

Thoracic Wall Reconstruction with Acellular Porcine Dermal Collagen Matrix

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Abstract

Background Major thoracic wall resections require the implantation of foreign materials for reconstruction and stabilization. Recently, biological collagen matrixes have emerged as an alternative to the routinely used synthetic materials.

Materials and Methods Retrospectively, we analyzed our initial experience of chest wall reconstruction on large defects using a cross-linked porcine dermal acellular collagen matrix mesh with a thickness of 1.5 mm.

Results Six sarcoma patients with a mean age of 46 (22–66) years underwent chest wall resections. Complete thoracic wall defects (mean area 149 cm²) ranged from 8 × 10 to 15 × 20 cm in size. In the majority of cases, only mobilized subcutaneous tissue and skin were used for soft-tissue coverage of the implanted porcine collagen matrix patches. Implantation and postoperative courses were uneventful in all patients. No local infections or wound healing problems occurred. The collagen material resulted in durable and good to excellent chest wall stability in clinical follow-ups, and on computed tomography scans spanning over 3.5 years. Histological examination showed integration, neovascularization, and long-term persistence of the collagen matrix on late reoperation of one patient.

Conclusion Acellular porcine dermal collagen matrix is a feasible and reliable biological patch material for reconstruction of the thoracic wall. Excellent wound healing and long-term stability are achieved even in large defects or complete sternal replacements.

Keywords

- ▶ chest wall
- ▶ sarcoma
- ▶ wound healing
- ▶ sternum
- ▶ tumor

Introduction

Chest wall resections due to malignancies require extended surgical procedures to ensure wide safety margins. Reconstruction of larger defects, and in particular complete sternal resections, presents a major challenge.¹ Sufficient chest wall stability, absence of respiratory impairments, adequate tissue coverage, and satisfactory cosmetics results must all be achieved.²

Synthetic materials combined with soft-tissue transfers, such as pectoralis or latissimus muscle flaps, have been employed in chest wall reconstructions for decades.^{2,3} This strategy has been associated with significant morbidity and mortality in 46 to 69% of patients.^{4,5} Respiratory impairments may pose major problems such as paradox chest wall movements and rigidity due to excessive encapsulation.⁶ Seroma formation and wound healing impairment are paving the way for infection of synthetic materials which

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Table 1 Patient characteristics

Patient	Sex (M/F)	Age (y)	Diagnosis	Location	Defect size (cm ²)	Pretreatment
1	M	22	Osteosarcoma (G3)	Ninth rib left	9 × 18 cm (162)	Preoperative chemotherapy
2	F	48	High-grade sarcoma (G3)	Dorsal chest wall left (ribs 7–9)	8 × 10 cm (80)	None
3	M	44	Chondrosarcoma (G2)	Sternum	7 × 19 cm (133)	None
4	F	50	Ewing sarcoma (G4)	Seventh rib right	14 × 10 cm (140)	Preoperative chemotherapy
5	M	66	Metastasis from synovial sarcoma (G3) of the right femur	Chest wall right (ribs 4–6)	14 × 18 cm (252)	Preoperative chemotherapy
6	F	46	Chondrosarcoma (G2)	Sternum	8 × 16 cm (128)	None

often jeopardizes long-term success and result in significant failure rates.⁷

In the past, the use of a wide variety of synthetic materials such as polypropylene, polytetrafluoroethylene (PTFE), solid methylmethacrylate sandwich constructions, as well as various composite absorbable meshes has been explored. PTFE materials have been most frequently used.⁸ However, due to the inconclusiveness of available studies, the type of allomaterial and the technique of reconstruction still depend largely on the expertise and preference of the individual surgeon.

Recently, collagen matrixes harvested from human or animal sources and processed for medical use have emerged as an alternative. The implanted matrix undergoes a remodeling process with cellular infiltration, neovascularization, and exchange of extracellular matrix. Some of these materials, such as the product used in the present study, have been chemically cross-linked to increase strength and durability.^{9–13}

The implantation of biological collagen matrixes has been described in abdominal hernia repair and various other fields of surgery.^{11,12,14} However, in thoracic surgery, experience is limited to single cases and small series.^{15–17} Unlike permanently fixated biological and synthetic materials, acellular collagen matrixes allow for integration and remodeling. The

long-term integrity, strength, and stability of a collagen matrix are unknown. In this pilot study, we evaluated the feasibility and long-term results in the usage of a porcine dermal collagen matrix for thoracic wall reconstruction.

Materials and Methods

Study Setting and Design

Beginning in December 2009, six consecutive sarcoma patients scheduled for major thoracic wall or sternum resection were enrolled in the study (►Table 1). Written informed consent was obtained from all patients. Data were analyzed retrospectively and included patient demographics, diagnoses, operative data, and both pre- and postoperative laboratory and technical examinations. All patients underwent preoperative and postoperative computed tomography (CT) scans required for tumor evaluation and oncological follow-up.

Characteristics of Biological Implant

Thoracic wall reconstructions were performed using collagen matrix patches (Permacol; Covidien, Mansfield, Massachusetts, United States; 1.5 mm thickness in sizes of up to 15 × 20 cm) (►Figs. 1 and 2). This collagen matrix is derived

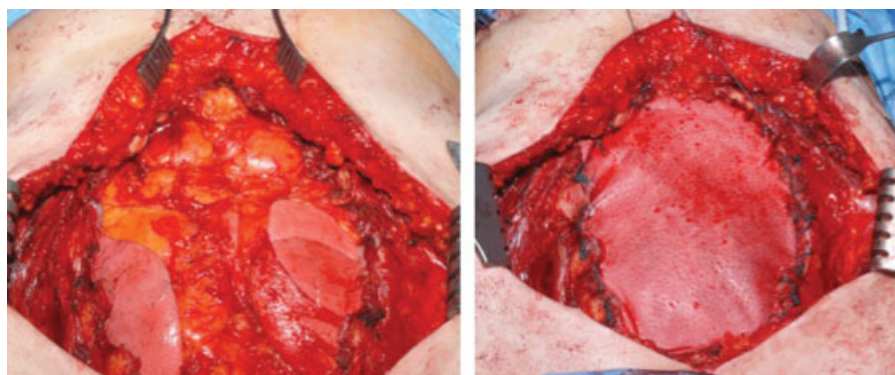


Fig. 1 Complete sternum resection in a patient with chondrosarcoma (left panel). Subsequent sternum reconstruction with a 15 × 20 cm porcine dermal derived patch (right panel).

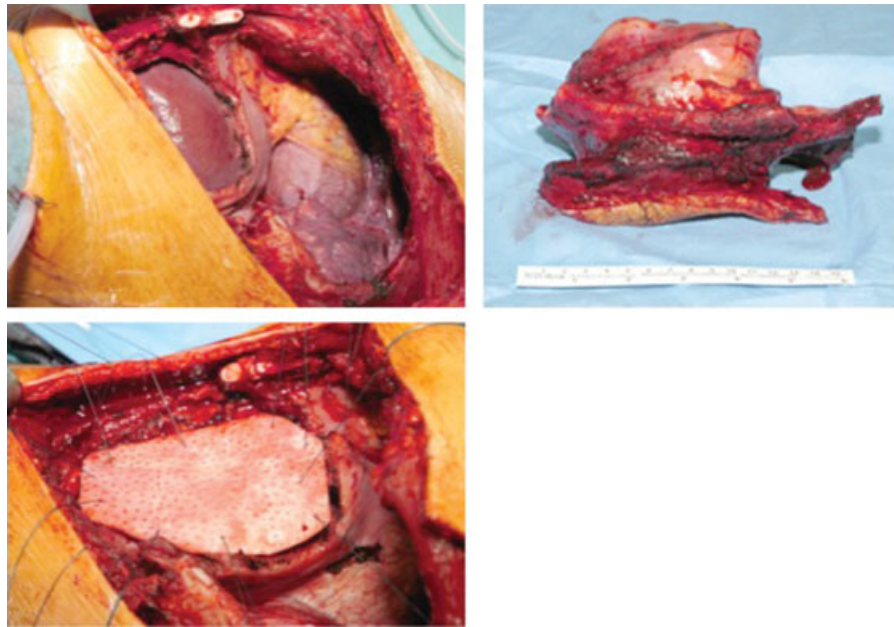


Fig. 2 Extended thoracic wall resection in a patient with osteosarcoma of the ninth left rib (upper panels). Partial diaphragm resection and pulmonary wedge resections were necessary. The chest wall and diaphragm defects were reconstructed using a 15 × 20 cm Permacol (Covidien, Mansfield, Massachusetts, United States) patches (lower panel). A pedicled latissimus dorsi transfer flap was used for soft-tissue coverage.

from porcine dermis in which cells, cell debris, DNA, and RNA were removed. The resulting acellular matrix with its constituent collagen fibers is cross-linked with hexamethylene diisocyanate for additional stability and reduction of collagenase degradation. The biomechanical characteristics of several collagen materials have been tested in experimental settings. The native collagen patch used in this series sustained a maximum load of 317.2 ± 23.6 N during uniaxial tensile testing. The tensile strength per unit width was 105.7 ± 7.9 N/cm and stiffness 58.3 ± 4.0 N/mm (mean \pm standard error of the mean). One month after abdominal hernia repair in a porcine animal model, the maximum tolerated force was 35.6 ± 3.5 N compared with the native abdominal wall with 16.8 ± 1.8 N, similarly the tensile strength was 11.9 ± 1.2 N/cm compared with 5.6 ± 0.6 N/cm and stiffness values were 5.8 ± 0.9 N/mm compared with 1.1 ± 0.2 N/mm.^{10–12,14,18,19}

Patients and Surgical Techniques

Indications for surgery were resection of primary chest wall sarcomas ($n = 5$) or sarcoma metastasis ($n = 1$). Patient data are listed in ▶Table 1. Lateral chest wall resections were performed via thoracotomies to ensure wide safety margins ($n = 4$). Complete sternal resections were performed through a midline incision (▶Figs. 1 and 2).

Before treatment, all patients had undergone biopsy to determine definite histopathological diagnosis. All tumor surgeries were en bloc resections, which included the biopsy sites.

Resections were performed with a minimum margin of 4 cm for ribs, sternum, and soft tissue. The underlying pleura was always resected, as were adherent parts of the lung, diaphragm, and mediastinum (▶Table 1).

Thoracic cavities were drained with 28 Charrière chest tubes. Patches were shaped with scissors to match the resected defect with an overlap of approximately 1 cm on all margins to ensure complete coverage. Under tension the patch was anchored with multiple single-tied coated nonabsorbable polyethylene terephthalate sutures (Ethibond; Ethicon, Norderstedt, Germany) to neighboring ribs and transosseously drilled holes in the adjoining rib stumps. The same sutures were additionally used as running stitches (▶Fig. 3) to increase tension and to approximate soft tissues to the patch.

Redon drainages were placed on top, and left in place for at least 7 days. Adjacent muscles, subcutaneous tissue, and skin were mobilized, and approximated with polyglactin (Vicryl, Ethicon, Norderstedt, Germany) sutures. In two cases, soft-tissue coverage was augmented by transposition of lifted muscle flaps.

Before incision, a single shot of cefuroxime was administered for perioperative antibiotic prophylaxis. All patients received continuous postoperative analgesia via a peridural catheter. Patients were mobilized without restrictions from postoperative day 1. Clinical wound assessment, laboratory tests, and radiological imaging were performed according to routine surgical procedures.

Follow-Up

Chest wall reconstructions were evaluated during postoperative oncological follow-up visits at 3, 6, 12, and 24 months. The subjective impressions or complaints from the patients were documented. Wound healing and soft-tissue coverage were examined. Chest wall stability was tested using deep breath maneuvers and coughing tests. The stability was classified as excellent, good, medium, or poor according to the surgical consultant's impression. Routine oncological CT

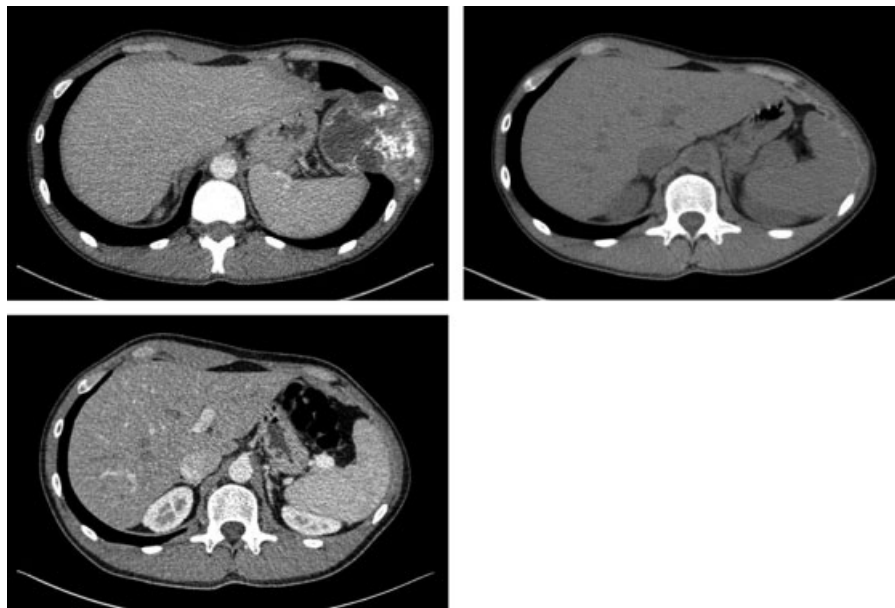


Fig. 3 Computed tomography (CT) scan of patient with osteosarcoma of the ninth rib showing the extent of the tumor mass (upper left panel). Postoperative follow-up CT scan after thoracic wall resection and reconstruction after 6 months (upper right panel) and after 12 months (lower panel).

scans were used to evaluate the patches for structural changes and integrity.

Histopathology and Immunohistochemistry

Formalin fixated and paraffin embedded sections of the explanted patch material were stained for hematoxylin and eosin and periodic acid Schiff reaction. Immunohistochemistry (IHC) was used to stain for CD31 positive capillary endothelial cells indicating neoangiogenesis. IHC was performed by means of a standardized avidin-biotin complex method.

Results

Resection of chest wall sarcomas, including complete removal of the sternum in two cases, was successfully performed in all patients. Details of patient data and surgical procedures are listed in **Tables 1** and **2**. A minimal area of three ribs with adjacent soft tissues was resected. Mean size of the defects was 149 cm² (range: 80–252 cm²). Complete resection (R0) and wide safety margins were confirmed by histopathological examination in all patients.

The collagen patch material proved to be implantable under tension. The material was pliable but not stretchable, and resulted in immediate stability of the thoracic wall.

Mobilized subcutaneous tissue and skin were sufficient to cover the patches in four patients. Pediculate muscle flaps were necessary for two patients (Musculus latissimus dorsi and bilateral M. pectoralis major flap). Primary skin closure was achieved in all patients. Mean duration of surgery was 178 (range: 110–305) minutes.

All patients were extubated in the operating room and transferred to the intensive care unit ($n = 3$) or surgical ward ($n = 3$). The postoperative course was uncomplicated in all

cases. In particular, no early or late respiratory impairment was observed. No postoperative bleeding, no infections, or wound healing problems were encountered. Inflammatory markers peaked in average (C-reactive protein [CRP] 29.2 mg/dL; white blood cell count [WBC] 12,950/ μ L) on postoperative day 2. Mean CRP value at 3 weeks postoperatively was 1.2 (range: 0.5–4) mg/dL and mean WBC was 7,270 (range: 4,310–11,500)/ μ L. Chest drains were removed after a mean of 5 (range: 2–8) days. Mean hospital stay was 10 (range: 8–15) days. The 30-day mortality was 0%.

Mean duration of follow-up was 27.6 (range 8–42) months. None of the patients suffered from subjective respiratory limitations or complaints. No fluid accumulation inside or outside the thorax, no excessive fibrous tissue formation, or signs of herniation were observed (**Table 2**).

Following lateral chest wall resections, provoking tests caused only minimal movements of the patch area. At 3-month follow-up, the stability was rated as good ($n = 2$) and excellent ($n = 2$).

Initially, both cases of complete sternal reconstruction presented with noteworthy visible respiratory movements of the anterior chest. Neither of the patients suffered from respiratory impairment. In the course of follow-up, the stability improved significantly. At 3-month follow-up, the stability was rated good ($n = 1$) and moderate ($n = 1$) by the surgeon under deep breath and coughing tests (**Table 2**). In all six patients, no change in stability was observed at follow-up visits beyond 3 months. On routine follow-up CT scans, all implanted patches were identified as intact without bulging, herniation, rupture, or loss of structural integrity. The appearance of the patch material in the CT scans did not change during follow-up. No excessive encapsulation or seroma formations were evident. A representative series of follow-up CT scans demonstrating the intact patch material is shown in **Fig. 3**.

Table 2 Surgical procedures and follow up

Patient	Resection	Additional resections	Reconstruction		Stability	Complications	Follow-up
			Allomaterial	Soft tissue coverage			
1	Chest wall tumor en bloc resection including skin spindle, musculature, partial resection of the 8th–10th ribs	Partial diaphragm resection, pulmonary wedge resection left lower lobe	15 × 20 cm × 1.5 mm Permacol and 10 × 10 cm × 1.5 mm Permacol for diaphragm	Latissimus dorsi flap graft	Excellent	None	Reoperation for local tumor recurrence at 14 mo, death at 32 mo due to distant metastasis
2	Chest wall tumor en bloc resection including the seventh–ninth ribs	None	10 × 10 cm × 1.5 mm Permacol	Direct (mobilized subcutaneous tissue and skin)	Good	None	Tumor relapse, patient alive under chemotherapy 42 mo
3	Complete sternum resection including skin	Partial resection of pleura and pericardium	15 × 20 cm × 1.5 mm Permacol	Pectoralis muscle	Good	None	Lost to regular follow-up, no CT scans, patient alive, no tumor relapse after 37 mo
4	Chest wall tumor en bloc resection including the complete seventh rib, partial resection of the sixth and eighth ribs	None	15 × 20 cm × 1.5 mm Permacol	Direct (mobilized subcutaneous tissue and skin)	Good	None	No local tumor recurrence, death at 17 mo due to cerebral metastasis
5	Chest wall tumor en bloc resection including partial resection of the fourth–sixth ribs	Pulmonary wedge resections right middle and lower lobes	15 × 20 cm × 1.5 mm Permacol	Direct (mobilized subcutaneous tissue and skin)	Moderate	None	No local tumor recurrence, death at 8 mo due to pelvic tumor relapse
6	Complete sternum resection	Partial resection of right pleura and pericardium	15 × 20 cm × 1.5 mm Permacol	Direct (mobilized subcutaneous tissue and skin)	Excellent	None	No local tumor recurrence, patient alive after 30 mo

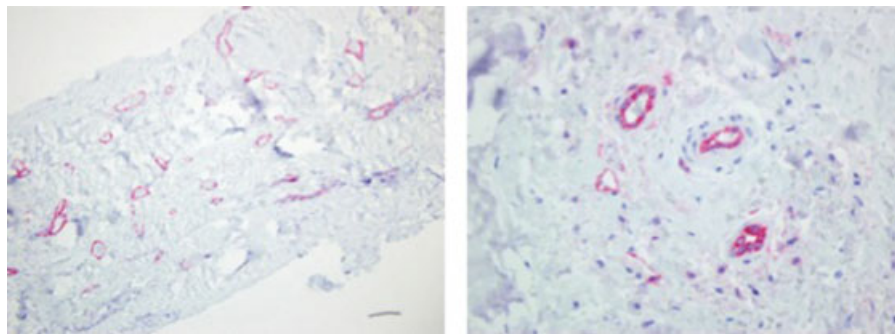


Fig. 4 Hematoxylin and eosin stain with immunohistochemistry of CD31 for neovascularization in explanted collagen matrix patch 14 months after initial implantation. Intimal cells are stained red. Tenfold magnification on left panel and 40-fold on right panel.

Follow-up and oncological outcome are shown in ► **Table 2**. Despite wide safety margins, patient 1 developed a local tumor relapse and underwent reoperation 14 months after his first tumor resection. The primary implanted patch was removed en bloc with the recurrent sarcoma. During gross and histological examination, the patch proved to be intact and well integrated into the surrounding tissues (► **Fig. 4**). IHC staining for CD31 showed remarkable neovascularization of the collagen matrix within the surrounding tissue. This observation is a substantial indication for biological integration of the collagen matrix patch.

Upon returning to his mid-eastern country of residence 4 months postoperatively, patient 3 was lost to personal follow-up. According to e-mail contact, the patient is healthy, without local impairments and is free of tumor recurrence.

Discussion

Following its introduction nearly 30 years ago, PTFE has emerged as the most frequently applied material for chest wall reconstructions. It allows for implantation under tension and results in a durable replacement of bony and soft tissues. Some surgeons even used methylmethacrylate sandwich techniques or large metal prostheses to create sufficient stability in large defects, especially in cases of sternal resections.^{2-6,17} Nevertheless, reconstructions with synthetic materials are associated with serious complications. Synthetic materials are known to cause seroma formation and excessive encapsulation by dense fibrous tissue. The latter may not only result in patient discomfort and impaired respiration but also in serious deformities such as scoliosis following chest wall replacement in children.^{15,16}

More importantly, PTFE materials do not overcome the main risk of all synthetic durable implants: infection. Although low complication rates have been described in some series, infection is a common problem, particularly in large reconstructions and sternal replacements ranging from 5 to 12%.^{2-6,8,9} Therefore, effective soft-tissue coverage with muscle flaps is essential, when applying synthetic allomaterials. A considerable number of synthetic patches had to be revised or explanted for these reasons. Mansour et al report 7% of flap complications or loss, and another 5% of surgical site infection.⁴ In 2006, Weyant et al showed that within 30 days complication rates were 38% for rigid methylmethacrylate

sandwich techniques and a 4.5% 90-day prosthesis removal rate was observed. For PTFE or polypropylene mesh, the 30-day mortality was 27% and the 90-day prosthesis removal rate was 4.1%.⁶ Supposedly, absorbable or composite meshes have a reduced infection risk. However, these implants may result in significant mid- and long-term instabilities, paradoxical respiratory movements, and finally herniation in the area of the reconstructed chest wall.^{1,3,4,8}

The rationale for employing collagen matrix patches in thoracic wall reconstruction is to combine the rigidity and durability of nonabsorbable synthetic materials with a reduced risk of infection.^{15,19}

A growing variety of biological collagen matrix meshes is commercially available. Unlike permanently fixated biological materials, this novel generation of materials allows for a remodeling process with neovascularization and complete integration. This process starts with the migration of host cells and the formation of new blood vessels. In this respect, our histological findings (► **Fig. 4**) in a patch explanted after 14 months support the data from other reports.^{7,19}

Our positive experiences with respect to strength, durability, and resistance to infection with this type of biological implant for thoracic wall reconstruction are in accordance with experimental and clinical findings of others.^{15-17,20} Most of the available data stem from the field of abdominal hernia repair.^{7,10,14,19} Only very few reports describe the application of collagen matrix patches in thoracic surgery.^{15-17,20} In abdominal hernia surgery, biological materials proved to be superior even to synthetic meshes with an overall success rate of 90%.²¹ However, to our knowledge, no experimental study exists which compares the biomechanical characteristics of collagen matrixes and synthetic materials directly. In an animal study of hernia repair contaminated by staphylococci, all cases with synthetic implants failed, whereas 67% of the animals with the biological patch type used by us experienced uncomplicated wound healing.²² Clinical studies in patients with contamination and overt infection of the surgical field resulted in similar outcomes.^{23,24}

However, for reconstruction of the thoracic wall characteristics of ideal materials and techniques of implantation are different. To minimize paradox respiratory movements, a patch must be implanted under tension and should not be stretchable. The ideal characteristics and strength of the biological material should resemble that of 1- to 2-mm-thick

PTFE membranes. Compared with other collagen matrixes, the product used in this study provides very good strength and durability owing to a thickness of 1.5 mm.

At this point, we would like to stress that origin and processing of a collagen matrix determines remodeling, stability, and durability. Whereas reduced susceptibility to infection is a common attribute of all these implants, strength and durability are not.

Tissues derived from dermis, intestinal submucosa, or pericardium of porcine, bovine, and human origin have been explored. The process of chemical cross-linking restricts the extent of degradation by collagenase digestion and the turnover of collagen fibers following implantation. On the contrary, cellular infiltration, neovascularization, and integration are delayed as well.^{7,17} Compared with a collagen matrix derived from porcine dermis, significantly higher failure rates were reported for non-cross-linked human acellular dermis in a systematic review of the published series of hernia repair. Non-cross-linked collagen mesh from human dermis, which undergoes extensive remodeling and is known to stretch with time, seems to be less suitable for use in thoracic surgery.²⁵

Application of collagen matrixes may also be beneficial for pediatric patients. Deformities of the spine are a well-known complication following thoracic wall reconstruction in children.¹⁵ Lin et al demonstrated that chest wall reconstructions with collagen matrix patches in pediatric patients did not lead to the development of clinically relevant scoliosis.

Handling and tailoring of the thick collagen patch was easy, it proved to be blood tight and a safe abutment for sutures. No seroma formation, wound healing problems, or infections were observed in this pilot study. The clinical, radiological, and histological findings in this study support long-term stability and effective integration of this type of collagen matrix implant. Our experience demonstrates that a porcine dermal-derived acellular collagen matrix is a viable alternative to PTFE for thoracic wall reconstructions. However, it is evident that this pilot study only allows limited conclusions. Also, the advantages of collagen matrix materials must be weighed against the considerably higher expense. Nevertheless, in complicated settings such as large defects, total sternal replacement, difficult soft-tissue coverage, contaminated surgical field, or pediatric surgeries, implantation of this biological patch appears to be justified.

Disclaimer

The German Society for Thoracic and Cardiovascular Surgery (DGTHG) and The Thoracic and Cardiovascular Surgeon neither endorse nor discourage the use of the new technology described in this publication.

Conflict of Interest

None of the authors has a conflict of interest to disclose.

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