BONEBANK

Result Report

German-Danish Biobank and Innovation Platform for Stem Cells in Bone Regeneration

Interreg
Deutschland - Danmark

EUROPEAN UNION

This project is funded by Interreg Deutschland-Danmark with money from the European Regional Development Fund.European Development Fund.

Imprint

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This document presents a compilation on the key findings provided by the partners.

BONEBANK – the project

Currently, bone marrow and bone fragments containing valuable stem cells are discarded as waste during routine bone operations. The potential of these stem cells lies primarily in their use for regenerative therapies, such as the treatment of bone fractures.

Our aim is to harvest these stem cells with new instruments and methods and to store them in cross-border biobanks. Thereby, this valuable resource can be made available for therapeutic purposes or for research into advanced therapies.

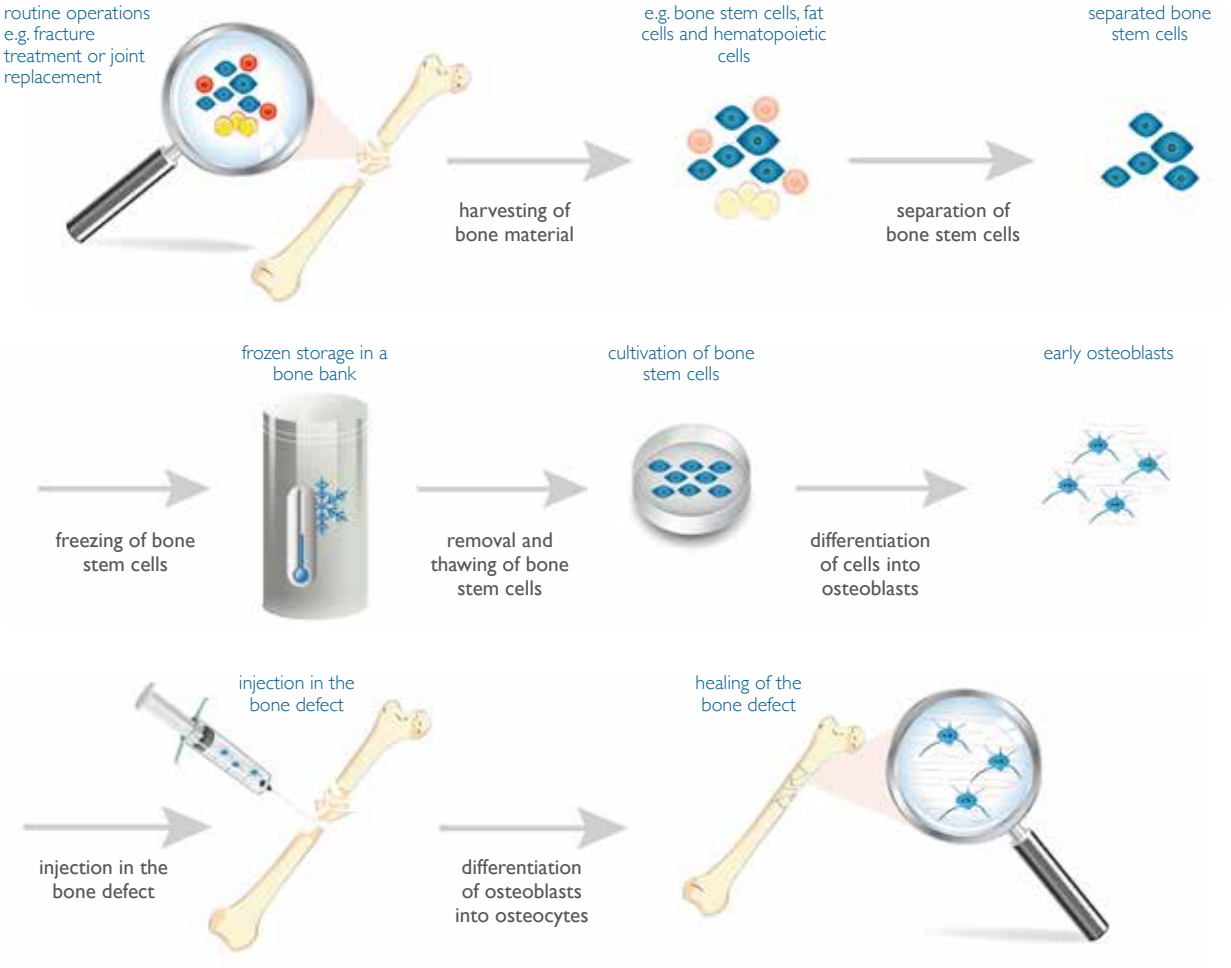

Figure 1: The BONEBANK value chain.

The results of BONEBANK are interesting for various target groups:

- Clinicians and hospitals implement the BONEBANK approach to harvest bone marrow stem cells during routine operations.
- Public and/ or private biobank operators are part of the BONEBANK value chain to store, use and / or market stem cells.
- Academic researchers use bone marrow stem cells for research purposes.
- Life Science Industry (medtech, biotech, pharma) companies purchase bone marrow stem cells for research and the development of therapies.
- Politicians and the general public understand the potential of bone marrow stem cells for regenerative medicine, and the value of the BONEBANK network for the cross-border region.

Harvesting bone material

1. Goal

In the first phase of the BONEBANK project, a unique value chain was created, in which bone and bone fragments that contain stem cells were harvested during routine operations. After harvesting, this bone material was transported to the corresponding lab and the stem cells were isolated. Finally, the isolated stem cells were stored in the cross-border biobank in Lübeck and Odense. The bone material was only harvested at the hospitals in Lübeck and Odense. In order to expand the scope of the BONEBANK project, the goal in the extension phase was to attract more hospitals to participate in the BONEBANK value chain as donor hospitals.

2. Results

BONEBANK aimed to attract more hospitals to become donor hospitals in the project. So the first step was to identify potentially interested hospitals and to provide them with information material about the BONEBANK project, and then to ask them about their willingness to participate in the project.

The next step was to determine the clinic-specific requirements that must be taken into account when integrating the hospital system into the BONEBANK value chain. A prerequisite for the collection of bone material is obtaining the approval of the ethics committee responsible for the clinic.

Therefore, for each clinical and ethical issue, a proposal must be prepared in cooperation with the respective clinic. Following a positive vote by the ethics committee, the transport containers for collection are sterilely sealed and packaged (according to GMP standards), and handed over to the new collection hospitals, where harvesting begins. The harvested bone material is then transported to the responsible laboratory by a logistics company, and the isolated stem cells are stored in the cross-border biobank.

This collected bone material, as well as the bone material collected in Lübeck and Odense, may only be harvested for research purposes, as the donor hospitals involved do not currently have a license for collecting human tissue for human application.

In order to expand the value chain developed for the collection of bone material for regenerative therapies, an SOP has been developed for the GMP-compliant collection of bone material.

3. Conclusion & Outlook

The next steps are to involve more donor hospitals in the BONEBANK value chain developed, to increase the scope of the BONEBANK project and to support the hospitals involved with obtaining a license for collecting human tissue for human application, and to expand the GMP-compliant harvesting of bone material for regenerative therapies.

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Clinical application of harvesting device and stem cell mapping

1. Goal

There is currently no clarity about the exact distribution of stem cells within the bone. Stem cell mapping aims to optimise the localisation of bone harvesting in such a way as to enable a highly-efficient extraction of potent stem cells of high quality, even with a small sample size. The activity builds on the human cells already collected as well as the cells from the animal experiments collected with the further developed harvesting device. The harvesting device which was successfully developed in the first phase of BONEBANK should be available in a series of 20-30 units in sterile packaging at the beginning of the project's extension, in the form of a revised prototype. However, as a result of the tightening of the EU Medical Devices Regulation (MDR) in May 2017, a significantly expanded approval programme is required (there is no equivalent reference product on the market). For this purpose, an explanation of the functionality and health safety of the device in animal experiments is required first.

2. Results

At the start of the extension phase of BONEBANK, the design of the BONEBANK harvesting device was optimised for injection moulding and glue-free assembly in the cleanroom. Current material standards changed at the beginning of 2020, and consequently material certificates and choices of injection moulding application had to be adjusted.

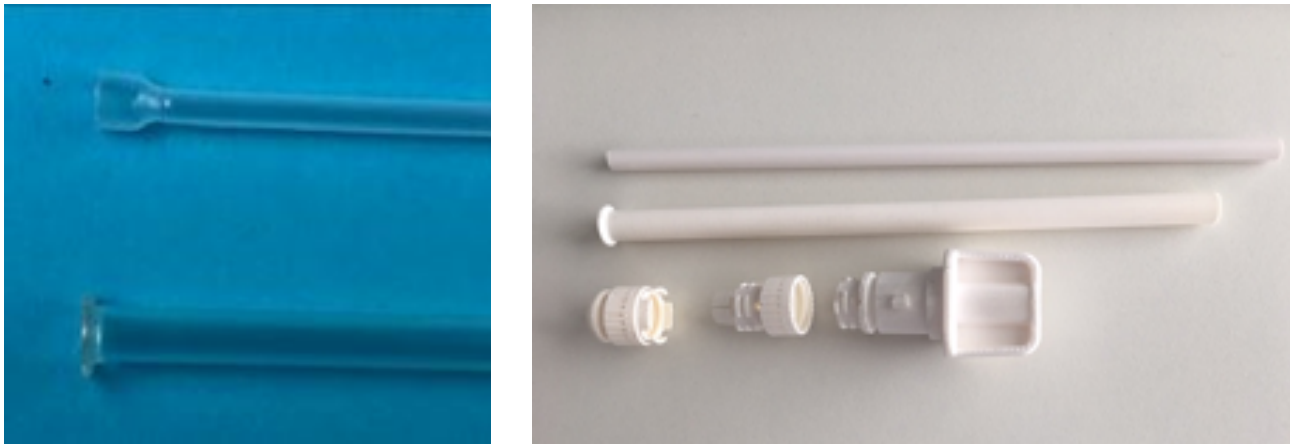

Figure 2: The extruded cannulas for the BONEBANK harvesting device. The tubes (inner and outer cannula) are manufactured from polypropylene (PP) and temperature-formed at their ends (see left) to allow glue-free assembly with the cannula adapter parts (shown on the right).

The transition of the cannula design from prototyping to standard production turned out to be more time-consuming than expected. The tube manufacturing was outsourced to a specialised sub-supplier, who initially had problems adhering to the narrow tolerances of the design specs. With an eye on risk mitigation and cost efficiency, the cannula assembly was switched to glue-free clamping, which requires precisely-extruded materials. Finally, this issue was solved.

Other material was ordered from medical device suppliers for the purchased parts (filters, seals) of the BONEBANK harvesting device. The entire product line was set up together with a sub-supplier specialised in cleanroom assembly. In addition, different sterilisation procedures and packaging templates were tested, to determine the correct process for the extension phase of BONEBANK.

Side logo: Accent Light Gray Logo on Stryker Body White Plastic

Logo and color considerations

Figure 3: Exploded view of the BONEBANK harvesting device and its components.

A "surgical technique" document was developed to describe the setup and use of the BONEBANK harvesting device. Three cadaveric workshops were presented in order to prepare/train the performing scientists in proper handling. The labs were performed in Aachen and in Kiel on full sheep carcasses and on sheep bones. The functional outcome as well as the training effect were successful.

The Institute of Health and Biomedical Innovation (IHBI) at Queensland University of Technology in Brisbane started and finalised preparations for the animal experiments for BONEBANK's extension phase. Due to the coronavirus crisis, the experiments will only be completed in the second half of the year.

The lab setup was adjusted to perform various analytical procedures on harvested material, among them viability analysis for bone grafts. Surgical equipment for intramedullary surgical approaches was provided by Stryker, along with the required consumables.

Stryker also supported the anatomical preparations by performing X-ray and CT scans of sheep bones and transferring this data into CAD formats for further processing. These models were printed in 3D-printing prototyping and provided to the IHBI, to support study planning and improve orientation and scaling.

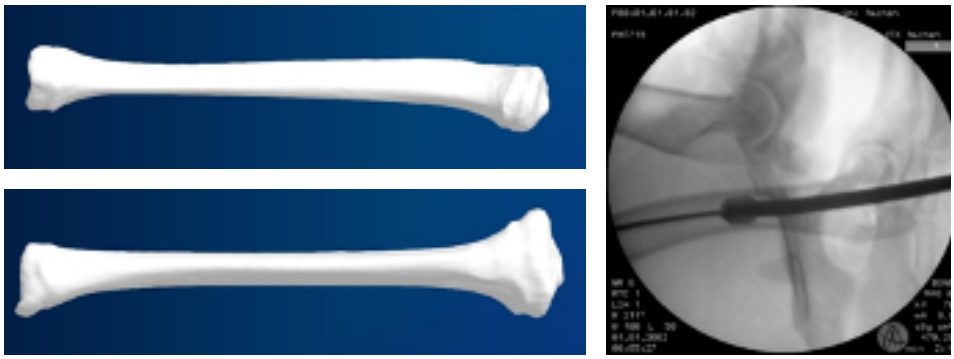

Figure 4: Sample sheep bones from additive manufacturing (left) and X-ray image from a sheep cadlab with master scale for dimension reference.

A study protocol was created. Based on this, an ethical application document was developed and successfully submitted to the Australian ethical committee UAEC. Ethical approval was granted on 17 March 2020 (Application no. 2000000013, valid until March 2023). In addition, the Stryker internal procedure DQP 21-001 for pre-clinical investigations according to quality management ISO 13485 was documented and initiated. This is an ongoing procedure, accompanying the entire study. Due to the coronavirus crisis, the experiments will only be completed in the second half of the year.

3. Conclusion & Outlook

From the results reported, we can conclude that the essential study preparations have been completed.

The next step will be the provision of the BONEBANK harvesting devices in five (5) lot sizes of 10. The product samples will be provided pre-assembled, labelled in sequential order and in a sterile condition - ready for use in the animal OR.

Subsequently, animal experiments will be carried out according to the study protocol, which will result in fresh tissue material samples for immediate analysis in the lab.

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Development of an injection device

1. Goal

Currently, in most cases trephines are used in clinical trials to inject a stem cell product into a non-union. Trephines were originally developed for biopsies taken from the bone, and therefore have some disadvantages for the injection of stem cells into non-unions. The trephines used are usually too long and inconvenient for injection into long tubular bones. Consequently, exact positioning - which must be verified by X-ray imaging - is difficult, and the precise injection of the stem cell product into the fracture gap is not guaranteed. For this reason, a new device to inject a stem cell product into a non-union must be developed.

Besides good handling of the injection device, a high number of vital mesenchymal stem cells are necessary for therapeutic success. But during the injection of stem cells into a non-union through a tubular cannula, shear forces act on the stem cells injected, which among other things can affect the viability of the cells - because these shear forces can lead to rup-turing of the cell membrane, and hence to necrosis of the stem cells.

One parameter which influences the level of the shear forces is the volume flow. The higher the volume flow, the higher the prevailing shear forces. In order to investigate whether volume flows influence the viability of the cells, a test setup was developed to carry out the injection process through the cannula with different volume flows.

2. Results

The injection device developed consists of the following components: connector, ergonomic handle, depth limiter and cannula (see Figure 5).

Figure 5: CAD model of the injection device developed with connector (a), ergonomic handle (b), depth limiter (c) and cannula (d).

The stem cell product needed for the injection is usually delivered in a syringe. To avoid a transfer of the product and the associated risk of contamination of the cell product, a connector (see Figure 5 a) was designed. A standardised connection system was used, known in medical technology as a Luer lock, with connecting pairs of "female" and "male" fittings. Since the syringes used in medicine have the "male" connection, the connection on the injection device was developed with the "female" counterpart.

To ensure good handling during the surgical procedure, an ergonomic handle was developed (see Figure 5 b). The design of the handle is based on the pistol grip model, where the whole hand grips the handle vertically. This makes it easier for the surgeon to position the cannula correctly in the non-union, and ensures optimal control of the pressure on the fracture gap.

With the devices currently used for the injection of stem cell products, it is not possible for the surgeon to determine the exact depth of penetration of the cannula during positioning in the non-union. Only by means of multiple X-rays can the surgeon find the optimal position of the cannula for the injection, which increases the radiation exposure for the patient and the surgical team. To minimise the radiation exposure, a depth limiter was integrated below the handle, which allows the surgeon to determine exactly how far the cannula should penetrate the non-union (see Figure 5 c). Accordingly, a single X-ray image is sufficient to determine the optimal position before inserting the cannula and before injecting the stem cell product.

Another component of the device is the cannula, through which the stem cell product is injected into the non-union (see Figure 5 d). The cannula must be sufficiently long to reach the non-union through the skin, fat layer, fascia and muscle groups, e.g. in the femur. Furthermore, the cannula is subjected to strong forces during insertion into the non-union, which must not cause it to bend.

A further aspect is the material used for the cannula. This must be visible in X-rays and the radiation must not lead to any material degradation. Therefore, stainless steel is suitable as a material for the cannula. An additional advantage of this material is the guaranteed biocompatibility, through its use in other approved surgical instruments.

For the commercialisation of the injection device developed on the European market, a concept was prepared indicating all required steps for the certification process and compliance with the legal requirements of the European Union.

In addition to the development of the injection device and the related approval concept, a test setup was developed to carry out the injection process through the cannula. This is due to the fact that during the injection of stem cells into a non-union through a tubular cannula, shear forces act on the MSCs injected, which among other things can affect the viability of the cells. These shear forces can lead to rupturing of the cell membrane, and hence to necrosis of the stem cells. One parameter which influences the level of the shear forces is the volume flow. The higher the volume flow, the higher the prevailing shear forces. In order to investigate whether volume flows influence the viability of the cells, experiments with the test setup developed were conducted with different volume flows.

To obtain an initial estimate of the order of magnitude of the volume flow during the injection of stem cells into a non-union, the injection pressure and the volume flow were determined with the help of a surgeon, who performed such injections as part of a clinical study.

The results of these experiments show an average volume flow of 15.81 ml/min with an average pressure of 93.6 kPa and a maximum volume flow at the highest pressure level of 38.65 ml/min. Since a higher volume flow leads to higher shear forces on the cells, the experiments were carried out with volume flows of 38 ml/min and 100 ml/min.

The measurements showed no decrease in cell viability after the injection via cannula with the two different volume flows.

3. Conclusion & Outlook

The device developed that is presented here features an ergonomically-designed handle, which allows precise control of the device. The extended length of the device enables the surgeon to place the needle under X-ray-based evaluation without exposure to the main radiation field, and the depth limiter ensures an exact injection depth. The next step will be the CE certification of the injection device, based on the approval concept prepared.

The viability measurements showed no impact on cell viability after injection with the two different volume flows. In a follow-up step, further parameters that could potentially lead to a decrease in viability will be investigated, e.g. a higher cell concentration, a greater length or a smaller diameter of the needle.

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CQ – Cell quality for biobanking

1. Goal

In the extension stage of BONEBANK, one aim was to validate cultivation and quality parameters determined during the first phase of the project. Furthermore, variances of individual parameters should be used to make the SOPs developed more specific, to define thresholds and to precisely measure the quality of unknown samples.

Therefore, the quality of mesenchymal stem cells (MSCs) was compared while using three different methods of sampling: a) direct isolation and cultivation of MSCs (fresh); b) storage of whole bone fragments in the vapour phase of liquid nitrogen with subsequent isolation and cultivation of MSCs (frozen bone) and c) cultivation of MSCs after isolation and storage in the vapour phase of liquid nitrogen (frozen cells). Based on this experimental setting, a score was defined in order to categorise samples according to their biological quality.

2. Results

Evaluation of quality parameters for the three sampling conditions was conducted using samples from eight patients (5 females and 3 males, mean age = 71.2) collected at the UKSH, Germany. The freshly collected cells were used as a reference for the analysis. Based on MSC criteria of the International Society for Cellular Therapy, colony-forming unit (CFU) assays, proliferation assays, osteogenic & adipogenic differentiation ability, as well the expression of CD44, CD73, CD34 and CD14 were analysed. Moreover, genomic stability of the cells was tested by means of Feulgen staining and subsequent image cytometry ploidy measurement.

The results showed that it is possible to isolate MSCs from frozen bone pieces, as well as to cultivate MSCs that were frozen directly after the isolation. While the sampling and storage method of MSCs did not affect their genomic stability and marker expression, it impacted their proliferation rate, colony-forming ability and differentiation ability. Overall, extracted MSCs from frozen bone presented a worse colony-forming ability, proliferation rate and differentiation ability compared to the other two sampling methods.

Based on these initial results, a quality score for MSCs was defined in order to detect MSCs with bad properties for therapy options. For the calculation of the score, each group of quality parameters was divided into quartiles and corresponds to a value from 1 to 4. The results showed a significant difference between the three sampling groups: while the frozen bone samples had the lowest score, fresh samples demonstrated the highest score, which thus allowed characterisation of the quality of cells. A subsequent validation of the score using an independent cohort of fresh samples was successful.

3. Conclusion & Outlook

All methods of MSC sampling are technically feasible, but with different impacts on proliferation and differentiation. Furthermore, the results showed that it is possible to establish a score to categorise the samples according to their quality parameters. A further validation of the score using a GMP-compliant product from Næstved Hospital, Denmark, is warranted. All results could support the establishment of MSC therapies in the future by ensuring good cell product quality.

Contact

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Production of a GMP-compliant cell product

1. Goal

The laboratory facility in the Department of Clinical Immunology of the Næstved Hospital includes cell culture and packaging facilities in cleanrooms of the corresponding air purity class. The processes for the GMP-compliant production of MSC cells with aseptic procedures and sterile disposable articles for all product contact steps are established, and the laboratory is ready for GMP approval. The manufacturing process includes the following measures: the activity will develop the optimal cell culture processes for the maximum output of MSC in a standardised product based on BONEBANK material. Patient selection is based on the results achieved in the first project phase of BONEBANK. Also, the preparation of the cells is based on previous processes and results.

2. Results

A process chain from donation of allogenic bone marrow to a final MSC product is established and validated. The harvesting of bone marrow follows a procedure setup in the operating theatre by the local Orthopaedic Department in Næstved Hospital, as a CE-marked device for use in this respect is still in development (by BONEBANK partner Stryker Trauma GmbH). A signed agreement regarding the inclusion of donors and the harvesting of cells between the local Orthopaedic Department and the Department of Clinical Immunology is in place. The selection of donors respects the results from the first BONEBANK phase regarding age and gender. The conclusion was that these variables do not have important implications; nevertheless, only donors below 65 years of age can donate.

Until the outbreak of the coronavirus pandemic, donors were actively recruited and a pool of eligible donors have given signed consent to donate. Unfortunately, all elective surgery has been postponed due to the situation. Therefore, production of MSCs awaits the resumption of this activity. Full traceability is ensured by the use of the Blood Bank IT system, and the final MSC products are labelled according to legal requirements using SEC (Single European Code) and ISBT128 component codes.

Analyses performed within the Department of Clinical Immunology confirm cell quality using the production method developed. Moreover, BONEBANK partners used samples to further characterise growth and differentiation characteristics.

All documentation of the production is complete, including a Product Specification File; thus, the laboratory is ready to apply for GMP approval of the MSC product. In addition, an Investigators Brochure (IB) has been prepared, and the required IMPD is in progress using the registration number in the Eudra-CT database. The parallel development of a clinical trial by BONEBANK partner Hagen Schmal, Odense University Hospital, is complete; this is a pre-requisite in order to apply for GMP approval. The outbreak of the coronavirus pandemic unfortunately put things on hold, but it is expected that parallel applications to the Ethical Board and to the health authorities (the Danish Medical Board and the Danish Board of Patient Safety) can be submitted within the timeframe of the project.

The delivery of products for an approved study will not be within the timeframe of the BONEBANK extension. The planned clinical study requires funding, which was not part of the development framework. Nevertheless, the products will be ready, thereby providing an option for use in other clinical trials which exploit clinical stem cell treatment.

The development of a BONEBANK data centre IT solution by Soventec GmbH is a parallel task within the BONEBANK network. The MCS production in Næstved provided input regarding relevant parameters for inclusion in the database solution.

3. Conclusion & Outlook

MSC production derived from allogenic bone marrow is established according to GMP. The quality of the cells meets international standards; furthermore, growth and differentiation characteristics are confirmed within the BONEBANK network. The Næstved Hospital will send this cell product for a further validation of the cell quality to the Interdisciplinary Center for Biobanking-Lübeck.

The parallel development of a clinical trial within the BONEBANK network is finalised; however, the coronavirus pandemic halted the activities temporarily. Nevertheless, the expectation is to apply for approval of the clinical study in parallel with application for GMP production of bone marrow-derived MSCs, within the project timeline.

The next step is to achieve funding for the clinical study. Again, such applications await the developments in Germany and Denmark regarding the coronavirus situation. Timeframes regarding inspections from the health authorities are currently difficult to predict. Moreover, scientific funding is very much affected, as many organisations are aiming to support projects related to this particular disease.

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"First in Human" clinical study

1. Goal

The latest studies have shown that certain fractures are associated with a high rate of complications such as pseudarthrosis. This applies, for example to proximal tibia fractures after high speed traumata with bone loss. This type of fracture therefore requires highly innovative strategies for bone healing, and constitutes the framework for the "First in Human" clinical study. Besides fracture complexity and epidemiological factors, synovial cell and cytokine regulation significantly influence the outcome of the fracture. The initial events of every articular fracture trigger both components by initiating an inflammatory reaction, leading to local debridement but also degradation of the cartilage matrix, a crucial starting point for osteoarthritis. Stromal (mesenchymal) stem cells (MSC) play a key role in controlling both inflammation and regeneration, and are present in the fractured joint. The hypothesis is that the intra-articular injection of allogeneic MSC supports the repair of fracture-associated damages in the joint. Additionally, MSC could attenuate the fracture-induced synovial inflammatory reaction and serve as a therapeutic option for patients with a risk of post-traumatic osteoarthritis (PTOA). In addition to improved treatment, the study aimed to increase knowledge about cellular reactions and cytokine cascades which cause post-traumatic osteoarthritis.

2. Results

The results achieved in the first phase of the BONEBANK project were used to determine case numbers and potential indications for the study protocol. Furthermore, advantages and disadvantages of allogeneic or autogenic application were analysed and the safety standards of the study defined. Results from in vitro studies provided input into immunology and MSC characteristics. Cell production was performed by the project partner Næstved Hospital. Patient recruitment in the different countries was planned and executed. Moreover, the administrative structures for a cross-border clinical trial were defined and evaluated. In Denmark (OPEN) and Germany (Clinic OUS, Center for Clinical Studies) there are excellent structures with years of study experience and skilled study teams.

The clinical indication for the use of cells in a clinical trial was defined as post-traumatic osteoarthritis following intra-articular proximal tibia and ankle fractures. This was done in cooperation with the project partners from Odense University Hospital, the University Medical Center Schleswig-Holstein, Næstved Hospital, and considered feasibility, expected case load and scientific novelty. To date, the study protocol was developed and finalised with the consent of all participants in the project activities. The application at the local ethical board (EB) was finalised, including patient information, protocol, Danish translation, Investigators Brochure, etc.

3. Conclusion & Outlook

The EB application must be submitted. Following approval from the authorities, the local workflows will be tested and finalised, and relevant participating staff will receive information to ensure the correct inclusion of patients. MSC products will be shipped for local storage according to defined instructions and agreements. Thus, products will be in place and ready for use on patients entering the study.

Contact

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(During BONEBANK, Hagen Schmal was employed at Odense University Hospital)

The data centre platform

1. Goal

In the first phase of the BONEBANK project, a concept for a cross-border IT infrastructure was developed. The hospitals involved in Odense and Lübeck have web-based access to the shared database. The partners agreed on a common set of parameters, which have been transferred to an IT data template. At the end of the project, technical requirements for a common IT system connecting independent hospitals with different existing IT systems were collected and implemented.

The technical implementation of the BONEBANK data centre and the training of future users was planned next, for the extension phase of BONEBANK. New and individually-adapted data templates are created automatically, IT training courses are conducted with future users, and a video has been created to enable them to understand the effective use of the BONEBANK system.

2. Results

The common BONEBANK data centre is technically implemented and released now. All partners and future partners can get access to shared data according to valid data processing agreements between the partners.

These data processing agreements are challenging in a cross-border project like BONEBANK. The BONEBANK organisation itself needs a data protection concept to prove its compatibility with EU data protection and data privacy regulations. A concept for this was created by soventec. The system must be described technically, the server used must meet certain security criteria, and the shared data must be fixed and ethically approved.

German and Danish staff have been trained on the BONEBANK system and know how to share data in the BONEBANK data centre.

It is important that hospital staff are virtually free of extra work when using the BONEBANK system. With their tough time schedules, they have no time for duplicated work such as data entry in an extra IT system like the BONEBANK data centre. Therefore, soventec created a toolkit to easily integrate (new) donor hospitals. Exported data files from local IT systems are uploaded to the BONEBANK data centre and used to create individual data templates and structured data.

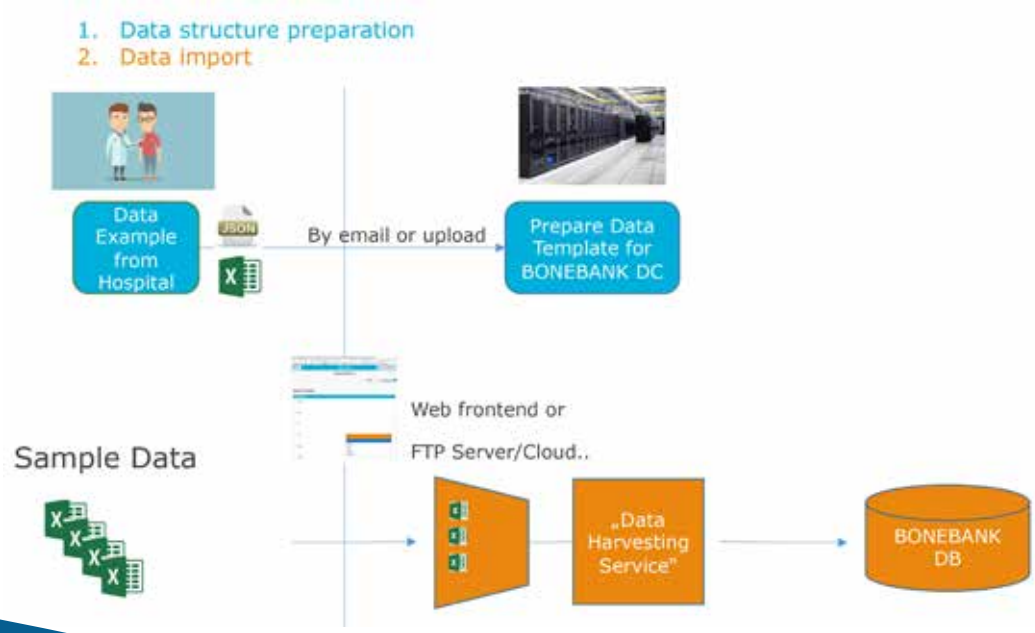

Figure 6: Toolset for external hospital integration.

All uploaded data is encrypted and stored on a safe server that is hosted according to ISO 27001.

Data is only accessible to users who have the relevant access rights.

Samples and sample information can be searched using the web portal of the BONEBANK data centre. If the "sources" (donor hospitals) want to share their material or sample information with a "user" they can contact each other.

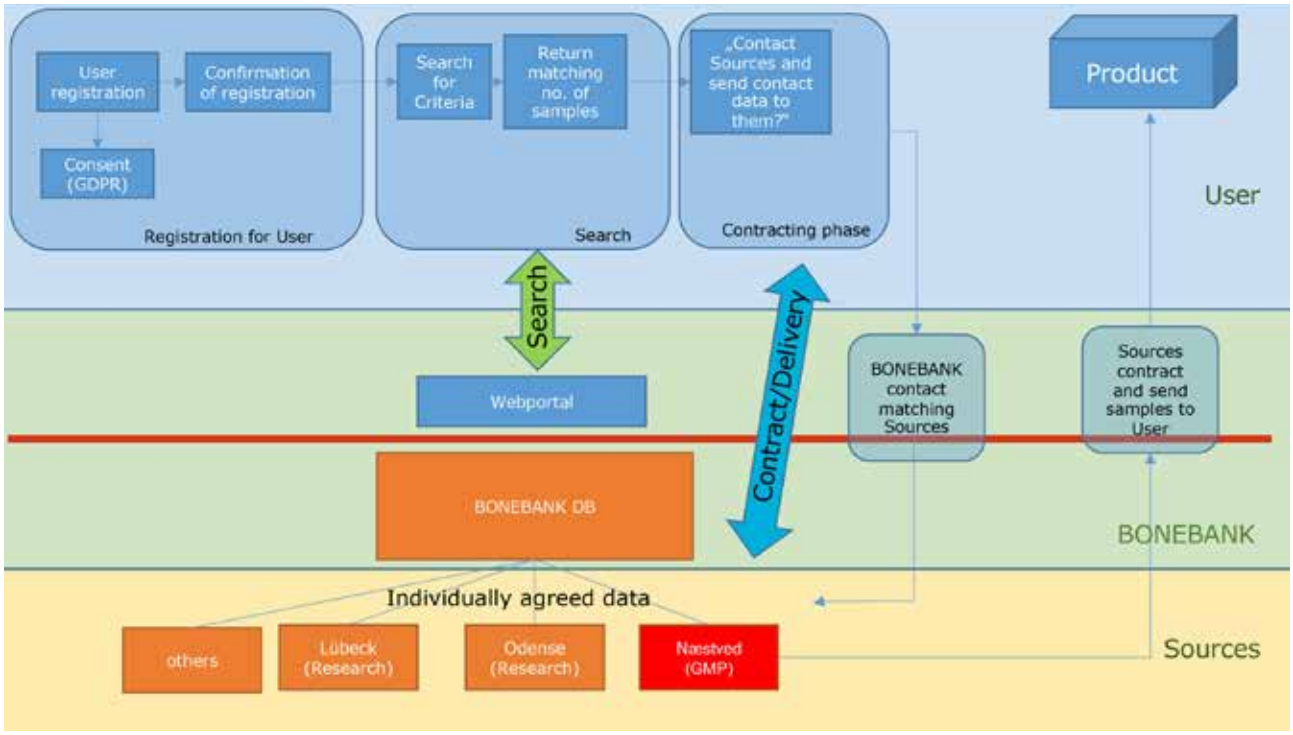

Figure 7: „Big Vision" - BONEBANK IT infrastructure.

Through the BONEBANK data centre, the BONEBANK organisation can act as a broker between "users" and "sources".

3. Conclusion & Outlook

The BONEBANK data centre is ready to provide access to uploaded data to authorised users. As a BONEBANK organisation could have valuable samples and/or sample information, there may be various interested users.

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Implementation of the organisational model

1. Goal

Research into the use of stem cells obtained from bone and bone marrow is currently making decisive progress. At present, bone marrow and bone fragments containing valuable stem cells are discarded as waste during routine bone operations. The potential of these stem cells lies primarily in their use for regenerative therapies, such as the treatment of bone fractures.

Our aim is to harvest these stem cells with new instruments and methods and to store them in cross-border biobanks. This valuable resource can thereby be made available for therapeutic purposes or for research into advanced therapies.

The main goal in the primary phase of the BONEBANK project was the development of a unique value chain in the programme region, from the innovative collection of bone stem cells to their storage in a cross-border biobank, right through to their utilisation by regional research institutions and companies.

The main objective of this activity is to establish this already developed BONEBANK value chain in the programme region, through the implementation of an organisational model and the establishment of an organisation.

2. Results

Various steps were required in order to determine and ultimately implement the appropriate organisational model for the BONEBANK project, together with all project partners.

The first step was to discuss the feasibility of the organisational model developed in the programme region. Subsequently, the Delphi process was started, which consisted of various surveys. All project partners had the opportunity to define the required structure and describe their ideas. The majority of the project partners are interested in continuing their work in a new BONEBANK organisation. According to the survey, an association or foundation have been shortlisted as the organisational form. Almost all project partners are willing to take on a supporting role in the new BONEBANK organisation.

For a further planned approach, the next step was to find a common goal for the organisation. For this reason, a strategy paper was developed, which will serve as a basis for the organisational model. The strategy paper examines different scenarios which consider the possible uses of harvested bone marrow material from an economic perspective. The paper was sent to all project partners. As there were still some questions arising from the paper, a more detailed discussion of the paper took place by means of an online survey, the results of which were then presented in a project meeting, where the next steps with regard to founding a new BONEBANK organisation were discussed. Among other things, the different potential business models presented were assessed by the project partners in the survey, with regard to their suitability for the future BONEBANK organisation.

A competence matrix was developed to get an overview of which skills can be contributed to the new organisation by each partner. This consists of seven main categories that are based on the BONEBANK value chain developed, with various sub-items defined for each category, so that all activities which take place in the related work are covered. The competence matrix was sent to the project partners, who each filled in the data in relation to their core business and their interests. For each sub-item in the seven categories, there is at least one project partner who can contribute relevant skills.

An essential component in the implementation of an organisational model is the cost analysis. For this analysis, all costs incurred in establishing the BONEBANK value chain developed were determined by each project partner. On the one hand, this cost analysis includes the costs incurred by the donor hospitals during the harvesting process, and the costs for the biological testing of the blood samples to exclude infections of the donor. On the other hand, it also includes the costs incurred for isolation of the stem cells and preparation of a GMP-compliant stem cell product, plus the costs for storage in a cross-border biobank. In addition, costs are incurred for the transport of the bone material from the donor hospital to the biobank, as well as for the transport from the biobank to the hospital where treatment is carried out. Moreover, there are costs incurred by the IT service for managing the exchange of the data between the individual partners. To estimate the costs for each of these steps, the personnel, consumables and room costs were determined.

At the end of the process, a new BONEBANK organisation, to be known as the BONEBANK interest group (BIG), will be established, with the goal of continuing the implementation of the value chain developed in the BONEBANK project through collaboration between German and Danish experts from research groups, industry and hospitals who are interested in the use of mesenchymal stem cells, and expanding the cross-border network and thereby promoting new collaborations in the border region, in order to accelerate research in the field of mesenchymal stem cell application. The project partners have therefore decided to perform email exchanges, video and telephone conferences and other activities towards achieving these objectives.

3. Conclusion & Outlook

After completion of the BONEBANK project, the goals achieved will form the basis for the new BONEBANK interest group (BIG), and building on this, further goals will be pursued to promote the expansion of the BONEBANK value chain in the German-Danish programme region by involving further experts from research groups, industry and hospitals who are interested in the use of mesenchymal stem cells.

Contact

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Competence atlas DE-DK on stem cells

1. Goal

The goal of this activity was to develop a competence atlas in the field of mesenchymal stem cells, therapy, manufacturing and other topics related to the BONEBANK project. This web-based tool enables identification of competences in clinics, industry and universities in the programme region in an automated and easy way.

2. Results

The project partner Life Science Nord successfully integrated the BONEBANK platform with the competence atlas into an existing networking tool. The competence atlas is available to the public for free after registration on the web page. The project consortium first developed a catalogue of well-defined and detailed keywords, which are related to the BONEBANK project. These keywords have been clustered in different overarching topics, e.g. surgery, cells or materials. Second, a list of German and Danish companies, research facilities, etc. was generated. As planned, the list covers the fields of medical technology, bone healing, stem cells and related areas. Project and network partners were involved in identifying relevant entries for this list. The keywords as well as the company list were integrated into the online search tool afterwards. More than 1,100 companies and research facilities were already listed at the launch of the competence atlas in January 2020. Based on the choice of the keyword(s) of interest, the web pages of companies and facilities are screened and then listed, and displayed on a geographic map. Users can see locations and basic information of the search results, and if the respective persons are registered on the platform, also contact them to facilitate knowledge exchange and collaboration. The BONEBANK competence atlas has been promoted in different ways to enhance its outreach, e.g. via social media like LinkedIn and Twitter, newsletters and the final conference.

3. Conclusion & Outlook

The BONEBANK competence atlas delivers a powerful tool to identify expertise in the programme region and to strengthen knowledge transfer within the related topics. The tool offers the possibil-ity for further and new cooperation. Moreover, the networking platform offers opportunities to exchange data and images, or to set up a discussion forum independent of the BONEBANK competence atlas. With the competence atlas, an innovative opportunity exists to enhance the visibility of expertise in Northern Germany and Denmark beyond the programme region itself. To date, the search tool has already attracted interest from outside the programme area, e.g. from Bavaria, Lower Saxony, Spain and the Czech Republic.

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Project Partners

- Life Science Nord Management GmbH
- Næstved Hospital
  Department of Clinical Immunology
- Odense University Hospital
- soventec GmbH
- Stryker Trauma GmbH
- University Medical Center Schleswig-Holstein, Campus Lübeck
  Laboratory for Biomechanics and Orthopaedic-Traumatological Research, Department for Orthopaedics and Trauma Surgery
- University of Lübeck
  Interdisciplinary Center for Biobanking-Lübeck (ICB-L) & Section for Translational Surgical Oncology and Biobanking (Department of Surgery)

Network Partners

- Health Innovation Centre of Southern Denmark
- Lübeck Chamber of Commerce and Industry
- WelfareTech

Project Data

BONEBANK – the German-Danish Biobank and Innovation Platform for Stem Cells in Bone Regeneration

- **7 Partner Organisations**
- **Duration: Sep 2015 – Aug 2020**
- **Budget: 3.9 Million Euros, thereof 2.2 Million Euros funding**

BONEBANK is supported by Interreg Deutschland-Danmark with funds from the European Regional Development Fund.