Clinical effect of Spherox treatment in patients with chondral lesions of the knee

A Data Management Plan created using DMPonline

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Funder: UMC Utrecht

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Project abstract:

Throughout the past decennia Autologous Chondrocyte Implantation (ACI) has become an increasingly used product for the treatment of cartilage defects in the knee. Literature shows superiority of ACI, particularly for larger defect sizes. Over the past ten years, several techniques have been developed involving ACI. More recently, a matrix-associated ACI procedure was introduced, based on spheroid technology. The general principle is based on the acquisition of the patient’s own healthy chondrocytes derived from a non-weight-bearing part of the knee, cultivated in vitro and condensed into 3-dimensional spheroids such as Spherox. In 2019, treatment with Spherox started in hospitals in Utrecht, Zwolle and Tilburg. For follow-up assessment, patients were included in the knee registry. It seems important to examine this new technique and to adduce scientific evidence for its safety and effectiveness.

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1. General features

1.1. Please fill in the table below. When not applicable (yet), please fill in N/A.

DMP template version	29 (don't change)
ABR number *(only for human-related research)*	
METC number *(only for human-related research)*	TBD
DEC number *(only for animal-related research)*	
Acronym/short study title	Spherox treatment in the Netherlands
Name Research Folder	xx-xxx_SPHEROX
Name Division	Surgical Division
Name Department	Orthopaedics
Partner Organization	Maastricht UMC, Elisabeth Tweesteden hospital (ETZ) in Tilburg
Start date study	01-07-2021
Planned end date study	
Name of datamanager consulted*	Dax Steins
Check date by datamanager	18-03-2021

1.2 Select the specifics that are applicable for your research.

- Observational study
- Use of Questionnaires
- Non-WMO
- Retrospective study
- Multicenter study

The knee registry (METC 17-005/C) from the UMC Utrecht collects and stores information of the knee from different departments (at least; orthopaedic surgery, physiotherapy, sports medicine, radiology and cast technician unit) for new research questions. All upper mentioned departments can request data from the knee registry for the reuse in new non-WMO research by contacting the PI.

Data will be collected from 3 different hospitals in the Netherlands:

1. University Medical Centre Utrecht (UMCU)
2. Maastricht UMC (MUMC)
3. Elisabeth Tweesteden Ziekenhuis in Tilburg

2. Data Collection

2.1 Give a short description of the research data.

The primary objective of this multicenter retrospective study is to evaluate the effect of this surgical technique on chondral defects in the knee for pain (NRS pain), patients' experienced symptoms and functional limitations (KOOS) and health related quality of life (EQ-5D) in the cohort of patients treated with Spherox that have a minimum follow-up of 9 months

Study population: Patients aged 18 years or older, undergoing ACI treatment using spheroid technology (Spherox), in the Netherlands. Follow up 9 months.

For the Spherox study, we intend to reuse the following health care data from the UMCU knee registry: Knee Injury and Osteoarthritis Outcome Score (KOOS), EQ-5D-5L and VAS. The assessment of patient reported outcomes (PROMs) took place at 3, 6, and 9 months after chondrocyte implantation via an online PROMs tool (OnlinePROMS: https://orthopedie.umcutrechtproms.nl/).

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Study subjects	Volume	Data Source	Data Capture Tool	File Type	Format	Storage space
Human	53	EPD	Research Data Platform (RDP)	Quantitative	.sas7bdat / .xls	0 -10 GB
Human	53	KOOS (OnlinePROMs Questionnaire)	SPSS / Excel	Questionnaire	.sas or .xls	0 - 10 GB
Human	53	EQ-5D-5L (OnlinePROMs Questionnaire)				
Human	53	OnlinePROMs VAS Score				

2.2 Do you reuse existing data?

- Yes, please specify

In this retrospective study, we will reuse pseudonymized data from the Knee Registry (METC: 17-005/C) made available by our Research Data Platform (RDP).

2.3 Describe who will have access to which data during your study.

Existing health data of patients are provided by the Research Data Platform. Selection is made

for patients that provided written broad consent. The data manager is authorized to link different datasets of the selected patientgroup and thus has access to the identifiable data such as patientID. Esmee Kester acts as the data manager for knee patients, with access to the selection of these patients and the patientID to link this data to the questionnaire data. Following data selection and 4-eyes control by our div. data manager, the data is stored in the designated research folder for the research team.

Tabel 1. Data Access Table

Type of data	**Who has access**
Direct identifying personal data	Research team, Datamanager. Datamanagers of department of orthopaedic surgery: Hans Pruijs, Hilde Stempels Esmee Kester, and dHS datamanager Dax Steins
Pseudonimized data	Research team, Datamanager
Key table linking study specific IDs to Patient IDs	Research team, Datamanager
Questionnaires OnlinePROMs	Research team, Datamanager

Data will be collected from the RDP. Only datamanagers have direct access to the RDP. The data will be pseudonomized with a study-specific study-id.

2.4 Describe how you will take care of good data quality.

1. Pseudonymized data from patients will be shared, merged, and collected in an Excel file. Data is checked by the division datamanager in conformidity with the data specifications. Data collection will be frozen before analysis.

#	**Question**	**Yes**	**No**	**N/A**
1.	Do you use a certified Data Capture Tool or Electronic Lab Notebook?		x	
2.	Have you built in skips and validation checks?		x	
3.	Do you perform repeated measurements?		x	
4.	Are your devices calibrated?			x
5.	Are your data (partially) checked by others (4 eyes principle)?	x		
6.	Are your data fully up to date?	x		
7.	Do you lock your raw data (frozen dataset)	x		
8.	Do you keep a logging (audit trail) of all changes?	x		
9.	Do you have a policy for handling missing data?	x		
10.	Do you have a policy for handling outliers?	x		

2.5 Specify data management costs and how you plan to cover these costs.

#	Type of costs	Division ("overhead")	Funder	Other (specify)
1.	Time of datamanager	X		
2.	OnlinePROMs license fee			X
3.	Storage / Archiving	X		

For research data originating from the Knee Registry, the department of Orthopeadics makes use of UMCU's Research Data Platform. No additional costs are associated with the use of this platform. The use of self-administered questionnaires from OnlinePROMs also falls under the scope of the Knee Registry. For this our department pays a licence fee.

2.6 State how ownership of the data and intellectual property rights (IPR) to the data will be managed, and which agreements will be or are made.

1. UMC Utrecht is and remains the owner of all collected data for this study. The data is collected in a relatively large patient group and is very valuable for future studies. Our data cannot be protected with IP, but its value will be taken into account when making our data available to others, when setting up Research Collaborations and when drawing up Data Transfer Agreement(s). IPR will be discussed with the PI and the contract manager.

3. Personal data (Data Protection Impact Assessment (DPIA) light)

Will you be using personal data (direct or indirect identifying) from the Electronic Patient Dossier (EPD), DNA, body material, images or any other form of personal data?

- Yes, go to next question

I will process personal data. I have consulted the div. datamanager and I do not have to complete a full DPIA. I therefore fill out this DPIA light and proceed to 3.1.

3.1 Describe which personal data you are collecting and why you need them.

Which personal data?	Why?
Patient demographics (Gender, age, BMI etc)	To describe our study population
Medical history	
Comorbidities	
Additional treatment	
Adverse events	

3.2 What legal right do you have to process personal data?

- Other, please explain

Broad consent Knee Registry (17-005/C)

3.3 Describe how you manage your data to comply to the rights of study participants.

1. The data are pseudonymized and the linking table to personal data is saved. An authorized person manages the linking table, can re-identify study participants when necessary and deliver, correct or delete the data.

CHECK PIF/IC van knieregister

Kopieer onderstaande tabel

3.4 Describe the tools and procedures that you use to ensure that only authorized persons have access to personal data.

We use the secured Research Folder Structure that ensures that only authorized personnel has access to personal data, including the key table that links personal data to the pseudoID.

3.5 Describe how you ensure secure transport of personal data and what contracts are in place for doing that.

1. We have a Data Transfer Agreement with Maastricht UMC and Elisabeth Tweesteden Ziekenhuis in Tilburg. The agreement is stored at location: .....

2. In case we need to transport personal data with colleagues, we use Surfdrive or surffilesender with encryption.

4. Data Storage and Backup

4.1 Describe where you will store your data and documentation during the research.

The digital files will be stored in the secured Research Folder Structure of the UMC Utrecht (L:\Onderzoek\Orthopaedie\xx_xxx_SPHEROX). The data manager uses the D-Folder with patient ID, a copy but with pseudonomized data will be stored in the E-folder. Researchers do not have access to the D-folders, therefore the privacy of data will remain secured. Versions will be tracked by using the date in the name of the file.

4.2 Describe your backup strategy or the automated backup strategy of your storage locations.

All (research) data is stored on UMC Utrecht networked drives from which backups are made automatically twice a day by the division IT (dIT).

5. Metadata and Documentation

5.1 Describe the metadata that you will collect and which standards you use.

5.2 Describe your version control and file naming standards.

We will distinguish versions by indicating the version in the filename of the master copy by adding a code after each edit, for example V1.1 (first number for major versions, last for minor versions). The most recent copy at the master location is always used as the source, and before any editing, this file is saved with the new version code in the filename. The file with the highest code number is the most recent version. Every month, we will move minor versions to a folder OLD. The major versions will be listed in a version document (projxVersDoc.txt), stating the distinguishing elements per listed version.

6. Data Analysis

6 Describe how you will make the data analysis procedure insightful for peers.

We will be using SPSS, version 26.0.0.1, for statistical analysis of the data. The scripts will contain comments, such that every step in the analysis is documented and peers can read why I made certain decisions during the analysis phase.

7. Data Preservation and Archiving

7.1 Describe which data and documents are needed to reproduce your findings.

The data package will contain: the raw data, the study protocol describing the methods and materials, the script to process the data, the scripts leading to tables and figures in the publication, a codebook with explanations on the variable names, and a ‘read_me.txt’ file with an overview of files included and their content and use.

7.2 Describe for how long the data and documents needed for reproducibility will be available.

Data and documentation needed to reproduce findings from this non-WMO study will be stored for at least 15 years.

7.3 Describe which archive or repository (include the link!) you will use for long-term archiving of your data and whether the repository is certified.

After finishing the project, the data package will be stored at the UMC Utrecht Research Folder Structure and is under the responsibility of the Principal Investigator of the research group. When the UMC Utrecht repository is available, the data package will be published here.

7.4 Give the Persistent Identifier (PID) that you will use as a permanent link to your published dataset.

I will be using a DOI-code and will update this plan as soon as I have the code.

8. Data Sharing Statement

8.1 Describe what reuse of your research data you intend or foresee, and what audience will be interested in your data.

TBD

8.2 Are there any reasons to make part of the data NOT publicly available or to restrict access to the data once made publicly available?

- No, all data generated in this project will be made publicly available without any restrictions

TBD

8.3 Describe which metadata will be available with the data and what methods or software tools are needed to reuse the data.

TBD

8.4 Describe when and for how long the (meta)data will be available for reuse

- (Meta)data will be available upon completion of the project
- (Meta)data will be available as soon as article is published
- (Meta)data will be available after completion of project (with embargo)

TBD

8.5 Describe where you will make your data findable and available to others.

TBD