



DIZG Annual Report 2024

**DEUTSCHES INSTITUT FÜR
ZELL- UND GEWEBEERSATZ**

Gemeinnützige Gesellschaft mbH





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Cover image: Macro absorption Corticalis granules



The year of progress

Dear friends of the DIZG,

Patience can be challenging, but it usually pays off. After establishing a partnership with a US non-profit donor program in early 2023 to address the critical shortage of safe allogeneic hard and soft tissues, we obtained regulatory approval in April 2024. Three departments were involved in this success: Tissue Donation, Regulatory Affairs and our Legal department. Your commitment was worth it: In September, the first post-mortem tissue donation from Oklahoma was released for processing.

Donors count

Our deepest thanks go to all those who donated their tissue after death. Without their selfless decision, surgeons would have no safe allogeneic avital transplants for national patient care. An equally important role is played by endoprosthetic femoral head donations, which serve as the basis for the production of urgently needed allografts. To guarantee stable provision again, we will keep engaging in new collaborations in this area.

New studies, new findings

Studies on the transplants Shark Screw® and Fascia lata show that their use is possible beyond the current indications. In particular, the clinical cases presented in a study on human acellular matrix (hADM) such as Epiflex® demons-

trate a broad spectrum of medical applications that far exceed the original indication, the treatment of skin defects.¹ Equally surprising was the success of Spongioflex® in partial meniscus replacement, which has been documented in more than 150 patient treatments with this innovative graft. With their experience and research, doctors make a decisive contribution to the further development of patient care with human tissue transplants.

A day for family & friends

Our employees, their families, and friends were invited on a Saturday in September to get to know our Facility 2025, the new production facility for human tissue transplants. Guided tours offered exciting insights into production, the various departments, and the transplants. The response was extremely positive.

Facility 2025

Anyone who has built or procured building materials during the COVID-19 pandemic will be familiar with the associated delivery delays. We also had to face this challenge and mastered it: Our Facility 2025 is scheduled to go into operation at the end of 2025. For DIZG, it will represent yet another milestone in the care of patients with severe tissue defects.

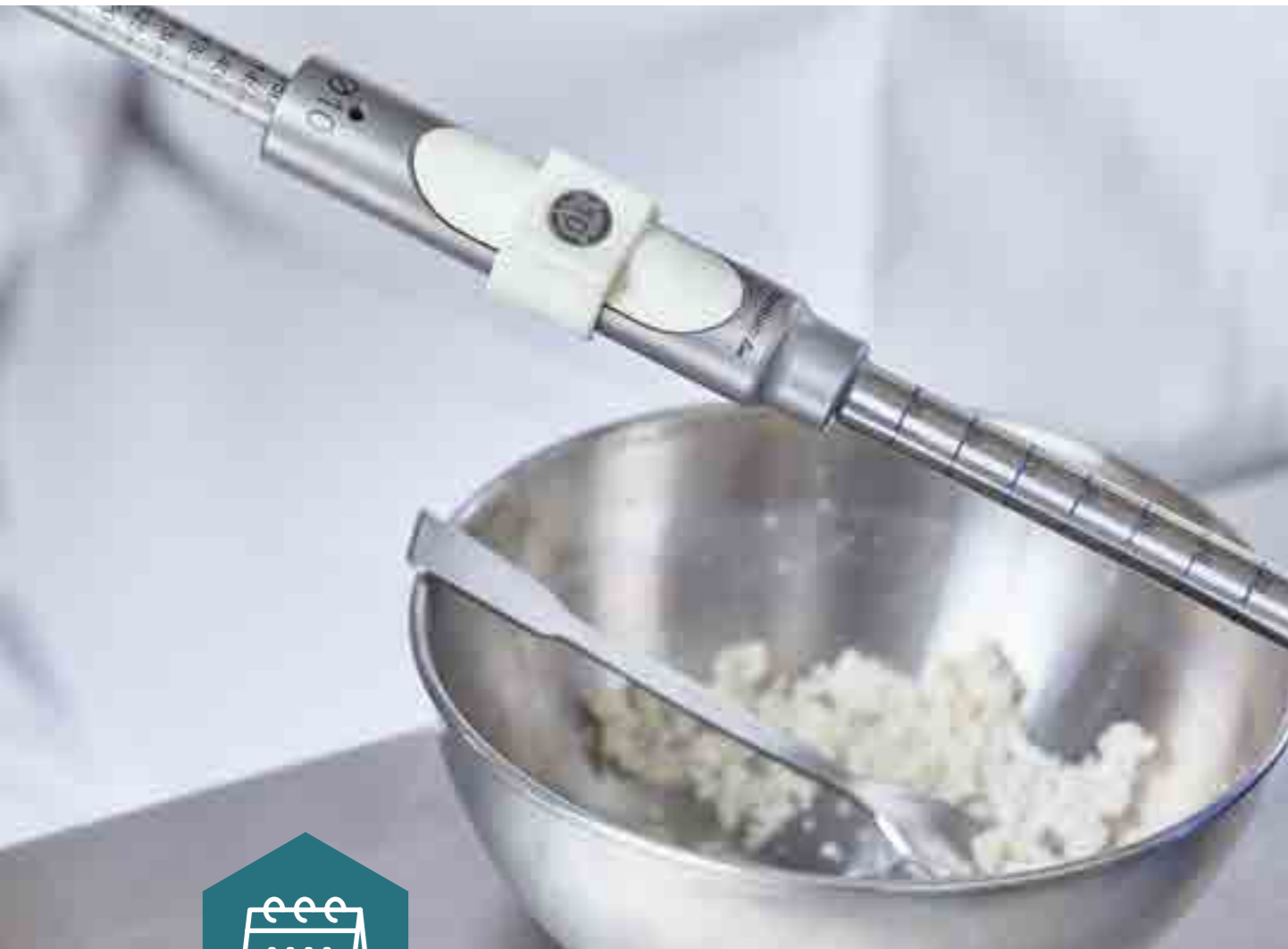
New DIZG service

We expanded our range of services at the start of 2025: Our previous sales manager, Dr. Michael Wolf, is now available to surgeons on request in his new role as Director of Surgical Education in the operating theater for our allogeneic avital transplants.

Last year, we produced almost 70,000 safe allogeneic tissue transplants, enabling clinical facilities to support the medical care of patients. We look forward to continuing our successful collaboration.

Yours sincerely

Jürgen Ehlers
Managing Director



Review and outlook

A year of steady progress

Spongioflex® for the knee

If they're injured, menisci tend to heal poorly due to their poor circulation, especially in the innermost area.² A meniscus loss in the short term causes functional limitations and, if left unaddressed, contributes to knee osteoarthritis.³ With Spongioflex® the DIZG provides surgeons with an allogenic avital graft that works as a partial meniscus replacement.

In a 2023 study, human meniscus cells were seeded on Spongioflex® and a bovine collagen meniscus implant (CMI) and cell viability was compared to the 2D culture control.² As in the 2D control, the viability / cell count of meniscus cells cultured on Spongioflex® increased over seven days – a finding that was not observed in CMI.

After one week, the meniscus cells cultured on Spongioflex® secreted significantly more Procollagen type 1 into the supernatant than those on the CMI.

A case study of a patient with bilateral medial meniscal lesions also indicates that Spongioflex® is rapidly integrated and leads to favorable radiographic and functional outcomes.⁴



Applicators: Hands-on training

Several training courses were offered by the DIZG last year, where participants observed the enrichment of allogeneic avital grafts and learned about the patient-specific, time-saving, and controlled filling of bone defects using the TITANIUM prime line* applicator.

The events enabled participants to gain practical experience with the high-quality applicator, which is suitable for Spierings chips (corticocancellous chips), corticalis granules, crushed cancellous bone chips, and DBM putty, as well as the application of transplants mixed with DBM putty. They were able to find out for themselves how the mixture with DBM makes handling easier thanks to the malleability

of this human transplant. This malleability enables the complete closure of bone defects caused by accidents, inflammation, tumors, or cysts without free spaces, which is essential for the complete and sustainable insertion and remodeling of the transplants. At the same time, this prevents the detachment of tissue particles.

In addition, the sodium hyaluronate contained in DBM putty supports the healing process,^{5,6,7} as well as the vascularization,⁸ and also has an anti-inflammatory effect.⁹

The TITANIUM prime line* applicator can be used for large, open operations such as a total hip arthroplasty, but also for arthroscopic procedures such as drill canal fillings.

It can be used, for example, in

- > orthopaedic surgery/trauma surgery,
- > spinal surgery,
- > sports medicine.



TITANIUM prime line*
BIOMEDIX® product, distributed in Germany and Austria by DIZG

One year of the organ and tissue donor registry

The federal organ and tissue donor registry went online on March 18, 2024. In this central electronic directory, citizens can document their decision for or against organ and tissue donation, voluntarily and free of charge. As of March 1, 2025, **270,315 people** have registered here. This registration marked the first phase of the registry.

In the second step, collection clinics were connected to the register by July 2024 to be able to search and retrieve declarations. The option of authentication with the health ID was added in the third step in summer 2024.

The fourth step, originally planned for January 2025, the integration of officially approved tissue facilities postponed indefinitely into 2025, as this first requires an amendment to the Transplantation Act (TPG). The corresponding legislative process had already been initiated but could not be completed due to the change in government.

The fact that these institutions can also access the register is thanks to the non-profit German Society for Tissue Transplantation (DGFG), which had issued a position paper long before the organ and tissue donor registry was launched, calling for the access mechanisms for donation facilities to be optimized.

The work of the DGFG was crucial to ensuring the future supply of human tissue transplants for German hospitals. Without the registry's optimizations, the number of post-mortem tissue donations, which is already significantly too low, would have been further reduced – with serious consequences for medically necessary surgical interventions.

2024 – 2025



A day for family & friends

Facility 2025, the new production facility for allogeneic avital tissue transplants, demanded a high level of commitment from everyone involved. To honor this commitment and to present the new building, the DIZG invited people to a Family & Friends Day on a Saturday in September 2024. Relatives and friends of the employees used the opportunity to get to know the new building on guided tours and take a look at the rooms where safe allografts will soon be created for patient care throughout Germany.

During the guided tours and a small exhibition, they learned how complex the daily tasks at the DIZG are – from tissue donation to the complex quality and safety requirements and legal specifications for the production of transplants. At the end of the successful event, everyone agreed that it had been a wonderful few hours that had flown by.



Fig. 1+2 Tour through the new DIZG building

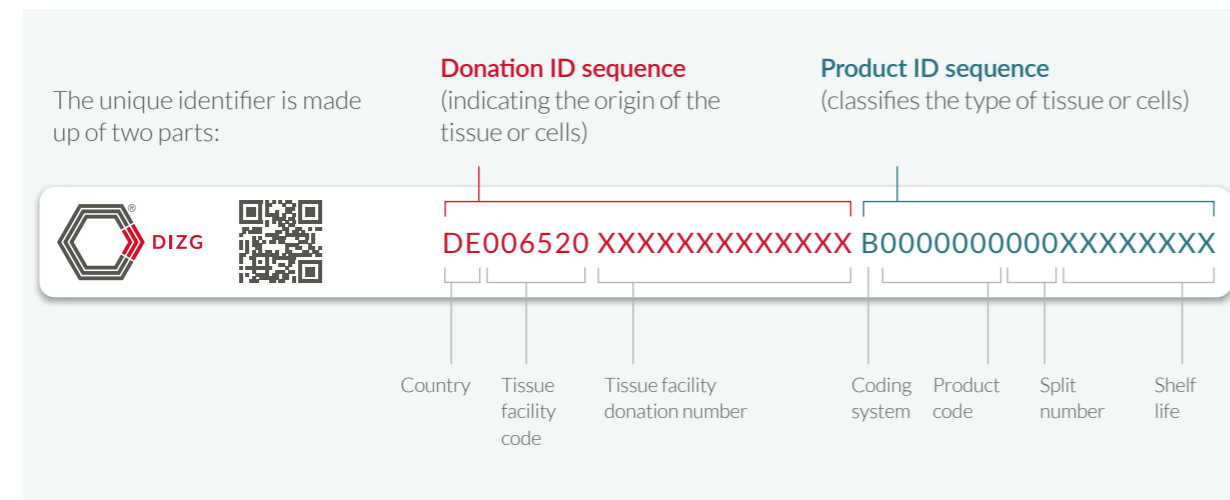
Fig. 3 Modern technology for the development of innovative transplants



Introduction of a machine-readable Single European Code

Human tissues and cells for patient care must be traceable from donor to recipient and from recipient to donor in the European Union in accordance with Directive 2006/86/EC. This is made possible by the Single European Code (SEC).

This uniform European Code must be machine-readable in accordance with Article 43 of the SoHO (Substances of Human Origin) Regulation adopted by the European Council in 2024. Implementation must take place by 2027. The top priority is always the safety of the tissue donor and the tissue recipient.



With the introduction of the machine-readable SEC in the form of a QR code at the end of October 2024, the DIZG met a regulatory requirement ahead of schedule.

The new DIZG website is online

By mid-December: The DIZG website has a new look and offers users and interested parties a clear and concise presentation. You can find in-depth information about the non-profit institute, postmortem and living tissue donation, medical devices, meniscus matching, upcoming events and much more. Visit us online: www.dizg.de.





We also support clinics in the operating theater

2024 2025 2026

Since January 2025, our former sales manager, Dr.phil.nat. Michael Wolf, will be advising surgeons in his new role as Director of Surgical Education. With this appointment, we want to support doctors in the practical application of our transplants where it counts: in the operating room. In particular, surgeons who are using a tissue graft for the first time will receive

effective support with their questions and benefit from Mr. Wolf's comprehensive knowledge on how to use various allografts in different areas of application.

Mr. Sönke Petersen is now responsible for sales management. He brings more than 30 years of experience in international medical device and pharmaceutical

companies, as well as extensive leadership expertise. For the past ten years, he has headed up sales for a global MedTech company in Germany and Switzerland.

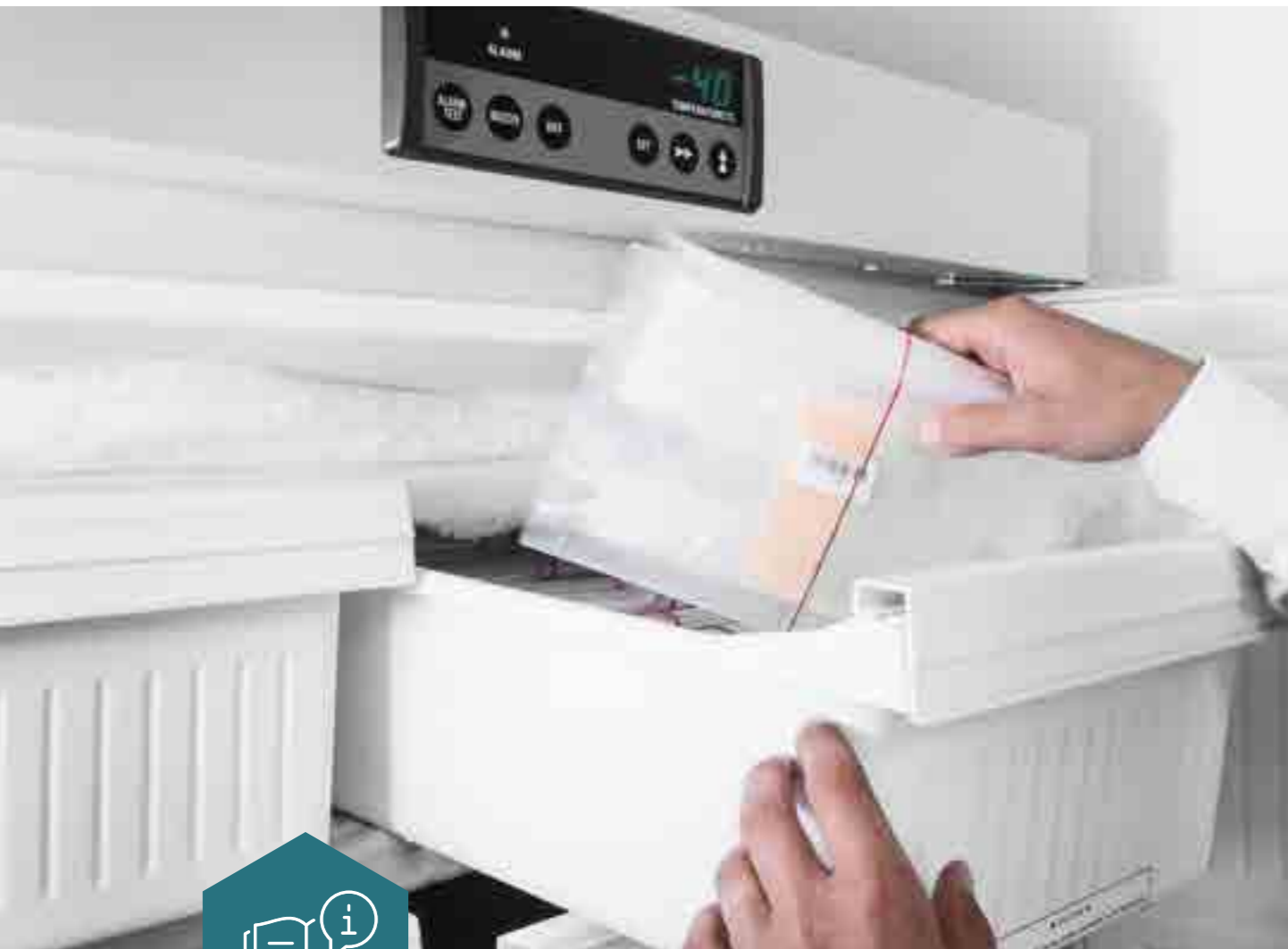
Facility 2025

The construction of our new, **2,526 m²** production facility for human bone and soft tissue was a major project with challenges that were overcome thanks to the tireless commitment of everyone involved. Preparations are currently in full swing to obtain the usage permit for the building from the building authority. The production area with its clean rooms is approx. 1,480 m² of the total area. Once commissioned in 2025, the facility

will enable significant redundancies and, in addition to the existing annual production of over **69,900** tissue transplants, generate an additional 100,000 human tissue transplants from bone, tendons, acellular dermis, and fascia for patient care across Germany.

Facility 2025: The new production facility of the DIZG





Figures 2024

Tissue donations are needed

The DIZG was once again able to provide more human transplants for national and international patient care, despite a slight decline in the number of tissue donations received.

How tissue can be donated

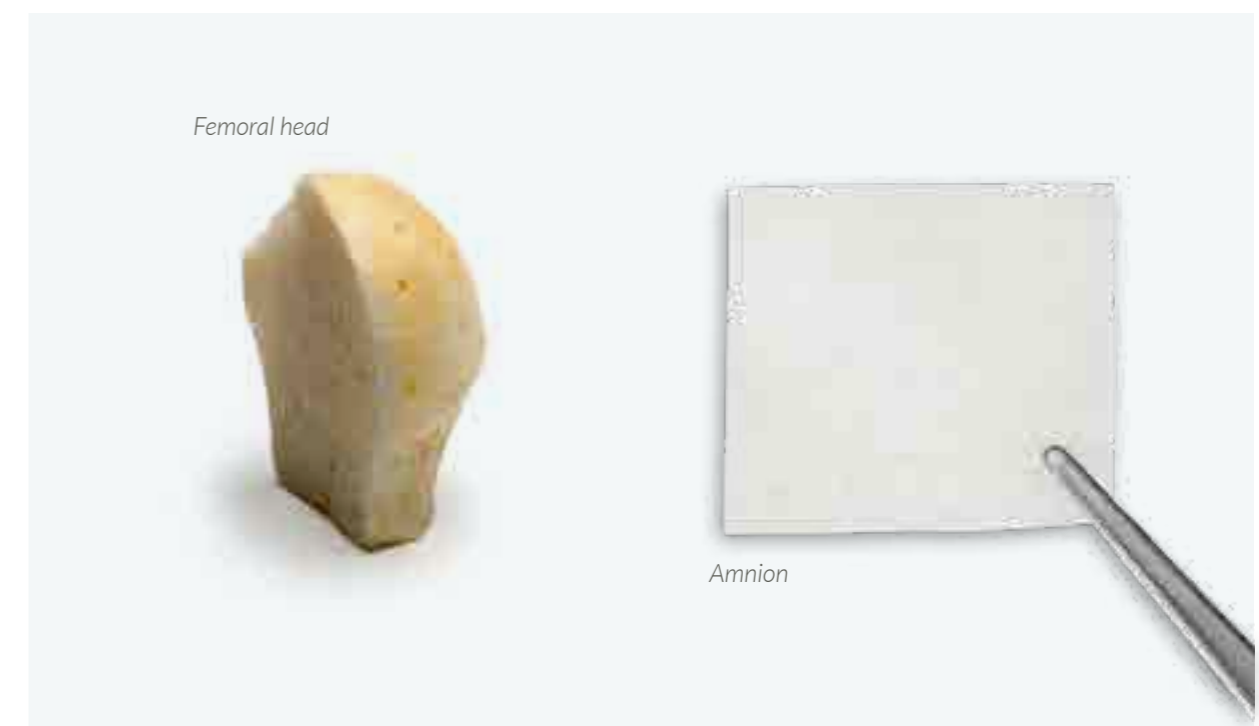
Tissue can be donated by living donors or post-mortem. Examples of living donations are:

- > Amnion donation and
- > femoral head donation.

Post-mortem tissue donation is only possible if it corresponds to the presumed will of the deceased. The willingness to donate can be documented in the federal organ and donor register, via the organ donor card or a living will. The next of kin are also contacted to express the presumed wishes of the deceased.

i The anonymization of the donation is enshrined in law. The recipient of a tissue transplant does not learn the name of the donor. The donor's relatives also do not know who receives the donated tissue.

In principle, any adult can donate tissue. These transplants are used, for example, in the fields of orthopaedics and traumatology, spinal surgery, sports medicine and oral and maxillo-facial surgery. Every donation is made free of charge.



Living and post-mortem tissue donation

In the reporting year, **3,278** individuals donated tissue, which is **15** fewer than in the previous year. The number of post-mortem donations decreased slightly from **353** to **349**. From these donations, **6,208** individual tissues were obtained.

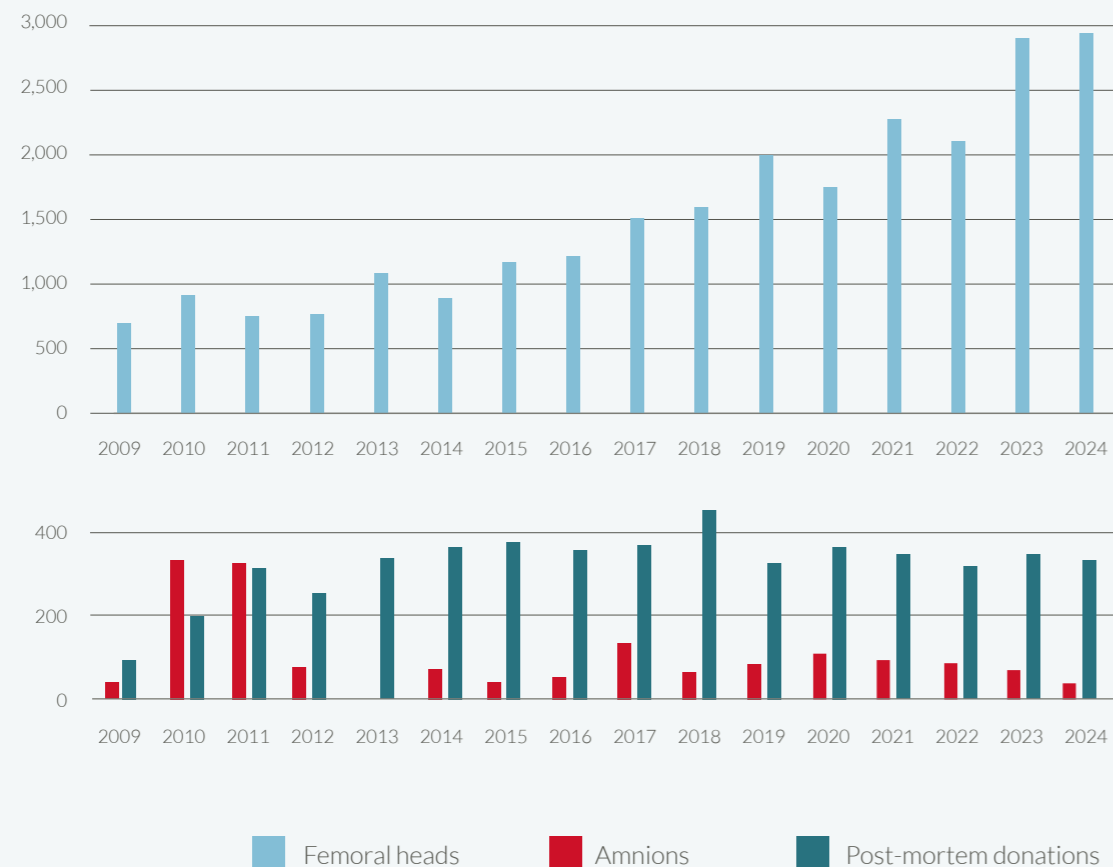
There was a slight increase in the number of donated femoral heads resulting from arthroplasty operations:

In the past year, **2,946** femoral heads were donated – **14 more than 2023**.

Unfortunately, there was another decline in amnion donations. **38** donations were released for further processing.

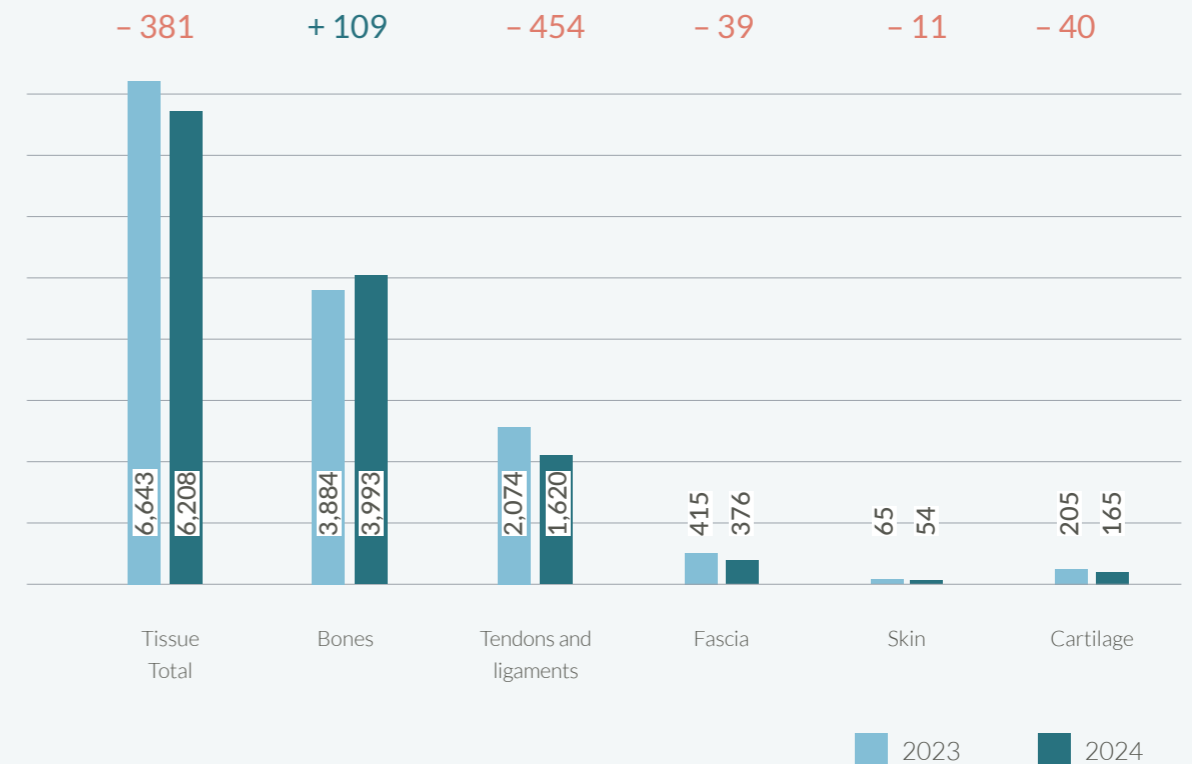
In contrast, there was an increase in bone donation, which rose from **3,884** to **3,993**.

Tissue donations per year 2009 - 2024



Which tissues were donated

Tissue donations compared to the previous year








A total of **9,192** individual musculoskeletal tissues (incl. skin) were received in the reporting year and were released for tissue processing in the same period.

Increased delivery of allogeneic transplants

In the reporting year, **69,912** allogeneic transplants were delivered – **2,084** more than in 2023. The DIZG made these available to clinical facilities throughout Germany and in **24** other countries. The increase in the human menisci provided is particularly impressive: While **28** were sold in the previous year, **82** were sold in the reporting year, of which **11** were sold abroad.

October was a very strong month in terms of sales, with **7,476** transplants provided. Ideally, this means that just as many patients could be helped.

TRANSPLANTS THAT WERE SPECIFICALLY REQUESTED

Place	Description	Quantity	
1.	Granulate	25,152	
2.	Chips	15,567	
3.	Cancellous bone blocks	7,948	
4.	DBMx press, putty	6,062	
5.	Femoral heads	4,901	

These transplants are used, for example, in the fields of orthopedics and traumatology, spinal surgery, sports medicine, and in oral and maxillofacial surgery.



OVERNIGHT DELIVERY

If necessary, the DIZG delivers the transplants required for medical care overnight.



SAFELY SUPPLIED

For clinical facilities that do not have their own bone bank, we are happy to take over the complete supply of safe allogeneic tissue transplants.



We are also happy to support you with the patient-specific supply of tissue transplants that are not available nationally on a doctor's prescription.



Tissue donation

Helping with tissue donations

The demand for human tissue transplants remains high. Tissue donation is a basic requirement for assuring patient care.

For improved health

Anyone who makes the decision to donate tissue enables other people to improve their quality of life. The transplantation of donor tissue means the end of a period of suffering for many patients and can even prevent amputations.

The surgical intervention using bone and tissue transplants allows patients to regain more mobility and thus the chance of a much more active life. This is precisely what DIZG is committed to.



DIZG patient information, education on femoral head donation



The relevance of our tissue donation partners

The DIZG works closely with partners throughout Germany, Europe and the USA. National and international donor centers and clinics participating in post-mortem and/or living tissue donation programs are very important partners: The donated tissue is the basic prerequisite for producing urgently needed human transplants for patient care.

In the end, the clinical institutions participating in donation programs contribute significantly to improving the health and quality of life of many patients with severe tissue defects.



The more clinics participate in the donation process, the more patients can be supplied with transplants throughout Germany and Europe. To achieve this, a nationwide expansion of tissue donation would be beneficial.

Clinics benefit from tissue donation

The enormous demand for safe human tissue transplants exceeds the supply. They are used in all specialist disciplines, but particularly in the following areas:



Trauma surgery



Maxillary and facial surgery



Reconstructive surgery



Orthopedics

These transplants are used in a variety of specialized areas such as endoprosthetic revision surgery, tumor surgery, and burn medicine.



Endoprosthetic femoral head donation

The femoral head is donated after medical consultation and with the patient's informed consent, as part of a necessary hip joint endoprosthesis procedure. This means the femoral head, which would otherwise be medically discarded, is made available.

This donation is a simple but very effective way of helping other people to improve their quality of life. After extensive screening and determination of donor suitability, the recovered femoral heads are released for further processing into human transplants.





Research and development

Our work centers on transforming knowledge into healing – with every innovation, we create new perspectives for patients.

Volker Eras,
Head of R&D Department

Every question about "how" and "what is required" is aimed at improving the health of patients with severe tissue defects and their quality of life.

Research: Developing the new, analyzing the familiar

The Research and Development (R&D) team is driven by the desire to optimize transplant properties, adapt them to constantly changing clinical requirements, identify new surgical applications for existing transplant forms and develop new transplants. The aim is to provide surgeons with the best possible supply of human transplants, in order to ultimately offer patients improved prospects of recovery, a more active life, and a higher

quality of life. Patience and persistence pay off. The development of a transplant can take several years. It's essential not to be discouraged by setbacks when conducting experiments. After all, not everything always goes as planned. Changing your point of view, staying interested, and asking questions, all while paying close attention to details and documenting and analyzing them, are the essence of research.

Working in this field requires meticulousness, self-critical thinking and a high level of self-motivation. Even when the results are disappointing, perseverance and the urge to discover new things prevail.



The aim is to answer questions about processes and transplants arising from manufacturing or projects. With the help of our own investigations and the use of available information from others, such as scientific studies and publications, we can answer these questions as clearly as possible.



Verified data for research

The DIZG's allograft registry now comprises 65,950 verified data on the use of allogeneic avital hard and soft tissue.

The allograft registry is highly valuable for both research and medical practice. Among other things, it enables the

- > identification of new areas of application for existing transplant forms for bone and soft tissue defects,
- > identification of vulnerabilities and risks to increase the safe use of human tissue transplants,
- > scientific evaluation of the application data,
- > targeted planning of new studies.

The data is determined via the transplant registration system, which is enclosed with every transplant ordered. This enables surgeons to provide information about the patient's age and gender, the diagnosis, indication, location, and any special features during the operation.

Each completed form supports the DIZG allograft registry and thus also the further development of human transplants. Based on the information received, trends in using specific graft groups can also be identified.

Clinical institutions that actively contribute to the data collection by submitting fully completed transplant forms to the DIZG can request data from the allograft registry free of charge. Please send your request by e-mail to allograftregister@dizg.de.



Allograft registry: data evaluation for the best possible patient care

New studies, new opportunities

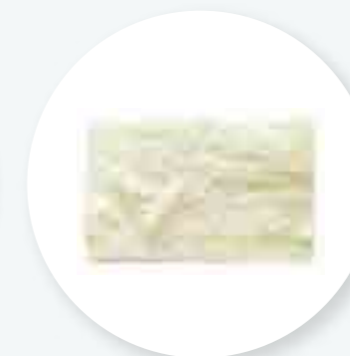
Transplants, which can be used for various indications, expand the treatment options for surgeons and patients. Three studies published in 2024 point to new potential applications for three human transplants from the DIZG.



DIZG transplants in focus



Shark Screw®



Fascia lata



Epiflex®
human skin, acellular

Shark Screw®

The allogenic avital bone screw, which was used surgically for the first time in Germany last year, can be used in a variety of orthopedic applications.

Like the body's own bones, the Shark Screw®, made from donated bone tissue, is subject to natural bone metabolism. Within a few weeks to months, it is completely converted into new endogenous tissue.¹⁰

The fact that there is no need for further surgery to remove the

material, such as metal plates, is particularly advantageous for patients.

As a study from 2024 shows, the Shark Screw® is a promising option for the treatment of pseudarthrosis in foot and ankle surgery, as well as in selected cases of the lower leg.¹¹ The data collected shows that it leads to a high rate of healing compared to conventional treatment of pseudarthrosis and tends to enable a shorter healing period after the operation.



Fascia lata

The human soft tissue graft Fascia lata is suitable for ligament reconstruction in chronic elbow instability.¹² This was the conclusion of a retrospective study also published in 2024, in which the biomechanical suitability of the graft was evaluated, among other things. In addition, the clinical and radiological results of ligament reconstructions were compared, in which a triceps tendon reinforced with FiberTape® was used on one hand and a fascia lata transplant reinforced with FiberTape® on the other.

To date, there is no gold standard for the optimal choice of graft in the surgical treatment of chronic elbow instability. The use of an allograft such as Fascia lata is advantageous in order to avoid the rare but serious complication of morbidity at the donor site, which can occur

in approximately one to four percent of cases when using an autologous graft.

Patients who had undergone reconstruction of the ligament of the elbow with allogenic fascia lata or autologous triceps tendon due to chronic instability were examined. Of the initial 117 patients, 80 were excluded due to other injuries or surgical techniques. Twenty-one patients remained for the follow-up: ten who had been treated with Fascia lata and were observed for twelve months, and eleven who had been treated with an autologous transplant and had an observation period of 25 months.

The clinical results showed no significant differences between the Fascia lata and triceps groups in terms of pain, mobility or measu-

ring the success of treatment from the patient's perspective (Patient-Reported Outcome Measures, PROMs for short).



Epiflex® Human skin, acellular

The first successful epidermis transplant was performed by Jacques-Louis Reverdin in 1869, when he removed two small epidermis flaps from a Patient's right arm and placed and attached them to a wound on the left elbow.¹³ At the time, this procedure was a huge step forward for wound healing. Human acellular dermal matrices (hADM) have long been established.

Epiflex® offers a wide range of applications

hADMs such as our Epiflex® can be used successfully for severe tissue defects in various medical specialties: for in breast reconstruction, visceral, thoracic and plastic reconstructive surgery as well as in the jaw. As a thick variant (≥ 3 mm), they are also used in superior capsular reconstruction (SCR). The paper "Human Acellular Collagen Matrices – Clinical Opportunities in Tissue Replacement"¹¹ shows further indications and thus also proves the potential of Epiflex®.

Several current clinical requirements were examined

The aim of the publication is to expand the range of applications of hADMs – in particular in view of the growing need for effective and tolerable tissue replacement materials in regenerative medicine. In this area, hADMs are proving to be particularly promising. The example of Epiflex® demonstrates the versatile clinical application

possibilities of the matrices, which go far beyond the original application for skin defects. It has been shown that this human tissue transplant is also suitable for the treatment of osteochondrosis-dissecans lesions and for ligament reconstruction in the hand.

In addition, Epiflex® has shown its value in bone reconstruction. Successful preclinical studies¹⁴ in rats with a five-millimeter femoral defect suggest that hADMs have clinical potential beyond the treatment of skin damage and collagenous tissue defects. The defect filled with Spongiosa and coated with Epiflex® was investigated. The bone healing showed a biomechanically impressive result, which was equivalent to the classic two-stage Masquelet technology and significantly better than without defect wrapping.

The application on patients also proved successful: Acellular collagen matrices can replace the two-stage Masquelet technique with a one-stage procedure.¹ The use of this human graft can enable the reconstruction of larger tissue defects without the need for extensive plastic reconstructive surgery. The current work presents an initial collection of relatively

heterogeneous clinical cases. However, it indicates that Epiflex® is well suited and very well tolerated for the treatment of various bone and soft tissue defects and can also improve patient care results.



Importance of allogeneic transplants in medical treatment

Interview with PD Dr. med. habil. René D. Verboket



For the treatment of severe tissue defects, allogeneic transplants have been used in almost all medical fields for decades. We interviewed PD Dr. med. habil. René D. Verboket from the Clinic for Trauma Surgery and Orthopedics at the University Hospital Frankfurt about the importance of allogeneic transplants in medical treatment.

DIZG: In your opinion, where is the development of regenerative bone replacement materials heading?

The development is increasingly moving toward so-called "Individual Smart Biomaterials," which are tailored to the specific needs of the bone regeneration process. Materials that are not only structurally and mechanically resilient but also exhibit bioactive properties are gaining importance. Materials that enable controlled release of growth factors or even stem cells are particularly in focus to accelerate healing and support personalized therapeutic approaches. The integration of cell technology plays a role here, as does the development of customized, patient-specific implants using 3D printing processes. These applications will become increasingly individualized in the future.

DIZG: In your view, what role do human transplants play in this?

Human transplants remain a standard in regenerative medicine, primarily due to their natural biological and immunological compatibility. In more complex cases, such as larger defects or infections, they provide an excellent foundation for regeneration through their inductive and conductive properties, and often create a more stable healing environment. Human transplants are still considered the gold standard for biological tissue replacement. With advancing technology, they could even become the basis for new hybrid solutions with synthetic components in the coming years.

DIZG: Your recent publication "Human Acellular Collagen Matrices – Clinical Opportunities in Tissue Replacement" highlights new areas of application. What others would be conceivable?

In our publication, the potential of human acellular collagen matrices (hADMs) in various application scenarios is detailed. Beyond the classic areas of use in reconstructive and aesthetic surgery, hADMs as collagen scaffolds have proven effective in bone reconstruction. Here, they can replace the complex but efficient induced Masquelet membrane through a one-stage procedure, proving clinically effective and safe.

The application of these membranes enables the reconstruction of significant bone defects without requiring repeated interventions. Furthermore, they have proven suitable for the treatment of bone-cartilage defects, such as osteochondrosis dissecans lesions, as well as for ligament reconstruction in the carpus.

The clinical examples presented in our study show that the application possibilities of human ADM extend far beyond the original use for treating skin defects. hADM has proven extremely successful and well-tolerated in the treatment

of bone and soft tissue defects of various etiologies and contributes significantly to improving patient care.

A promising future field could be the combination of hADMs with bioactive molecules or stem cells. This

would expand the application possibilities. Studies indicate that hADMs provide a favorable environment for cell colonization and could thus promote regeneration in various tissues. The integration with bioactive molecules could establish hADMs as versatile matrices for different tissue types, paving the way for new treatment strategies.

"Beyond the classic areas of use in reconstructive and aesthetic surgery, hADMs as collagen scaffolds have proven effective in bone reconstruction."

DIZG: Which other human transplants do you see as having more potential?

Human transplants offer diverse possibilities in several areas beyond the established applications in bone and skin transplants. Acellular nerve matrices, for instance, hold significant promise in treating nerve defects and neuropathies. They provide a natural guide structure for the growth and regeneration of nerve fibers and could thus represent a valuable alternative to autologous nerve transplantation.

Similarly, acellular heart valves have the potential to revolutionize the treatment of heart valve diseases.

Acellular heart valves have reduced immunoreactivity and connect with the recipient's tissue, making them more durable and functional than conventional artificial valves.

Acellular blood vessel transplants also offer exciting possibilities, especially for patients requiring vascular reconstruction. Such transplants could be useful as bypass options for peripheral arterial occlusions or in cardiac surgery and represent a possible alternative to synthetic vascular prostheses.

Another promising field is the use of acellular cartilage matrices in orthopedics for treating cartilage defects. Their natural structure promotes the regeneration of cartilage cells, contributing to the restoration of joint function. Acellular tendon and ligament transplants are valuable options in trauma

surgery and sports medicine. They accelerate healing and reduce the risk of rejection reactions. These areas hold tremendous potential for future innovations, especially when human acellular transplants are combined with modern bioactive and growth-promoting technologies to further enhance regenerative capacity.

DIZG: What clinical evidence do you expect to incorporate such new applications into the medical routine?

To integrate new applications for human transplants into the medical routine, convincing clinical evidence is required that demonstrates both

safety and efficacy in the long term. This necessitates studies with a sufficiently large number of patients and a long observation period to document the durability and functionality of the transplants. Long-term data showing that the transplants remain stably integrated in the recipient tissue and do not trigger negative immune reactions are particularly relevant. The basic applicability and tissue compatibility have already been proven, so these aspects do not need to be demonstrated again for each indication.

Multicenter studies are essential to confirm applicability and efficacy in different clinical contexts and patient groups. These studies will provide valuable information on complications or risks and help identify optimal indications and treatment strategies. Ideally, we should conduct randomized,

controlled studies. However, due to the sometimes very heterogeneous indications and courses, this is not always possible. Other clinical study concepts, such as registry studies, can be useful to demonstrate the benefits of new transplant technologies. It is essential to ensure that innovative transplants are included in standard care and benefit a wide range of patients. This can only be achieved through comprehensive, high-quality clinical evidence.

Dr. Verboket, thank you for the interview.



Scan the QR code to read the study

Scientific publications in international journals featuring contributions from DIZG staff or research partners – selected examples

- 1 **Verboket RD, Henrich D, Janko M, Sommer K, Neijhoft J, Söhling N, Weber B, Frank J, Marzi I, Nau C.** Human Acellular Collagen Matrices – Clinical Opportunities in Tissue Replacement. *International Journal of Molecular Sciences*. 2024 Jun 28;25(13):7088.
- 2 **Ahrens P, Borchert GH, Freutel C, Ahmed N, Brune JC.** Peracetic acid sterilized tendon and ligament allografts for knee reconstruction: For anterior cruciate ligament (ACL), posterior cruciate ligament (PCL) and complex knee surgery. *Die Orthopädie*. 2024 May;53(5):341-347.
- 3 **Mayer SA, Thomas B, Heuer M, Brune JC, Eras V, Schuster K, Knoedler L, Schaefer RL, Thiele W, Sleeman JP, Dimmler A, Heibel P, Kneser U, Bigdeli AK, Falkner F.** In Vivo Engineering and Transplantation of Axially Vascularized and Epithelialized Flaps in Rats. *Tissue Engineering Part A*. 2024 May 2.
- 4 **Labmayr V, Huber E, Wenzel-Schwarz F, Holweg P, Ornig M, Jakob G, Palle W, Borchert GH, Pastl K.** Non-Union treatment in the Foot, Ankle, and Lower Leg: A Multicenter Retrospective Study Comparing Conventional Treatment with the Human Allogeneic Cortical Bone Screw (Shark Screw®). *Journal of Personalized Medicine*. 2024 Mar 27;14(4):352.
- 5 **Kirschbaum S, Gerhardt C, Akgün D, Eras V, Kaltenhäuser D, Thiele K.** Fascia lata allograft: a suitable alternative in ligamentous reconstruction for chronic elbow instability? *JSES International*. 2024 May 24;8(5):1137-1144.
- 6 **Heuer M, Stiti M, Eras V, Scholz J, Ahmed N, Berrocal E, Brune JC.** High-Speed Fluorescence Imaging Corroborates Biological Data on the Influence of Different Nozzle Types on Cell Spray Viability and Formation. *Journal of Functional Biomaterials*. 2024 May 14;15(5):126.
- 7 **Penna-Martinez M, Kammerer A, Stützle P, Fees S, Behr S, Schaible I, Schröder K, Verboket RD, Neijhoft J, Marzi I, Nau C, Henrich D.** Enhancement of a one-step membrane technique for the treatment of large bone defects by pre-seeding the membrane with CD8 lymphocyte depleted bone marrow mononuclear cells in a rat femoral defect model. *Frontiers in Immunology*. 2024 Oct 23;15:1488611.
- 8 **Falkner F, Mayer SA, Heuer M, Brune J, Helt H, Bigdeli AK, Dimmler A, Heibel P, Thiele W, Sleeman JP, Bergmeister H, Schneider KH, Kneser U, Thomas B.** Comparison of Decellularized Human Dermal Scaffolds versus Bovine Collagen/Elastin Matrices for Engineering of Soft-Tissue Flaps. *Plastic and Reconstructive Surgery*. 2024 Jan 1;153(1):130-141.
- 9 **Bormann N, Schmock A, Hanke A, Eras V, Ahmed N, Kissner MS, Wildemann B, Brune JC.** Analysis of the Ability of Different Allografts to Act as Carrier Grafts for Local Drug Delivery. *Journal of Functional Biomaterials*. 2023 Jun 1;14(6):305.
- 10 **Söhling N, Heilani M, Fremdling C, Schaible A, Schröder K, Brune JC, Eras V, Nau C, Marzi I, Henrich D, Verboket RD.** One Stage Masquelets Technique: Evaluation of Different Forms of Membrane Filling with and without Bone Marrow Mononuclear Cells (BMC) in Large Femoral Bone Defects in Rats. *Cells*. 2023 Apr 30;12(9):1289.
- 11 **Barski D, Tsauro I, Boros M, Brune J, Otto T.** Functional Recovery after the Application of Amniotic Tissues and Methylene Blue during Radical Prostatectomy—A Pilot Study. *Biomedicines*. 2023 Aug 13;11(8):2260.
- 12 **Dabaghi M, Eras V, Kaltenhaeuser D, Ahmed N, Wildemann B.** Allografts for partial meniscus repair: an in vitro and ex vivo meniscus culture study. *Frontiers in Bioengineering and Biotechnology*. 2023 Oct 12;11:1268176.
- 13 **Behrendt S.** MRI follow up of bilateral partial meniscal substitution with a demineralized bone block. A case report. *Radiology Case Reports*. 2022 Oct 27;18(1):21-26.
- 14 **Vogt W, Borchert GH, Ahmed N, Brune JC.** Anatomical acromioclavicular joint stabilization with chemically sterilized tendon allografts: A retrospective study. *Shoulder & Elbow*. 2023 Aug;15(4):411-423.
- 15 **Ahmed N, Eras V, Pruß A, Perka C, Brune J, Vu-Han TL.** Allografts: expanding the surgeon's armamentarium. *Cell and Tissue Banking*. 2023 Mar;24(1):273-283.
- 16 **Huber T, Hofstätter SG, Fiala R, Hartenbach F, Breuer R, Rath B.** The Application of an Allogenic Bone Screw for Stabilization of a Modified Chevron Osteotomy: A Prospective Analysis. *Journal of Clinical Medicine*. 2022 Mar 3;11(5):1384.
- 17 **Pastl K, Pastl E, Flöry D, Borchert GH, Chraim M.** Arthrodesis and Defect Bridging of the Upper Ankle Joint with Allograft Bone Chips and Allograft Cortical Bone Screws (Shark Screw®) after Removal of the Salto-Prosthesis in a Multimorbidity Patient: A Case Report. *Life (Basel)*. 2022 Jul 11;12(7):1028.
- 18 **Falkner F et al.** A Comparative Study of Decellularized Human Dermal Scaffolds versus Bovine Collagen/Elastin Matrices for in vivo Engineering of Axially Vascularized Soft Tissue Flaps in Rats. 2022 (accepted, not published yet).
- 19 **Minkus M, Akgün D, Thiele K, Karpinski K, Moroder P.** Bankart-Plus zur Behandlung von Patienten mit anteriorer Schulterinstabilität und kleinen bis moderaten Glenoiddefekten. *Obere Extremität*. 2022 Oct 6;17(4):243-249.
- 20 **Beier L, Faridi A, Neumann C, Paepke S, Mau C, Keller M, Strittmatter HJ, Gerber-Schäfer C, Bauer L, Karsten MM, Kümmel S, Blohmer JU.** Human Acellular Dermal Matrix (Epiflex®) in Immediate Implant-Based Breast Reconstruction after Skin- and Nipple-Sparing Mastectomy and Treatment of Capsular Fibrosis: Results of a Multicenter, Prospective, Observational NOGGO-AWOGyn Study. *Breast Care (Basel)*. 2021 Oct;16(5):461-467.
- 21 **Blohmer JU, Beier L, Faridi A, Ankel C, Krause-Bergmann B, Paepke S, Mau C, Keller M, Strittmatter HJ, Karsten MM.** Patient-Reported Outcomes and Aesthetic Results after Immediate Breast Reconstruction Using Human Acellular Dermal Matrices: Results of a Multicenter, Prospective, Observational NOGGO-AWOGyn Study. *Breast Care (Basel)*. 2021 Aug;16(4):335-342.
- 22 **Eras V, Graffunder J, Ahmed N, Brune JC.** Influence of peracetic acid-ethanol sterilisation on the biomechanical properties of human meniscus transplants. *Journal of Experimental Orthopaedics*. 2021 Mar 5;8(1):18.
- 23 **Verboket RD, Irrle T, Busche Y, Schaible A, Schröder K, Brune JC, Marzi I, Nau C, Henrich D.** Fibrous Demineralized Bone Matrix (DBM) Improves Bone Marrow Mononuclear Cell (BMC)-Supported Bone Healing in Large Femoral Bone Defects in Rats. *Cells*. 2021 May 19;10(5):1249.
- 24 **Barski D, Gerullis H, Ecke T, Boros M, Brune J, Beutner U, Tsauro I, Ramon A, Otto T.** Application of Dried Human Amnion Graft to Improve Post-Prostatectomy Incontinence and Potency: A Randomized Exploration Study Protocol. *Advances in Therapy*. 2020 Jan;37(1):592-602.
- 25 **Söhling N, Leiblein M, Schaible A, Janko M, Schwäble J, Seidl C, Brune JC, Nau C, Marzi I, Henrich D, Verboket RD.** First Human Leucocyte Antigen (HLA) Response and Safety Evaluation of Fibrous Demineralized Bone Matrix in a Critical Size Femoral Defect Model of the Sprague-Dawley Rat. *Materials (Basel)*. 2020 Jul 13;13(14):3120.
- 26 **Verboket RD, Leiblein M, Janko M, Schaible A, Brune JC, Schröder K, Heilani M, Fremdling C, Busche Y, Irrle T, Marzi I, Nau C, Henrich D.** From two stages to one: acceleration of the induced membrane (Masquelet) technique using human acellular dermis for the treatment of non-infectious large bone defects. *European Journal of Trauma and Emergency Surgery*. 2020 Apr;46(2):317-327.
- 27 **Ackermann C, Frings J, Alm L, Frosch KH.** Arthroscopic Controlled Closed Reduction and Percutaneous Fixation of Posterolateral Tibia Plateau Impression Fractures. *Arthroscopy Techniques*. 2019 Jul 19;8(8):e867-e874.
- 28 **Anavi Lev K, Chaushu L, Schwarz F, Artzi Z.** Bone-implant-contact and new bone formation around implants placed in FDB blocks compared to placement at the adjunction of particulate FDB. *Clinical Implant Dentistry and Related Research*. 2020 Feb;22(1):21-28.
- 29 **Wagner JM, Conze N, Lewik G, Wallner C, Brune JC, Dittfeld S, Jaurich H, Becerikli M, Dadras M, Harati K, Fischer S, Lehnhardt M, Behr B.** Bone allografts combined with adipose-derived stem cells in an optimized cell/volume ratio showed enhanced osteogenesis and angiogenesis in a murine femur defect model. *Journal of Molecular Medicine (Berlin)*. 2019 Oct 1;97(10):1439-1450.
- 30 **Janko M, Sahn J, Schaible A, Brune JC, Bellen M, Schroder K, Seebach C, Marzi I, Henrich D.** Comparison of three different types of scaffolds preseeded with human bone marrow mononuclear cells on the bone healing in a femoral critical size defect model of the athymic rat. *Journal of Tissue Engineering and Regenerative Medicine*. 2018 Mar;12(3):653-666.

- 31 Verboket R, Leiblein M, Seebach C, Nau C, Janko M, Bellen M, Bönig H, Henrich D, Marzi I.** Autologous cell-based therapy for treatment of large bone defects: from bench to bedside. *European Journal of Trauma and Emergency Surgery: Official Publication of the European Trauma Society*. 2018 Oct;44(5):649-665.
- 32 Knels R, Stüpmann K, Pruß A, Klerke J, Kardoeus J, Hiller J.** Coding of Tissue and Cell Preparations Using Eurocode. *Transfusion Medicine and Hemotherapy*. 2017 Nov;44(6):401-405.
- 33 Paprottka FJ, Krezdorn N, Sorg H, Könniker S, Bontikous S, Robertson I, Schlett CL, Dohse NK, Hebebrand D.** Evaluation of Complication Rates after Breast Surgery Using Acellular Dermal Matrix: Median Follow-Up of Three Years. *Plastic Surgery International*. 2017;2017:1283735.
- 34 Pruß A.** Coding of Tissue and Cell Products. *Transfusion Medicine and Hemotherapy*. 2017 Nov;44(6):382.
- 35 Schroeter J, Schulz T, Schroeter B, Fleischhauer K, Pruß A.** Implementation of the Single European Code in a Multi-Tissue Bank. *Transfusion Medicine and Hemotherapy*. 2017 Nov;44(6):396-400.
- 36 Vitacolonna M, Belharazem D, Hohenberger P, Roessner ED.** In-vivo quantification of the revascularization of a human acellular dermis seeded with EPCs and MSCs in co-culture with fibroblasts and pericytes in the dorsal chamber model in pre-irradiated tissue. *Cell and Tissue Banking*. 2017 Mar;18(1):27-43.
- 37 Vitacolonna M, Doyon F, Belharazem D, Tsagogiorgas C, Hohenberger P, Roessner ED.** Transplanted fibroblasts proliferate in host bronchial tissue and enhance bronchial anastomotic healing in a rodent model. *The International Journal of Artificial Organs*. 2017 Sep 15;40(9):515-521.
- 38 Hohenberger P, Rössner E, Nowak K.** 9.7 Tumoren der Thoraxwand. In: *Expertise Thoraxchirurgie*, edited by Müller MR, Watzka SB. Thieme Verlag 2016, 331-338.
- 39 Smith MD, Brune JC, Petschke B, Mönig HJ, Hartmann B.** 21 Kultivierte autologe Hautzellentransplantate: Historie, Regulativa und Praxis. In: *Verbrennungschirurgie*, Lenhardt M, Hartmann B, Reichert B. Springer Verlag 2016, 195-220
- 40 Henrich D, Verboket R, Schaible A, Konradowitz K, Oppermann E, Brune JC, Nau C, Meier S, Bonig H, Marzi I, Seebach C.** Characterization of bone marrow mononuclear cells on biomaterials for bone tissue engineering in vitro. *BioMed Research International*. 2015;2015:762407.
- 41 Kasetty G, Kalle M, Mörgelin M, Brune JC, Schmidtchen A.** Anti-endotoxic and antibacterial effects of a dermal substitute coated with host defense peptides. *Biomaterials*. 2015;53:415-25.
- 42 Vitacolonna M, Belharazem D, Hohenberger P, Roessner ED.** Effect of dynamic seeding methods on the distribution of fibroblasts within human acellular dermis. *Cell and Tissue Banking*. 2015 Dec;16(4):605-14.
- 43 Vitacolonna M, Belharazem D, Maier P, Hohenberger P, Roessner ED.** 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 May 8;10(5):e0125689.
- 44 Bormann N, Schwabe P, Smith MD, Wildemann B.** Analysis of parameters influencing the release of antibiotics mixed with bone grafting material using a reliable mixing procedure. *Bone*. 2014 Feb;59:162-72.
- 45 Roessner E, Vitacolonna M, Schulmeister A, Pilz L, Tsagogiorgas C, Brockmann M, Hohenberger P.** Human acellular dermis seeded with autologous fibroblasts enhances bronchial anastomotic healing in an irradiated rodent sleeve resection model. *Annals of Surgical Oncology*. 2013 Dec;20 Suppl 3:S709-15.
- 46 Vitacolonna M, Belharazem D, Hohenberger P, Roessner ED.** Effect of static seeding methods on the distribution of fibroblasts within human acellular dermis. *BioMedical Engineering Online*. 2013 Jun 24;12:55.
- 47 Brune JC, Hesselbarth U, Seifert P, Nowack D, von Versen R, Smith MD, Seifert D.** CT Lesion Model-Based Structural Allografts: Custom Fabrication and Clinical Experience. *Transfusion Medicine and Hemotherapy*. 2012 Dec;39(6):395-404
- 48 Roessner ED, Vitacolonna M, Hohenberger P.** Confocal laser scanning microscopy evaluation of an acellular dermis tissue transplant (Epiflex®). *PLoS One*. 2012;7(10):e45991.
- 49 Roessner ED, Thier S, Hohenberger P, Schwarz M, Pott P, Dinter D, Smith M.** Acellular dermal matrix seeded with autologous fibroblasts improves wound breaking strength in a rodent soft tissue damage model in neoadjuvant settings. *Journal of Biomaterials Applications*. 2011 Jan;25(5):413-27.
- 50 Roessner E, Smith MD, Petschke B, Schmidt K, Vitacolonna M, Syring C, von Versen R, Hohenberger P.** Epiflex® a new decellularised human skin tissue transplant: manufacture and properties. *Cell and Tissue Banking*. 2011 Aug;12(3):209-17.
- 51 Karbe T, Braun C, Wulff B, Schröder AS, Püschel K, Bratzke H, Parzeller M.** Practical experience in post-mortem tissue donation in consideration of the European tissue law. *Forensic Science, Medicine, and Pathology*. 2010 Mar;6(1):3-8.
- 52 Putzier M, Strube P, Funk JF, Gross C, Mönig HJ, Perka C, Pruß A.** Allogenic versus autologous cancellous bone in lumbar segmental spondylodesis: a randomized prospective study. *European Spine Journal*. 2009 May;18(5):687-95.
- 53 Von Versen-Höynck F, Steinfeld AP, Becker J, Hermel M, Rath W, Hesselbarth U.** Sterilization and preservation influence the biophysical properties of human amnion grafts. *Biologicals*. 2008 Jul;36(4):248-55.
- 54 Pruß A, von Versen R.** Einfluss europäischer Regulativa auf Qualität, Sicherheit und Verfügbarkeit allogener Zell- und Gewebetransplantate in Deutschland [Influence of European regulations on quality, safety and availability of cell and tissue allografts in Germany]. *Handchirurgie, Mikrochirurgie, plastische Chirurgie*. 2007 Apr;39(2):81-7.
- 55 Scheffler S, Trautmann S, Smith M, Kalus U, von Versen R, Pauli G, Pruß A.** No influence of collagenous proteins of Achilles tendon, skin and cartilage on the virus-inactivating efficacy of peracetic acid-ethanol. *Biologicals*. 2007 Oct;35(4):355-9.
- 56 Galambos B, Csöngé L, von Versen R, Olah A, Tamas L, Zsoldos P.** Preservation of vein allograft viability during long-term storage. *European Surgical Research*. 2005 Jan-Feb;37(1):60-7.
- 57 Scheffler SU, Scherler J, Pruß A, von Versen R, Weiler A.** Biomechanical comparison of human bone-patellar tendon-bone grafts after sterilization with peracetic acid ethanol. *Cell and Tissue Banking*. 2005;6(2):109-15.
- 58 Von Versen-Höynck F, Hesselbarth U, Möller DE.** Application of sterilised human amnion for reconstruction of the ocular surface. *Cell and Tissue Banking*. 2004;5(1):57-65.
- 59 Pruß A, Göbel UB, Pauli G, Kao M, Seibold M, Mönig HJ, Hansen A, von Versen R.** Peracetic acid-ethanol treatment of allogeneic avital bone tissue transplants – a reliable sterilization method. *Annals of Transplantation*. 2003;8(2):34-42.
- 60 Pruß A, Kao M, Gohs U, Koscielny J, von Versen R, Pauli G.** Effect of gamma irradiation on human cortical bone transplants contaminated with enveloped and non-enveloped viruses. *Biologicals*. 2002 Jun;30(2):125-33.
- 61 Pruß A, Perka C, Degenhardt P, Maronna U, Büttner-Janz K, Paul B, Müller K, Klumpp C, Bruck JC, von Versen R.** Clinical efficacy and compatibility of allogeneic avital tissue transplants sterilized with a peracetic acid/ethanol mixture. *Cell and Tissue Banking*. 2002;3(4):235-43.
- 62 Von Versen-Höynck F.** *Humanes Amnion – Experimentelle Untersuchungen und klinische Erfahrungen*. 1–111, Dissertation an der Medizinischen Fakultät Charité der Humboldt-Universität Berlin, 2002.
- 63 Pruß A, Baumann B, Seibold M, Kao M, Tintelnot K, von Versen R, Radtke H, Dörner T, Pauli G, Göbel UB.** Validation of the sterilization procedure of allogeneic avital bone transplants using peracetic acid-ethanol. *Biologicals*. 2001 Jun;29(2):59-66.
- 64 Pruß A, Hansen A, Kao M, Gürtler L, Pauli G, Benedix F, von Versen R.** Comparison of the efficacy of virus inactivation methods in allogeneic avital bone tissue transplants. *Cell and Tissue Banking*. 2001;2(4):201-15.
- 65 Pruß A, Kao M, Kiesewetter H, von Versen R, Pauli G.** Virus safety of avital bone tissue transplants: evaluation of sterilization steps of spongiosa cuboids using a peracetic acid-methanol mixture. *Biologicals*. 1999 Sep;27(3):195-201.
- 66 Thielicke U, Thielicke B, von Versen R, Denner K.** Klinische Studie zum Einsatz von demineralisierter Knochenmatrix (DBM) in der Chirurgischen Stomatologie [Clinical study on the application of demineralized bone matrix (DBM) in surgical orthodontics]. *Beiträge zur Orthopädie und Traumatologie*. 1990 Aug;37(8):461-5.
- 67 Denner K, von Versen R, Freistedt B, Klein W, Dehmlow R.** Relevanz labordiagnostischer Methoden zur Bewertung der Osteoinduktivität von Knochenmatriximplantaten [Relevant laboratory diagnostic methods for the evaluation of the osteoinductivity of bone matrix implants]. *Zeitschrift für medizinische Laboratoriumsdiagnostik*. 1989;30(3):159-64.
- 68 Von Versen R, Denner K, Freistedt B, Seht B, Matthes G.** Verfahren zur Präparation demineralisierter Knochenmatrix [A method for the preparation of demineralized bone matrix]. *Zeitschrift für medizinische Laboratoriumsdiagnostik*. 1989;30(3):154-8.
- 69 Von Versen R, Starke R.** The peracetic acid/low pressure cold sterilization – a new method to sterilize corticocancellous bone and soft tissue. *Zeitschrift für experimentelle Chirurgie, Transplantation, und künstliche Organe*. 1989;22(1):18-21
- 70 Starke R, Hackensellner HA, von Versen R.** Experimentelle Untersuchungen zur Entkeimung von Transplantationsmaterial mit Peressigsäure [Experimental studies of the sterilization of transplantation material with peracetic acid]. *Zeitschrift für experimentelle Chirurgie, Transplantation, und künstliche Organe*. 1984;17(5):254-8.

Student projects and theses at the DIZG as part of university education— selected examples

YEAR	TITLE	NAME	DEGREE
2024	Einfluss der Sterilisationstemperatur auf biologische und physikalische Eigenschaften kortikaler mineralisierter Gewebe	Hermine Coenders	Forschungsprojekt
2024	Einfluss einer Pufferbehandlung auf biologische und physikalische Eigenschaften von demineralisierter Knochenmatrix	Justus Krekeler	Bachelor
2024	Einfluss von Sterilisations- und Gefriertrocknungszyklen auf die biologischen und physikalischen Eigenschaften spongiöser Gewebe	Celina Garbaden	Masters
2023	Influence of a spray application for primary human dermal fibroblasts on their behaviour in a wound healing model	Thilo Brill	Master
2023	Qualität von Röhrenknochen in Abhängigkeit der Reinigungsmethode	Hanan Kdouh	Bachelor
2023	Optimierung der Medienzusammensetzung bei der Kultivierung humaner Keratinozyten	Felix Hüttig	Bachelor
2022	Etablierung eines Verfahrens zur Trocknung von allogenen Knochenpräparaten	Dominik Lehmann	Bachelor
2022	Entwicklung eines Entfettungsprozesses für dermales Gewebe zur Herstellung humaner Allografts unter Verwendung superkritischer Fluidextraktion	Leon Unger	Master
2022	Xeno-freie Kultivierung von humanen Keratinozyten	Emily Elise Pgetz	Bachelor
2022	Bewertung von serumfreien und feederfreien Kultivierungsalternativen humaner Keratinozyten	Christina Leonie Frohn	Bachelor
2021	Etablierung von Methoden zur objektiven Zustandsbeschreibung des proliferativen Potentials von Keratinozyten in Kultur	Nora Gaertner	Bachelor
2021	Behandlung von Surrogaten und Hartgewebe mittels scCO ₂	Lennart Suckow	Praktikum
2021	Delipidierung humaner dermaler Matrices durch mechanische Verfahren – Einfluss auf die biomechanischen Eigenschaften der Matrices	Leon Schäfer	Bachelor
2021	Progenitorfrequenzanalyse in humaner Keratinozyten-Zellkultur	Henrike Keil	Master
2020	Optimierung einer Dezellularisierungsmethode für die Herstellung einer humanen azellulären dermalen Matrix	Svenja Ebeling	Bachelor
2020	Etablierung einer Holoklonfrequenzanalyse von Humanen Epidermalen Keratinozyten	Jan Renziehausen	Bachelor
2019	Optimierung der Herstellung von Amnion-Transplantaten	Ngoc Hai Chu	Bachelor

YEAR	TITLE	NAME	DEGREE
2019	Untersuchung verschiedener Einflussparameter auf die Entfettung humaner Spalthaut während der Prozessierung der hADM Epiflex®	Sarah Köhler	Projektarbeit
2019	Untersuchung der biomechanischen Eigenschaften humaner Sehnentransplantate	Kassandra Hoetzel	Bachelor
2019	Delipidierung humaner dermaler Matrices durch Triglycerid-Hydrolyse – Einfluss auf den residualen TG-Gehalt und die biomechanischen Eigenschaften der Matrices	Lena Schollmeyer	Bachelor
2018	Comparison of nozzle types used in cell spray applications	Miriam Heuer	Master
2017	Entfettung humaner Gewebetransplantate – Methodvalidierung einer enzymatischen Triglyceridbestimmung in hADM-Transplantaten als Grundlage für die Kontrolle der Restfettgehaltreduktion	Mandy Kästorf	Bachelor
2016	Entwicklung von Tests für die objektive Beurteilung biologischer und physikalischer Eigenschaften von Knochentransplantaten	Anja Hanke	Master
2016	Isolation und Nachweis von therapeutisch relevanten Proteinen aus Amnion	Sabrina Engel, geb. Pfeffer	Bachelor
2015	Optimierung von Qualitätsstandards und des Hilfsstoffes Choleratoxin in der Kultivierung von epidermalen Sheets	Emelie Maximiliane Landmann	Master
2015	Entwicklung eines Assays zur Beurteilung der Eignung von Feederzellen für die Kultur humaner Keratinozyten für Verbrennungsoffer	Constanze Dermitzel	Projektarbeit
2015	Biomechanische Beurteilung von ausgewählten Hartgewebetplantaten. Eignung zum Einsatz beim Impaction Bone Grafting	Anne Grünberg	Projektarbeit
2015	Erfassung und Analyse von Rückmeldungen zur Anwendung von Transplantaten	Emelie Maximiliane Landmann	Projektarbeit
2014	Entwicklung eines Antikörper-Panels zur Beurteilung der Qualität humaner Keratinozytensheets	Christin Gävert	Master
2013	Prüfung der Einflüsse verschiedener Medienmengen auf das Wachstum von Keratinozyten	Jenny Hoffmann	Bachelor
2012	Isolation und Charakterisierung von Zellen aus humanem Amnion	Alexandra Wagner	Bachelor
2011	Einfluss extrakorporaler Stoßwellen auf das Proliferationsverhalten von Keratinozyten in vitro	Sandra Münch	Diplomarbeit
2005	Tissue Engineering von autologen Fibroblasten in allogenen Matrices: Untersuchungen zum Stofftransport in Weichgewebetplantaten	Doris Kappelt	Diplomarbeit



Autologous cell cultures

The provision of cell cultures for clinical applications is an integral part of providing basic necessities.

The German Society for Burn Surgery confirmed the relevance of keratinocytes to the DIZG in a letter in spring 2023. You can find out how the Department of Biotechnology enables their provision with the utmost care on the following pages.

Grafts for burns medicine and hard-to-heal wounds

Autologous cell cultures are often the only treatment option for severely burned patients.¹⁵ With these and with donated (allogeneic) skin grafts for hard-to-heal wounds, the DIZG makes a significant contribution to improving patient care.

Medical treatment of extensive burns is extremely complex and requires multimodal therapy with multiple surgical interventions. In burn surgery, the use of autologous cell cultures has proven to be essential in many cases. The DIZG is the only institution in Germany to provide these. This enables us to offer clinics and burn centers a life-saving therapy option and an improved chance of recovery for patients, where there is not enough healthy skin to transplant elsewhere (autografting).

We provide autologous keratinocyte transplants as sheets and as a suspension. The suspension applied with the Cell Spray allows several doctors to spray at the same time, significantly reducing the application time – and with a lower risk of infection for the patient.



Keratinozyten as a sheet



Keratinozyten as a suspension

i For third-degree burns, it is particularly advantageous when regeneration of the dermis occurs before the transplantation of autologous keratinocytes. This can be achieved through the transplantation of dermis substitute materials or by applying keratinocytes combined with autologous skin. The goal is to increase the elasticity of the regenerated skin and reduce scarring.



Microscopic control of cell growth

Manufactured under the highest requirements

The cultivation and provision of keratinocytes are subject to strict regulatory requirements. Among other things, these make it necessary for the DIZG to have a separate clean room area just for them.



Processing the cells

The production of autologous keratinocytes is a process that requires extreme care and takes time. This process already begins during the biopsy with the removal of cells from the patient. The skin sample must be sterile be taken from clinically healthy areas. Suitable sites include the upper arms, lower abdomen, thighs, lower legs, or other intact, unburned area.

During collection, microbiological contamination must be avoided at all costs, as this can lead to possible complications, and may delay the delivery of cultivated keratinocytes.

This can be achieved by transplanting dermis substitutes or by using keratinocytes in combination with autologous skin. The aim is to increase the elasticity of the regenerated skin and reduce scarring.



Our autologous keratinocytes are registered as orphan medicinal products for the treatment of partial-thickness and full-thickness burns (Orphan Drug: EU/3/21/2483).

The recognition by the European Commission, based on a favorable opinion from the European Medicines Agency (EMA) confirms the relevance of the life-saving therapy option that DIZG offers severely injured patients.

The keratinocyte sheets

The autologous keratinocyte sheets fixed to a carrier are suitable for the treatment of extensive skin wounds and for the care of patients with severe burns. They are indicated:

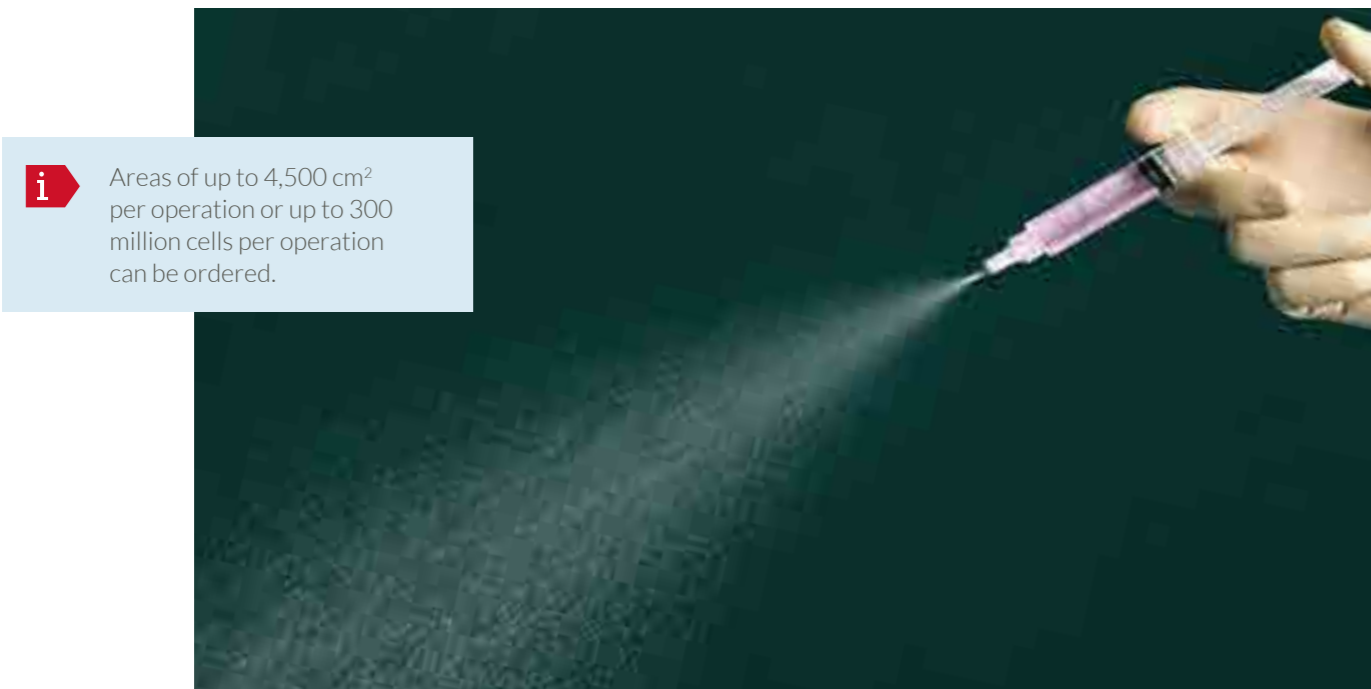
- > In case of extensive burns on the body surface.
- > In case of insufficient or poorly healing skin sampling sites.¹⁶
- > To accelerate the re-epithelialization of dermal wounds in combination with widely expanding autologous skin grafts.¹⁶
- > In children, the use of autologous keratinocyte grafts is indicated even for smaller areas because of the often-limited donor sites.¹⁶



Keratinocyte sheet

The keratinocyte suspension

The ready-to-use autologous keratinocytes, prepared as a suspension, are indicated for the treatment of skin wounds and grade 2b burns. The use of Cell Spray for burns in visible areas of the body, such as the face, hands, neck, and décolleté, or in regions with complex topography, achieves good results.¹⁶



i Areas of up to 4,500 cm² per operation or up to 300 million cells per operation can be ordered.

Uniform application of cultured cells with the Cell Spray

Nozzles influence the success of therapy

The nozzle of the spray system is crucial for cell viability, good metabolic activity and optimum spray distribution in the treatment of patients with severe skin defects.

This is confirmed by a study published in 2024 that compared air-assisted and unsupported nozzles.¹⁷

The success of the cell sprays, particularly in topographically complex wound regions, depends to a large extent on efficient cell delivery and complete wound coverage.¹⁵

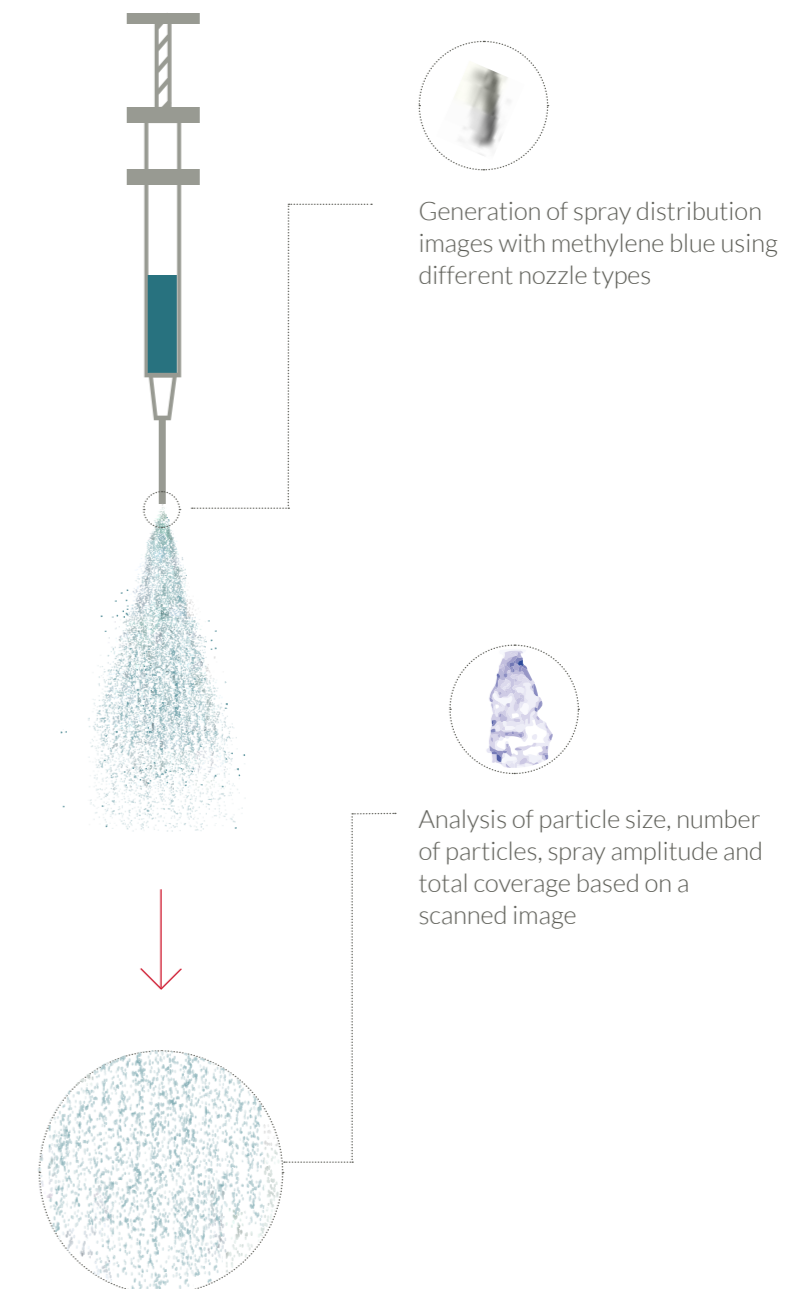
A good spray distribution is required with

- > low droplet size,
- > high particle count and
- > high surface coverage.

These parameters can be influenced by the nozzle. There are two main types of nozzles: non-assisted nozzles, which produce a mist without the help of additional air, and air-assisted nozzles, which use an additional air stream. The study compares different nozzle variants and concludes that nozzle shapes without additional air flow are also ideally suited for the application of clinical cell suspensions with regard to the spray pattern and cell health.

The choice of nozzle in keratinocyte suspension therapy is therefore crucial for the successful treatment of severe burns.

The distribution analysis



The production steps of autologous cell cultures

1. EXTRACTION/PREPARATION



Extraction kit

The DIZG extraction kit contains biopsy tubes, documents such as the consent form, the collection form and a collection guide.



Shipping of the biopsies to the DIZG

The biopsies are sent to the DIZG refrigerated (5-22 °C). Temperature control is performed when the kit is received in the DIZG.



Preparation of the biopsy specimen for cell isolation

Prior to cell isolation, biopsies are gently decontaminated by incubation in various buffer solutions.

2. PROCESSING



Processing the cells

The cells are processed in a class A clean room.



Cell proliferation

The autologous cells are incubated in previously sterilized incubators at 37 °C.



Control of culture growth

The growth and proliferation of the cells are controlled microscopically.

3. PREPARATION OF SHEETS FOR TRANSPLANTATION



Sheet preparation

Preparation begins with culturing the cells until they form a thin membrane.



Keratinocyte sheet

It takes an average of about three weeks from sowing the cells to the formation of a firmer membrane.



Fastening to the gauze

With the enzymatic treatment of the keratinocyte sheets, the preparation begins: each sheet is dissolved and bound to a support. Afterwards, the sheets are ready for transplantation.



Shipment

A special courier is used to send the finished transplants under refrigeration. These can remain in the box until transplantation.

4. PREPARATION OF THE SUSPENSION FOR TRANSPLANTATION



Time of preparation

The keratinocyte suspension can be prepared for transplantation after ten (+/-two) days.



Filling the syringes

On the day before transplantation, the cells are enzymatically treated and separated, and the concentration and viability are determined. The finished suspension is filled into the syringes.



Packing & shipping

The finished suspension is shipped refrigerated. It can remain in the box until use.

Helping severely burned people

In 2024, **17 cases** were processed. Keratinocyte sheets with a total area of **19,140 cm²** and keratinocyte suspensions with a total cell count of **960 billion cells** were delivered. The latter were applied using the Cell Spray, which enables easy handling.



COMPREHENSIVE SUPPORT FOR BURN CLINICS

When using autologous cell cultures, burn clinics must meet regulatory requirements. This means: Each clinic must have its own permit for the collection and provision of biopsies for the cultivation of autologous cells in accordance with § 20b (1) of the German Medicines Act (AMG) or a license through a contractual obligation with a manufacturer such as the DIZG in accordance with § Section 20b (2) AMG. The DIZG assists burn clinics in obtaining this certificate. The clinics benefit in particular from our many years of experience.



Quality and safety

Patient safety is the top priority

Strict donor selection, comprehensive serological screening, precise manufacturing processes and experienced quality management ensure safe allogeneic avital transplants.

Maximum quality standards for safe allografts

Since it was founded in 1993, the DIZG has manufactured 868,000 allogeneic tissue transplants.

Since then, no graft application has ever evidently resulted in graft-derived transmission of microbiological or viral infection. This impressively demonstrates that quality and safety are our top priority.

DIZG grafts are produced to the highest quality standards, in part under Class A cleanroom conditions. The DIZG is subject to monitoring by the Paul Ehrlich Institute and the LAGeSo Berlin; it has permits and approvals

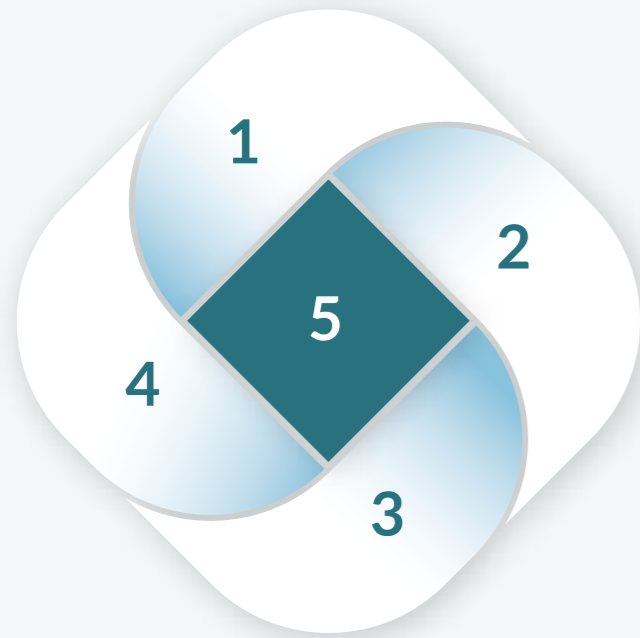
pursuant to § 21 und § 21a AMG as well as the corresponding manufacturing authorizations according to § 13 and § 20c AMG. A large number of laws, regulations, and standards are taken into account during the manufacturing process.

Besides numerous other safety precautions, we use a validated and published inactivation procedure for viruses and microorganisms which simultaneously protects the biological integrity of the tissue.

Reviewing the donor file for donor exclusion criteria



The following safety aspects form the basis of this high level of safety:



1 Medical background screening

Assessment of the anamnesis and medical history according to strict internationally standardized exclusion criteria by doctors in clinics as part of an agreed quality management system.

2 Serologic screening in certified laboratories

The scope of serological screening for tissue donations conducted by DIZG exceeds the requirements of EU Directive 17/2006/EC. In addition to the legally required serological tests, DIZG also performs PCR tests to exclude HIV, Hepatitis B and C.

Furthermore, after preparation/ before sterilization, a bioburden analysis is completed on the donated tissue, in which all viable germs are counted. Only when the colony-forming units (CFU) are below the defined threshold values are the tissues released for further processing.

3 Validated sterilization and inactivation procedure

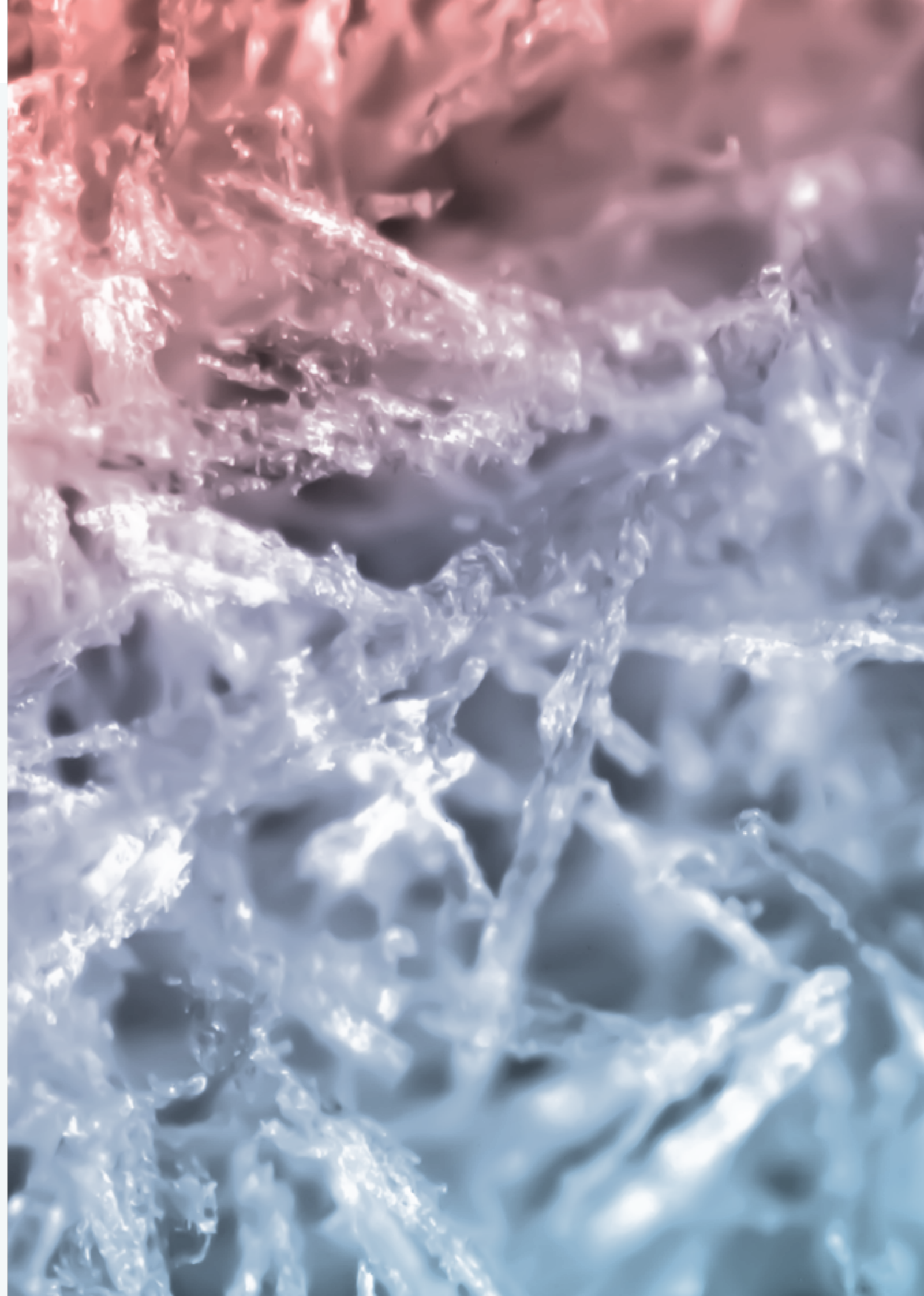
The validation study was conducted in cooperation with Charité and the Robert Koch Institute. The effectiveness of the procedure was examined using model organisms (enveloped and non-enveloped viruses as well as bacteria and spore-formers) according to European guidelines and official recommendations. The results were published.

4 Sterility testing

The release of a manufactured batch for clinical application requires confirmation of the batch's sterility according to the test specifications in the European Pharmacopoeia. This testing is carried out in certified laboratories.

5 Quality management

DIZG operates a quality management system in accordance with the requirements of GMP and GFP regulations. Processes for obtaining tissue donations, transport of tissues, manufacturing of allogeneic and autologous transplants, testing, release and distribution, as well as the procedure for process changes are strictly regulated and monitored. Based on the aforementioned safety levels, the responsible pharmaceutical authorities and state health authorities have issued pharmaceutical approvals and authorizations according to § 21 and § 21a of the German Medicines Act (AMG) and manufacturing permits according to § 13 and § 20c.





As a non-profit manufacturer of medicinal products, according to Articles 20c and 13 of the German Medicinal Products Act, DIZG is subject to regulatory oversight. All DIZG tissue grafts have marketing authorizations according to Article 21 AMG or approvals according to Article 21a AMG.

Safety for Clinics and physicians

The Patient Rights Act passed in 2013 strengthened patient rights. This also gave new significance to user safety. This means: Clinics are forced to protect themselves well against potential damage cases. Surgery is particularly affected. Errors in the storage of femoral heads manufactured internally by clinics due to incorrect temperatures, faulty or insufficient documentation in the in-house production of femoral head transplants, for example, and the signatures associated with the release process gained new legal relevance with the Patient Rights Act.

DIZG transplants are of human origin

A SELECTION OF OUR DIZG TRANSPLANTS FROM AROUND 230 DIFFERENT PACKAGE SIZES



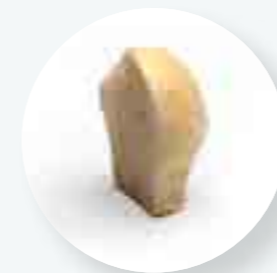
Cancellous bone blocks



DBM putty



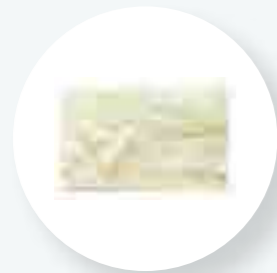
DBMx press



Femoral heads



Cancellous chips



Fascia lata



Spierings chips



Amnion



Epiflex® human skin, acellular



Fiberfill®



Epiflex® ≥ 3 mm



Shark Screw®



Menisci



Spongioflex®



Spongioflex®

The transplants approved according to § 21 AMG and those authorized according to § 21a AMG are manufactured using a validated virus inactivation process. They have the following properties:

- > Free of preservatives and antibiotics
- > Safe because of the validated sterilization process
- > Free of animal components
- > Manufactured without thermal treatment
- > Storage of the freeze-dried grafts at room temperature

i You can find a complete overview in our transplant catalog.

DIZG at a glance

FOUNDED

August 1993 as a non-profit GmbH company in Berlin

MANAGING DIRECTOR

Jürgen Ehlers

HEADQUARTERS

Innovationspark Wuhlheide in Berlin

NUMBER OF EMPLOYEES

As of March 1, 2025, there are 137 employees.

FIELDS OF ACTIVITY

The German Institute for Cell and Tissue Replacement (DIZG) is a non-profit manufacturer of allogeneic tissue transplants and autologous cell cultures. The focus is on research and development, with the goal of offering people with severe tissue defects improved recovery prospects. The basis for using a DIZG transplant must always be the surgeon's assessment that the use of human tissue transplants is medically indicated. The variety of transplants is constantly being expanded. Currently, more than 69,900 patients benefit annually from around 230 different types of transplants from the DIZG cleanrooms.

MARKETING AUTHORIZATIONS FOR MEDICINAL PRODUCTS

Eleven marketing authorizations for medicinal products in accordance with Article 21 AMG

Musculoskeletal tissue

- > Human cortical bone, freeze-preserved, DIZG
- > Human cortical bone, lyophilized, DIZG
- > Human cancellous bone, freeze-preserved, DIZG
- > Human cancellous bone, lyophilized, DIZG
- > Human ligament/tendon tissue, freeze-preserved, DIZG
- > Human fascia, lyophilized, DIZG
- > Demineralized human bone matrix, lyophilized, DIZG
- > Human cartilage, freeze-preserved, DIZG

Tissue for wound healing and soft tissue reconstruction

- > Human amnion, dried, DIZG
- > Human skin, freeze-preserved, DIZG
- > Human acellular dermis Epiflex®, lyophilized, DIZG

Two drug approvals according to § 21a AMG

Tissue preparation

- > Bone screw (Shark Screw®) freeze-dried, DIZG
- > Fiberfill®, freeze-dried, DIZG

LEGAL FORM

Non-profit limited liability company (Gemeinnützige GmbH)

MANUFACTURING AUTHORIZATION

Authorization according to Articles 13 and 20c AMG for the manufacture of allogeneic tissue grafts and autologous cell cultures.

CUSTOMER SERVICE

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distribution@dizg.de

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Gemeinnützige Gesellschaft mbH
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References

1. **Verboket RD, Henrich D, Janko M, Sommer K, Neijhoft J, Söhling N, Weber B, Frank J, Marzi I, Nau C.** Human Acellular Collagen Matrices – Clinical Opportunities in Tissue Replacement. *International Journal of Molecular Sciences* 2024 Jun 28;25(13):7088.
2. **Dabaghi M, Eras V, Kaltenhäuser D, Ahmed N, Wildemann B.** Allografts for partial meniscus repair: an in vitro and ex vivo meniscus culture study. *Frontiers in Bioengineering and Biotechnology*. 2023 Oct 12;11:1268176.
3. **Feeley BT, Lau BC.** Biomechanics and Clinical Outcomes of Partial Meniscectomy. *Journal of the American Academy of Orthopaedic Surgeons*. 2018 Dec 15;26(24):853-863.
4. **Behrendt S.** MRI follow up of bilateral partial meniscal substitution with a demineralized bone block. A case report. *Radiology Case Reports*. 2022 Oct 27;18(1):21-26.
5. **Kyyak S, Pabst A, Heimes D, Kämmerer PW.** The Influence of Hyaluronic Acid Biofunctionalization of a Bovine Bone Substitute on Osteoblast Activity In Vitro. *Materials (Basel)*. 2021 May 27;14(11):2885.
6. **Aslan M, Şimşek G, Dayi E.** The effect of hyaluronic acid-supplemented bone graft in bone healing: experimental study in rabbits. *Journal of Biomaterials Applications*. 2006 Jan;20(3):209-20.
7. **Alcântara CEP, Castro MAA, Noronha MS, Martins-Junior PA, Mendes RM, Caliarí MV, Mesquita RA, Ferreira AJ.** Hyaluronic acid accelerates bone repair in human dental sockets: a randomized triple-blind clinical trial. *Brazilian Oral Research*. 2018 Sep 13;32:e84.
8. **Park D, Kim Y, Kim H, Kim K, Lee YS, Choe J, Hahn JH, Lee H, Jeon J, Choi C, Kim YM, Jeoung D.** Hyaluronic acid promotes angiogenesis by inducing RHAMM-TGFβ receptor interaction via CD44-PKCδ. *Molecules and Cells*. 2012 Jun;33(6):563-74.
9. **Altman R, Bedi A, Manjoo A, Niazi F, Shaw P, Mease P.** Anti-Inflammatory Effects of Intra-Articular Hyaluronic Acid: A Systematic Review. *Cartilage*. 2019 Jan;10(1):43-52.
10. **Brcic I, Pastl K, Plank H, Igréc J, Schanda JE, Pastl E, Werner M.** Incorporation of an Allogenic Cortical Bone Graft Following Arthrodesis of the First Metatarsophalangeal Joint in a Patient with Hallux Rigidus. *Life (Basel)*. 2021 May 24;11(6):473.
11. **Labmayr V, Huber E, Wenzel-Schwarz F, Holweg P, Ornig M, Jakob G, Palle W, Borchert GH, Pastl K.** Non-Union Treatment in the Foot, Ankle, and Lower Leg: A Multicenter Retrospective Study Comparing Conventional Treatment with the Human Allogenic Cortical Bone Screw (Shark Screw®). *Journal of Personalized Medicine*. 2024 Mar 27;14(4):352.
12. **Kirschbaum S, Gerhardt C, Akgün D, Eras V, Kaltenhäuser D, Thiele K.** Fascia lata allograft: a suitable alternative in ligamentous reconstruction for chronic elbow instability? *JSES International*. 2024 May 24;8(5):1137-1144.
13. **Mudry A.** Jacques-Louis Reverdin (1842-1929) und die Epidermis-Transplantation. *Schweizerisches Medizin-Forum*. 2014;14(36):651-653.
14. **Verboket RD, Leiblein M, Janko M, Schaible A, Brune JC, Schröder K, Heilani M, Fremdling C, Busche Y, Irrle T, Marzi I, Nau C, Henrich D.** From two stages to one: acceleration of the induced membrane (Masquelet) technique using human acellular dermis for the treatment of non-infectious large bone defects. *European Journal of Trauma and Emergency Surgery*. 2020 Apr;46(2):317-327.
15. **Hartmann B, Ekkernkamp A, Johnen C, Gerlach JC, Belfekroun C, Küntscher MV.** Sprayed cultured epithelial autografts for deep dermal burns of the face and neck. *Annals of Plastic Surgery*. 2007 Jan;58(1):70-3.
16. **Hartmann B.** Arzneimittelzulassung autologe Hautzellprodukte – Stellungnahme zum klinischen Einsatz von autologen Keratinozyten-Suspensionen sowie von Sheets von humanen Keratinozyten zur autologen Anwendung. 2021, unpublished.
17. **Heuer M, Stiti M, Eras V, Scholz J, Ahmed N, Berrocal E, Brune JC.** High-Speed Fluorescence Imaging Corroborates Biological Data on the Influence of Different Nozzle Types on Cell Spray Viability and Formation. *Journal of Functional Biomaterials*. 2024 May 14;15(5):126.

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