Original Article

3D-printing on human acellular dermis for chest wall reconstructions—an *in vitro* and *in ovo* study

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Background: Massive bone or tissue defects caused by trauma, tumors or infections are a frequently occurring clinical problem. Novel biomaterials combined with new technologies offer new treatment options especially regarding reconstruction of bone and tissue. Aim of this study was to establish the stable and biocompatible combination of decellularized human dermis with a stable polymer via three-dimensional (3D) printing.

Methods: Polylactide (PLA) models were 3D-printed onto human acellular dermis (hAD) membranes using FreeCAD (computer-aided design) software for modeling and Ultimaker 2+ for printing. Cytotoxicity was assessed using L929 fibroblast cells in an 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumbromid (MTT) assay analogue to DIN EN ISO 10993-5 guidelines. Laser microtome sectioning was performed to enable histological analysis involving hematoxylin-eosin (HE) staining for tissue morphology assessment. The chorioallantoic membrane (CAM) assay was conducted on fertilized chicken eggs to evaluate cytotoxic effects and vascular ingrowth, by microscopic imaging.

Results: PLA was successfully 3D-printed onto hAD, forming a stable bond. After 72 hours of incubation in PBS, the printed structure remained securely attached. Histological analysis confirmed the integrity of the collagen structure after printing with high temperatures, with only slight compression in the top layer of the hAD. Cytotoxicity testing according to ISO 10993-5 showed no significant reduction in cell viability (83%), thereby demonstrating biocompatibility. The CAM assay demonstrated vascular integration, with vessels forming around and connecting to the hybrid material.

Conclusions: The successful 3D printing of PLA onto hAD resulted in a stable hybrid material with preserved structural integrity and good fluid resistance. Histological and cytotoxicity analyses confirmed biocompatibility, while the CAM assay demonstrated vascular integration. These findings suggest that the hAD-PLA composite holds potential for biomedical applications, particularly in tissue engineering.

Keywords: Three-dimensional-printing (3D-printing); chest wall reconstruction; human acellular dermis (hAD); biocompatibility; chorioallantoic membrane-assay (CAM-assay)

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Introduction

Background

Massive bone or tissue defects caused by trauma, tumors or infections are a frequently occurring clinical problem. New biomaterials combined with new technologies offer new treatment options especially regarding reconstruction of bone and tissue (1). One option is the combination of decellularized human dermis with 3D printing.

Research on decellularised human acellular dermis (hAD) used as transplant started at the end of last century. The advantage is that they are non-immunogenic, demonstrate a good biocompatibility and enhance growth of host cells and blood vessels (2,3). They are attractive for recellularization, which has been first demonstrated for resurfacing and reconstruction after massive burns (4). The first description of a standardized production of such a decellularized dermis was described in 2011, confirming the biocompatibility as well as *in vivo* tissue reactivity following implantation in a murine model (5). This so-called Epiflex membrane was approved as a drug in Germany (6). Further analyses confirmed that the processing described in this study neither influenced the collagen structure network nor the extracellular matrix or biomechanical properties (7). Since then these decellularised tissues have been used in the treatment of various diseases for tissue reconstruction, for example: Peyronie's disease (8), thoracic surgery (9-12), breast reconstruction (13), after proctocolectomy (14), in oral soft tissue augmentation (15) and potentially for critical size bone defects (16). hAD is used for chest wall reconstruction and demonstrates resistance to infections. Moreover, it's potential in promoting bronchial anastomotic healing in the presence of pre- operative radiotherapy (17). The potential of human acellular collagen matrices for clinical applications has been reviewed shortly (16). However, while decellularized human skin tissue does not trigger allo-reactive immune responses and is generally biocompatible, the underlying immunological mechanism controlling hAD integration, effective tissue repair, and wound healing remain poorly understood (18).

Despite the potential benefits of hAD compared to artificial reconstructive materials in cases of chest wall reconstruction many clinical issues remain. These issues arise from the fact that the chest consists of soft tissue and cartilaginous and bony structure. This combination of different tissues with differing stiffness ensure the biomechanical properties of the chest wall facilitating breathing mechanics as well as it provides a protecting for the vital chest viscera. A soft reconstruction material alone cannot mimic these features of the chest wall. Therefore, in cases of larger lateral defects or defects including the sternum different methods are used for the reconstruction. A traditional commonly used form of reconstructions, are non-resorbable surgical meshes augmented with bone cementwhich are sutured to the chest wall. The resulting biomechanical properties are poor, since inverse movements of the chest during the breathing cycle are frequently occurring and the construction is susceptible to infection. The combination of titanium bars and human or

Highlight box

Key findings

- It is possible to print polylactide (PLA) on human acellular dermis (hAD), offering a non-toxic and biocompatible solution. After printing, the acellular dermis maintains its structural integrity and remains stable in fluids for up to seven days of incubation. Additionally, the observed connection to vessels in ovo further supports its biocompatibility, making it a promising material for various applications.

What is known and what is new?

- It is known that hAD can support wound healing, particularly in soft tissue reconstruction. However, due to the lack of mechanical stability/stiffness, it cannot be used in areas with different mechanical requirements, such as the thorax, without an additional stabilising component.
- This study demonstrates the feasibility of printing hard materials like PLA directly onto an hAD without destroying its structure. By combining hAD with a 3D printed PLA scaffold, mechanical stability and improved wound healing and angiogenesis could be achieved.

What is the implication, and what should change now?

- This pilot in vitro study shows the potential of the hybrid material combining hAD and PLA, especially regarding the prospect of individualized medicine with implants printed for the individual tissue injuries of the patient. Nevertheless, the potential of this hybrid material has to be confirmed in *in vivo* studies.

porcine AD is an appealing alternative method (19,20), yet there is only one commercially available device (Stratos®, MedXpert, Germany). Fixation of these bars to the rib stumps by clamps induce a soft tissue damage impairing the blood supply. Moreover, the bars themselves and the quite bulky joints are a threat to the covering soft tissue. Especially in cases with limited local soft tissue coverage or in cases where free soft tissue flaps are used. the constant shear stress of the sharp metal bar and especially on the bulky joints can cause erosion of the soft tissue reconstruction exposing the metal implants.

An alternative could be provided with the help of the 3D printing technology. In the field of surgery, this technology has emerged as a new tool, enabling remarkable levels of customization, precision, and innovation. By creating three-dimensional objects layer by layer from digital models, 3D printing allows for the production of patient-specific anatomical models, surgical tools, implants, and prosthetics (21). Nevertheless, although many advantages exist various challenges still have to be overcome (22). One promising material for 3D-printing in medicine is polylactide (PLA). It is widely used in the field of medicine as it is biocompatible and cost effective. Regarding 3D-printing in tissue engineering and regenerative medicine, PLA has been mostly applied to manufacture bone tissue scaffolds, sometimes combined with other materials like hydrogels (23).

By combining the advantages of hAD with the PLA 3D-printing technology the above described problems, difficulties and negative effects can be addressed and eliminated.

Rationale and knowledge gap

Despite the potential benefits of hAD compared to artificial reconstructive materials in cases of chest wall reconstruction many clinical issues remain. These issues arise from the fact that the chest consists of soft tissue and cartilaginous and bony structure. These combination of different tissues with differing stiffness ensure the biomechanical properties of the chest wall facilitating breathing mechanics as well as it provides a protecting for the vital chest viscera. A soft reconstruction material alone cannot mimic these features of the chest wall.

Objective

Goal of this study was to test, whether it is possible to produce a hybrid material that combines the positive aspects of hAD with a hard material to avoid the described clinical problems. Therefore 3D-printing technology was utilized to print PLA-structures onto hAD and to test how stable the connection is, whether this combination is biocompatible and whether the printing process destroys the hAD structure. We present this article in accordance with the MDAR reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-767/rc).

Methods

Printing of PLA models on hAD membrane

For 3D printing of commercially available PLA (Ultimaker white PLA, iGo3D, Hannover, Germany) onto the Epiflex membrane, models were created using an open-source 3D modelling software (FreeCAD) to produce the Epiflex/PLA models. Round plates with a diameter of 5 mm and a height of 1 or 0.5 mm were created, which were then prepared for 3D printing in Cura (Ultimaker B.V., Geldermasen, The Netherlands). The standard settings and a Z-offset of 1.8 mm were set in the slicing program for printing. The models were printed with the Ultimaker 2+ (Ultimaker B.V., Geldermasen, The Netherlands) on Epiflex pieces (Deutsches Institut für Zell- und Gewebeersatz, Berlin, Germany, DIZG) which were fixed to the print bed. Before the subsequent tests, the models were incubated in saline solution for 1 hour. This incubation time was chosen in accordance with the manufacturer (https://dizg.de/gewebetransplantat/epiflex-perforiert/) and former experiments (6).

Tensile testing

Tensile tests were performed in accordance with DIN EN ISO 527-1 using the ZWICK Roell Z010 tensile testing machine (ZwickRoell, Ulm, Germany) equipped with force transducer Xforce P 500 N. The samples were positioned centrally within the clamping device (Type 8033, F_{max} =200 N) featuring a vulcanized coating and were securely fixed to prevent slippage. The tensile testing parameters included a preload of 5 N, an extension module speed of 5 mm/min, a testing speed of 5 mm/min, and a clamping length of 20 or 10 mm at the start position. Data were recorded using the testXpert software.

Tests were performed on samples with an approximately size of 1 cm × 3 cm. Different samples were tested: Epiflex and Epiflex loaded with PLA. Some samples were tested

without any further pretreatment, others were soaked in PBS for 30 minutes at room temperature. For Epiflex samples loaded with PLA the clamping differs between only clamping the Epiflex membrane (20 mm) or clamping both (Epiflex and PLA – 10 mm). The positioning of the clamping during tensile testing influenced the mechanical behavior. In some cases, clamping the sample at the PLA lattice results in initial breakage of the PLA component, followed by further stretching of the Epiflex membrane, highlighting the importance of test setup and mechanical interface. Ethical approval is not required for the in ovo study.

Cytotoxicity

For *in vitro* cytotoxicity tests, L929 cells (Mouse fibroblast cell line, NCTC clone 929, CCL-1, ATCC, Manassas, USA) were used in an assay according to DIN EN ISO 10993-5. The printing of the Epiflex/PLA models was performed as described above. Ten thousand cells/well were seeded in a 96-well plate for 24 h. Subsequently, the L929 medium was replaced with supernatants from Epiflex/PLA models, incubated for 24 h. Following incubation, the treatment fluid was exchanged with 100 µL/well of a 1 mg/mL 3-(4,5- dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Sigma-Aldrich, St. Louis, MO, USA) solution in serum-free medium. The treated L929 cells were incubated with the MTT solution for 3h before the solution was replaced by 100 µL isopropanol/well (Thermo Fisher Scientific, Waltham, MA, USA). Finally, absorbance was measured with the Tecan (570/560 nm; Tecan).

Histology

For histological examination the sample was cut in slices by a laser microtome and then subjected to hematoxylin and eosin (HE) staining (LLS Rowiak LaserLabSolutions GmbH, Hannover, Germany), and the stained sections were examined under a microscope to analyze the tissue morphology and identify any abnormalities.

Proliferation/microscopy

Proliferation was measured with alamarBlue-assay (Invitrogen, Karlsruhe, Germany) according to the manufacturer's protocol. Normal human dermal fibroblasts (5×10^4 cells) were seeded on the printed scaffolds, which were placed in ultra-low-attachment 24-well plates (Corning Life Sciences, Corning, NY). After 1 and 4 days the cell culture media was removed. The cells were incubated with 500 mL of a 10% solution of alamarBlue in cell culture media (DMEM-F12, 10% FCS and 1% P/S) for 4 h at 37 ℃. Subsequently, the media were transferred into 96-well plates and the fluorescence intensity was measured using the GlomaxVR-Multi Detection System (filter with 525 nm extinction and 580–640 nm emission, PromegaVR, Madison, WI, USA).

To allow analysis by fluorescent microscopy cells were transduced with lentiviral vectors encoding the enhanced green fluorescent protein. Vector supernatants were collected and concentrated from transfected 293T producer cells as previously described (24). For gene transfer, 15,000 normal human dermal fibroblasts (NHDF) were seeded into 24-well tissue culture plates (Greiner, Frickenhausen, Germany) in 500 µL media supplemented with 5 g/mL protamine sulfate. Two rounds of transduction on day 1 and 3 were performed at a cumulative multiplicity of infection (MOI) of ~100 to achieve >98% gene marking. Transduction efficiency was confirmed by fluorescence microscopy (Wilovert AFL30, Hundt, Wetzlar, Germany) and flow cytometry FACSCalibur (BD Biosciences, San Jose, CA, USA) using the CellQuestPro Software (BD Biosciences, San Jose, CA, USA). Transduced cells were seeded onto the scaffolds and the spreading, morphology and distribution of the cells analyzed microscopically with a fluorescent microscope.

Chorioallantoic membrane (CAM) assay

The CAM assay is a widely used *in vivo* model for studying angiogenesis and biocompatibility of materials as the CAM itself is a highly vascularized membrane, where interactions with implanted materials, such as biomaterials, can be easily and cost effectively analyzed. The CAM assay was performed to evaluate possible cytotoxic effects on an organism based on the printed models and to observe possible vascular ingrowth. Fertilised white Leghorn chicken eggs (LSL Rhein-Main, Dieburg, Germany) were used for the CAM assay. As previously described, the eggs were incubated horizontally at 37 ℃ and 60% humidity in an egg incubator (25) (Brutmaschine-Janeschitz GmbH, Hammelburg, Germany). On day 3 of incubation, approximately 6mL of albumin was aspirated from the egg using a sterile 10 mL syringe and a small window was cut into the shell using sterile scissors. The eggs were then incubated further. On day 7, the objects were placed on the

Figure 1 PLA structure printed on hAD. hAD, human acellular dermis; PLA, polylactide.

Figure 2 Hybrid material of hAD with printed PLA-structure after a 72-hour incubation in PBS. hAD, human acellular dermis; PBS, phosphate buffered saline; PLA, polylactide.

CAM. The eggs were incubated until day 14. Microscopic analyses were taken at 10× magnification with a digital microscope (KEYENCE, Neu-Isenburg, Germany). Subsequently, the embryos were euthanized by cutting the main vessels.

Statistical analysis

For the assessment of *in vitro* cytotoxicity and cell proliferation, three biological replicates with three technical replicates, respectively, were conducted for each sample. The mean was calculated from the values, and the standard deviation was determined and displayed in the bar chart.

Results

Printing results

As described in materials and methods PLA was 3D-printed onto the hAD. The theory was that the PLA melts into the material due to the high printing temperature, resulting in a stable bond between the two materials. *Figure 1* shows the printed PLA structure on the hAD.

Stability in fluids

Although the PLA structure was stably connected to the dry hAD directly after printing, the question was, whether this connection is also stable after incubation in fluids. After incubation for 72 h in PBS the printed structure was still stably connected to the hAD as shown in *Figure 2*.

Tensile testing

Tensile testing was performed to detect the influence of incubation in buffer as well as the influence of the printed structure on the stability of the hAD. Young's Modulus and tensile strength were determined and compared. *Figure 3* and *Table 1* show the results obtained:

A comparative analysis between the samples 'Epiflex–untreated' and 'Epiflex–soaked in PBS' reveals that soaking the Epiflex membrane in PBS for 30 minutes leads to a significant increase in flexibility. This is evidenced by a notable decrease in Young's modulus from 186.92 to 10.34 MPa. While the impact on tensile strength is minor, a slight decrease is observed, indicating that the material becomes less rigid upon soaking.

When comparing pure Epiflex samples with composites consisting of Epiflex and PLA, distinct differences emerge. In the untreated state, the addition of PLA does not alter the tensile strength but significantly increases the Young's modulus from 186.92 to 413.24 MPa, resulting in a more rigid composite material. For samples soaked in PBS, both tensile strength and Young's modulus are slightly reduced, indicating that the PBS pretreatment affects not only the Epiflex membrane but also the composite's overall stiffness, albeit to a lesser extent.

Across all untreated samples, the tensile strength ranges narrowly between 10.56 and 13.17 MPa. In contrast, PBS-treated samples show a slight reduction in tensile strength. However, the most pronounced change is observed in the Young's modulus, which clearly distinguishes untreated and

Table 1 Mechanical properties of tested samples including maximum force, tensile strength and Young's modulus

Sample	Maximum force (N)	Tensile strength (MPa)	Young's modulus (MPa)
Epiflex–untreated	130.02	11.04	186.92
Epiflex–soaked in PBS	128.60	9.03	10.34
Epiflex/PLA–untreated–clamped at Epiflex	160.32	10.56	413.24
Epiflex/PLA–soaked in PBS–clamped at Epiflex	140.07	7.10	9.68
Epiflex/PLA–untreated–clamped at PLA	189.27	13.17	459.88
Epiflex/PLA–soaked in PBS–clamped at PLA	43.50	2.26	127.43

Values are presented as mean. PBS, phosphate buffered saline; PLA, polylactide.

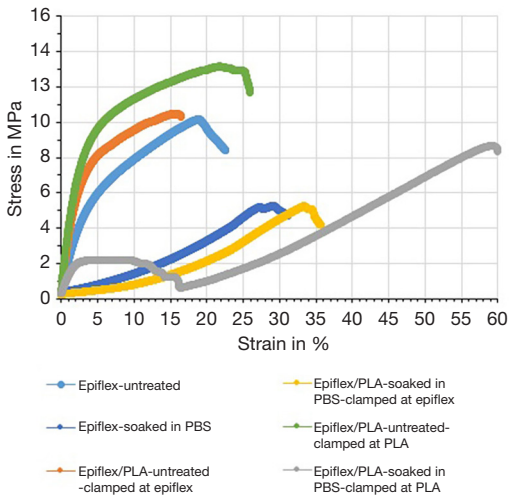

Figure 3 Stress strain diagram of tested samples. The diagram shows the mean values of all tested samples of each kind. PBS, phosphate buffered saline; PLA, polylactide.

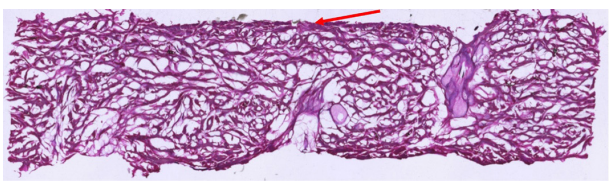

Figure 4 HE staining of the hAD after printing processes. The red arrow indicates the compressed structure of the top layer whereas the other parts of the hAD demonstrate the normal collagen structure. Magnification 10×. hAD, human acellular dermis; HE, hematoxylin and eosin.

soaked samples. Untreated specimens demonstrate higher stiffness and lower flexibility, while PBS-soaked samples exhibit significantly increased flexibility due to their lower Young's modulus.

Histology

To the next step was to analyze the tissue morphology and to identify any abnormalities caused by high printing temperatures. *Figure 4* shows that the collagen structure of hAD is still intact. Only the top layer of the collagen structure of the hAD seems to be slightly compressed due to the PLA printing process at high temperatures.

Cytotoxicity

The next step was to confirm the biocompatibility of the 3D-printed hybrid material. The viability of the L929 cells incubated in medium supernatants of the hAD-PLA was marginally yet not significantly decreased (83%) compared to the viability of the cells cultured in the normal culture medium. As a reduction in cell viability exceeding 30 % is indicative of cytotoxicity, this assay confirmed the biocompatibility of the hybrid material (*Figure 5*).

Seeding and proliferation of fibroblasts

NHDF were seeded on the printed material and analyzed for their proliferation capacity and microscopically. *Figure 6A* demonstrates that the cells proliferate from day 1 to day 4 after seeding. This is confirmed by the microscopic analyses of the cells (*Figure 6B,6C*), showing the adhered and morphological typical fibroblasts.

CAM-assay

The printed hybrid material was placed onto the CAM and after several days the integration was analyzed micorscopically. *Figure 7* shows that the hybrid material is surrounded by vessels that also connect directly to the material. This can be observed with the material lying on

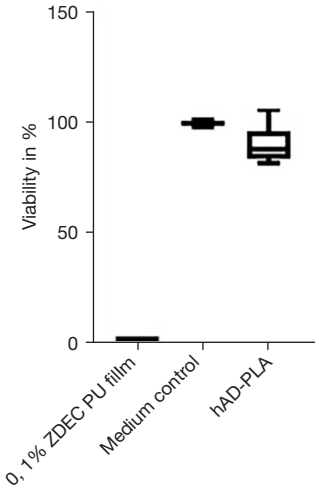

Figure 5 *In vitro* cytotoxicity assessment of the tested hybrid material consisting of hAD-PLA, presented as the percentage relative to the control (normal culture medium). hAD, human acellular dermis; PLA, polylactide.

the CAM and is also confirmed by the excised part of the membrane together with the material.

Discussion

Key findings

It is possible to print PLA on hAD, offering a non-toxic and biocompatible solution. After printing, the acellular dermis maintains its structural integrity and remains stable in fluids for up to seven days of incubation. Fibroblasts adhere to the material demonstrating their typical morphology and proliferate. Additionally, the observed connection to vessels in ovo further supports its biocompatibility, making it a promising material for various tissue reconstruction applications.

Strengths and limitations

To our knowledge, this is the first study describing a layer-by-layer printing strategy on hAD. Our pilot study shows the general feasibility of the approach first by demonstrating the printing strategy forming a stable bond between the two distinct materials without destroying most parts of the hAD structure. Only the layer directly connected to the printed material shows compression and densening. Tensile strength studies demonstrated that soaking the membranes

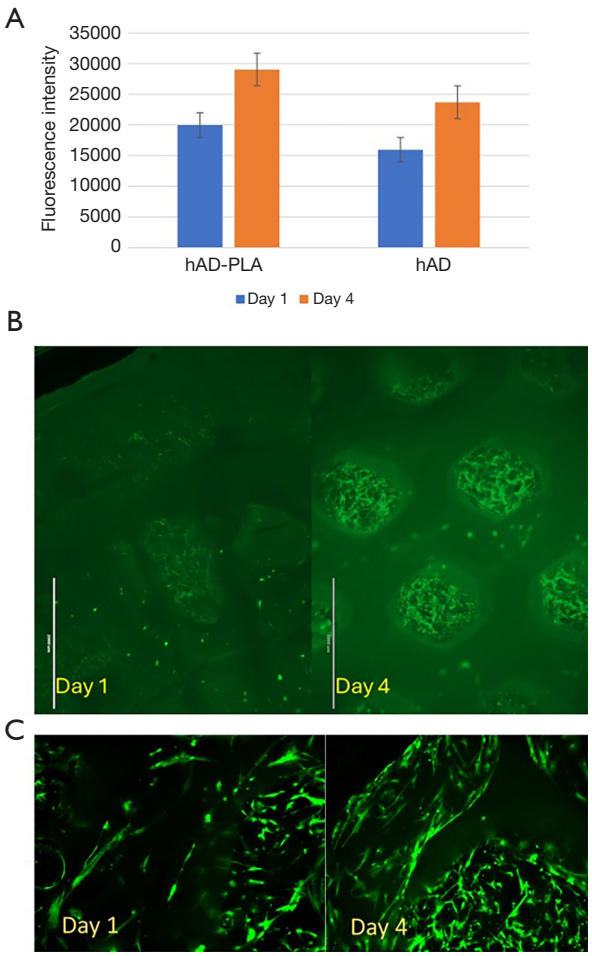

Figure 6 Proliferation and images of seeded fibroblasts. (A) Fluorescence intensity of the PLA hAD hybrid models colonised with NHDFs on days 1 and 4 after seeding the fibroblasts onto the models. (B,C) Fluorescence images of the PLA hAD models. Left: day 1, right: day 4 (B, 2× magnification, C; 10× magnification). hAD, human acellular dermis; NHDFs, normal human dermal fibroblasts; PLA, polylactide.

significantly increases their flexibility by greatly reducing the Young's modulus, while having minimal impact on tensile strength. Adding PLA to Epiflex increases stiffness. Secondly, biocompatibility of the hybrid material was demonstrated *in vitro* and in ovo. Fibroblasts adhered to the material and proliferated and in ovo assays showed integration into the vascular system. Limitation of the study is the fact, that it is a pilot study, and its results need to be confirmed in further studies.

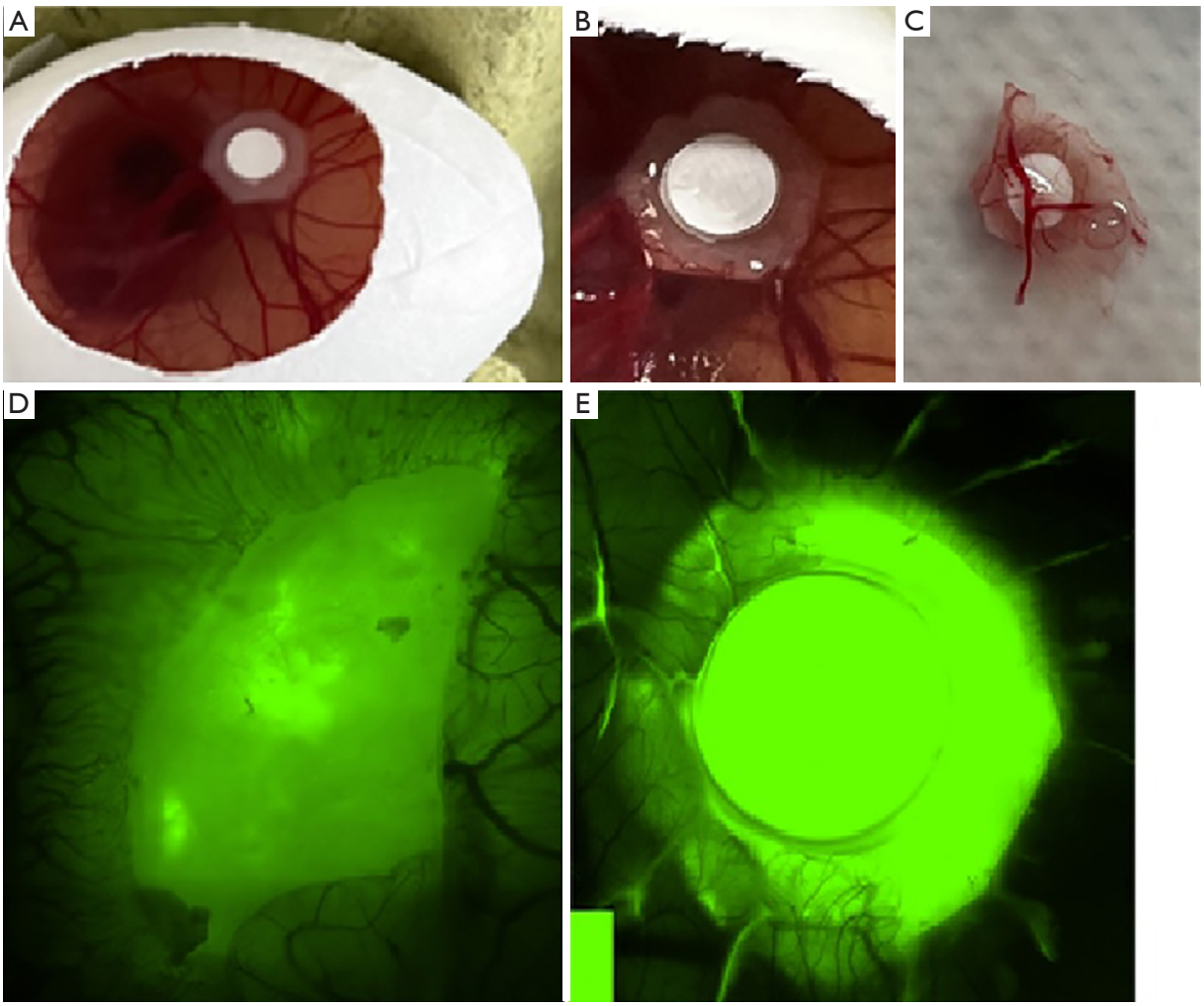

Figure 7 CAM assay. (A,B) Hybrid material on the CAM. (C) Excised material after 14 days of incubation, with vessels surrounding the whole material. (D,E) Hybrid material on the CAM at (D) 7 days, and (E) at 14 days after the start of the experiment. CAM, chorioallantoic membrane.

Comparison with similar researches

To our knowledge, only few studies exist combining acellular dermis with 3D-printing. Their approaches differ significantly from our research project. Song *et al.* grinded hAD material into powder, reconstructed it via 3D-printing and embedded this structure into PLA meshes. Their scaffold material produced cytotoxic effects *in vitro* but not *in vivo*. Similar to our results, they demonstrated a positive effect on vessel formation (26). A similar approach was chosen by Hu *et al.* They combined PLA with thermoplastic polyurethane (TPU) and hAD powder to design three dimensional meshes for hernia repair. They demonstrated their biocompatibility as well as elasticity and strength (27). To overcome and treat skin defects Jin *et al.* combined gelatin methacrylamide with hAD and produced a functional skin model (28). A similar bioink was produced by Liu *et al.*, who used this bioink for abdominal wall reconstruction in rats (29). What these studies have in common is that they use a lyophilized powder grinded from hAD. They use the advantages of hAD—high concentration of growth factors, VEGF and TGF-beta (30)—but destroy the structure of hAD by fabrication of a powder, which they combine with different materials. This fact distinguishes our approach, as we utilize the natural structure of the hAD and print a stable PLA structure onto the membrane, assuming that cells and tissues will interact with the hAD. Thus, our hybrid material represents a promising candidate for tissue engineering, particularly in thoracic surgery.

Explanations of findings

Our work confirms the feasibility of printing hard materials like PLA onto a hAD. In this combination the hybrid material consists of a soft and a hard part similar to the chest that consists of soft tissue and cartilaginous and bony structure. It might be an option for reconstruction in cases of larger lateral defects or defects including the sternum. Including 3D-printing technology enables the fabrication of complex scaffold structures and implants that can be individually adapted to the patient's injuries.

Implications and actions needed

To further evaluate the potential of this approach, several key steps are necessary. Additionally, further biomechanical testing, will provide insights into its mechanical properties. Testing with different cell types will be crucial to assess cell proliferation and the structural stability of the material in biological environments especially regarding the degradation behaviour. PLA usually degrades in a time span of 3–5 years *in vivo* depending on temperature, crystallinity and manufacturing processes (31). Especially 3D printing can change degradation processes and therefore these processes have to be analyzed in further studies to get more insight in the mechanical properties for long-term application (32,33).

Exploring various structural designs for printing will help optimize functionality and performance. Furthermore, animal studies will be required to assess biocompatibility, while immunological evaluations will help to determine potential immune responses. These steps are essential to ensure the material's suitability for future applications.

Conclusions

This study demonstrates *in vitro* and *in ovo* that 3D-printing on hAD is possible and represents a promising tool in tissue engineering. The 3D-printed hybrid material is biocompatible and indicates a pro-angiogenic effect. By combining soft and hard materials it might be an attractive alternative for structural reconstructions in various surgical applications.

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Footnote

Reporting Checklist: The authors have completed the MDAR reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-767/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-767/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-2025-767/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethical approval is not required for the *in ovo* study.

References

1. Sun J, Chen C, Zhang B, et al. Advances in 3D-printed scaffold technologies for bone defect repair: materials, biomechanics, and clinical prospects. Biomed Eng Online 2025;24:51.
2. Morris AH, Stamer DK, Kyriakides TR. The host

response to naturally-derived extracellular matrix biomaterials. Semin Immunol 2017;29:72-91.
3. Luijendijk RW, Hop WC, van den Tol MP, et al. A comparison of suture repair with mesh repair for incisional hernia. N Engl J Med 2000;343:392-8.
4. Sheridan RL, Choucair RJ. Acellular allogenic dermis does not hinder initial engraftment in burn wound resurfacing and reconstruction. J Burn Care Rehabil 1997;18:496-9.
5. Hogg P, Rooney P, Ingham E, et al. Development of a decellularised dermis. Cell Tissue Bank 2013;14:465-74.
6. Rössner E, Smith MD, Petschke B, et al. Epiflex(®) a new decellularised human skin tissue transplant: manufacture and properties. Cell Tissue Bank 2011;12:209-17.
7. Roessner ED, Vitacolonna M, Hohenberger P. Confocal laser scanning microscopy evaluation of an acellular dermis tissue transplant (Epiflex®). PLoS One 2012;7:e45991.
8. Adamakis I, Tyritzis SI, Stravodimos KG, et al. A novel approach for the surgical management of Peyronie's disease using an acellular, human dermis tissue graft: preliminary results. World J Urol 2011;29:399-403.
9. Vitacolonna M, Mularczyk M, Herrle F, et al. Effect on the tensile strength of human acellular dermis (Epiflex®) of in-vitro incubation simulating an open abdomen setting. BMC Surg 2014;14:7.
10. Vitacolonna M, Belharazem D, Maier P, et al. In vivo Quantification of the Effects of Radiation and Presence of Hair Follicle Pores on the Proliferation of Fibroblasts in an Acellular Human Dermis in a Dorsal Skinfold Chamber: Relevance for Tissue Reconstruction following Neoadjuvant Therapy. PLoS One 2015;10:e0125689.
11. Velotta JB, Hammer J, Mukhatyar V. Chest Wall Reconstruction Using Biologic Mesh to Cover Soft Tissue Defects: A Narrative Review. J Surg Res 2025;311:98-105.
12. Semlacher RA, Nuri MAK. Successful management of absent sternum in an infant using porcine acellular dermal matrix. Arch Plast Surg 2019;46:470-4.
13. Eichler C, Schulz C, Thangarajah F, et al. A Retrospective Head-to-head Comparison Between TiLoop Bra/TiMesh® and Seragyn® in 320 Cases of Reconstructive Breast Surgery. Anticancer Res 2019;39:2599-605.
14. Hardt J, Kienle P. Laparoscopic ventral pouch pexy with acellular dermal matrix (ADM)-a novel technique for the treatment of full-thickness pouch prolapse after restorative proctocolectomy and j-pouch. Int J Colorectal Dis 2018;33:1643-6.
15. Sagheb K, Noelken R, Schröger SV, et al. Biomechanical analysis of the human derived soft tissue graft Epiflex for use in oral soft tissue augmentation. Int J Implant Dent 2024;10:16.
16. Kammerer A, Hartmann FA, Nau C, et al. The Impact of Defect Size on Bone Healing in Critical-Size Bone Defects Investigated on a Rat Femur Defect Model Comparing Two Treatment Methods. Bioengineering (Basel) 2024;11:287.
17. Roessner E, Vitacolonna M, Schulmeister A, et al. Human acellular dermis seeded with autologous fibroblasts enhances bronchial anastomotic healing in an irradiated rodent sleeve resection model. Ann Surg Oncol 2013;20 Suppl 3:S709-15.
18. Kim A, Downer MA, Berry CE, et al. Investigating Immunomodulatory Biomaterials for Preventing the Foreign Body Response. Bioengineering (Basel) 2023;10:1411.
19. Ong K, Ong CS, Chua YC, et al. The painless combination of anatomically contoured titanium plates and porcine dermal collagen patch for chest wall reconstruction. J Thorac Dis 2018;10:2890-7.
20. Weksler B. Commentary: Acellular porcine mesh for chest wall reconstruction. JTCVS Tech 2022;13:261-2.
21. Prządka M, Pająk W, Kleinrok J, et al. Advances in 3D Printing Applications for Personalized Orthopedic Surgery: From Anatomical Modeling to Patient-Specific Implants. J Clin Med 2025;14:3989.
22. Kanumilli SLD, Kosuru BP, Shaukat F, et al. Advancements and Applications of Three-dimensional Printing Technology in Surgery. J Med Phys 2024;49:319-25.
23. Barcena AJR, Ravi P, Kundu S, et al. Emerging Biomedical and Clinical Applications of 3D-Printed Poly(Lactic Acid)-Based Devices and Delivery Systems. Bioengineering (Basel) 2024;11:705.
24. Brendel C, Müller-Kuller U, Schultze-Strasser S, et al. Physiological regulation of transgene expression by a lentiviral vector containing the A2UCOE linked to a myeloid promoter. Gene Ther 2012;19:1018-29.
25. Grandjean T, Perumal N, Manicam C, et al. Towards optimized tissue regeneration: a new 3D printable bioink of alginate/cellulose hydrogel loaded with thrombocyte concentrate. Front Bioeng Biotechnol 2024;12:1363380.
26. Song Z, Yang D, Hu Q, et al. Reconstruction of Abdominal Wall Defect with Composite Scaffold of 3D Printed ADM/PLA in a Rat Model. Macromol Biosci 2023;23:e2200521.
27. Hu Q, Zhang R, Zhang H, et al. Topological Structure Design and Fabrication of Biocompatible PLA/TPU/ADM Mesh with Appropriate Elasticity for Hernia Repair. Macromol Biosci 2021;21:e2000423.

28. Jin R, Cui Y, Chen H, et al. Three-dimensional bioprinting of a full-thickness functional skin model using acellular dermal matrix and gelatin methacrylamide bioink. Acta Biomater 2021;131:248-61.
29. Liu S, Zhang H, Hu Q, et al. A facile strategy for fabricating composite patch scaffold by using porcine acellular dermal matrix and gelatin for the reconstruction of abdominal wall defects. J Biomater Appl 2020;34:1479-93.
30. Turner NJ, Yates AJ Jr, Weber DJ, et al. Xenogeneic extracellular matrix as an inductive scaffold for regeneration of a functioning musculotendinous junction. Tissue Eng Part A 2010;16:3309-17.
31. Farah S, Anderson DG, Langer R. Physical and mechanical properties of PLA, and their functions in widespread applications - A comprehensive review. Adv Drug Deliv Rev 2016;107:367-92.
32. Moetazedian A, Gleadall A, Han X, et al. Effect of environment on mechanical properties of 3D printed polylactide for biomedical applications. J Mech Behav Biomed Mater 2020;102:103510.
33. Moetazedian A, Gleadall A, Han XX, et al. Mechanical performance of 3D printed polylactide during degradation. Addit Manuf 2021;38:101764.

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