醫療器材仿單標籤粘貼表

產品名稱	"奧林柏斯泰爾茂" 貼得適人造真皮	申請廠商	日商泰爾茂股份有限公司台北分公司
衛生署給證號碼	衛署醫器輸　　字　第　　008900　　號		

"奧林柏斯泰爾茂" 貼得適人造真皮
"OLYMPUSTERUMO" Terudermis Artificial Dermis
製造批號：如包裝所示 有效期限：如包裝所示
許可證字號：衛署醫器輸字第 008900 號
藥商名稱：日商泰爾茂股份有限公司台北分公司
藥商地址：台北市松山區敦化北路 170 號 7 樓
製造廠名稱：(O) OLYMPUS TERUMO BIOMATERIALS CORP.
(P)OLYMPUS TERUMO BIOMATERIALS CORP. MISHIMA FACTORY
製造廠地址：(O) Shinjuku Monolith, 3-1 Nishi-Shinjuku 2-Chome, Shinjuku-ku Tokyo, 163-0914, Japan
(P)454-1 Higashino, Nagaizumi-cho, Sunto-Gun, Shizuoka 411-0931, Japan

99.12.14

衛生署 醫療器材 輸 食品藥物管理局

OLYMPUS TERUMO BIOMATERIALS

テルダーミズ 真皮欠損用グラフト

TERUDERMIS™ Artificial Dermis Silicone Membrane Type

ｺｰﾄﾞ番号/Code No.：TD*A013SJ　ｻｲｽﾞ/Size：2.5cm×5cm

製造番号/Lot No.：M10042

製造年月日/Production Date 100419

使用期限/Expiry：2013.3

(01)04562456555561(17)130300(30)1(10)M10042

シリコーン膜付 タイプ
Silicone Membrane Type

■添付文書の内容を確認の上、使用すること。
<保管・保管方法>
●水ぬれ、直射日光、過大な圧力下で室温で保管すること。

■Please carefully read the instructions for use before using.
Storage
● Keep dry. Keep away from heat. Avoid direct sunlight.

高度管理医療機器　再使用禁止
一般的名称：コラーゲン使用人工皮膚
販　売　名：テルダーミス真皮欠損用グラフト
製造販売元：オリンパステルモバイオマテリアル株式会社
東京都新宿区西新宿2-3-1 新宿モノリス
医療機器承認番号　20400BZZ00406000

OLYMPUS TERUMO
BIOMATERIALS CORP
Shinjuku Monolith
3-1 Nishi-Shinjuku 2-chome
Shinjuku-ku Tokyo 163-0914 JAPAN
Made in Japan

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本アルミ包装は、遮光・遮湿のためのものです。製品の無菌保証は内包装の内部のみとなります。

This aluminum pouch is for shading and moisture prevention. An aseptic guarantee of the product is only inside of inner paper pouch

※ 外文仿單應檢附中文譯文

“奧林柏斯泰爾茂”貼得適人造真皮

“OLYMPUSTERUMO” Terudermis Artificial Dermis

衛署醫器輸字第：008900 號

使用前請務必詳閱原廠之使用說明書並遵照指示使用。

產品概述

TERUDERMIS 是以低抗原 atelocollagen 製造，材料來自小牛皮膠原，並以蛋白酶製劑去除 telopeptide。由於是用熱交叉鍵結程序的製劑進行處理，膠原本身的生物相容性並未減低，因此 TERUDERMIS 能夠讓病人本身的細胞自己重建類真皮組織（類顆粒組織）。

＜特性＞

TERUDERMIS；

1. 讓病人本身的細胞自己重建類真皮組織。
2. 完全附著於患部，減輕疼痛。
3. 可用於深部傷口。（暴露出來的骨骼、肌腱和肌肉等）
4. 熱交叉鍵結程序的製劑，提供良好的生物相容性。
5. 低或無抗原性。
6. 在無菌狀態下製造，可立即用於移植。

產品類型和材料

產品類型：：

膠原單層型

由膠原層組成，以增加結構穩定性，加速纖維母細胞及微血管的滲透。

材料：

- 膠原層：來自小牛皮膠原製造，以熱交叉鍵結處理的 atelocollagen。

矽膠膜型

由膠原層和矽膠膜層組成，以預防感染，控制濕氣流出及體液散失。

材料：

- 膠原層：來自小牛皮膠原製造，以熱交叉鍵結處理的 atelocollagen。
- 矽膠層：矽膠。

網眼強化型

由膠原層和矽膠膜層組成，並以插入網眼強化。

材料：

- 膠原層：來自小牛皮膠原製造，以熱交叉鍵結處理的 atelocollagen。
- 矽膠膜以網眼強化：矽膠，以及聚酯網眼。

排水狹縫型

由膠原層和矽膠膜層組成，以預防感染，控制濕氣流出及體液散失。

具有許多排水小孔透過膠原層和矽膠膜層。

- 膠原層： 來自小牛皮膠原製造，以熱交叉鍵結處理的 atelocollagen。
- 矽膠層： 矽膠。

適應症

燒傷、外傷、手術創傷及口蓋裂手術創傷等零度皮膚，黏膜缺損修復。

告誡

- 本產品應避免美容目的的使用。
- 當出現過敏時，請立即移除 TERUDERMIS 。
- 不可使用於過去曾對動物來源所製造的蛋白質過敏之病人。
- TERUDERMIS 使用期間，如有發燒反應時，請立即執行抗感染治療，並檢視是否有感染的徵兆。
- 用於支氣管過敏或具有過敏症狀傾向如蕁麻疹的病人時，請特別注意。
- 在使用 TERUDERMIS 排水狹縫型、TERUDERMIS 矽膠膜型或網眼強化型，上面具有排水孔的產品時，可能會有顆粒化組織生長穿過排水孔、到達矽膠層的風險，因而難以移除。因此使用 TERUDERMIS 一週後，應小心留意顆粒化組織的形成，並在顆料化組織長過矽膠層之前即行移除矽膠層。如果矽膠層上已長有顆粒化組織時，以手術完全移除矽膠層後，再移植裂片厚的皮膚移植片。如未將長到矽膠層的顆粒化組織移除，即進行裂片厚的皮膚移植片移植時，在殘留矽膠層周邊可能發生壞死或潰瘍。
- TERUDERMIS 用於臉部時，可能引起傷口的嚴重攣縮。請避免用於臉部。

注意

- 請勿將軟膏塗在傷口上或 TERUDERMIS 下。【軟膏可能會干擾膠原層的細胞滲透。】
- 完全移除或割去傷口上的任何破碎組織、污染、水疱、焦痂、疙瘩、壞死組織或感染部位，小心進行止血、清潔、殺菌和清洗等。
- 如果 TERUDERMIS 使用部位的骨骼或肌腱廣泛暴露，不可能有來自鄰近組織的血流供應，或有血流阻塞現象時，微血管及細胞將不會滲透 TERUDERMIS ，因而類真皮組織不會形成。此時，以傳統治療方法確保血液的流通。【否則，TERUDERMIS 可能會脫落。】
- 存放於室溫，避免過度潮濕或直射陽光。
- 請勿滅菌。
- 如果包裝破損或污染，請勿使用。開封後立即使用。如未立即使用，請予以丟棄。
- 鋁袋之作用乃在於光線及潮濕的保護。無菌的保證僅於鋁袋內。

使用說明

真皮缺損

1) 充分小心進行止血及傷口清潔。在有感染傷口的情況下，請切除所有感染部位。

如爲灼傷，切除所有壞死組織再予以小心止血。

告誡： 在有細菌感染的情況，應對感染部位進行切除，再予以小心止血。

2) 將 TERUDERMIS 切成和傷口形狀相同，但尺寸較大一點，再將其貼到傷口上。

告誡： 在使用矽膠膜型的產品時，膠原側應面向下貼在傷口表面，請勿放顛倒了。（若將亮面的矽膠層貼到傷口表面，TERUDERMIS 移除時則不會有類真皮組織的形成。）

3) 以傳統技術進行移植，並縫妥或訂好。

告誡： 在需要有良好排水以移除多餘的滲出物，或當移除感染部位後，可能有傷口感染復發的風險時，請在整個 TERUDERMIS 製作排水孔（類似皮膚移植片上的排水孔）、採用 TERUDERMIS 排水狹縫型，或將 TERUDERMIS 切成貼片狀移植片再予使用。【否則可能會感染復發。滲出物的蓄積可能會將 TERUDERMIS 推起遠離傷口、洗掉或脫離膠原層。】

4) 以非黏性敷料覆蓋區域，輕輕施壓並以厚紗布敷料包紮。若傷口需要保持濕潤狀態，應將濕棉花或紗布置於非黏性敷料和紗布敷料之間。

告誡： 以適當壓力將 TERUDERMIS 置於傷口表面，過大壓力、傷口和 TERUDERMIS 間的死角，或者 TERUDERMIS 於傷口表面脫落等，都會干擾微血管滲透以形成類真皮組織的情況。

5) 外部敷料應視 TERUDERMIS 上滲出物的量進行更換。

告誡： 當移除感染部位後，可能有傷口感染復發的風險時，請蓋上吸收性敷料以吸收並移除來自傷口的滲出排水，每天進行敷料更換直到滲出物減少。更換敷料時，應清洗傷口上的 TERUDERMIS【否則可能會感染復發。】

6) 更換外部敷料時，如觀察到有血腫或滲出物滯留在 TERUDERMIS 下，請將其移除，清潔該部位，再重複步驟 4) 及 5)。

告誡： 每天監控以 TERUDERMIS 治療的傷口，TERUDERMIS 下如有感染現象或膿狀滲出物，應立即將其移除，並在清潔及消毒傷口表面後，更換一個新的產品。

7) 在類真皮組織形成後，應立即取下矽膠層，且進行分層植皮術。

告誡：
- 使用 TERUDERMIS 後不可立即進行分層植皮術，否則移植片可能會脫落。
- 如果使用 TERUDERMIS 後，類真皮形成並未在 7-10 天內重建，請予以移除，並重新再使用 TERUDERMIS 或採其他傳統治療方法。
- 在使用 TERUDERMIS 排水狹縫型和膠原單層型時，小心避免細菌的入侵及乾燥。

8) 分層植皮術之術後護理應遵照傳統自體移植規範進行。

口腔黏膜缺損

1) 完全小心進行止血及清潔傷口。

2) 將 TERUDERMIS 切成和傷口形狀相同，但尺寸較大一點，再將其貼到傷口上。

告誡： 膠原側應面向下貼在傷口表面。

（若將亮面的矽膠層貼到傷口表面，TERUDERMIS 移除時則不會有類真

皮組織的形成。）

3) 以傳統技術進行移植，並縫妥或訂好。

警告： 請確認 TERUDERMIS 完全固定，脫落時可能引起吞嚥困難而窒息。

告誡：

- 以適當壓力將 TERUDERMIS 置於傷口表面，過大壓力、傷口和 TERUDERMIS 間的死角，或者 TERUDERMIS 於傷口表面脫落等，都會干擾微血管滲透以形成類真皮組織的情況。
- 每天監控以 TERUDERMIS 治療的傷口，TERUDERMIS 下如有感染現象或膿狀滲出物，應立即將其移除，並在清潔及消毒傷口表面後，更換一個新的產品。
- 口腔黏膜缺損的情況，請勿使用 TERUDERMIS 排水狹縫型及膠原單層型。【TERUDERMIS 用於口腔黏膜缺損時，可能因爲咀嚼、食物殘渣或唾液而脫落或污染。】
- 將 TERUDERMIS 切成和口腔黏膜缺損形狀相同，但尺寸較大一點，將其固定，讓矽膠層能覆蓋傷口邊緣。【否則表皮層可能延伸到矽膠層上，以至於難以移除。】

＜存放條件＞

保持乾燥，遠離熱及避免直射陽光。

包裝

＜膠原單層型＞

產品編號	TD*A006NJ	TD*A013NJ	TD*A025NJ	TD*A100NJ
尺寸（cm）	2.5 x 2.5	2.5 x 5	5 x 5	10 x 10
包（每盒）	5	1	1	1

＜矽膠膜型＞

產品編號	TD*A006SJ	TD*A013SJ	TD*A025SJ	TD*A100SJ
尺寸（cm）	2.5 x 2.5	2.5 x 5	5 x 5	10 x 10
包（每盒）	5	1	1	1

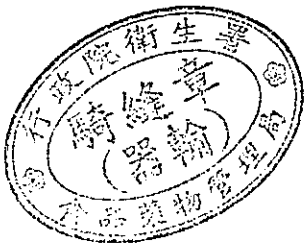
＜網眼強化型＞

產品編號	TD*M006SJ	TD*M013SJ	TD*M025SJ	TD*M100SJ
尺寸（cm）	2.5 x 2.5	2.5 x 5	5 x 5	10 x 10
包（每盒）	5	1	1	1

＜排水狹縫型＞

產品編號	TD*A100SDJ
尺寸（cm）	10 x 10
包（每盒）	1

藥商名稱：日商泰爾茂股份有限公司台北分公司
藥商地址：台北市敦化北路 170 號 7 樓
總公司名稱：OLYMPUS TERUMO BIOMATERIALS CORP.
總公司地址：SHINJUKU MONOLITH, 3-1 NISHI-SHINJUKU 2-CHOME, SHINJUKU-KU, TOKYO, 163-0914, JAPAN
製造廠名稱：OLYMPUS TERUMO BIOMATERIALS CORP. MISHIMA FACTORY
製造廠地址：454-1 HIGASHINO, NAGAIZUMI-CHO, SUNTO-GUN, SHIZUOKA, 411-0931, JAPAN



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hours at room temperature, and examined according to Pyrogen Test in General Tests of the Pharmacopoeia of Japan. There was no report of pyrogenic substance in TERUDERMIS™.

* For preparation of the extract, TERUDERMIS™ was cut into strips and extracted with 0.67 mL of saline per 1 cm^2 for 24 hours at 37degrees C.

** For preparation of the suspension, the TERUDERMIS™ was cut into strips, added with 0.67 mL of saline per 1 cm^2, and suspended by a glass mortar.

Clinical Studies

Efficacy Clinical Trials of TERUDERMIS™ Artificial Dermis

TERUDERMIS™ Artificial Dermis was applied to 96 cases in 6 facilities for efficacy test.

The subjects were 67 patients with full-thickness dermal defect, 27 patients with oral mucosal defect, and 2 patients requiring concavity reconstruction.

50 out of 67 cases with full-thickness dermal defect were treated with thin split-thickness skin graft transplantation.

1) Evaluation Items

All cases were evaluated for the following four items:

Granulation (dermis-like tissue)

Adhesion

Analgesic effect

Amount of exudate

The following four additional items were also evaluated for the graft transplantation cases.

Degree of graft taking

Success rate of graft taking

Degree of contracture

Effects of contracture

2) Total Evaluation

For full-thickness dermal defect, 35 out of 67 cases were evaluated to be "Usefulness satisfactorily" (52%).

For oral mucosal defect, 24 out of 27 cases were evaluated to be "Usefulness satisfactorily " (89%).

For concavity reconstruction, all 2 cases were evaluated to be "Usefulness satisfactorily " (100%).

<Storage Conditions>

Keep dry. Keep away from heat. Avoid direct sunlight.

Packaging

<Collagen Monolayer Type>

Code number	TD*A006NJ	TD*A013NJ	TD*A025NJ	TD*A100NJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

<Silicone Membrane Type>

Code number	TD*A006SJ	TD*A013SJ	TD*A025SJ	TD*A100SJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

<Mesh Reinforced Type>

Code number	TD*M006SJ	TD*M013SJ	TD*M025SJ	TD*M100SJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

< Drainage Slits Type>

Code number	TD*A100SDJ
Size (cm)	10x10
Packages (per box)	1

OLYMPUS TERUMO BIOMATERIALS

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OLYMPUS TERUMO BIOMATERIALS CORP.
Mishima Factory
454-1 Higashino, Nagaizumi-cho, Sunto-gun,
Shizuoka, 411-0931, Japan

FK2053-02

Manufacturer:
OLYMPUS TERUMO BIOMATERIALS CORP.
Shinjuku Monolith
3-1 Nishi-shinjuku 2-chome
Shinjuku-ku, Tokyo
163-0914 JAPAN

TERUDERMIS™ Artificial Dermis

Please carefully read these instructions before using.

Product Overview

TERUDERMIS™ is made of a low antigenic atelocollagen that is produced from a calf hide collagen eliminated the telopeptide by a preparation of protease. Due to treated by a preparation of thermal cross - linkage process, biocompatibility of the collagen itself is not compromised, a thus enabling TERUDERMIS™ to reconstruct dermis-like tissue (granulo-like tissue) by the patient's own cells.

< Characteristics >

TERUDERMIS™ ;

1. reconstructs dermis-like tissue by the patient's own cells.
2. alleviates pain by well adherence to the wound.
3. apply to deep wounds (exposed bone, tendon, muscles, etc.).
4. good biocompatibility offered by the preparation of thermal cross-linkage process.
5. low or absent antigenicity.
6. due to manufactured in aseptic condition, immediately available for grafting.

Product Type and Materials

Product Type:

Collagen Monolayer Type

Composed of collagen layer to increase structural stability and accelerate infiltration of fibroblasts and capillaries.

Materials:

• Collagen layer: thermally cross-linked atelocollagen produced from a calf hide collagen

Silicone Membrane Type

Composed of collagen layer and silicone membrane layer to prevent infection and control moisture flux and fluid loss.

Materials:

• Collagen layer: thermally cross-linked atelocollagen produced from a calf hide collagen
• Silicone membrane: silicone

Mesh Reinforced Type

Composed of collagen layer and silicone membrane layer enforced with mesh inserted.

Materials:

• Collagen layer: thermally cross-linked atelocollagen produced from a calf hide collagen
• Silicone membrane enforced with mesh: silicone, and polyester mesh

Drainage Slits Type

Composed of collagen layer and silicone membrane layer to prevent infection and control moisture flux and fluid loss with.

Have many drainage holes through collagen layer and silicone membrane layer.

Materials:

• Collagen layer: thermally cross-linked atelocollagen produced from a calf hide collagen
• Silicone membrane: silicone

Indications

Dermal defects due to burns, traumas and operational wounds, and for cleft palate operation and mucosal defects.

Cautions

• Immediately remove TERUDERMIS™ when allergy appears.
• Must not use for a patient who has a hypersensitivity to protein, produced from an animal, in the past.
• Carry out anti-infection therapy when develop a fever rapidly and find a sign of infection during TERUDERMIS™ has been applied.
• Pay careful attention when applying to the patients with bronchial asthma or disposition to allergy symptoms such as urticaria.
• When using the TERUDERMIS™ Drainage Slits Type,TERUDERMIS™ Silicone Membrane Type or Mesh Reinforced Type with drainage holes made in them, there is a risk of granulation tissue growing through the drainage holes and involving the silicone layer, making it difficult to remove. Be careful of the formation of granulation tissue after one week has passed since application of TERUDERMIS™, and remove the silicone layer before granulation tissue growth over it. If the silicone layer is involved in the granulation tissue, transplant a split-thickness skin graft after complete surgical removal of the silicone layer. If the split-thickness skin graft is transplanted without removing the granulation tissue involving the silicone, necrosis or ulcer could occur in the periphery of the residue silicone.
• TERUDERMIS™ applied to the face could cause severe contracture of the wound.

Precautions

• Do not apply ointment to the wound or under TERUDERMIS™. [Ointment could interfere with

cellular infiltration in the collagen layer.]

• Completely remove or excise any crushed tissue, contamination, blister, eschar, scab, necrotic tissue or infected site in the wound, if any. Perform careful hemostasis, cleansing , disinfection, washing, etc.

• If the bone or tendon in the site to which TERUDERMIS™ is applied is extensively exposed with no possibility of blood inflow from the adjacent tissues or there is blood flow obstruction, the capillaries and cells will not infiltrate TERUDERMIS™ and dermis-like tissue will not be formed. In such a case, provide the means to secure blood flow using conventional treatment. [Otherwise TERUDERMIS™ may peel off.]

• Store at room temperature, avoid excess humidity and direct sunlight.

• Do not sterilize

• Do not use if the package is damaged or contaminated. Use immediately after opening the package. Discard if not used immediately.

• The aluminum pouch is for shading and moisture prevention. An aseptic guarantee of the product is only inside of inner paper pouch.

Instructions for Use

Dermal Defects

1) Complete careful hemostasis and cleaning to the wound. In case of an infected wound, excise all infection sites.

In case of burn, excise all necrotic tissue followed by careful hemostasis.

Caution : In case of bacterial infection, excision should be done at the infected sites followed by careful hemostasis.

2) Cut TERUDERMIS™ to the same shape but a slightly larger size than the wound, and apply it to the wound.

Caution : In case of Silicone Membrane Type, the collagen side should be put face down onto the wound surface. Do not apply upside down.
(If the shiny silicone layer is placed onto the wound surface, TERUDERMIS™ will be removed without dermis-like tissue formation.)

3) Graft by conventional techniques and sutured or stapled.

Caution: When good drainage is required to remove excessive exudate or there is a risk of infection recurrence in the wound after removal of the infected sites, make drainage holes all over TERUDERMIS™ (similar to the drainage on a skin graft), use the TERUDERMIS™ Drainage Slits Type, or cut TERUDERMIS™ into patch grafts and apply them. [Otherwise infection could recur. Accumulated exudates could push TERUDERMIS™ up away from the wound or wash out or eliminate the collagen layer.]

4) Cover the area with non-adhesive dressing and lightly press and wrap with thick gauze dressing. For wounds requiring wet conditions, wet cotton or gauze should be placed between non-adhesive dressing and gauze dressing.

Caution: Place TERUDERMIS™ on the wound surfaces with adequate pressure. Capillary infiltration to form dermis-like tissue is interfered by excessive pressure, dead space between the wound and TERUDERMIS™, or TERUDERMIS™ slips off the wound surface.

5) The outer dressing should be exchanged depend on the amount of exudate on TERUDERMIS™

Caution: When there is a risk of infection recurrence in the wound after removal of the infected sites, apply an absorptive dressing to absorb and remove the exudate draining from the wound. Exchange the dressing every day until the exudate is reduced. Wash the TERUDERMIS™ applied to the wound every time the dressing is changed. [Otherwise infection could recur.]

6) Hematoma or stagnation of exudate is observed under the TERUDERMIS™ when changing the outer dressing, remove it, cleanse the site and repeat procedures 4) and 5).

Caution: Monitor the wound treated with the TERUDERMIS™ everyday. If there is evidence of infection, or purulent exudate under the TERUDERMIS™, it should be removed and exchanged with a new one after cleansing and disinfecting the wound surface immediately.

7) The silicone layer should be detached after a dermis-like tissue forms, and split-thickness skin graft should be transplanted.

Cautions: • Must not transplant split-thickness skin graft immediately after applying TERUDERMIS™, since the graft may be separated.

• If dermis-like formation is not reconstructed 7-10 days after applying TERUDERMIS™, remove and reapply TERUDERMIS™ or another conventional treatment.

• Take caution to prevent invasion of bacteria, and drying after applying the TERUDERMIS™ Drainage Slits Type and Collagen Monolayer Type.

8) Postoperative care of the split-thickness skin graft should follow the protocol for conventional autograft.

Oral Mucosal Defects

1) Complete careful hemostasis and cleaning to the wound.

2) Cut TERUDERMIS™ to the same shape , but a slightly larger size than the wound, and apply it to the wound.

Caution: The collagen side should be put face down onto the wound surface.
(If the shiny silicone layer is placed onto the wound surface, TERUDERMIS™ will be removed without dermis-like tissue formation.)

3) Graft by conventional techniques and sutured or stapled.

Warning: Make sure TERUDERMIS™ is fixed completely. Detachment may cause suffocation by dysphagia.

Cautions: • Place TERUDERMIS™ on the wound surfaces with adequate pressure. Capillary infiltration to form dermis-like tissue is interfered by excessive pressure, dead space between the wound and TERUDERMIS™, or TERUDERMIS™ slips off the wound surface.

• Monitor the wound treated with the TERUDERMIS™ everyday. If there is evidence of infection, or purulent exudate under the TERUDERMIS™, it should be removed and exchanged with a new one after cleansing and disinfecting the wound surface immediately.

• Do not apply the TERUDERMIS™ Drainage Slits Type and Collagen Monolayer Type to an oral mucosal defect wound. [TERUDERMIS™ applied to an oral mucosal defect could be removed or contaminated by mastication, food residue, or saliva.]

• Cut TERUDERMIS™ to the same shape as, but a slightly larger size than the oral mucosal defect, and fix TERUDERMIS™ so that its silicone layer covers the wound margins. [Otherwise the epithelium may extension on the silicone layer, making it difficult to be removed.]

Nonclinical Studies

<Implantation and Transplantation Test>

Two studies were undertaken in the study of TERUDERMIS™: subcutaneous implantation study on rats, and the applying to dermal defects prepared on rats.

- Neither rejection to the TERUDERMIS™ nor histological abnormalities were reported.
- TERUDERMIS™ enabled early fibroblast infiltration, capillary formation and the reconstruction of dermis-like tissue on histological observation were reported.

<Acute Toxicity Test >

Extract* of TERUDERMIS™ was administered intravenously to male and female rats (30 mL/kg) and mice (50 mL/kg), and suspension** (mice; 100 mL/kg, rat; 30 mL/kg) was administered subcutaneously. There were no report of mortality and abnormality of body weight loss.

<Subacute Toxicity Test >

Extract of TERUDERMIS™ was administered subcutaneously into male rats for 28 consecutive days. There were no report of adverse events in abnormality, body weight changes, urinalysis data, hematological data, macroscopic findings, organ weights, and histopathological observation.

<Cytotoxicity Test >

TERUDERMIS™ was immersed in Eagle's minimum essential medium (MEM) with 2.5% calf fetal serum, and incubated at 37 degrees C for 24 hours. After cooled and filtrated, put it on the culture medium and incubated HeLa-S3 cells. There were no report of interfere of cell growth in increase of the number of dead cells, cell deformation, poor growth, etc.

<Skin Irritation Test >

Extract of TERUDERMIS™ was administered intracutaneously to male Japanese White rabbits. There were no report of abnormality in administration sites such as reddening, edema, bleeding, necrosis, etc.

<Antigenicity Test >

Antigenicity was studied by heterologous PCA reaction and subcutaneous reaction to implanted material. Good biocompatibility of TERUDERMIS™ with low or absent antigenicity and foreign body reaction were reported.

<Hemocompatibility study>

After suspension** was administered subcutaneously to guinea pigs. There were no report of hematological and blood biochemical response.

<Pyrogen Test >

TERUDERMIS™ was extracted with saline for 72

List of References about TERUDERMIS

TERUDERMIS™ Artificial Dermis

OLYMPUS TERUMO BIOMATERIALS

Dermal defect

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Basic study

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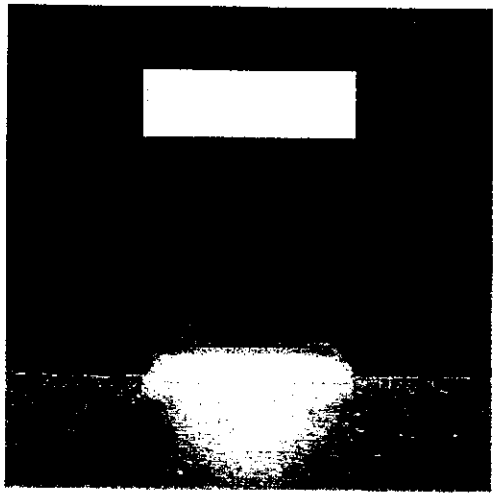
18) Ishikawa T. et al; Production of a Biologically Active Epidermal Growth Factor Fusion Protein with High Collagen Affinity, J Biochem, 129, p627-633, 2001
19) Yanaga H. et al; Take Percentage and Conditions of Cultured Epithellum Were Improved When Basement Membrane of the Graft Was Maintained and Anchoring Mesh Was Added, Plastic and Reconstructive Surgery, 107(1), p105-115, 2001

Applicable to deep dermal defects and mucosal defects caused by burns, trauma or surgical operations.



TERUDERMIS™ Artificial Dermis

Manufacturer

OLYMPUS TERUMO BIOMATERIALS

OLYMPUS TERUMO BIOMATERIALS CORP.
Mishima Factory
454-1 Higashino, Nagaizumi-cho, Sunto-gun,
Shizuoka, 411-0931, Japan

OLYMPUS TERUMO BIOMATERIALS CORP.
Shinjuku Monolith, 3-1 Nishi-Shinjuku 2-chome
Shinjuku-ku, Tokyo, 163-0914 JAPAN
http://www.biomaterial.co.jp/en/

TERUMO KOREA CORPORATION
TERUMO CORPORATION Taipei Branch
TERUMO (THAILAND) CO., LTD

OTB0039H-0309

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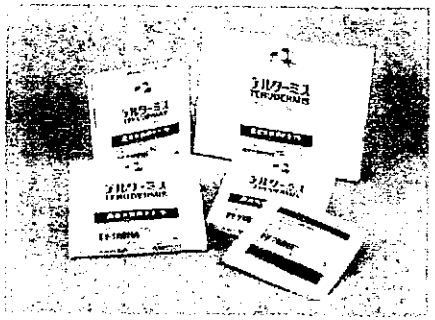
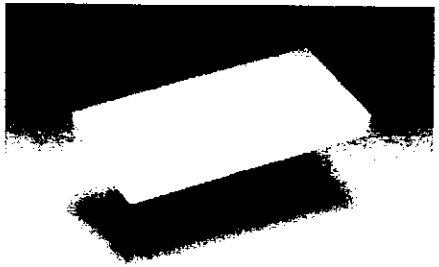


TERUDERMIS™ Artificial Dermis



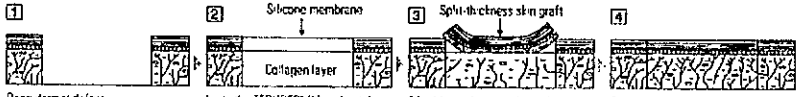
Product Overview

Features

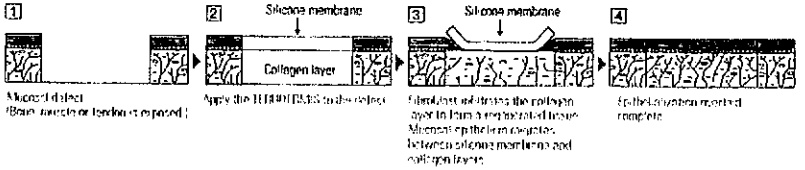
1. The collagen layer is made of a low antigenic atelocollagen that is produced from a calf dermal collagen eliminated the telopeptide by a preparation of protease.
2. Due to treatment by preparation of thermal cross-linkage process, biocompatibility of the collagen itself is not compromised, thus enabling the TERUDERMIS collagen layer itself to reconstruct dermis-like tissue (granulo-like tissue) by the patient's own cells infiltration.
3. Offers excellent adhesion and reduces pain.
4. Applicable to deep wounds (exposed bone, tendon, muscles, etc.)
5. Four types are available: Silicone Membrane Type, Mesh Reinforced Type, Collagen Monolayer Type and Drainage Slits Type.
6. Silicone Membrane Type and Mesh Reinforced Type are equipped with a silicone membrane layer (or silicone membrane reinforced with polyester mesh) to prevent infection and control moisture flux like exudates
7. The Drainage Slits Type has many drainage holes penetrating through collagen layer and silicone membrane layer to drain excessive exudates.
8. Due to manufactured in aseptic conditions, TERUDERMIS is immediately usable for application.

Application Example

Reconstruction example of dermal defect

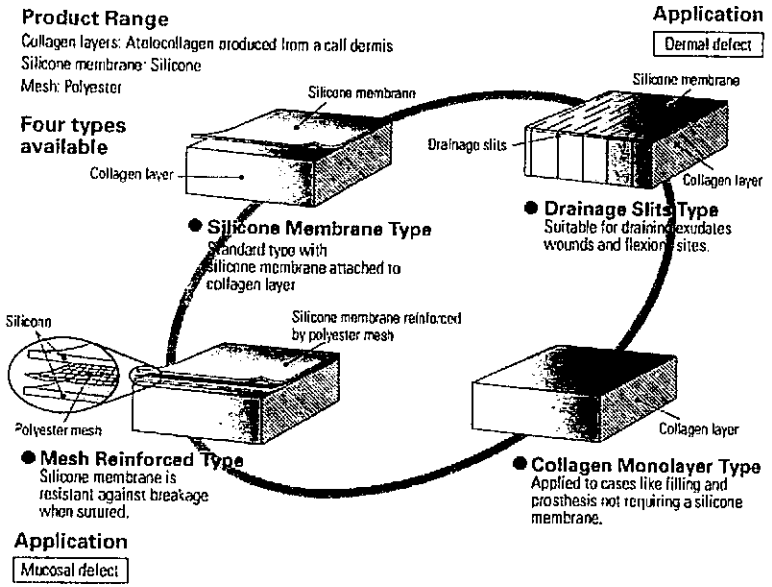


Application example of mucosal defect



Composition, Structure and Others [1)]

TERUDERMIS Artificial Dermis consists of the bottom layer, which is made of a low antigenic atelocollagen that is produced from a calf hide collagen eliminated the telopeptide by a preparation of protease, and the silicone top layer that prevents infection from outside and controls permeability of water such as exudation, etc. Collagen Monolayer Type (consisting of the bottom layer only), Mesh Reinforced Type (with mesh reinforcement in the top layer) and Drainage Slits Type (for draining exudates) are also available.



Indications

Dermal defects due to burns, traumas and operational wounds, and for cleft palate operation and mucosal defects.

Cautions

- Immediately remove TERUDERMIS when allergy appears.
- Must not use for a patient who has a hypersensitivity to protein, produced from an animal, in the past.
- Carry out anti-infection therapy when develop a fever rapidly and find a sign of infection during TERUDERMIS has been applied
- Pay careful attention when applying to the patients with bronchial asthma or disposition to allergy symptoms such as urticaria.
- When using the TERUDERMIS Drainage Slits Type, TERUDERMIS Silicone Membrane Type or Mesh Reinforced Type with drainage holes made in them, there is a risk of granulation tissue growing through the drainage holes and involving the silicone membrane, making it difficult to remove. Be careful of the formation of granulation tissue after one week has passed since application of TERUDERMIS, and remove the silicone membrane before granulation tissue growth over it. If the silicone membrane is involved in the granulation tissue, transplant a split-thickness skin graft after complete surgical removal of the silicone membrane. If the split-thickness skin graft is transplanted without removing the granulation tissue involving the silicone, necrosis or ulcer could occur in the periphery of the residue silicone
- TERUDERMIS applied to the face could cause severe contracture of the wound.

Precautions

- Do not apply ointment to the wound or under TERUDERMIS. (Ointment could interfere with cellular infiltration in the collagen layer.)
- Completely remove or excise any crushed tissue, contamination, blister, eschar, scab, necrotic tissue or infected site in the wound, if any. Perform careful hemostasis, cleansing, disinfection, washing, etc.
- If the bone or tendon in the site to which TERUDERMIS is applied is extensively exposed with no possibility of blood inflow from the adjacent tissues or there is blood flow obstruction, the capillaries and cells will not infiltrate TERUDERMIS and dermis-like tissue will not be formed. In such a case, provide the means to secure blood flow using conventional treatment. (Otherwise TERUDERMIS may peel off.)
- Store at room temperature, avoid excess humidity and direct sunlight.
- Do not sterilize.
- Do not use if the package is damaged or contaminated. Use immediately after opening the package. Discard if not used immediately.

Instructions for Use

Dermal Defects [2)]

1. Complete careful hemostasis and cleaning to the wound.

Caution In case of bacterial infection, excision should be done at the infected sites followed by careful hemostasis.

2. Cut TERUDERMIS to the shape but a slightly larger size than the wound, and apply it to the wound.

Caution In case of Silicone Membrane Type, the collagen side should be put face down onto the wound surface. Do not apply upside down. (If the shiny silicone layer is placed onto the wound surface, TERUDERMIS will be removed without dermis-like tissue formation.)

3. Graft by conventional techniques and sutured or stapled.

Caution When good drainage is required to remove excessive exudates or there is a risk of infection recurrence in the wound after removal of the infected sites, make drainage holes all over TERUDERMIS (similar to the drainage on a skin graft), use the TERUDERMIS Drainage Slits Type, or cut TERUDERMIS into patch grafts and apply them. (Otherwise infection could recur. Accumulated exudates could push TERUDERMIS up away from the wound or wash out or eliminate the collagen layer.)

4. Cover the area with non-adhesive dressing and lightly press and wrap with thick gauge dressing. For wounds requiring wet conditions, wet cotton or gauze should be placed between non-adhesive dressing and gauze dressing.

Caution Place TERUDERMIS on the wound surfaces with adequate pressure. Capillary infiltration to form dermis-like tissue or cells is interfered by excessive pressure, dead space between the wound and TERUDERMIS, or TERUDERMIS slips off the wound surfaces.

5. The outer dressing should be exchanged depend on the amount of exudates on TERUDERMIS.

Caution When there is a risk of infection recurrence in the wound after removal of the infected sites, apply an absorptive dressing to absorb and remove the exudates draining from the wound. Exchange the dressing everyday until the exudates are reduced. Wash the TERUDERMIS applied to the wound every time the dressing is changed. (Otherwise infection could recur.)

6. Hematoma or stagnation of exudates is observed under the TERUDERMIS when changing the outer dressing, remove it, cleanse the site and repeat procedures 4 and 5.

Caution Monitor the wound treated with the TERUDERMIS everyday. If there is evidence of infection, or purulent exudates under the TERUDERMIS, it should be removed and exchanged with a new one after cleansing and disinfecting the wound surface immediately.

7. The silicone layer should be detached after a dermis-like tissue forms, and split-thickness skin graft should be transplanted.

Caution

- Must not transplant split-thickness skin graft immediately after applying TERUDERMIS, since the graft may be separated.
- If dermis-like formation is not reconstructed 7-10 days after applying TERUDERMIS, remove and reapply TERUDERMIS or another conventional treatment.
- Take caution to prevent invasion of bacteria, and drying after applying the TERUDERMIS Drainage Slits Type and Collagen Monolayer Type.

8. Postoperative care of the split-thickness skin graft should follow the protocol for conventional autograft.

Oral Mucosal Defects [8-9]

1. Complete careful hemostasis and cleaning to the wound.

Caution In case of an infected wound, excise all infection sites. In case of burn, excise all necrotic tissue followed by careful hemostasis.

2. Cut TERUDERMIS to the shape but a slightly larger size than the wound, and apply it to the wound.

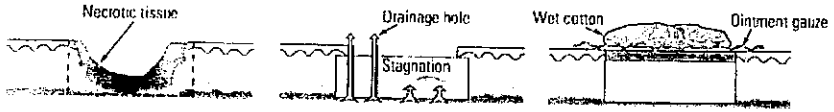
Caution The collagen side should be put face down onto the wound surface. (If the shiny silicone membrane is placed onto the wound surface, TERUDERMIS will be removed without dermis-like tissue formation.)

3. Graft by conventional techniques and sutured or stapled.

Caution

- Place TERUDERMIS on the wound surfaces with adequate pressure. Capillary infiltration to form dermis-like tissue is interfered by excessive pressure, dead space between the wound and TERUDERMIS, or TERUDERMIS slips off the wound surface.
- Monitor the wound treated with the TERUDERMIS everyday. If there is evidence of infection, or purulent exudates under the TERUDERMIS, it should be removed and exchanged with a new one after cleansing and disinfecting the wound surface immediately.
- Do not apply the TERUDERMIS Collago Monolayer Type or Drainage Slits Type to an oral mucosal defect wound. (TERUDERMIS applied to an oral mucosal defect could be removed or contaminated by mastication, food residue, or saliva.)
- Cut TERUDERMIS to the same shape as, but a slightly larger size than the oral mucosal defect, and fix TERUDERMIS so that its silicone membrane covers the wound margins. (Otherwise the epithelium may extension on the silicone layer, making it difficult to be removed.)

Keys to Success

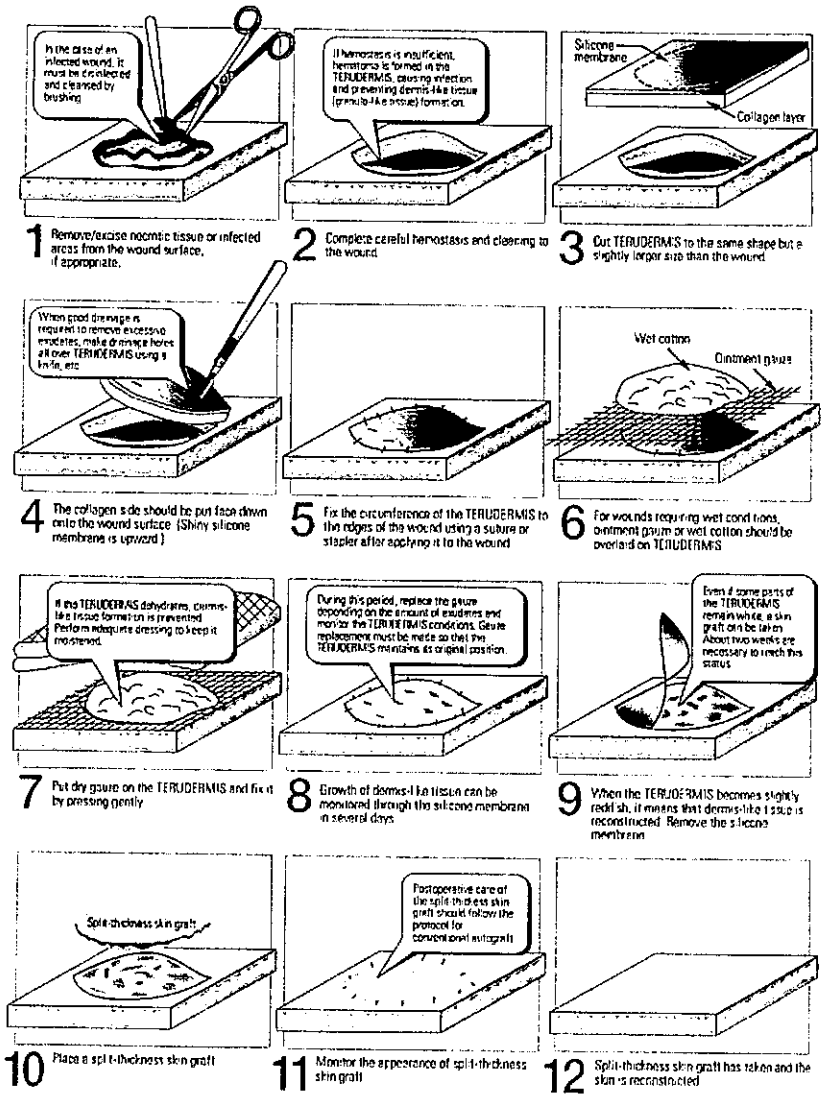


1) Excise necrotic tissue.
Before applying the TERUDERMIS to the wound, remove or excise the necrotic or infected tissues completely.

2) Control drainage.
Stagnation of exudates or blood (hematoma) not only interrupts the infiltration of cells and capillaries but also causes a risk of infection. Make drainage holes on the TERUDERMIS to drain them.

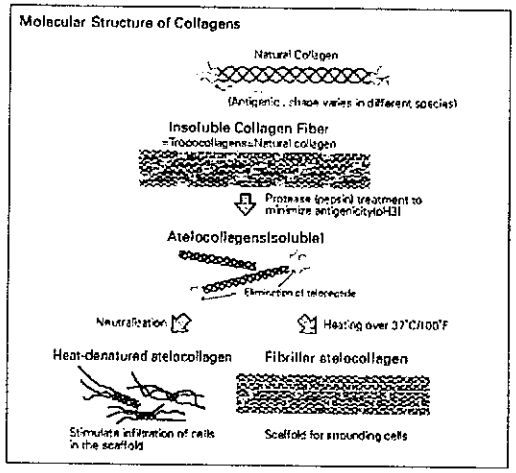
3) Keep moistened.
If TERUDERMIS dehydrates, dermis-like tissue formation is prevented. Place ointment gauze or wet cotton over the TERUDERMIS to keep it moistened.

Examples of Standard Usage (Silicone Membrane Type)



Structure and properties of collagens

Collagen is a protein that exists most abundantly in animal skin, tendon, and bone. The figure on the right shows the structure of collagen: a long, slender, cylindrical triple helix at the center and peptides known as "telopeptide" at both ends. In general, the antigenicity of the telopeptide region is assumed to be high because its shape varies from species to species.



The structure of collagen from animal skin or tendon is found to differ depending on the extraction method used. Under certain extraction conditions, fibrous collagen is obtained, it is known as "insoluble collagen", and collagen is often regularly aggregated and mutually coupled in this structure. Insoluble collagen molecules strongly combine with each other by crosslinking at the telopeptide region, and it is natural collagen structure of the skin and tendon. Enzymes like pepsin enable the resolution and removal of telopeptides. Such collagen that lacks the telopeptides is referred to as "atelocollagen". Atelocollagen exhibits low antigenicity because it lacks telopeptides. The triple-helix structure of collagen disintegrates when a solution of atelocollagen is heated. This is known as "heat-denatured collagen" (HAC). On the other hand, under conditions of neutral pH and 37°C, atelocollagen molecules aggregate mutually and regularly and form a structure similar to that of insoluble collagen. This is referred to as "fibrillar atelocollagen" (FAC). The collagen layer in TERUDERMIS is composed of a mixture of FAC and HAC.

Characterization of spongy materials

Sample	Mechanical properties		Degradation of collagenase	Infiltration* of cells	Cellular activity*
	Stress [g/cm²]	Elongation [%]			
Atelocollagen	18 (1.8)	155	100	+	+
Heat-denatured atelocollagen	15 (1.5)	62	100	++	++
Fibrillar atelocollagen	1776 (174)	82	4	−	−

* : In vitro studies using fibroblasts

The upper table indicates various characteristics of each collagen formed by sponge shape. HAC has low mechanical strength and resistance to collagenase, but it was found to increase the infiltrating ability and activity of fibroblasts in an in vitro study. In contrast, FAC did not affect any property of fibroblasts, but it has high mechanical strength and resistance to collagenase, and it was shown to contribute to the in vivo stability of the sponge.

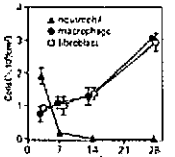
We prepared a sponge composed of only FAC and one composed of FAC with 10% HAC, and we then compared the characteristics of these sponges. The mechanical strength and resistance to collagenase of the mixed composition sponge were equal to those of the sponge composed of only FAC. However, the infiltration ability and activity of the cells in the former were higher.

The photographs on the right are histological cross sections of the FAC sponge containing 10% HAC and the sponge containing only FAC that were subcutaneously placed in rats and removed 3 days later.
Only a few neutrophils existed in the sponge containing only FAC (upper image), but several fibroblasts had infiltrated into the mixed composition sponge (lower image). In an in vivo test, excellent infiltration of fibroblasts into the mixed composition sponge was observed due to the presence of HAC.

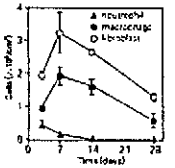

FAC:HAC=10:0


FAC:HAC=9:1

The graph on the right shows the cell population in the sponge containing only FAC and that including 10% HAC that were subcutaneously implanted in rats and removed 3, 7, 14, and 28 days after implantation. The number of cells within a constant area in the histological cross section was measured, and this value was converted into the cell population per square centimeter. The cell types were judged based on shape.
In the sponge containing only FC, the number of neutrophils that had infiltrated the sponge was greater than the number of monocytes and fibroblasts at day 3 after implantation; at day 7, the number of neutrophils decreased, and the number of monocytes and fibroblasts continued to increase until day 28. Therefore, this sponge was almost completely absorbed by day 28.
In the sponge containing FC and 10% HAC, the number of neutrophils that had infiltrated the sponge was considerably less than the number of the other cells by day 3, and decreased neutrophils thereafter.
The number of monocytes and fibroblasts increased until day 7, and it gradually decreased thereafter. Therefore, it was suggested that this sponge was retained for substantially until day 28 and contributed to tissue filling.



FAC:HAC=10:0



FAC:HAC=9:1

FAC: Fibrillar atelocollagen
HAC: Heat-denatured atelocollagen

Normal dermis and dermis-like tissue

Observation of normal rat skin under a scanning electron microscope revealed that the collagen fibrils in the rat dermis are bundled into heavy-fiber forms and that they assume a wavy, folded structure. It is thought that this structure of collagen contributes greatly to the flexibility of the dermis.
In an experiment in which TERUDERMIS was grafted into a full-thickness skin wound in a rat, we found that at 8 weeks after the implantation, the wavy, folded structure of collagen had formed at the region where TERUDERMIS had been applied. This tissue was flexible. We distinguish this connective tissue from a mere "scar tissue" and designate it "dermis-like tissue".
On the other hand, in another case, the full-thickness skin wound was allowed to heal without any treatment. We found that the collagen fibers formed horizontally lines at the region in which the wound was first created. This structure is known as a scar tissue, and it is hard and lacks flexibility.


Intact dermis

Biocompatibility Tests

<Implantation and Transplantation Test>[11-13]
Two studies were undertaken in the study of TERUDERMIS: subcutaneous implantation study on rats, and the applying to dermal defects prepared on rats

- Neither rejection to the TERUDERMIS nor histological abnormalities were reported.
- TERUDERMIS enabled early fibroblast infiltration, capillary formation and the reconstruction of dermis-like tissue on histological observation were reported.

<Acute Toxicity Test>
Extract* of TERUDERMIS was administered intravenously to male and female mice (50 mL/kg) and rats (30 mL/kg), and suspension** (rats, 30 mL/kg, mice, 100 mL/kg) was administered subcutaneously. There were no report of mortality and abnormality of body weight loss.

<Subacute Toxity Test>
Extract* of TERUDERMIS was administered subcutaneously into male rats for 28 consecutive days. There were no report of adverse events in abnormality, body weight changes, urinalysis data, hematological data, macroscopic findings, organ weights, and histopathological observation.

<Cytotoxicity Test>
TERUDERMIS was immersed in Eagle's minimum essential medium (MEM) with 2.5% calf fetal serum, and incubated at 37°C for 24 hours. After cooled and filtrated, put it on the culture medium and incubated HeLa-S3 cells. There were no report of interfere of cell growth in increase of the number of dead cells, cell deformation, poor growth, etc.

<Skin Irritation Test>
Extract* of TERUDERMIS was administered intracutaneously to make Japanese White rabbits. There were no reports of abnormality in administration sites such as reddening, edema, bleeding, necrosis, etc.

<Antigenicity Test>
Antigenicity was studied by heterologous PCA reaction and subcutaneous reaction to implanted material. Good biocompatibility of TERUDERMIS with low or absent antigenicity and foreign body reaction were reported.

<Hemocompatibility Study>
After suspension** was administered subcutaneously to guinea pigs. There were no report of hematological and blood biochemical response.

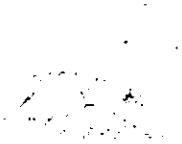
<Pyrogen Test>
TERUDERMIS was extracted with saline for 72 hours at room temperature, and examined according to Pyrogen Test in General Tests of the Pharmacopeia of Japan. There was no report of pyrogenic substance in TERUDERMIS.

* For preparation of the extract, TERUDERMIS was cut into strips and extracted with 0.67 mL of saline per 1 cm^2 for 24 hours at 37°C.

** For preparation of the suspension, the TERUDERMIS was cut into strips, added with 0.67 mL of saline per 1 cm^2, and suspended by a glass mortar.

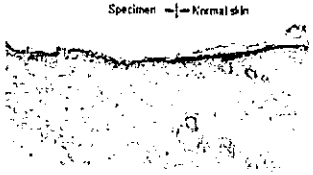
Applying TERUDERMIS to dermal defects prepared on rat (HE dyed)

3rd day
Cells infiltrated through the bottom of collagen layer. Collagen sponge shape is still maintained.



7th day
Sponge structure of collagen deformed and changed to gel structure. Fibroblast and capillarins infiltrated to the center of the collagen.

10th day
Fibroblast and capillaries infiltrated throughout the collagen layer, and the dermis-like tissue is reconstructed with minimum inflammation.



28th day
Extension of epidermis on the dermis like tissue is observed.

Clinical Studies (Efficacy Clinical Trials of TERUDERMIS Artificial Dermis)

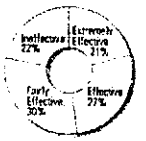
TERUDERMIS Artificial Dermis was applied to 96 cases in 6 facilities for efficacy test.
The subjects were 67 patients with full-thickness dermal defect, 27 patients with oral mucosal defect, and 2 patients requiring concavity reconstruction.
50 out of 67 cases with full-thickness dermal defect were treated with thin split-thickness skin graft transplantation.

1) Evaluation Items
All cases were evaluated for the following four items;
- Granulation (dermis-like tissue) • Adhesion • Analgesic effect • Amount of exudates

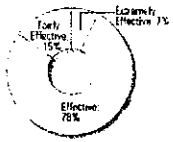
The following four additional items were also evaluated for the graft transplantation cases
- Degree of graft taking • Success rate of graft taking
- Degree of contracture • Effects of contracture

2) Evaluation Result on Effectiveness
For full-thickness dermal defect, 32 out of 67 cases were evaluated to be "Effectiveness satisfactorily" (48%). For oral mucosal defect, 23 out of 27 cases were evaluated to be "Effectiveness satisfactorily" (85%). For concavity reconstruction examples, two out of two cases were evaluated to be "Effectiveness satisfactorily" (100%).

Dermal defects



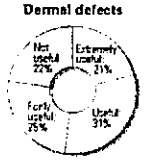
Oral mucosal defects



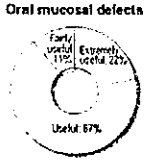
3) Evaluation Result on Safety
Abnormal fluctuation of clinical study values or side effects that result from TERUDERMIS were not found in all cases.

4) Total Evaluation
For full-thickness dermal defect, 35 out of 67 cases were evaluated to be "Usefulness satisfactorily" (52%). For oral mucosal defect, 24 out of 27 cases were evaluated to be "Usefulness satisfactorily" (89%). For concavity reconstruction, all 2 cases were evaluated to be "Usefulness satisfactorily" (100%).

Dermal defects

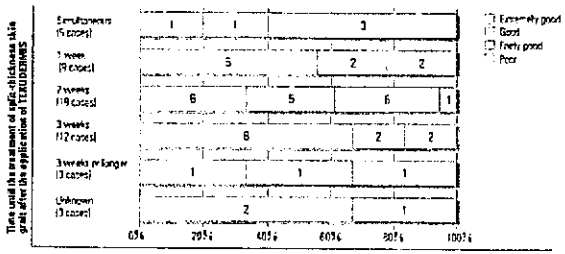


Oral mucosal defects

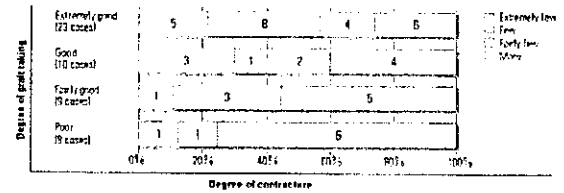


5) Evaluation Results of the Graft Transplantation Cases
Following correlations were confirmed on 50 (with thin split-thickness skin graft transplantation) out of 67 cases (with full-thickness dermal defect).

Correlation between time until the treatment of split-thickness skin graft after the application of TERUDERMIS and degree of graft taking



Correlation between degree of graft taking and degree of contracture

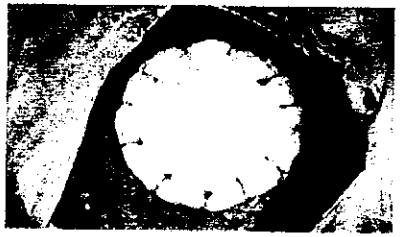


Clinical Applications

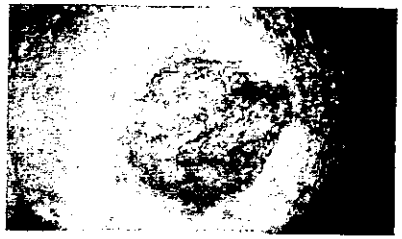
Example 1: The Wound after Scalp Tumor was Excised (bone was exposed) / Patient: 59 year-old male

1 Wound where scalp tumor was excised.
The split-thickness skin graft had not taken on the wound where the periosteum was excised. (Wound in which bone was exposed after the split-thickness skin graft did not take.)

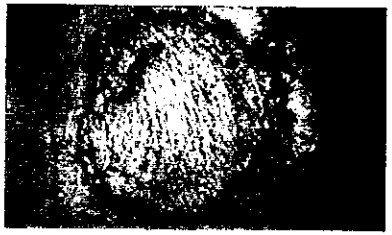
2 Affixation of TERUDERMIS.
TERUDERMIS was affixed to the wound in which the bone was exposed.



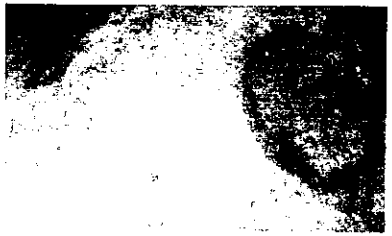
3 Three weeks after application of TERUDERMIS.
Good granulation was seen and mesh split-thickness skin graft was transplanted.



4 Three days after the graft.
The mesh split-thickness skin graft has taken completely.



5 Eight weeks after the graft.

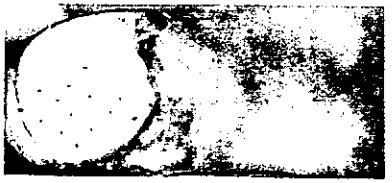


(Courtesy: Department of Plastic and Reconstructive Surgery, Hokkaido University)

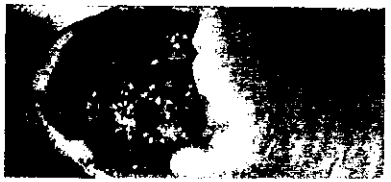
Example 2: Diabetic Ulcer (tendon was exposed) / Patient: 60 year-old male

1 Before application: diabetic ulcer of a sole exposed aponeurosis. The patient had diabetes and arteriosclerosis obliterans (ASO).

2 TERUDERMIS was made drainage holes and applied onto the ulcer. The second application was performed within a few weeks.



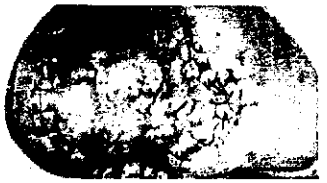
3 A few weeks after the second application: good granulation was seen though blood flow obstruction due to ASO was strong.



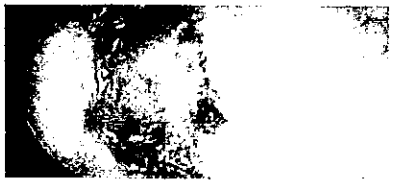
4 TERUDERMIS was put into the narrow strips and the third application was performed onto the concavity whose granulo-like tissue is insufficient.

5 About ten weeks after the first application, the concavity was flattened.

6 Split-thickness skin graft was placed.



7 Three months after the skin graft.
A part of edge of the skin graft was inflamed.



8 One year after the skin graft.
Recurrence of diabetic ulcer was not seen.

(Courtesy: Department of Plastic and Reconstructive Surgery, Seirei Hamamatsu Hospital)

Clinical Applications

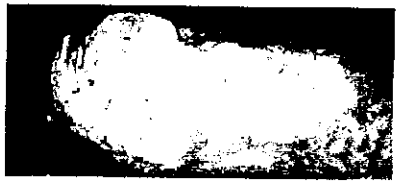
Example 3: Degloving Injury (wound where tendon was exposed) / Patient: 66 year-old female

1 Degloving injury occurring between the left crus and heel. Left tendo Achillis was ruptured (with no aponeurosis) One month after having got injury (when the patient was introduced to the Department of Plastic Surgery).

2 After debridement. Tendo Achillis was exposed (with no aponeurosis).

3 Immediately after application of TERUDERMIS. TERUDERMIS was attached over the wound where the tendon was exposed and its surroundings, then it was sutured. Drainage slits were provided on the TERUDERMIS.

4 Three weeks after the application. Capillaries infiltrated and the reddish area enlarged. Seven weeks after the application, mesh split-thickness skin graft was placed.



5 One week after the graft. Over 80% of the skin graft has taken.

6 Four weeks after the graft. Since a part of the tendo Achillis was exposed, thin split-thickness skin graft was applied again to that part only (two weeks after the first graft).

7 Four months after the operation. Rehabilitation was commenced from three weeks after the operation. The patient recovered so that she could stand, and left the hospital.

8 Six months after the operation. Dorsiflexion and plantar-flexion of the ankle joint were same as those of the side tendon. The patient could stand and walk using a sole plate.

(Courtesy: Department of Plastic Surgery, Kurume University)

Example 4: Excisional Biopsy of Skin Tumor / Patient: 89 year-old male

1 Before application: skin tumor (squamous cell carcinoma (SCC)) on the back of left hand.

2 The defect wound, without aponeurosis after excisional biopsy, was applied with TERUDERMIS.

3 Seven days after the application. The TERUDERMIS is protected with silicone gauze and ointment, and affixed with plaster bandage.

4 Eleven days after the application; the silicone layer was removed and the site was protected with a wet ointment gauze. Fourteen days after the application, rehabilitation was started twice a week.

5 One month after the application; split-thickness skin graft was placed.

6 Three months after the skin graft.

(Courtesy: Department of Plastic Surgery, Almeida Hospital)

Clinical Applications

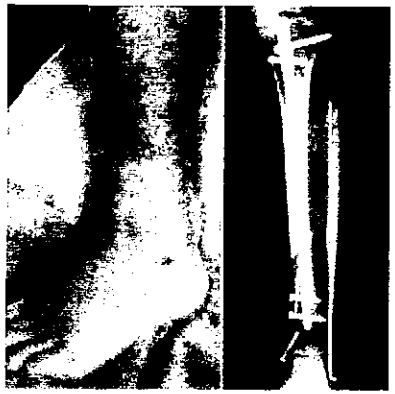
Example 5: Open Fracture / Patient: 26 year-old male [7]

1 Gustilo IIIb open fracture by a traffic accident.

2 The fractures were internally fixed. To close the original open wound, double pedicle flap was removed after adequate irrigation and two relaxing incisions.

3 The incised wounds were applied with TERUDERMIS. Two weeks after the application, the silicone membrane was removed, and split-thickness skin grafts were placed.

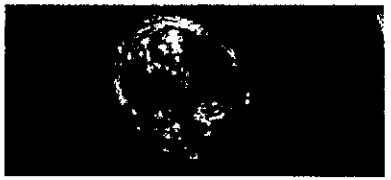
4 Four months after the application.



(Courtesy: Department of Emergency and Critical Care Medicine, Nippon Medical School)

Example 6: Deep Sacral Pressure Ulcer / Patient: 53 year-old male [8]

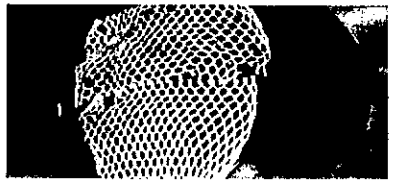
1 Deep sacral pressure ulcer of 314 cm^2 with subcutaneous pocket.



2 The necrotic tissue and unhealthy granulation, including subcutaneous pocket, were completely removed surgically, and the bony prominence was planed by an osteotome.

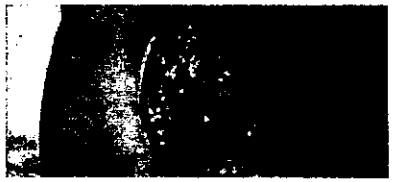
3 After debridement.

4 TERUDERMIS was meshed by a mesh dermatome, applied onto the wound and covered with absorptive dressing for quick absorption of pus and exudates.

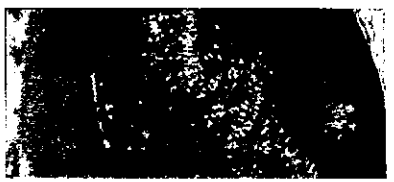


5 Dressings were changed daily in the early postoperative stage, and the wound was irrigated. Two weeks after the application, TERUDERMIS was added.

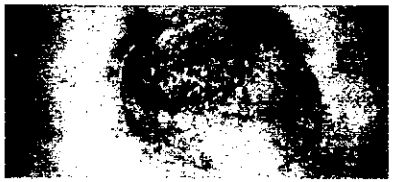
6 Five weeks after the first application: Healthy granulation was induced. The exposed bone was covered with the vascularized tissue.



7 After meshed split-thickness skin graft was applied, the wound closed in six weeks.



8 One year after the skin graft. No recurrence had seen.



(Courtesy: Department of Plastic and Reconstructive Surgery, Saitama Medical School)

Clinical Applications

Example 7: Tongue Tumor Excision (the wound where muscle is exposed) / Patient: 46 year-old male

1 Before tumor excision (T2N0, 32X20mm) was performed.

2 Hemiglossectomy (mND) was conducted using an electric knife under general anesthesia condition.

3 Excised tumor (55X30mm)

4 TERUDERMIS was affixed on the excised site by suture.

5 TERUDERMIS was fixed with a tie-over. Silicone membrane was removed seven days after the operation.

6 Four and a half months after the operation. Epithelialization on the site, to which TERUDERMIS was applied, was good with minimum scar contracture. Even after eight months, there were no problems in mastication and articulation.

(Courtesy: Department of Otolaryngology, Nara Medical University)

Example 8: Fenestration for Mandibular Cyst / Patient: 14 year-old female [10]

1 Bone is exposed in the fenestrated site from which the mandibular cyst was excised.

2 TERUDERMIS was applied to the site from which the cyst was excised. It was not sutured with the surrounding mucosa.

3 TERUDERMIS was adhered to the wound and pressed/fixed with the gauze containing antibiotic ointment to prevent infection. A part of the excised mucosa around the wound was sutured.

4 Three days after the application. Tissue infiltrated from the stump of peripheral mucosa. No bleeding was confirmed in case of gauze replacement.

5 Seven days after the application, silicone membrane was peeled off. No pain and bleeding had been confirmed during gauze replacement.

6 Eight weeks after the application. Epithelialization was completed and concavities were reduced. The fenestrated site was covered with the mucosa. Slight cavities were found only in a part of the site.

(Courtesy: Department of Oral Surgery, School of Medicine, Kobe University)

Clinical Applications

Example 9: Alveoplasty / Patient: 67 year-old male

1 Denture insertion was impossible due to a lapse of five years after tumor excision. Photo shows the site before conducting mandibular alveoplasty.

2 Wound exposed as the result of mandibular alveoplasty.

3 Immediately after the TERUDERMIS was applied. After the operation, hemostasis and alleviation of pain were observed.

4 10 days after the operation. Silicone membrane was removed.

5 19 days after the operation. Good granulation was confirmed.

6 35 days after the operation. Epithelialization was completed. Good alveolar ridge was formed. Appearance and jaw function were satisfactory.

(Courtesy: Department of Oral Surgery, School of Medicine, Yokohama City University)

Example 10: Vestibular Extension Surgery: Substitution of Gingival Free Flap / Patient: 22 year-old female

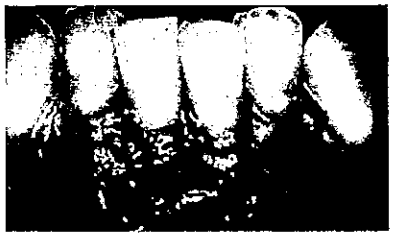
1 Before operation: gingiva was retracted and roots of the front teeth were exposed. The width of keratinized gingiva was about 1.5mm.

2 Incision was performed in the mucogingival junction. Vestibuloplasty was performed toward mucosa.

3 TERUDERMIS was sutured to the gingival wound edge. The mucosal wound edge was down to make open wound of 3mm between TERUDERMIS and mucosa, and sutured to periosteum.

4 1 week later, TERUDERMIS was red due to infiltration of capillaries in collagen layer, and silicone membrane was started peel.

5 Immediately after removal of stitches and silicone membrane (1 week later), peripheral epithelium extended onto the collagen layer of TERUDERMIS.



6 6 months after the gingival flap was surgically removed toward tooth crown in 3 months after the application of TERUDERMIS, the width of keratinized gingiva was about 3mm.

(Courtesy: Kodama Dental Clinic, Japan)

Clinical Applications

Example 11: Keratinized Tissue of the Alveolar Crest. Extension Surgery with Apical Repositioning / Patient: 43 year-old female

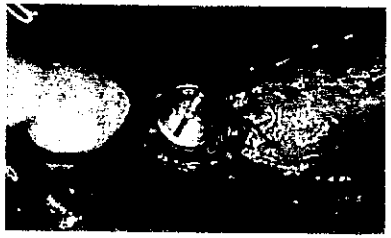
1 Before operation : edentulous mandible with narrow keratinized tissue.

2 The keratinized tissue of the alveolar crest was transversely incised along its width for approximately about 1 mm. A partial thickness flap was prepared from the buccal site. The edge of the flap was sutured to the periosteum of the bottom of the alveolar border.

3 Mesh Reinforced Type TERUDERMIS was cut so that it was slightly larger than the defect, and it was sutured to the surrounding keratinized tissue.

4 Eight weeks after the operation.

5 After dental implantation (12 weeks after the operation).



6 Final prosthesis (5 years after the operation).

(Courtesy: Kodama Dental Clinic, Japan)

Storage Conditions

Keep dry. Keep away from heat. Avoid direct sunlight

Packaging

<Collagen Monolayer Type>

Code number	TD•A006NJ	TD•A013NJ	TD•A025NJ	TD•A100NJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

<Silicone Membrane Type>

Code number	TD•A006SJ	TD•A013SJ	TD•A025SJ	TD•A100SJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

<Mesh Reinforced Type>

Code number	TD•M006SJ	TD•M013SJ	TD•M025SJ	TD•M100SJ
Size (cm)	2.5x2.5	2.5x5	5x5	10x10
Packages (per box)	5	1	1	1

< Drainage Slits Type>

Code number	TD•A100SDJ
Size (cm)	10x10
Packages (per box)	1

TERUDERMIS Artificial Dermises (actual size) Unit: cm