Interactive CardioVascular and Thoracic Surgery 2022, 35(4), ivac196
https://doi.org/10.1093/icvts/ivac196 Advance Access publication 27 July 2022

ORIGINAL ARTICLE

EXPERIMENTAL

Cite this article as: Suzuki A, Konishi H, Suzuki T, Katsumata T, Hanaoka N, Nakamura K *et al.* A combination of polyglycolic acid fabric and fibrin glue prevents air leakage from a lung defect. Interact CardioVasc Thorac Surg 2022; doi:10.1093/icvts/ivac196.

A combination of polyglycolic acid fabric and fibrin glue prevents air leakage from a lung defect

Akiyo Suzuki[a], Hayato Konishi[a], Tatsuya Suzuki[a], Takahiro Katsumata[a], Nobuharu Hanaoka[a], Koichiro Nakamura[b], Chisa Matsubara[b], Shota Fujii[b] and Shintaro Nemoto [a,*]

[a] Department of Thoracic and Cardiovascular Surgery, Osaka Medical and Pharmaceutical University, Takatsuki, Osaka, Japan
[b] Division of Research and Development, Kyoto Medical Planning Co., Ltd., Kyoto, Japan

* Corresponding author. Department of Thoracic and Cardiovascular Surgery, Osaka Medical and Pharmaceutical University, 2-7 Daigaku-machi, Takatsuki, Osaka 569-8686, Japan., Tel: +81-72-6846264; fax: +81-72-6846542, e-mail: snemoto@ompu.ac.jp (S. Nemoto).

Received 8 February 2022; received in revised form 12 May 2022; accepted 22 July 2022

Key question

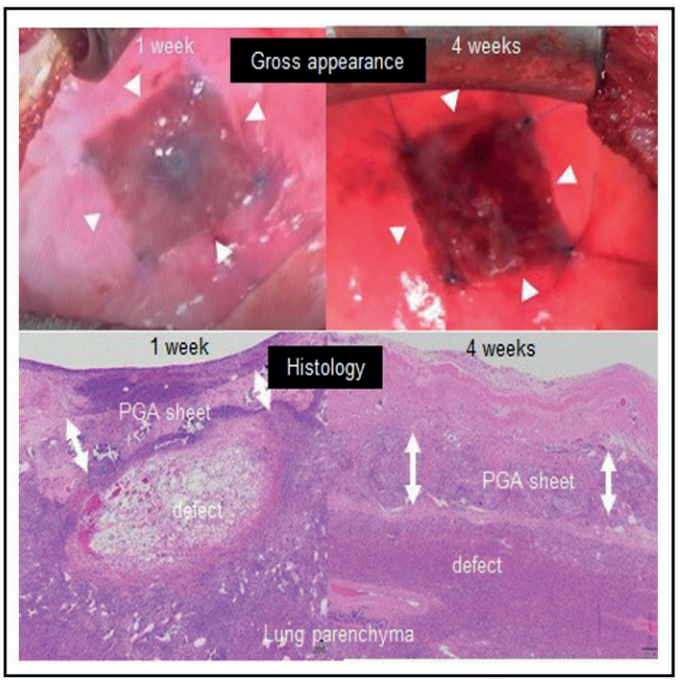
Is a combination of polyglycolic acid (PGA) fabric and fi brin glue (FG) effective for sealing a lung defect?

Key finding(s)

The PGA-FG combination prevented air leakage in a ca nine lung defect model and facilitated repair of the def ect.

Take-home message

Use of PGA fabric and FG may be a safe and non-toxic approach for prevention of air leakage in the critical pe riod after lung surgery.



Abstract

OBJECTIVES: Air leakage after lung resection is a common morbidity that may lengthen hospital stay. Applying sealant to a lesion is an effective prophylaxis in clinical practice. This study aimed to examine the effect of a combination of a bioabsorbable polyglycolic acid (PGA) fabric and fibrin glue (FG) on air sealing by measuring the *in vitro* mechanical strength and degradation of the fabric, and *in vivo* histological changes after implantation.

METHODS: A defect was created in the canine left upper lung lobe, and then filled with a fibrinogen solution and covered with a PGA sheet spray-coated with fibrinogen and thrombin. After 1 and 4 weeks, air leakage from the lesion was examined *in vivo* under airway pressure. Tissue samples were harvested for histological assessment.

RESULTS: The mechanical strength of the PGA fabric remained at 80–90% of the baseline level for 1 week in phosphate-buffered saline, and then rapidly decreased to zero thereafter. Air leakage from the lung defect was prevented by the combination of PGA fabric and FG at

1 and 4 weeks. Histological examinations showed that PGA bundles persisted with a non-specific inflammatory response for 2 weeks and then gradually broke into sparse yarns surrounded by collagen fibres and capillaries by 8 weeks. The lung defect was filled with FG at 1 week and by granulation tissue thereafter.

CONCLUSIONS: These results provide evidence for the efficacy of a combination of PGA fabric and FG for the prevention of air leakage in the critical period after lung surgery.

Keywords: Air leakage • Lung surgery • Sealant • Polyglycolic acid • Fibrin glue

ABREVIATIONS

FG	Fibrin glue
PBS	Phosphate-buffered saline
PEG	Polyethylene glycol
PGA	Polyglycolic acid

INTRODUCTION

Air leakage after lung resection is a common complication that may cause adverse events and increase medical costs [1, 2]. Various methods are used to prevent this leakage, including applying sealant to the lesion, which is widely recognized to be effective in clinical practice. Fibrin glue (FG) [3, 4], a collagen sheet with fibrinogen and thrombin [5], a cross-linked hydrogel using a biodegradable polymer (PEG: polyethylene glycol) [6–8] and a fabric sheet using biodegradable polymer (PGA: polyglycolic acid) with fibrinogen and thrombin [9–12] are used as sealant materials. Commercial synthetic products are the preferred and convenient choice, but PEG-based products are not available in Japan. Thus, a combination of a bioabsorbable PGA fabric and FG is the preferred method for covering a lung lesion in clinical practice. The plausibility of this approach has been reported [9], but its efficacy and safety are not proven beyond limited *ex vivo* data [9] and *in vivo* results in the acute phase at 24 h [10, 11] and in the long term at 6 months after implantation [12]. Therefore, this study aimed to measure the *in vitro* mechanical strength of the PGA fabric and evaluate *in vivo* histological changes for up to 8 weeks after implantation to examine the air sealing effect of the PGA fabric-FG combination.

The experimental study protocol and the quality assurance of the PGA fabric comply with the regulatory requirements for clinical approval in Japan.

MATERIALS AND METHODS

Ethical statement

The study was approved by the Institutional Animal Care and Use Committee of Osaka Medical and Pharmaceutical University (approval ID #21114-A). The animals received humane care based on the guidelines of this committee and the National Institute of Health Guidelines for the Care and Use of Laboratory Animals.

Design and fabrication of the polyglycolic acid sheet

The PGA sheet is a weft-knitted fabric composed of biodegradable PGA yarns. The fabric was needle-punched to control stretchability and improve dimensional stability. The ultimate tensile strength of the sheet was designed to decrease gradually to almost zero by hydrolysis in phosphate-buffered saline (PBS; Nacalai Tesque, Kyoto, Japan). The PGA sheet was manufactured under a quality management system stipulated by the International Organization of Standardization (ISO) 13485 protocol and was sterilized and packaged to meet standards for clinical use. The PGA sheets prepared for this study were manufactured by Kyoto Medical Planning Co., Ltd., Kyoto, Japan. Product quality was confirmed through strict spot inspection, following clinical product regulations in Japan.

Mechanical properties of the polyglycolic acid sheet

Mechanical properties of the PGA sheet were measured by uniaxial tensile testing, as previously described [13]. Samples were cut as 1 × 4 cm rectangles in the machine direction and traverse direction of the sheet and hung in a tensile test machine (SV-52NA-5M, Imada Seisakusho Corp., Aichi, Japan). The test was performed by stretching the samples at a speed of 20 mm/min at room temperature. The strain–stress relationship was obtained for each sample ($N = 6$).

In vitro mechanical strength and degradation of the polyglycolic acid sheet

To evaluate *in vitro* degradation, the PGA sheet was cut to 1 × 4 cm and immersed in PBS at pH 7.4 and 37°C ± 1°C for 4 weeks. After immersion in PBS, the samples were rinsed with distilled water and stored in a vacuum desiccator. The tensile test was performed in the machine direction and the ultimate tensile strength was determined for each sample ($N = 6$).

Application of the polyglycolic acid sheet with fibrin glue to a lung defect

Ten in total adult male beagles (age 15–19 months, body weight 10–13 kg, Oriental Bioservice Inc., Kyoto, Japan) were used in the study. Animals were intubated after induction with an intravenous injection of thiamylal sodium (25 mg/kg), general anaesthesia was maintained with inhaled sevoflurane. The left chest was opened by a standard thoracotomy, and then a round-shaped defect was made in the left upper lung lobe using a 6-mm biopsy punch [11]. Air leakage from the defect was confirmed under positive airway pressure. The defect was filled with 0.2 ml of fibrinogen solution (BOLHEAL, KM Biologics, Kumamoto, Japan) and then covered with the PGA sheet (1.5 × 1.5 cm), with the 4 corners of the sheet fixed using a 6–0 polypropylene suture (Ethicon, NJ, USA). Then, 3 ml of fibrinogen and thrombin solution (BOLHEAL) were sprayed on the PGA sheet and left for

5 min to allow fibrin gelation. This method was based on reports of the most effective sequential technique for use of the PGA fabric-FG combination [9–11]. After confirmation of no air leakage at 15 cmH_2O of airway pressure, the chest was closed. An intramuscular injection of butorphanol tartrate (0.2 mg/kg) was given for analgesia before the animals were awakened. Meloxicam (2.5 mg) was given orally for analgesia for 3 days after surgery. All animals were awakened and housed until further evaluations, as described below.

Histological examination

All animals were humanely euthanized by intravenous administration of a fatal dose of thiamylal sodium (100 mg/kg) in addition to inhaled sevoflurane. The PGA sheet and surrounding lung tissue were excised *en bloc*, with excision perpendicular to the sheet. After macroscopic observation, the excised tissue block was fixed with 10% formaldehyde. A sample slice was cut from the centre of the PGA sheet along the longitudinal direction of the sheet and embedded in paraffin. Slices were prepared by microtome sectioning and stained with haematoxylin and eosin. An inflammatory reaction to the PGA sheet, degradation of the sheet and changes in the surfaces of the lung injury and lung parenchyma were examined.

Evaluation of air leakage from the lung defect

Six animals were anaesthetized and mechanically ventilated as described above, and then the left chest was re-explored at 1 or 4 weeks after implantation ($N = 3$ each). The PGA sheet-implanted lung lesion was submerged in saline in the thoracic cavity. Air pressure was applied to the lung in steps of 5 cmH_2O up to 30 cmH_2O, and air bubbles from the implanted PGA sheet were checked. Tissue samples were obtained for histological examination after euthanasia, as described above.

Biological tissue reactions to the polyglycolic acid sheet

Four animals were used to evaluate fundamental biological reactions to the PGA sheet on the injured lung parenchyma. At 2 or 8 weeks after application of PGA with FG to a lung defect ($n = 2$ each), the animals were intubated, connected to a ventilator under general anaesthesia and euthanized as described above. A histological examination was then performed as described above.

RESULTS

Mechanical properties of the polyglycolic acid sheet

Scanning electron microscope images of fibres and the fabric structure of the PGA sheet (Fig. 1A) showed that the sheet was a porous and knitted fabric. Stress–strain curves (Fig. 1B) indicated differences between the machine direction and traverse direction of the sheet due to its weft-knitted structure. The sheet exhibited stretchability of 2–4 times the original length and had satisfactory ultimate tensile strength in both directions.

Changes in mechanical strength and degradation of the polyglycolic acid sheet *in vitro*

Measurements of the ultimate tensile strength (Fig. 1C) showed that PGA sheets maintained their initial shape in PBS for 4 weeks, but the sheets collapsed into fragments when retrieved from PBS. Therefore, a tensile test could not be performed at 4 weeks. The ultimate tensile strength of the sheet gradually decreased to about zero after 3 weeks of immersion in PBS.

Air leakage from the lung defect

Adhesion of the PGA-implanted area to the parietal pleura or intercostal muscle was not apparent at 1 week after implantation, but there was tight adhesion after 4 weeks. Air leakage from the PGA-implanted site did not occur under all tested airway pressures in all animals at both time points (Fig. 2).

Macroscopic findings in the air leakage test

The gross appearances of implanted PGA sheets upon completion of the air leakage test in all animals are shown in Fig. 3. The sheets were clearly recognizable at 1 week after implantation. At 4 weeks, after the careful release of the adhesion, the sheet was covered with fibrous tissue without a clear border and the lung defect beneath the sheet was not visible.

Histological findings in the air leakage test

Representative findings for specimens across the PGA sheet at 1 and 4 weeks after implantation are shown in Fig. 4. At 1 week, granulation tissue was present, and an acute inflammatory response was observed around the sheet. The bundles of PGA yarns remained unchanged in numbers and density. In contrast, at 4 weeks, the PGA bundles were fragmented into gracile and sparse yarns, with fibroblasts and collagen fibres infiltrated among the yarns, with the presence of macrophages and capillaries. Fibrin that filled the lung defect at 1 week after implantation was replaced by granulation tissue at 4 weeks. Of note, tissue dissection between the pulmonary injury surface and the PGA sheet did not occur, even under excessive positive airway pressure at both 1 and 4 weeks.

Histological findings for the implanted polyglycolic acid sheet

In a gross examination, the PGA sheets were clearly recognizable along with the lung defect area at 2 weeks after implantation, but the defect beneath the thickened PGA sheet was not visible at 8 weeks after implantation (Fig. 5A). Representative findings for specimens across the PGA sheet at 2 and 8 weeks after implantation (Fig. 5B) included inflammatory cells infiltrated around PGA bundles, along with foreign body giant cells and fibroblasts at 2 weeks, and reduced reactions with mild fibrotic changes at 8 weeks. Dense bundles of PGA yarns remained after 2 weeks, but these had loosened, and inflammatory cells had infiltrated among the yarns at 8 weeks. Inflammatory cells and fibroblast infiltration covered the surface of the injured lung at 2 weeks, but inflammation was reduced, and a connective tissue layer was

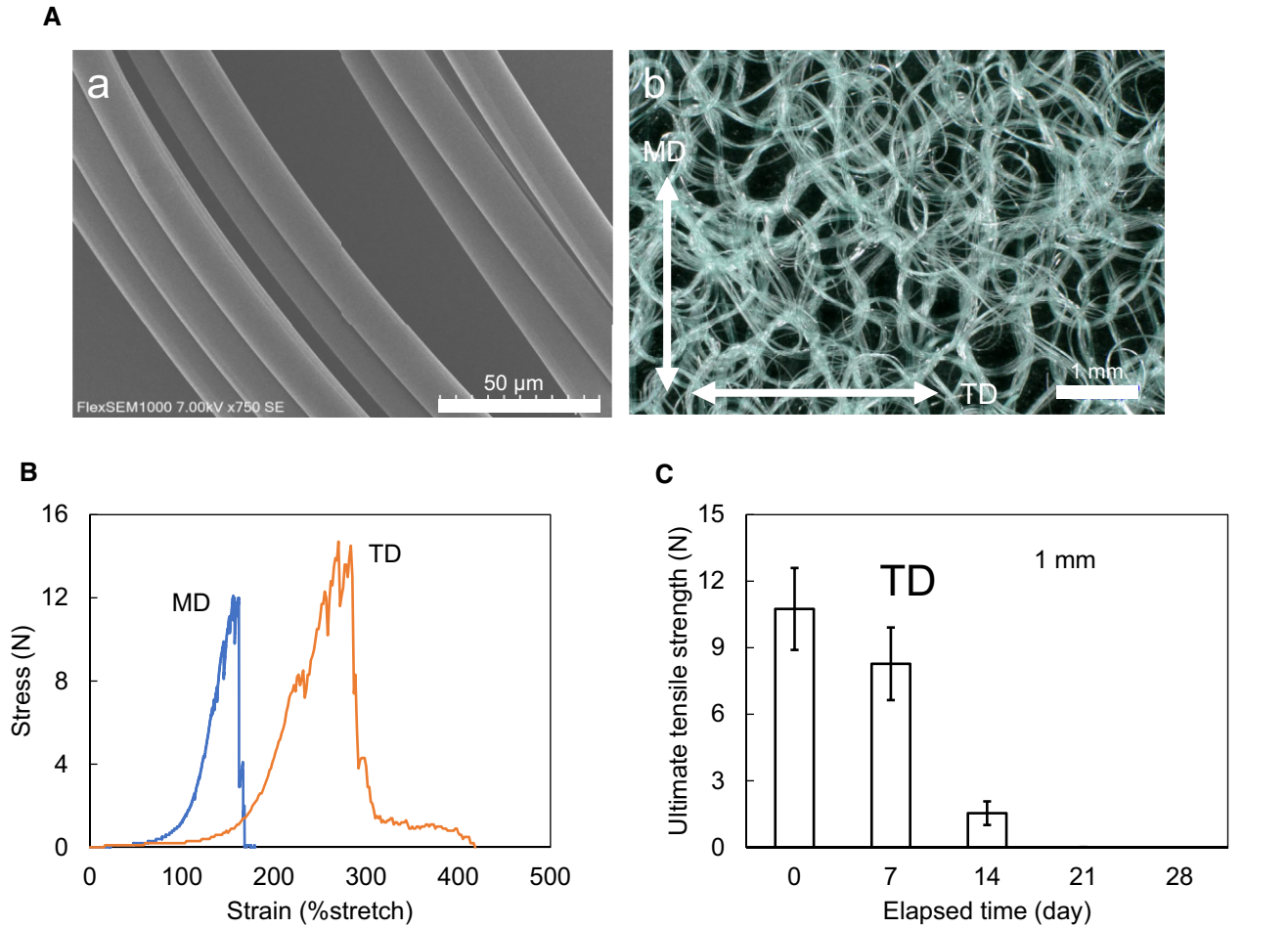


Figure 1: (**A**) Representative scanning electron microscope (**a**) and microscopic (**b**) findings for the polyglycolic acid (PGA) sheet. Double-ended arrows indicate the MD and TD of the PGA sheet. (**B**) Mechanical properties of the PGA sheet. Representative stress–strain curves of the MD and TD of the PGA sheet. (**C**) Changes over time in ultimate tensile strength of the PGA sheet by evaluation of *in vitro* degradation. MD: machine direction; TD: traverse direction.

present on the surface at 8 weeks. There were no significant changes in the lung parenchyma at both time points. FG remained at 2 weeks but had almost disappeared at 8 weeks after implantation.

DISCUSSION

The major findings of this study are as follows. First, *in vitro* mechanical strength of the PGA fabric was maintained at 80–90% of the baseline level for 1 week in PBS, but rapidly decreased to zero thereafter, along with degradation. Second, air leakage from a lung defect was prevented by a combination of PGA fabric and FG for 4 weeks after implantation. Third, serial histological examinations showed that PGA bundles persisted with non-specific inflammatory responses for 2 weeks after implantation and then gradually broke into sparse yarns surrounded by infiltrated collagen fibres and capillaries by 8 weeks. The lung defect was first filled with FG that firmly connected the PGA bundles to the lung parenchyma at 2 week, and granulation tissue gradually replaced the glue thereafter.

The prerequisites of sealant materials for lung air leakage have been described elsewhere [6, 8]. The sealants must be flexible and compliant to accommodate a volume change of the lung, providing a uniform surface tension to avoid tearing at the border of the application site, and must be sufficiently strong and adherent to the inflated lung with an airway pressure of 30–40 cmH_2O. The sealants must also bond to lung tissue rapidly and firmly, irrespective of underlying blood or moisture. Along with these mechanophysical properties, the materials used in sealants must be locally non-irritating, systemically non-toxic, non-antigenic and absorbable as chemically synthesized products. The effective duration or lifetime of sealants is also important. Most air leaks occur within 1 week after lung surgery, but 15–18% of patients suffer prolonged air leakage at more than 1 week [14, 15]. Therefore, air seal methods must work immediately after surgery until at least 1–2 weeks after surgery.

Given the mechanophysical, biochemical and temporal requirements, PEG-hydrogel or a PGA fabric-FG combination are viewed as potential sealants. Commercial PEG-hydrogel and FG alone have similar *in vitro* mechanical properties of compliance, stretchability, tensile strength and peel strength [16, 17]. However, the shear strength of FG is one-fourth to one-fifth that of PEG-hydrogel [16], which might explain the failure of FG alone for preventing air leak after lung surgery [3, 4]. PEG-hydrogel is used in clinical practice [6–8], but several concerns remain. First, it can be difficult to create a uniform layer thickness and area of the sprayed PEG-hydrogel because of cumbersome preparation and quick crosslinking and gelation times, which are within 5–10 s. This is important because the thickness and area may have significant influences on mechanical strength and adhesiveness.

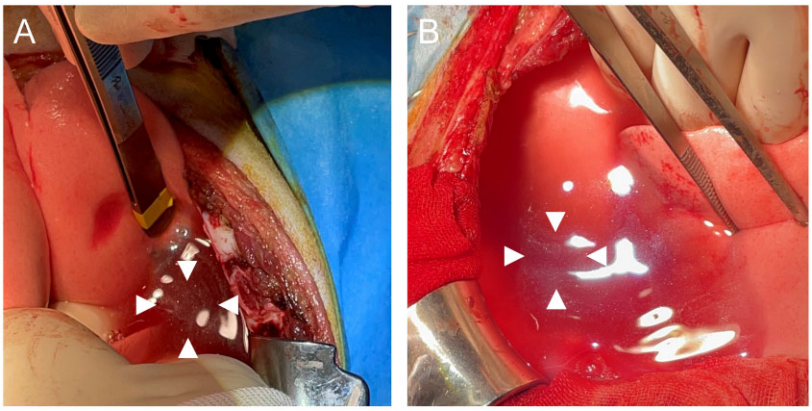


Figure 2: Gross appearance of air leakage at a pressure of 30 cmH_2O. The lung in the area (white arrowheads) implanted with a polyglycolic acid sheet was submerged in saline after implantation for 1 week (**A**) and 4 weeks (**B**).

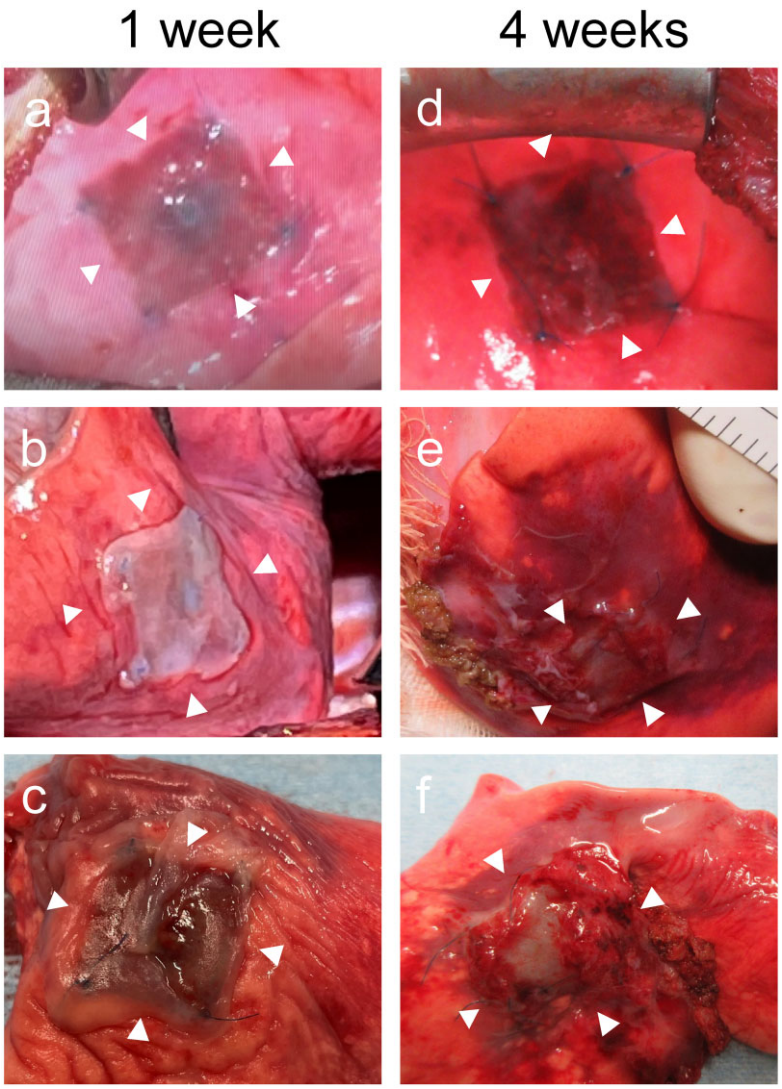


Figure 3: Gross appearance of the surface of the lung-implanted polyglycolic acid (PGA) sheet (white arrowheads) at implantation (**A**, **D**), at explantation (**B**, **E**) and after implantation for 1 and 4 weeks (**C**, **F**).

Second, PEG-hydrogel degrades completely within a relatively short period of about 6 days, and this may be accelerated by marked swelling of the baseline mass by 220–270% [16].

There are no similar concerns with the PGA sheet used in this study. The mechanical strength and stretchability are sufficient, and the product specification is consistent without specific

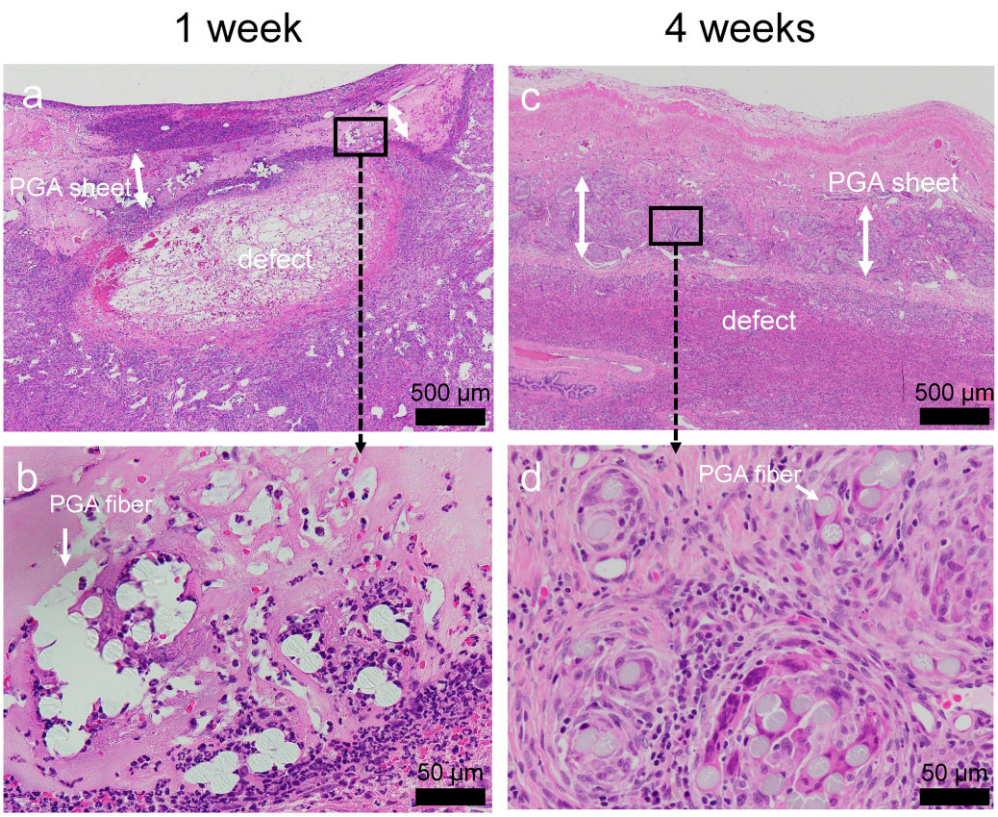


Figure 4: Histology of the polyglycolic acid (PGA) sheet explanted from the lung after 1 week (**A**, **B**) and 4 weeks (**C**, **D**) using haematoxylin and eosin staining: (**A**, **C**) low-power field (**B**, **D**) high-power field.

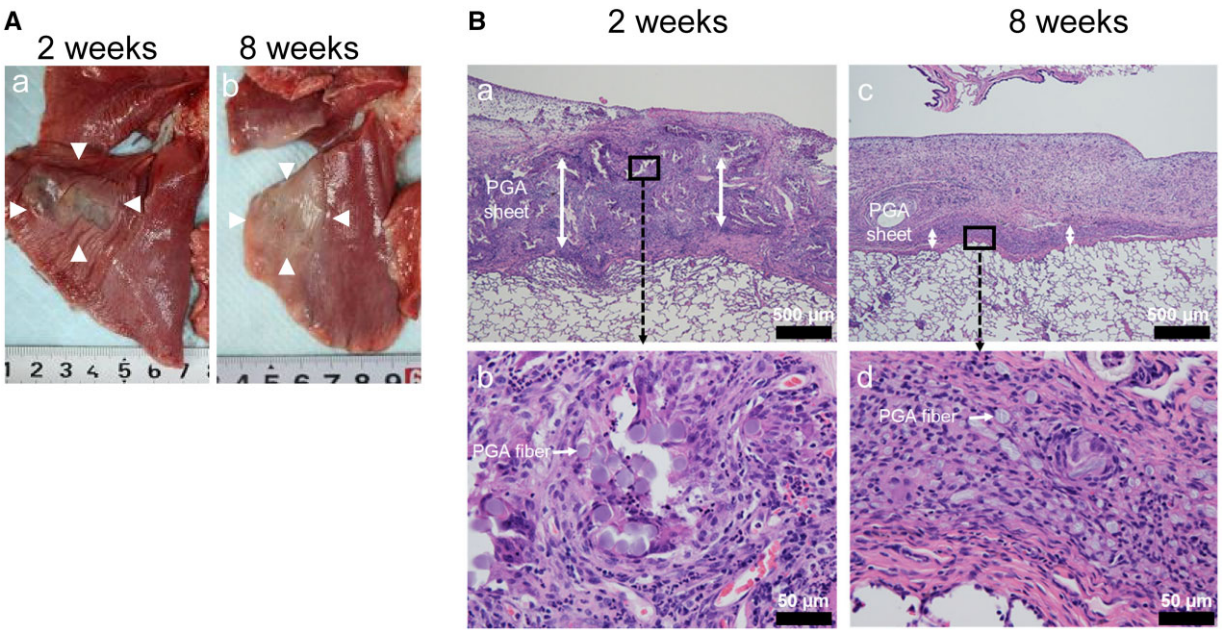


Figure 5: (**A**) Gross appearance of the PGA sheet (white arrowheads) implanted on the lung. Surfaces of the explanted PGA sheet after implantation for 2 weeks (**a**) and 8 weeks (**b**). (**B**) Histology of the explanted PGA sheet after 2 weeks (**a**, **b**) and 8 weeks (**c**, **d**) using haematoxylin and eosin staining: (**a**, **c**) low-power field, (**b**, **d**) high-power field. PGA: polyglycolic acid.

preparation, as shown in the study. In particular, the degradation period of the PGA sheet covers the clinically critical period of postoperative air leakage. The efficacy of the PGA fabric-FG combination for the prevention of air leakage from lung parenchyma has been shown in experimental and clinical settings.

In addition to the prerequisites in mechanopysical properties, the synthetic polymer used as a tissue sealant must have a potential inducing tissue healing initiated by cell attachment over the injured lung parenchyma. It is well known that various cells attach the surface of aliphatic polymers (PGA, poly-ε-caprolactone, etc.) and PGA has been used as a scaffold in tissue engineering [18]. Histology clearly revealed the incremental tissue healing by the combination in our *in vivo* experimental model. On the other hand, hydrophilic polymers, especially PEG, easily swell as hydrogel and typically exhibit bio-inert and poor bioactive characteristics of inhibiting cell attachment due to the non-adhesive nature of the PEG chains [19]. While PEG has been recognized as an excellent material for anti-adhesion [20], a various meticulous modification to add bioactivity to PEG have been attempted in tissue engineering but not succeeded for the practical use [21]. Therefore, we prefer to use PGA for the lung sealant with an increment of adhesiveness with the aid of FG.

In summary, this study suggests that the mechanism of air sealing by the PGA fabric-FG combination may involve strong bonding by FG between the compliant and strong PGA fabric and the damaged lung parenchyma in the early postoperative period of 4 weeks. PGA fabric-induced granulation tissue may then prevent air leakage during the postoperative period. After 2 months, the lung defect was covered completely with a newly developed connective tissue layer containing sparse and weak PGA fibres. These results add evidence for the efficacy of the PGA fabric–FG combination in the critical period for air leakage after lung surgery and may stimulate further developments of synthetic polymers for surgical use.

Limitations

A simple injury created in the normal healthy lung parenchyma was used in this study. Therefore, it is not certain that the air sealing effect of the combination of the PGA fabric and FG will be replicated in patients with lung parenchyma disease, because of difficulty in establishing experimental settings. However, we have been applying the combination therapy in the daily clinical practice and have witnessed the effectiveness of the air sealing even in the patients with emphysema or heavy smokers, in whom the fragile pleura easily tears by sutures. Taken together with the clinical facts, the air sealing effect of the combination is likely irrespective of the physical nature of the lung.

ACKNOWLEDGEMENTS

We are grateful to Fumiyo Shimada for coordinating the animal studies and data collection, and Takafumi Ogawa (Kyodo Byori Inc., Kobe, Japan) for the histological preparations.

Funding

This work was partially supported by Kyoto Medical Planning Co., Ltd., Kyoto, Japan.

Conflict of interest: Shintaro Nemoto received a consultation fee from Kyoto Medical Planning for the regulatory approval of the PGA fabric in Japan. Koichiro Nakamura, Chisa Matsubara and Shota Fujii are employees of Kyoto Medical Planning. The other authors declared no conflict of interest.

Data availability

All relevant data are within the manuscript. The data underlying this article will be shared on reasonable request to the corresponding author.

Author contributions

Akiyo Suzuki: Data curation; Investigation. **Hayato Konishi:** Data curation; Investigation. **Tatsuya Suzuki:** Data curation; Investigation. **Takahiro Katsumata:** Supervision. **Nobuharu Hanaoka:** Supervision; Validation. **Koichiro Nakamura:** Data curation; Formal analysis; Investigation; Writing—original draft. **Chisa Matsubara:** Data curation; Formal analysis; Investigation; Methodology. **Shota Fujii:** Data curation; Formal analysis; Investigation. **Shintaro Nemoto:** Conceptualization; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Writing—review & editing.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Cai Cheng, Roman Gottardi, Vanessa Diaz-Ravetllat and the other anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

[1] Okereke I, Murthy SC, Alster JM, Blackstone EH, Rice TW. Characterization and importance of air leak after lobectomy. Ann Thorac Surg 2005;79:1167–73.
[2] Yoo A, Ghosh SK, Danker W, Kassis E, Kalsekar I. Burden of air leak complications in thoracic surgery estimated using a national hospital database. Clinicoecon Outcomes Res 2017;9:373–83.
[3] Fleisher AG, Evans KG, Nelems B, Finley RJ. Effect of routine fibrin glue use on the duration of air leaks after lobectomy. Ann Thorac Surg 1990; 49:133–4.
[4] Wong K, Goldstraw G. Effect of fibrin glue in the reduction of postthoracotomy alveolar leak. Ann Thorac Surg 1997;64:979–81.
[5] Anegg U, Lindenmann J, Matzi V, Smolle J, Maier A, Smolle-Jüttner F. Efficiency of fleece-bound sealing (TachoSil) of air leaks in lung surgery: a prospective randomized trial. Eur J Cardiothorac Surg 2007;31: 198–202.
[6] D'Andrilli A, Andreetti C, Ibrahim M, Ciccone AM, Venuta F, Mansmann U *et al.* A prospective randomized study to assess the efficacy of a surgical sealant to treat air leaks in lung surgery. Eur J Cardiothorac Surg 2009;35:817–21.
[7] Lequaglie C, Giudice G, Marasco R, Morte AD, Gallo M. Use of a sealant to prevent prolonged air leaks after lung resection: a prospective randomized study. J Cardiothorac Surg 2012;7:106–12.
[8] Wain JC, Kaiser LR, Johnstone DW, Yang SC, Wright CD, Friedberg JS et al Trial of a novel synthetic sealant in preventing air leaks after lung resection. Ann Thorac Surg 2001;71:1623–9.
[9] Kawai H, Harada K, Ohta H, Tokushima T, Oka S. Prevention on alveolar air leakage after video-assisted thoracic surgery: comparison of the efficacy of methods involving the use of fibrin glue. Thorac Cardiovasc Surg 2012;60:351–5.
[10] Itano H. The optimal use of combined application of fibrin sealant and bioabsorbable felt against alveolar air leakage. Eur J Cardiothorac Surg 2008;33:457–60.
[11] Sakai T, Matsutani N, Kanai E, Yamauchi Y, Uehara H, Iinuma H *et al.* Efficacy of a sheet combined with fibrin glue in repair of pleural defect at the early phase after lung surgery in a canine model. Gen Thorac Cardiovasc Surg 2018;66:103–7.

[12] Kanai E, Matsutani N, Aso T, Yamamoto Y, Sakai T. Long-term effects of pleural defect repair using sheet material in a canine model. Gen Thorac Cardiovasc Surg 2020;68:615–22.
[13] Nemoto S, Konishi H, Shimada R, Suzuki T, Katsumata T, Yamada H *et al.* In situ tissue regeneration using a warp-knitted fabric in the canine aorta and inferior vena cava. Eur J Cardiothorac Surg 2018;54:318–27.
[14] Brunelli A, Monteverde M, Borri A, Salati M, Marasco RD, Fianchini A. Predictors of prolonged air leakage after pulmonary lobectomy. Ann Thorac Surg 2004;77:1205–10.
[15] Isowa N, Hasegawa S, Bando T, Wada H. Preoperative risk factors for prolonged air leak following lobectomy or segmentectomy for primary lung cancer. Eur J Cardiothorac Surg 2002;21:951–4.
[16] Vakalopoulos KA, Wu Z, Kroese L, Kleinrensink G-J, Jeekel J, Vendamme R *et al.* Mechanical strength and rheological properties of tissue adhesives with regard to colorectal anastomosis. Ann Surg 2015;261: 323–31.
[17] Azadani AN, Matthews PB, Ge L, Shen Y, Jhun CS, Guy S *et al.* Mechanical properties of surgical glue used in aortic root replacement. Ann Thorac Surg 2009;87:1154–60.
[18] Mikos AG, Bao Y, Cima LG, Ingber DE, Vacanti JP, Langer R. Preparation of poly (glycolic acid) bonded fiber structures for cell attachment and transplantation. J Biomed Mater Res 1993;27:183–9.
[19] Lee JH, Lee HB, Andrade JD. Blood compatibility of polyethylene oxide surfaces. Prog Polym Sci 1995;20:1043–79.
[20] Lih E, Oh SH, Joung YK, Lee JH, Han DK. Polymers for cell/tissue anti-adhesion. Prog Polym Sci 2015;44:28–61.
[21] Zhu J. Bioactive modification of poly (ethylene glycol) hydrogels for tissue engineering. Biomaterials 2010;31:4639–56.