Bo-Balance: Botulinum toxin for children with cerebral palsy: a delicate balance between clinical benefits and muscular harm

A Data Management Plan created using DMPonline.be

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Project abstract:

Intramuscular Botulinum Neuro-Toxin type A [BoNT] injection has become a widely used first-line treatment of focal spasticity in children with cerebral palsy [CP]. Our, as well as other groups, indicated clinical benefits of BoNT treatment in CP, including a reduction in muscle tone, increased joint range of motion and improved gait. However, an increasing number of animal studies have raised concern that BoNT may be harmful for muscle size and muscle integrity. The proposed project will tackle internationally recognized research challenges, to allow us to determine whether clinical benefits of BoNT treatment in CP counterweigh potential risks at the muscular level.

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1. Research Data Summary

List and describe all datasets or research materials that you plan to generate/collect or reuse during your research project. For each dataset or data type (observational, experimental etc.), provide a short name & description (sufficient for yourself to know what data it is about), indicate whether the data are newly generated/collected or reused, digital or physical, also indicate the type of the data (the kind of content), its technical format (file extension), and an estimate of the upper limit of the volume of the data.

				Only for digital data	**Only for digital data**	**Only for digital data**	**Only for physical data**
Dataset Name	**Description**	**New or reused**	**Digital or Physical**	**Digital Data Type**	**Digital Data format**	**Digital data volume (MB/GB/TB)**	**Physical volume**
		Please choose from the following options: • *Generate new data* • *Reuse existing data*	*Please choose from the following options:* • *Digital* • *Physical*	*Please choose from the following options:* • *Observational* • *Experimental* • *Compiled/aggregated data* • *Simulation data* • *Software* • *Other* • *NA*	*Please choose from the following options:* • *.por, .xml, .tab, .cvs,.pdf, .txt, .rtf, .dwg, .gml, ...* • *NA*	*Please choose from the following options:* • *<100MB* • *<1GB* • *<100GB* • *<1TB* • *<5TB* • *<10TB* • *<50TB* • *>50TB* • *NA*	
Informed consent form	Paper ICF Scanned ICF	Generate new data	Physical Digital	Other	.pdf	<100MB	1 paper sheet per subject
Muscle biopsy	Micro muscle biopsies of medial gastrocnemius	Generate new data	Physical	NA	NA	NA	5 biopsies per participant, 3 muscle samples per biopsy
3DfUS	3D freehand ultrasound images	Generate new data Reuse existing data	Digital	Observational: images Numerical: analysis output	Software specific (Stradwin): .sw .sxi .csv	.sw: <100MB .sxi: <100GB .csv: <100MB	NA
2DUS	2D ultrasound images	Generate new data	Digital	Observational: images	.dcm	<100GB	NA
Shearwave Elastography	Shearwave elastography (Ultrasound)	Generate new data	Digital	Observational: images Numerical: analysis output	.dcm .avi .csv	.dcm:<100GB .avi: <1GB .csv: <100MB	NA
mDixon MRI	mDixon MRI	Generate new data	Digital	Observational: images Numerical: analysis output	to be defined during project	to be defined during project	NA
Gait analysis	Gait analysis data (kinematics, kinetics, electromyography)	Generate new data	Digital	Numerical: assessment and analysis output Observational: video	Software specific files (Vicon) .c3d .avi	Vicon:<100GB .c3d: <100GB .avi: <100GB	NA
Clinical exam	Clinical examination results	Generate new data	Digital	Numerical	.xls .pdf	<100MB	NA
ISA	Instrumented spasticity assessment	Generate new data Reuse existing data	Digital	Numerical: assesment and analysis output	Software specific (custom made): .info .lsmeas .hsmeas .mat .csv .png	Software specific: <100GB .mat:<1GB .csv: <1GB .png:<1GB	NA
Patient medical records	Patient medical records	Generate new data Reuse existing data	Digital	Texts	.pdf .xls	<100MB	NA
Histological and cell culture analysis	Histological and cell culture analysis	Generate new data	Digital	Experimental: Images	.Tiff .mp3 .bmp .lif	<100GB	NA
Gel electrophoresis	Gel electrophoresis	Generate new data	Digital	Experimental: images	.tiff	<100GB	NA
Western Blot	Western Blot	Generate new data	Digital	Experimental: images	.tiff	<100GB	NA
DNA sequences	DNA sequences	Generate new data	Digital	Experimental: Molecular assessments	.ape .fas .seq .FASTQ	<50TB	NA
Gene expression	Gene expression	Generate new data	Digital	Experimental: qRT-PCR	.tiff .xls .csv	<100GB	NA
RNA seq analysis	RNA seq analysis	Generate new data	Digital	Experimental: Molecular assessment	.bam .FASTQ .xls	<5TB	NA

If you reuse existing data, please specify the source, preferably by using a persistent identifier (e.g. DOI, Handle, URL etc.) per dataset or data type:

The reused existing data is extracted from clinical and normal reference databases (established during TAMTA project FWO-TAMTA, 3M160415, S59945 and during the 3D-MMAP project 3M180752&3M180321, S62187&S62645) as well as from the UZ Leuven medical record system.

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? Describe these issues in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes, human subject data

We will conduct research experiments on humans (children).
Physical data of human subjects include microbiopsies containing muscle tissue from the medial gastrocnemius.
Digital data include muscle imaging with ultrasound, microscopic analysis and instrumented assessments.
An amandement will be requested for the already approved study with number s62645.

Will you process personal data? If so, briefly describe the kind of personal data you will use in the comment section. Please refer to specific datasets or data types when appropriate.

- Yes

Individual's name, phone number of the parents, birth date, type of disease, grade of involvement, level of functionality, body mass, body length and treatment history.
This data is both exported from UZ Leuven medical record and obtained via standard interview.

Does your work have potential for commercial valorization (e.g. tech transfer, for example spin-offs, commercial exploitation, …)? If so, please comment per dataset or data type where appropriate.

- No

Do existing 3rd party agreements restrict exploitation or dissemination of the data you (re)use (e.g. Material/Data transfer agreements/ research collaboration agreements)? If so, please explain in the comment section to what data they relate and what restrictions are in place.

- No

Are there any other legal issues, such as intellectual property rights and ownership, to be managed related to the data you (re)use? If so, please explain in the comment section to what data they relate and which restrictions will be asserted.

- No

2. Documentation and Metadata

Clearly describe what approach will be followed to capture the accompanying information necessary to keep data understandable and usable, for yourself and others, now and in the future (e.g., in terms of documentation levels and types required, procedures used, Electronic Lab Notebooks, README.txt files, Codebook.tsv etc. where this information is recorded).

All data will be coded.

Approved Ethical Commission: description of study protocol (.pdf)
Informed Consents Form: original black copies (.pdf) and signed hardcopies (printed paper)
Experimental protocols: description how the data are collected and generated (software, materials, set-up, settings (.docx) and how data are processed (software, protocol, guidelines, ...) (.docx, read.me text files)
Measurement forms: notes during data collection (printed paper)
Raw experimental data: storage of original physical data and folders with original digital data in software-specific files
Processed data: folder with digital data in the software-specific files, spreadsheets with results (.csv, .xls)
Subject recruitment files: only subject study code, personal data (for example, age, weight, height, …,) short overview of assessments. The subject recruitment files described the measurements info for each patient, whereby the patient's identiy is coded.

Will a metadata standard be used to make it easier to find and reuse the data? If so, please specify (where appropriate per dataset or data type) which metadata standard will be used. If not, please specify (where appropriate per dataset or data type) which metadata will be created to make the data easier to find and reuse.

- Yes

At the Clinical Motion Analysis Laboratory, raw experimental data are managed on a lab-specific generic data management platform, guiding researchers through data

collection and initial processing workflows, ensuring efficient safe storage, keeping track of data use and associated extra processing related to each experimental step, and enabling data query filtering of the collected data.
At the Pneumology Laboratory, muscle biopsies data and processed data are managed on a lab-specific generic data management platform, guiding researchers through data collection and processing workflows, ensuring efficient safe storage, keeping track of data use and associated processing related to each experimental step, and enabling data query filtering of the collected data. This has been developed based on an existing workflow that was been established at FIBER (Flanders Institute for Biomechanical Experimentation, KU Leuven, Department of Mechanical engineering) and has been be expanded to muscle biopsies as part of the 3DMMAP project (3M180321, S62645).
The generic data management platforms will generate metadata and this will be done in a uniform and consistent way for all datasets.
Metadata will follow Data Cite's recommendations.

3. Data storage & back-up during the research project

Where will the data be stored?

Raw and processed physical and digital data will be collected per assessment.
Physical data, derived from muscle microbiopsies will be stored in freezers at the Pneumology lab and Laboratory of Translation Cardiomyology.
Digital data files will be stored on secure KU/UZ Leuven servers and networks. (UZ Leuven Drive: UZ/admin/ganglaboresearch)
Hard copies of the Informed Consent forms, measurement forms and paper lab notebooks are kept in locked cabinets in the lab of the PIs concerned.

How will the data be backed up?

We will use the back-up facilities of the KU Leuven and UZ leuven IT services. The KU/UZ Leuven servers and netwerks are backed up automatically.
Physical muscle biopsy data and the analyzed specimens will be kept for 10 years post-project in freezer (temperature ranging from -20° till -150°, depending on the sample type), at the Pneumology Lab.
Digital data automatically stored on the acquisition laptop during data collection, will be manually transferred via external hard drive to the secure servers. This external hard drive is provided as automatic back-up of the acquisition laptop.

Is there currently sufficient storage & backup capacity during the project? If yes, specify concisely.
If no or insufficient storage or backup capacities are available, then explain how this will be taken care of.

- Yes

Yes. Suffcient storage and backup capacity is provided on the UZ/KU Leuven servers and networks.

How will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

All physical data, printed forms and notebooks are present in the labs, which are secured.
The access to the KU Leuven server is u-number and password controlled.
Data on the UZ Leuven networks is only accessible for researchers with personalized UZ Leuven login and password, and thus secured by a strict acces right management controlled by the PI.
Patient record files will be stored with password security only accessable for researchers involved in the projects and controlled by the PI .

What are the expected costs for data storage and backup during the research project? How will these costs be covered?

The expected costs at the University Hospital networks are +/- 1000€ per year
The expected costs for the L- and K-drives at the KU leuven are +/- 1000€ per year

The costs for data storage are covered by the current project funding (FWO) as well as by left rest budget from previous projects.

4. Data preservation after the end of the research project

Which data will be retained for at least five years (or longer, in agreement with other retention policies that are applicable) after the end of the project? In case some data cannot be preserved, clearly state the reasons for this (e.g. legal or contractual restrictions, storage/budget issues, institutional policies...).

All data (physical and digital), will be retained for the minimum preservation term of 10 years after the end of the project.

Where will these data be archived (stored and curated for the long-term)?

The physical muscle sample will be stored for a long term in freezer (temperature ranging from -20° till -150°, depending on the sample type), at the Pneumology Lab.
The digital data will be archived at special space provided by KU/UZ Leuven networks with restricted access, controlled by the PI.
Hard copies (eg. the Informed Consent forms, measurement forms and paper lab notebooks) are kept in locked cabinets in the lab of the PIs concerned.

What are the expected costs for data preservation during the expected retention period? How will these costs be covered?

The expected costs at the University Hospital networks are +/- 1000€ per year
The expected costs for the L- and K-drives at the KU leuven are +/- 1000€ per year

The costs for data storage are covered by running project funding as well as by left rest budget from previous projects.

5. Data sharing and reuse

Will the data (or part of the data) be made available for reuse after/during the project? In the comment section please explain per dataset or data type which data will be made available.

- Yes, in an Open Access repository

During the project as well as after the end of the project, the published data will be available via an open access repository (KU Leuven repositories, https://rdr.kuleuven.be/) and upon request by email. These published data contain the results of processed coded data presented in tables.
Reference databases for ultrasound measurements (containing typically developing data and clinical data) have been established. The reference database of ultrasound data of typically developing children (Peeters et al. (2022) - A comprehensive normative reference database of muscle morphology in typically developing children aged 3-18 years – a cross sectional ultrasound study) is published and openly accessible on Figshare (https://figshare.com/articles/dataset/Peeters_et_al_2022_-_A_comprehensive_normative_reference_database_of_muscle_morphology_in_typically_developing_children_aged_3-18_years_a_cross_sectional_ultrasound_study/21770450).
Data to reveal patient-specific reports will be available for clinicans who are treating the study patients and for the patient-specific caregivers in the hospital.
Patient-specifc data will only be shared ensuring the privacy of the healthy children and patients (e.g. body weight, body length). Decoded personal data will never be shared.
In addition, Python and Matlab scripts will be uploaded on GitHub, which is a standard hosting service to share scripts in the scientific community.

If access is restricted, please specify who will be able to access the data and under what conditions.

Acces to published data will not be restricted.
All project partners will have access to the data during the project and the post-project phase. Data access will be regularly discussed during the project steering group meetings.
Access to unpublished data by other KU Leuven colleagues (who are not part of the project consortium) and/or international partners will be arranged through special user and data-sharing agreements, developed in collaboration with Leuven research and Development. During the project, such data sharing is not foreseen.

Are there any factors that restrict or prevent the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)? Please explain in the comment section per dataset or data type where appropriate.

- Yes, Privacy aspects

Patient-specifc data will only be shared ensuring the privacy of the healthy children and patients (e.g. body weight, body length). Decoded personal data will never be shared.

Where will the data be made available? If already known, please provide a repository per dataset or data type.

The published data will be available via an open access repository (KU Leuven repositories, https://rdr.kuleuven.be/) and upon request by email. These published data contain the results of processed coded data presented in tables.
Python and Matlab scripts will also be available on GitHub.

When will the data be made available?

Published data will be made available at the time of publication in case of open access or upon request for other publications.
Additional, not-published data will be made available for external users upon request during the post-project trajectory (based on data sharing agreements developed in colabration with LRD).

Which data usage licenses are you going to provide? If none, please explain why.

There is no license associated to the use of the digital datasets that will be created during the project.
Python and Matlab scripts wil be licensed under specific software licenses.

Do you intend to add a PID/DOI/accession number to your dataset(s)? If already available, you have the option to provide it in the comment section.

- No

DOI will be provided upon acceptance for publication of the related research papers.
In the post project pahse, some data may be publsihed and may thus have a DOI access number.

What are the expected costs for data sharing? How will these costs be covered?

No cost are expected for data sharing.

6. Responsibilities

Who will manage data documentation and metadata during the research project?

Prof. Kaat Desloovere, Dr. Karen Maes

Who will manage data storage and backup during the research project?

Prof. Kaat Desloovere, Dr. Karen Maes

Who will manage data preservation and sharing?

Prof. Kaat Desloovere, Dr. Karen Maes

Who will update and implement this DMP?

Prof. Kaat Desloovere

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Application DMP

Questionnaire

Describe the datatypes (surveys, sequences, manuscripts, objects …) the research will collect and/or generate and /or (re)use. (use up to 700 characters)

We will collect primary, quantitative, experimental data. Raw data will be processed in type-specific software (MeVisLab, Python, Matlab, Vicon, GraphPad, statistical software). PHYSICAL DATA include micro-biopsies containing muscle tissue. DIGITAL DATA include: [1] Instrument-specific data from muscle ultrasound and MRI images (saved as dcm & tiff) and from electromyography, dynamometry and motion analysis and biopsy analysis (saved as software- specific formats); with extracted numerical data saved as xls; [2] histological images saved as tiff [3] numerical data from clinical examination saved as txt; and [4] movie data from motion analysis saved as multimedia files.

Specify in which way the following provisions are in place in order to preserve the data during and at least 5 years after the end of the research? Motivate your answer. (use up to 700 characters)

1. Designation of responsible person (If already designated, please fill in his/her name.)
2. Storage capacity/repository
    - during the research
    - after the research

Karen Maes is responsible for muscle biopsy data and Kaat Desloovere for all other data. All anonymized digital data (raw, processed, meta) will be preserved for >5 years, also after project completion, with separate storage of patient identifier record (PIR), with password-protected access for the PI. The required 5TB computer storage space is provided by KU/UZ Leuven networks, ensuring regular automatic back-up. Histological specimens will be kept for 5 years post-project in a -80°C freezer, at the Pneumology Lab, or at the UZ Leuven Biobank. Upon publication, anonymized numerical datasets will be put available via KU Leuven research data repository.

What’s the reason why you wish to deviate from the principle of preservation of data and of the minimum preservation term of 5 years? (max. 700 characters)

Not applicable.
We will not deviate from the principle of preservation of data and of the minimum preservation term of 5 years.

Are there issues concerning research data indicated in the ethics questionnaire of this application form? Which specific security measures do those data require? (use up to 700 characters)

No issues concerning research data have been indicated in the ethics questionnaire. The medical ethics committee, as well as the biobank (for muscle biopsies) of UZ Leuven/KU Leuven, are aware of the project and of the data collection and storage procedure (S62187). Ethical approval has also been obtained for muscle imaging by means of 3D ultrasound, gait analyses, and instrumented assessments of spasticity and strength in the context of ongoing research (S62645).

Which other issues related to the data management are relevant to mention? (use up to 700 characters)

All data are anonymized. The patient identifier record (PIR) is stored separately, using the ‘digital vault for private data’ service from IT KU Leuven, which offers a secure, standard infrastructure to keep private data safe. Strict rules of data access are applied making the vault fully compliant with the privacy law.
Measurement data are managed on a GDPR-prove lab-specific generic data management platform, guiding researchers through measurement workflows, ensuring efficient safe storage, keeping track of data use and associated processing related to each experimental step, and enabling data query filtering of the collected data. Metadata will follow Data Cite’s recommendations.

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DPIA

DPIA

Have you performed a DPIA for the personal data processing activities for this project?

- Not applicable

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GDPR

GDPR

Have you registered personal data processing activities for this project?

- Not applicable