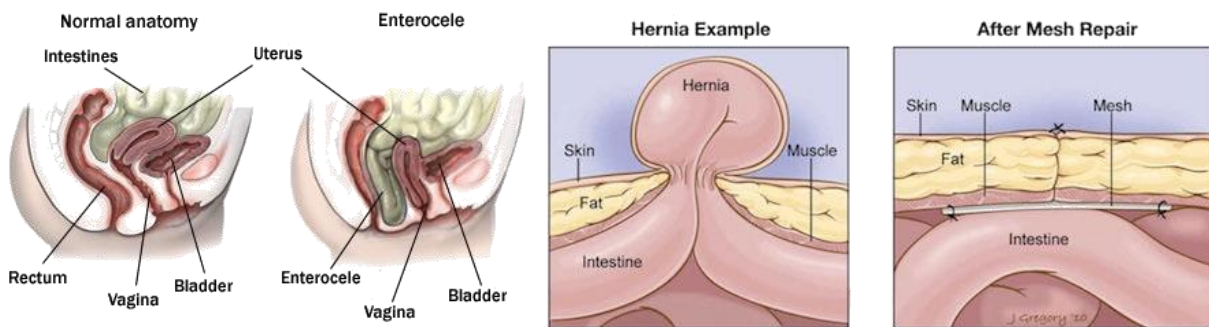
This can be done in two different ways:

- keyhole (laparoscopic) surgery – the operation is carried out through small incisions (cuts) in the lower abdomen
- open surgery – a larger incision is made in the lower abdomen.



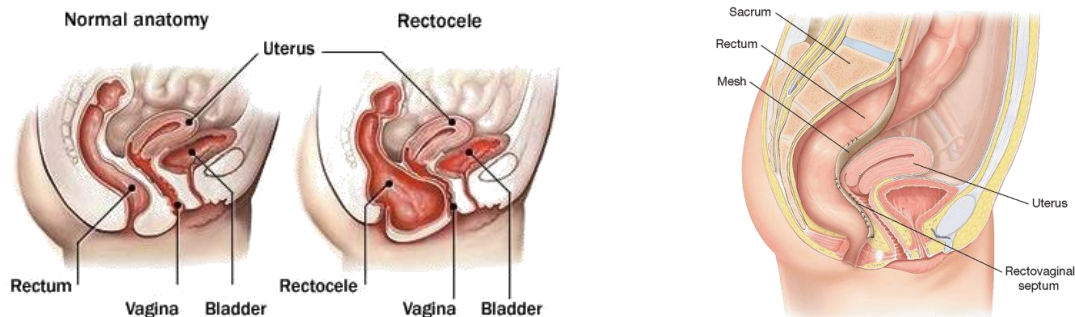
✓ **Enterocoe (Small bowel prolapse):**

An enterocoe (small bowel prolapse) occurs when the small bowel presses against and moves the upper wall of the vagina (ref 8). **Surgicoll-Mesh®** stabilizes and strengthens the area, supports organs and muscles, and acts as a scaffold for new tissue growth.



✓ **Rectocoe (Rectum prolapse):**

A rectocoe is a bulging of the front wall of the rectum into the back wall of the vagina (ref 9). The posterior mesh rectopexy involves insertion of **Surgicoll-Mesh®** behind a completely mobilized rectum and its fixation to the sacrum as well as to the sides of the rectum (ref 10).



Mesh Rectopexy



Complications of other meshes (ref 11):

Local irritation at wound site	Migration of the device
Infection	Pain
Urinary tract obstruction and urine retention	Recurrence of incontinence
Vaginal extrusion	Nerve damage
Erosion through the urethra	Swelling and redness at the wound site
Scarring	Vaginal discharge
Scar contracture	Fatigue
Inflammation	Shortness of breath
Fistula formation	Bleeding

Surgicoll-Mesh® Available Sizes (in cms):

5x5	2x25	5x10	10x10	10x15	10x20	15x15
10x25	15x20	20x20	15x30	20x25	20x30	

References:

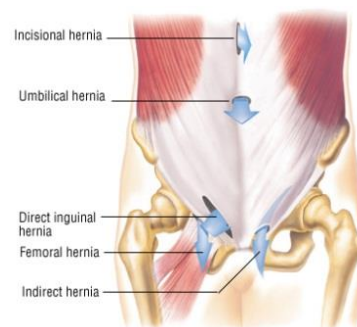
1. <https://www.webmd.com/urinary-incontinence-oab/qa/what-are-the-types-of-pelvic-organ-prolapse>
2. <https://www.mayoclinic.org/diseases-conditions/pelvic-organ-prolapse/in-depth/transvaginal-mesh-complications/art-20110300#:~:text=Surgical%20mesh%20can%20be%20used,reinforce%20the%20weakened%20vaginal%20wall.>
3. <https://link.springer.com/article/10.1007/s00192-020-04236-1>
4. https://cdn.ymaws.com/www.abdominalradiology.org/resource/resmgr/education_dfp/pelvicfloor/complications/posterior_vaginal_mesh_manag.pdf
5. <https://www.uofmhealth.org/health-library/tv1498>
6. <https://www.medicalnewstoday.com/articles/305971#:~:text=A%20uterine%20prolapse%20is%20when,able%20to%20support%20the%20uterus.>
7. <https://www.nice.org.uk/guidance/ng123/resources/surgery-for-uterine-prolapse-patient-decision-aid-pdf-6725286112>
8. [https://www.uofmhealth.org/health-library/tv1532#:~:text=Surgery%20Overview&text=An%20enterocele%20\(small%20bowel%20prolapse,muscles%20are%20weakened%20by%20aging.](https://www.uofmhealth.org/health-library/tv1532#:~:text=Surgery%20Overview&text=An%20enterocele%20(small%20bowel%20prolapse,muscles%20are%20weakened%20by%20aging.)
9. <https://fascrs.org/patients/diseases-and-conditions/a-z/rectocele>
10. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902550/>
11. <https://www.drugwatch.com/transvaginal-mesh/bladder-sling>



SURGICOLL-MESH® FOR HERNIA REPAIR

Types of Hernias

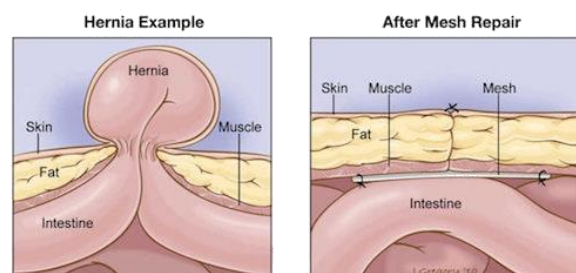
- ✓ **Inguinal:** occurs in the inner groin
- ✓ **Femoral:** occurs in the upper thigh/outer groin
- ✓ **Incisional:** occurs through an incision or scar in the abdomen
- ✓ **Ventral:** occurs in the general abdominal/ventral wall
- ✓ **Umbilical:** occurs at the belly button
- ✓ **Hiatal:** occurs inside the abdomen, along the upper stomach/diaphragm



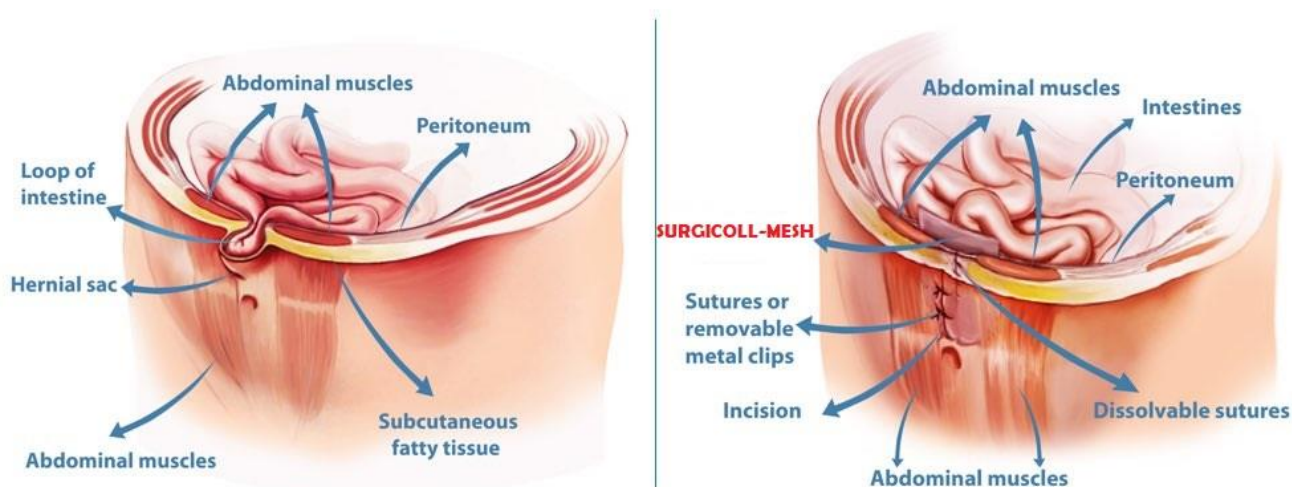
Abdominal Hernia:

Open Surgery:

An open incision is made in the abdomen at the hernia site and the protruded intestine or abdominal tissue is pushed back in place. Depending on the hernia's size, a component separation procedure (cutting through some of the abdominal wall muscles along the side of the body) may be performed. **Surgicoll-mesh** material is placed to reinforce the damaged site and reduce hernia recurrences. The skin is typically closed with dissolvable stitches and glue (ref 1).



Absorbable **Surgicoll-Mesh** would meet the clinical need to provide the physical support. As this product gradually degrades over time, it will trigger the new tissue growth that is intended to provide strength to the damaged site.



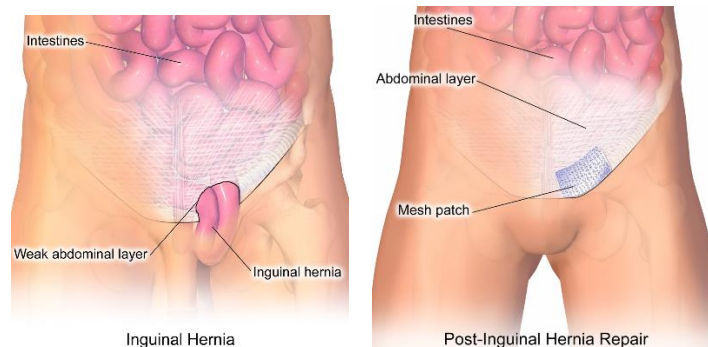
Laparoscopic Surgery (ref 2):

Several small incisions are made at locations away from the hernia site. A laparoscope (a thin lighted tube with a camera on the tip) is inserted through one of the openings to help guide the surgery. **Surgicoll-Mesh** material may be inserted to strengthen the weakened area in the abdominal wall.

Inguinal Hernia Repair:

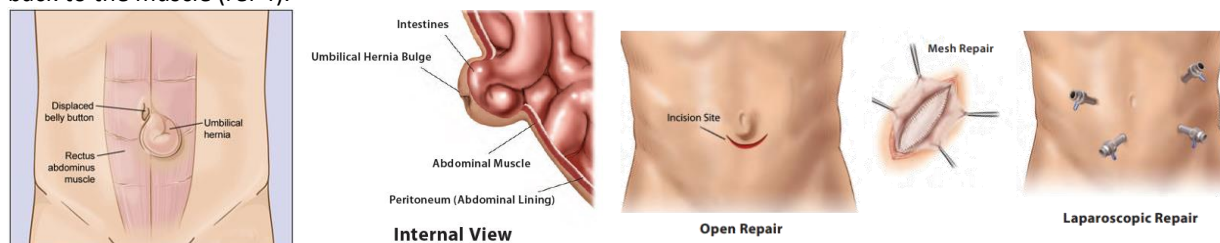
The procedure involves making an approximate 10-cm incision in the groin. Once exposed, the hernia sac is pushed to the abdominal cavity or excised. The abdominal wall is then reinforced (ref 3) with **Surgicoll-mesh**.





Umbilical Hernia:

Hernia sac is removed and **Surgicoll-Mesh** is placed on the site. It is attached using sutures to the stronger tissue surrounding the hernia. **Surgicoll-Mesh** extends 3 to 4 cm beyond the edges of the hernia and the umbilicus is fixed back to the muscle (ref 4).



Compared to this product, SurgiMend (ref 5), our product Surgicoll-Mesh is clinically more advantageous due to following reasons:

1. Physical Structure:

Surgicoll-Mesh fibrils are organized in parallel like in-vivo with native configuration with 20μ porosity through sedimentation process. On the other hand, SurgiMend has random, non-native fibrillar structure due to lyophilization.

2. Collagen Type:

SurgiMend has significant amount of type-III collagen which may not be highly biocompatible compared to pure Type-I collagen of Surgicoll-Mesh which is non-immunogenic and highly biocompatible for tissue infiltration.

3. Enhanced Bioactivity:

Surgicoll-Mesh is the only collagen product with advanced bioactivity as a result of collagen phosphorylation that induces cell signal transduction. This phenomenon makes the collagen implant encourage new tissue formation within 4 to 5 days.

Complications of other meshes (ref 6):

Bowel obstruction	Migration of the device
Infection	Pain
Scarring	Bleeding
Bowel perforation	Recurrence
Inflammation	Swelling and redness at the hernia site
Fistula formation	Rejection

References:

1. www.clevelandclinic.org/healthinfo/pdfv2/pdfs/16458.pdf
2. <https://c8g3e5x4.rocketcdn.me/wp-content/uploads/posters/2010/28634.jpg>
3. https://en.wikipedia.org/wiki/Inguinal_hernia_surgery#Open_hernia_repair
4. www.integralife.com/file/general/1453800269.pdf

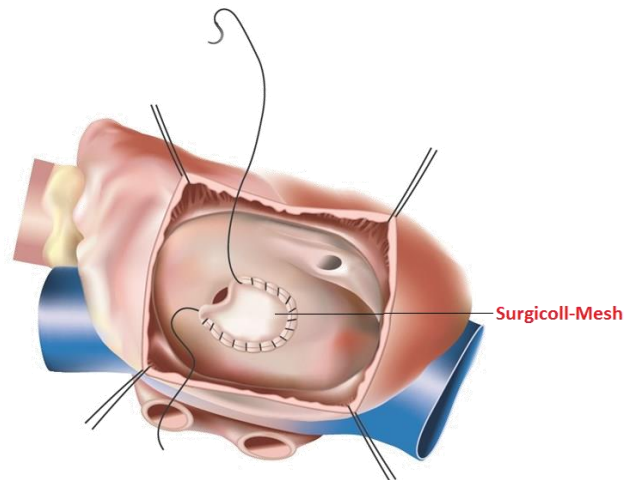


5. <https://www.facs.org/~media/files/education/patient%20ed/adultumbilical.ashx#:~:text=The%20repair%20can%20be%20done,adding%20a%20piece%20of%20mesh.&text=The%20surgeon%20makes%20an%20incision,used%20to%20close%20the%20muscle.&text=For%20an%20open%20mesh%20repair%3A%20The%20hernia%20sac%20is%20removed.>
6. <https://www.drugwatch.com/hernia-mesh/complications/>

CARDIOVASCULAR & NEUROSURGICAL APPLICATIONS OF SURGICOLL-MESH®

Cardiac Application:

Surgicoll-mesh applications may also be extended for use in Atrial, ventricular and arterial patch repair, suture line buttress, intra-cardiac patch, thoracic wall etc.

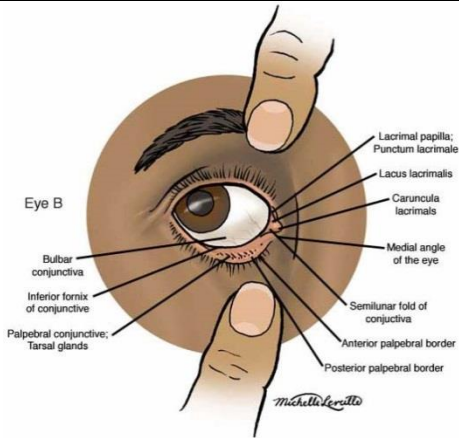
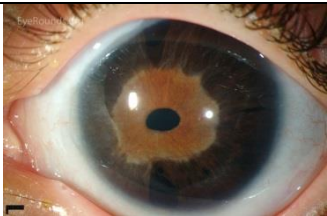


Neurological Application:

Surgicoll-mesh can also be used as a substitute for dura repair and nerve wrap.



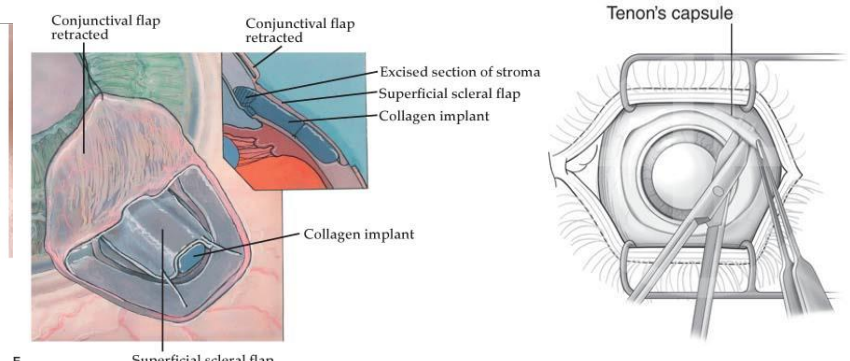
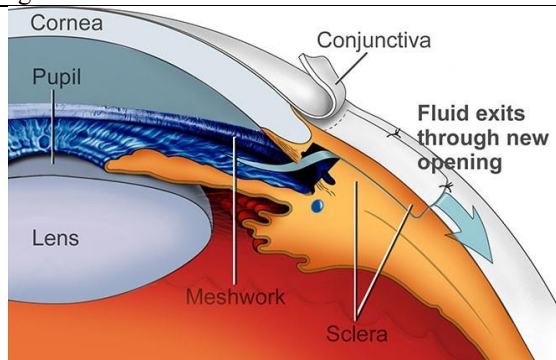
OPHTHALMIC APPLICATION OF SURGICOLL-MESH®

APPLICATION	PROCEDURE	REFERENCE
Trabeculectomy Primary Open-Angle Glaucoma	General Trabeculectomy 1. Fornix-based conjunctival flap was raised 2. Sclera was exposed, and a rectangular ($5 \times 5 \text{ mm}^2$ and $300 \mu\text{m}$ deep scleral flap was dissected at 12-o'clock position 3. $2 \times 3 \text{ mm}$ sclerostomy was created followed by peripheral iridectomy 4. Sclera flap was closed using 10-0 nylon sutures 5. Surgicoll-Mesh was placed above fornix-based sclera flap and conjunctiva was sutured	http://www.aeonastron.com/data/publications/201603/14579480584hq5x.pdf
		
Management of glaucoma in an unusual case of Axenfeld–Rieger Syndrome	Underwent trabeculectomy with Surgicoll-Mesh® implant under local anaesthesia	http://www.aeonastron.com/data/publications/201408/1407385393jysi1.pdf
		
Tube exposure repair in Boston Keratoprosthesis type 1	1. Using Westcott scissors, a superotemporal oval subconjunctival pocket beginning with the existing open conjunctiva and extending approximately 2–3 mm beyond the edge of the exposed tube in every direction 2. Surgicoll-Mesh sheet ($10 \times 10 \text{ mm}$ sheet with approximately 1.5 mm thick) was cut ($6 \times 8 \text{ mm}$) and placed in the subconjunctival pocket to fully cover the area of tube exposure. No sutures needed. 3. After careful measurement of the conjunctival opening, a conjunctival autograft of $5 \times 3 \text{ mm}$ is dissected from the super-nasal quadrant was then placed on the Surgicoll-Mesh matrix. 4. Using 10-0 nylon sutures, the autograft along with underlying Surgicoll-Mesh implant were secured to the sclera 5. The bed of the conjunctival autograft was primarily closed using 10-0 Vicryl sutures 6. Finally an amniotic membrane was carefully cut to cover an area twice as large as the area of tube exposure 7. The amniotic membrane was then placed on the conjunctival autograft and secured using 10-0 Vicryl sutures	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6104558/

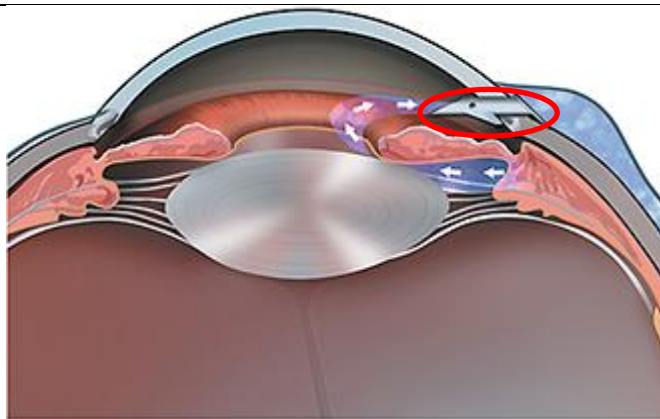


Cornea Iris Tube Plate Fluid exits the eye onto plate A glaucoma drainage implant creates a new way for aqueous fluid to drain from the eye.		
Glaucoma Drainage Device (GDD) Revision surgery	1. Treatment involves excision of the capsule (removal of the fibrous capsule overlying the plate), topical mitomycin C application, and implantation of Surgicoll-Mesh matrix (10 x 10 x sheet with approximately 1.5 mm thick)	http://www.aeonastron.com/data/publications/201112/1324287577dnk03.pdf
Recurrent symblepharon w/ pterygium	1. Excision of symblepharon with temporal pterygium right eye 2. Conjunctiva over symblepharon was conserved as much as possible 3. Conjunctiva was sutured superiorly and inferiorly to episclera about 6mm from limbus leaving a pocket for implantation of Surgicoll-Mesh 4. Collagen matrix of 6 mm diameter was placed in the pocket 5. Square shaped autologous limbal stemcell graft was harvested with 6mm conjunctiva from superior limbus and placed at temporal limbus 6. The conjunctiva was sutured with 10 '0 vicryl	http://www.aeonastron.com/data/publications/201301/13594528491anfc.pdf
Deep sclerectomy in treatment of open angle glaucoma	Limbal-based deep sclerectomy with Surgicoll-Mesh implantation in the scleral bed 1. The conjunctiva and Tenon's capsule is opened at the limbus to expose sclera. 2. A limbus based superficial 5 × 5 mm scleral flap of one-third thickness is fashioned and extended 1.5 mm into clear cornea. 3. A 2nd deep scleral flap is dissected leaving only a 50-100 µm thick scleral bed. This flap should be 4 × 4 mm leaving a step for closure of the superficial flap. 4. The trabeculo-Descemet's membrane (TDM) is fashioned by extending the dissection up to 1-1.5 mm into clear cornea. 5. Once this dissection is completed the deep flap is excised using a blade or fine scissors. At this stage aqueous should be percolating through the trabeculum.	http://www.aeonastron.com/data/publications/201112/1324288187msb4u.pdf, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2813598/



	6. Once dried, the inner wall of Schlemm's canal and the juxta canalicular trabecular meshwork can be grabbed by fine forceps and peeled off the underlying trabeculum. 7. Surgicoll-Mesh is sutured in the scleral bed to act as a space maintainer during the initial healing period, keeping the intrascleral space open 8. The superficial scleral flap is then closed with 10/0 nylon sutures. 9. Finally the conjunctiva is closed with 10/0 vicryl sutures.	
		
End Stage Glaucoma	1. limbal - or a fornix-based conjunctival flap are accepted 2. A loose stitch sclera flap is done in order to encourage aqueous flow for the filtering surgery 3. Surgicoll-Mesh collagen matrix disc is implanted over the scleral flap. 4. No suture is required to secure the implant, and as soon as it touches the sclera, it absorbs aqueous and molds to cover the scleral tissue 5. Collagen matrix therefore need not be presoaked or prepared in any way 6. After the collagen matrix's placement, the surgeon closes the conjunctiva to ensure that the wound is watertight	http://www.aeonastron.com/data/publications/201212/13559941827ec76.pdf
		
Glaucoma tube shunt surgery	1. The glaucoma drainage implant of choice was placed 2. Once the tube was secured to the sclera, Surgicoll-Mesh (10×10× sheet with approximately 1.5 mm thick) was used to cover the tube. 3. Presoaking the collagen is not necessary and is, in fact discouraged because once wet, the collagen becomes difficult to cut and can tear easily. 4. While dry, the collagen sheet was cut to size to cover the tube. 5. Great care is taken to ensure that the collagen is fully covered and the conjunctiva covering it is not under tension. 6. Once the conjunctiva was closed, a small amount of saline was placed in the anterior chamber and a fluorescein strip was used to verify the absence of leakage.	https://www.ncbi.nlm.nih.gov/pubmed/28184280

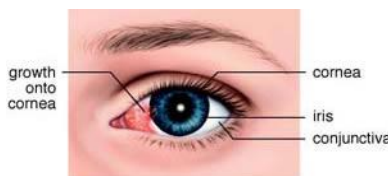




Scleral necrosis after pterygium excision

1. The size of the scleral defect was measured and its margin was marked with a 3-mm dia biopsy punch to determine the boundary of conjunctivectomy
2. The margin of scleral thinning area was trimmed by Vannas scissors
3. Surgicoll-Mesh was cut with a circular-shaped biopsy punch of the same size (3-mm dia) Surgicoll-Mesh was trimmed and fitted to cover the scleral defect
4. Surgicoll-Mesh was sutured with a recipient scleral wall using six stitches of 10-0 nylon interrupted sutures
5. A 4-mm dia, circular, free Conjunctival autograft was harvested from the superonasal bulbar conjunctiva with a punch biopsy 1 mm larger in dia than that of the piece of Surgicoll-Mesh
6. The autograft was carefully positioned over the previously sutured Surgicoll-Mesh bed
7. The autograft was anchored to the scleral wall and the healthy conjunctival margin through the Surgicoll-Mesh bed with 11 stitches of interrupted sutures of the 10-0 nylon

<https://www.ncbi.nlm.nih.gov/pubmed/26499993>

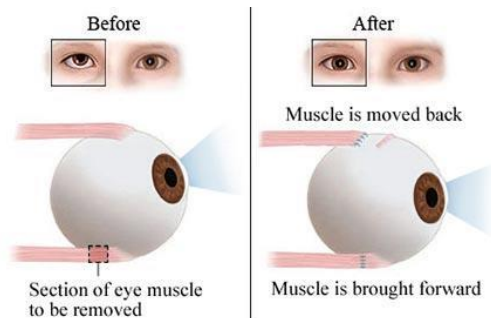
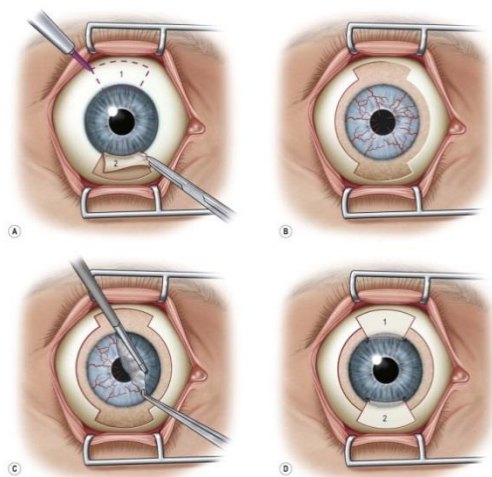


Strabismus Surgery

1. Forced duction test to exclude restrictive strabismus - that was negative
2. Wide fornix based periotomy of the conjunctiva to expose the area of original insertion
3. The sclera was very thin at this area with a bluish discoloration due to the proximity of uveal tissues
4. After proper isolation of lateral rectus (LR) and separation from inferior oblique muscle, LR was advanced 5mm to a point 11 mm from the limbus
5. Once LR was sutured to the sclera by vicryl 6/0 sutures, rupture of the thin scleral tissue occurred accidentally while manipulating the eye and uveal exposure of was encountered
6. As the complication occurred, a scleral graft was not available
7. A biodegradable collagen matrix (CM) implant (Surgicoll-Mesh™) measuring 10 x 10 x with approximately 1.5 mm thick was available.
8. It was used to cover the scleral defect and conjunctiva was closed over it using vicryl 8/0 stitches

<http://www.journalor.com/index.php/OR/article/view/22230>

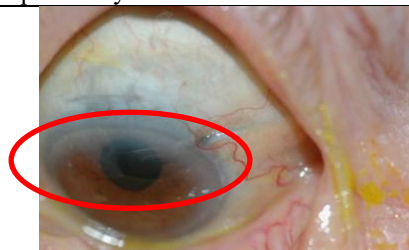




Ocular hypotony
after filtration
glaucoma surgery

1. Standard sub-Tenon anesthesia was induced using 2% lidocaine
2. The adhesion between the sclera and conjunctiva around the bleb was dissected through a small conjunctival peritomy made away from the bleb using a spring scissors or needling knife to release pressure inside the bleb and form a subconjunctival space for implantation
3. The Surgicoll-Mesh Collagen Matrix (10 × 10 x sheet with approximately 1.5 mm thick) was placed beneath the bleb using Gaskin forceps
4. When inserted, the Surgicoll-Mesh was folded to fit the size of the bleb and conjunctival entry
5. The conjunctiva was closed with a 10-0 polyglactin suture
6. At the end of surgery, 1.65 mg of dexamethasone sodium phosphate was injected subconjunctivally and 0.3% ofloxacin ointment was applied
7. Finally, 1.5% levofloxacin and 0.1% betamethasone were applied topically four times daily for 3–4 weeks postoperatively in all cases

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5639202/>



Gold standard trabeculectomy procedure with low dose anti-metabolites and ologen™ CM



Surgical technique unchanged until closure of scleral flap. Consider strategy to allow laser suture lysis. Consider lowering the dose of anti-metabolites.

Surgery by Dr. M.I. Canut



Place ologen™ CM directly posterior of scleral flap.

Surgery by Dr. M.I. Canut



Close and reform anterior chamber.

Surgery by Dr. M.I. Canut



Opportunities	DESCRIPTION
1	Placement of aqueous shunt, extraocular reservoir
2	Revision of aqueous shunt, extraocular reservoir
3	Scleral reinforcement; with graft
4	Excision or transportation of pterygium; with graft
5	Conjunctivoplasty with graft or rearrangement
6	Correction of lid retraction
7	Trabeculectomy, no previous sx
8	Trabeculectomy, with scarring, previous sx
9	Wound revision, anterior segment (bleb revision)
10	Treatment of Corneal Scars
11	Treatment of Corneal Ulcers



CLINICAL EVIDENCE FOR SURGICOLL-MESH®

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

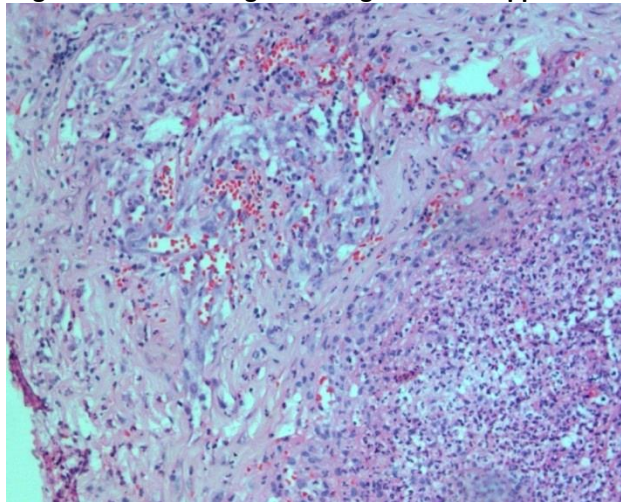
General Disclaimer:

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.⁷

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



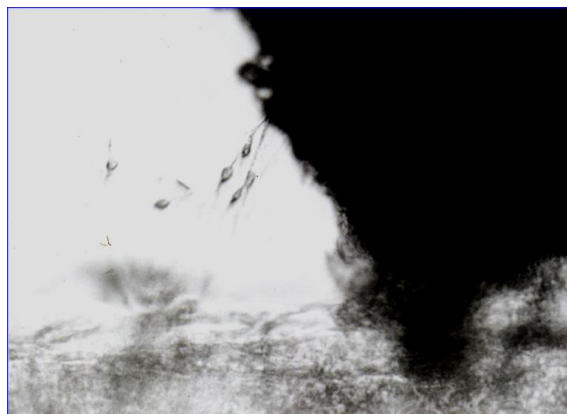
After **Surgicoll-Mesh** application the acute inflammatory cells, fibroblasts and blood vessels proliferate into the collagen matrix. (50x). Absence of Lymphocytes indicates the non-immunogenic property of the collagen in **Surgicoll-Mesh**.⁷

SURGICOLL-MESH PRESENTATION



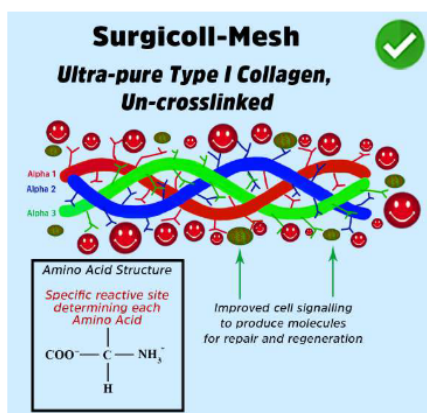
Figure 2: Bio Effects of Purified & modified EnColl COLLAGEN

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®

BIOCHEMICAL ADVANTAGES



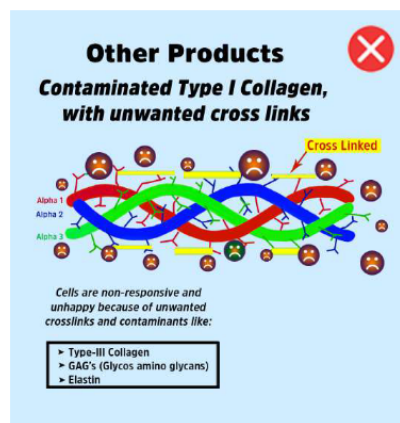
- Surgicoll-Mesh is a bioengineered bio-resorbable high purity Type-I collagen (> 97% pure and free of lipids, elastin and other immunogenic proteins) membrane.

- 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.

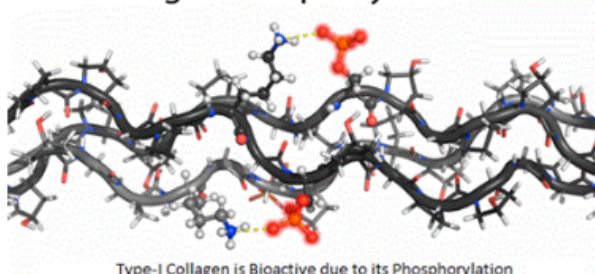
- This process restrains the bio-effectivity of the useful Type-I collagen and its biological regenerative use in the host tissue.



SURGICOLL-MESH®

COLLAGEN PHOSPHORYLATION AND BIOACTIVITY

Collagen Phosphorylation

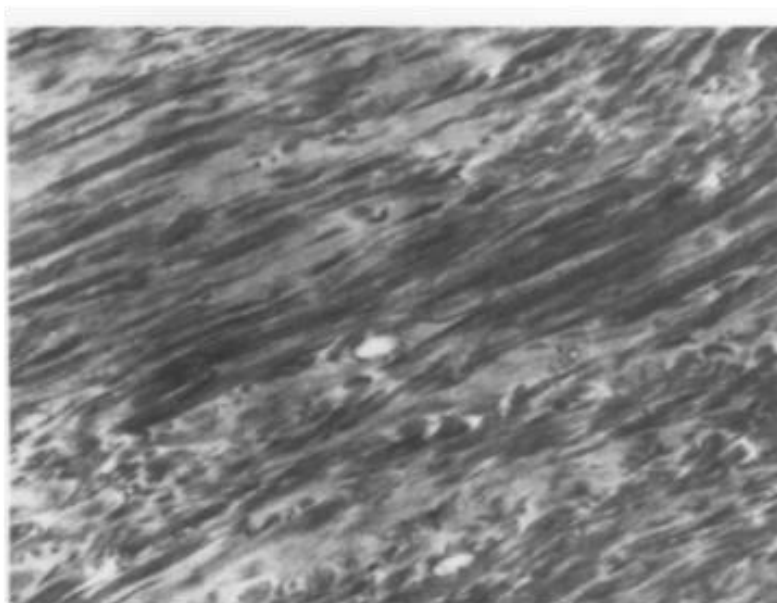


- The patented process yields high purity Type-I Collagen for maximum biocompatibility.
- Such collagen when phosphorylated results in cell signal transduction.
- Exceptional bioactivity of Surgicoll-Mesh collagen is derived due to its phosphorylation

SURGICOLL-MESH®

ELECTRON MICROSCOPY OF THE SHEET

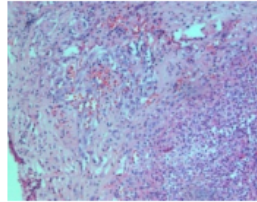
Shows meshwork of
collagen fibrils in the Product



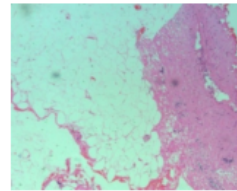
SURGICOLL-MESH®

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)

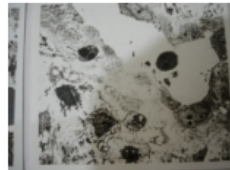


Control Histology: Before Surgicoll-Mesh application, only fibroadipose tissue is seen



Electron microscopy of tissue after Surgicoll-Mesh application

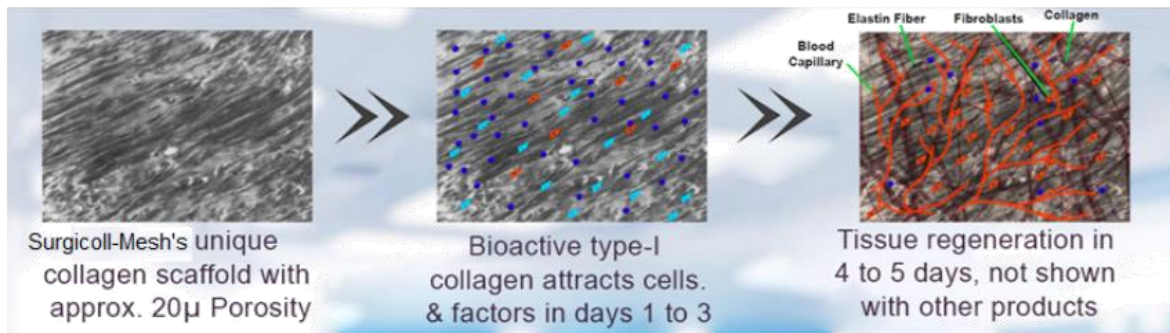
Scattered macrophages, monocytes, neutrophils fibroblasts & capillaries on day 4 and 5



SURGICOLL-MESH®

HOW IT DIFFERS FROM OTHER EXTRACTED COLLAGEN PRODUCTS?

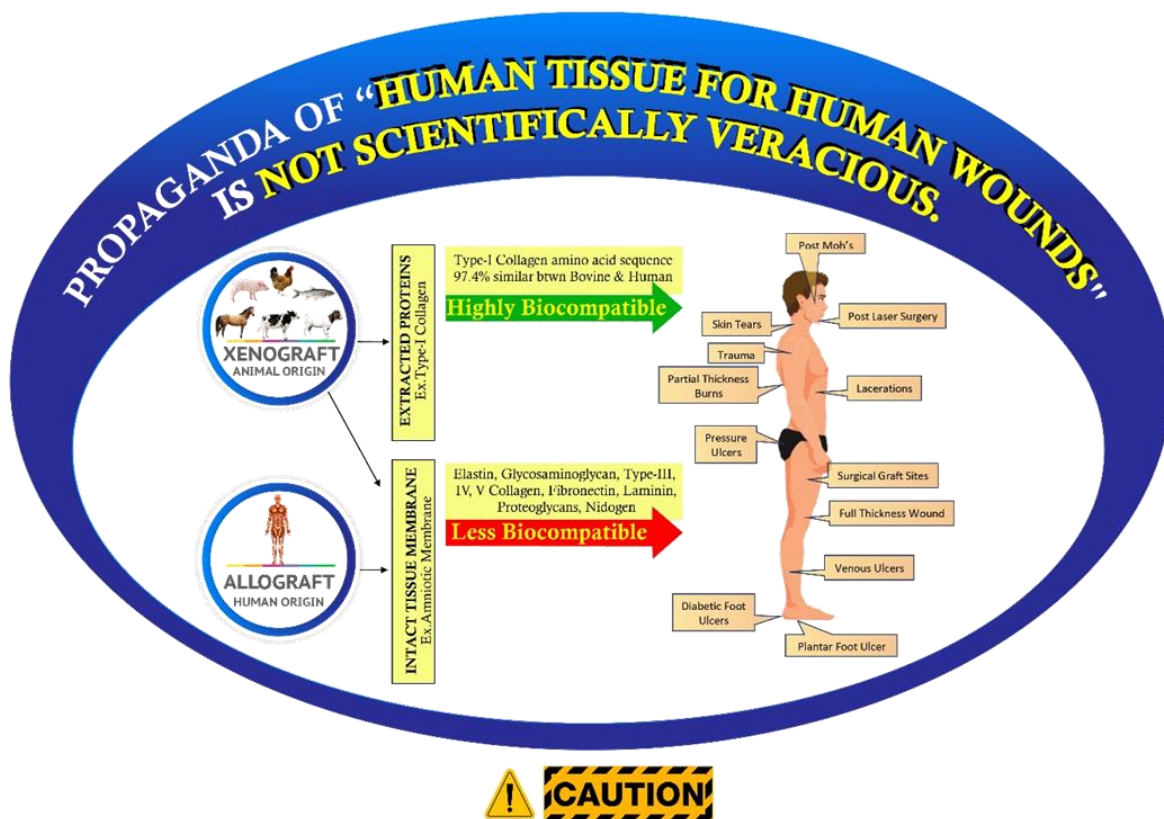
STRUCTURAL ADVANTAGE OF SURGICOLL-MESH COLLAGEN COMPARED TO OTHERS



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. Collagen when cross-linked, the natural bioactivity may be significantly minimized.

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





The risk seems to outweigh the benefits of using "Human tissue for human wound".
Intact human allograft tissue rich in **Elastin** is not appropriate for human wound treatments.
Elastin is not an ideal matrix compared to biocompatible native Type-I collagen.

1. Risk of Carcinogenicity:

All tissue derived intact membranes from amnion (Amnioxif, Epifix, Amnioexcel, Xwrap), placenta (Grafix), umbilical cord (Cellesta Cord), pericardium (Architect from Equine), urinary bladder (Cytal from Porcine), intestinal wall (Oasis from porcine SIS) and even skin (Kerecis from fish, EZ Derm from porcine, Apligraf from human) do possess at least 15% elastin (w/w). The peptides (Elastokines) derived during the process of disintegration by an enzyme (Elastase) may all be carcinogenic [1] and could cause various pathological conditions including emphysema, chronic obstructive pulmonary disease, atherosclerosis, metabolic syndrome, etc. [2]. There is no successful elastin based biomaterial available until now for tissue replacement/repair applications.

2. Less biocompatibility:

Most biomolecules in intact tissue derived membranes are incompatible compared to Type-I collagen matrix. For example, only some proteins are proven to be immunologically safe based on the amino acid sequence homology with the host tissue proteins. Too many isoforms [3] of Elastin could cause incompatibility.

3. Living cells from placental membrane may cause adverse response:

Incorporation of third person's tissue cells as a tissue regenerative scaffold are detrimental [4] for the treatment of wounds and it could cause Graft-versus-host disease [5]. The genome makeup of fibroblast differs between individuals and thus, fibroblast of one person will not express similar proteins in another person. Several company products failed while using fibroblast of a third person in their matrices to function as a universal tissue regenerative cell system.

Reference:

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3. <https://en.wikipedia.org/wiki/Elastin#:~:text=Elastin%20is%20a%20key%20protein,it%20is%20poked%20or%20pinched.>
4. <https://pubmed.ncbi.nlm.nih.gov/18971876/>
5. <https://www.lls.org/treatment/types-of-treatment/stem-cell-transplantation/graft-versus-host-disease>



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3. Gunasekaran S KM, Dhanraj P. Bioactive Collagen Dressing for the Treatment of Burns, Donor Sites, and Ulcers. *World Biomaterials Congress Meeting*. 2008.
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