DMP

Project Name Neurocognition-sparing radiotherapy of brain and base of skull tumours: based on mathematical modelling and advanced brain imaging - DMP

Project Identifier S65664

Grant Title 1SE5722N

Principal Investigator / Researcher Laurien De Roeck

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Description Long-term survival can be achieved in an increasing number of primary brain tumour patients after treatment. Therefore, safeguarding these survivorsâ€™ quality of life is essential. One of the key elements in the multimodal treatment of these patients is radiotherapy (RT). However, neurocognitive decline arises in up to half of all these cranial irradiated patients, placing a heavy burden on the social and economic aspects of the patientsâ€™ lives. To date, neither the pathologic processes nor the brain structures most important for neurocognition have been accurately identified. Together with the use of highly conformal radiotherapy techniques, this knowledge would allow us to selectively spare them from excess dose and thus decrease radiotherapy-related toxicity. In this project, we will combine neuropsychological testing with (micro)structural and functional MRI in adult brain tumour patients in a multicenter longitudinal trial (n=120). Based on these findings, we aim to increase our knowledge on the extent and pathogenesis of neurocognitive decline after RT and identify brain structures correlated with this long term toxicity. If successful, we aim to create a mathematical normal tissue complication probability (NTCP) model that can be used to select the optimal RT treatment plan, limiting neurotoxic sequelae and providing patient-tailored care in future RT patients.

Institution KU Leuven

1. General Information

Name applicant

Laurien De Roeck

FWO Project Number & Title

Project number: 1SE5722N

Project title: Neurocognition-sparing radiotherapy of brain and base of skull tumours based on mathematical modelling and advanced brain imaging

Affiliation

- KU Leuven

2. Data description

Will you generate/collect new data and/or make use of existing data?

- Generate new data

Describe in detail the origin, type and format of the data (per dataset) and its (estimated) volume. This may be easiest in a table (see example) or as a data flow and per WP or objective of the project. If you reuse existing data, specify the source of these data. Distinguish data types (the kind of content) from data formats (the technical format).

Type of data	Format	Volume	How created
(A) Magnetic resonance imaging (MRI)	NIfTI, DICOM	100 GB	MRI imaging of the participants' brains, more specifically: • anatomical scans (T1, T2, FLAIR) • susceptibility-weighted imaging (SWI) • diffusion-weighted imaging (DWI) • functional magnetic resonance imaging (fMRI)
(B) Behavioral data	paper/ .docx/ REDCap	2 GB	• docx for test instructions of neuropsychological tests • paper records will be transferred to the REDCap platform
(C) Questionnaire data	REDCap survey/paper	2 GB	questionnaires for behavioural measures associated with the study questions, via: • Redcap survey (online) • paper records will be transferred to the REDCap platform
(D) Analysis scripts and code for medical imaging (MRI) and statistical analysis	m(at), .py(w), .r, .sav, .sps	5 GB	Already existing in-house script (UZ Leuven) that is adapted; self-written code and statistics datasets
(E) Metadata	.txt/.docx	100 MB	See below, section 4
(F) Radiotherapy plan	DICOM	2 MB	Radiotherapy plans of the participant will be exported from the clinical database (ARIA)

3. Legal and ethical issues

Will you use personal data? If so, shortly describe the kind of personal data you will use. Add the reference to your file in KU Leuven's Register of Data Processing for Research and Public Service Purposes (PRET application). Be aware that registering the fact that you process personal data is a legal obligation.

- Yes

Ethical commission reference: S65664

All data that will be collected during this study, will be treated confidentially. The existing CRF’s (clinical) and acquired data will first be coded, so there continues to be a link between the data and the individual (pseudonymisation). The subject’s name and other identifiers will then be stored separately (on-site file) from their research data and replaced with a unique code to create a new identity for the subject. The original database (on-site file) with personal details will be stored on the local hospital network only (in every centre). The local PI's (Maarten Lambrecht, Katrien Erven and Tom Boterberg) are the owners and will maintain these databases.

Demographics (age, gender), medical history, data regarding diagnosis, treatment are collected retrospectively from the clinical database (KWS) and after coding, these pseudonymous data will be documented by the study team in REDCap. Only the pseudonymous data will be shared with the central centre (UZ Leuven). Paper questionnaires, test materials and documents are stored in a key-closed closet. These data are only approachable by the involved investigator using the specific study login code. The structural MR images are stored on PACS for the physician to review the images on potential abnormalities. Furthermore, MR imaging DICOMs and radiotherapy plans will be stored on a secured platform Onco Place (Aquilab), but only after pseudonymisation. Data are collected by the applicant under prof. Lambrecht‘s supervision (UZ Leuven) and by the study team of UZ Gent and Gasthuiszusters Antwerpen (GZA) and stored until at least ten years after the end of the research.

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? If so, add the reference to the formal approval by the relevant ethical review committee(s)

- Yes

Ethical Commission reference: S65664 (pending)

Does your work possibly result in research data with potential for tech transfer and valorisation? Will IP restrictions be claimed for the data you created? If so, for what data and which restrictions will be asserted?

- No

Do existing 3rd party agreements restrict dissemination or exploitation of the data you (re)use? If so, to what data do they relate and what restrictions are in place?

- No

4. Documentation and metadata

What documentation will be provided to enable reuse of the data collected/generated in this project?

The following documentation will be provided to enable reuse of the data:

All information regarding this study (IFC, protocol, questionnaires) will be kept on a central secured Google Cumulus Drive of UZ Leuven, shared with the study team of the participating centres. Documenys will be updated by a member of the research team.

The coding documents will only be uploaded on the protected internal server of the local hospital (UZ Leuven, UZ Gent, GZA). For storage and collection of pseudonymous data, REDCap will be used. Every time a new subject is enrolled and/or measurements take place the clinical, behaviour and questionnaire data will be transferred to REDCap. The imaging data and radiotherapy plans will be uploaded after pseudononymisation on a central platform 'Onco Place', which will be provided by Aquilab. Pseudonymous data in the REDCap and the Oncoplace platform will only be shared with the study team of UZ Leuven (central centre).

(A): The raw imaging data will be exported from the scanner and regularly saved with back-ups, so that these can always be reused for additional checks. The brain imaging data structure (BIDS) will be used to save medical imaging data (https://bids.neuroimaging.io/index.html). An additional .txt or docx. file explaining the scanning protocol, image reconstruction, data storage, primary data processing and generic descriptions of the applied data analysis processes will be stored for each imaging type. Pseudonymous data will be uploaded on the Onco Place platform (Aquilab) and only shared with the central centre (UZ Leuven)

(B and C): The complete pseudonymized dataset containing the questionnaire and behavioural data, will be stored in REDCap. This will be complemented with a codebook containing the specific variable definitions and their possible values/categories. The research protocol provides a detailed overview of all the variables that are collected and stored in the database. Together with the paper data, a printed version of these instructions will be stored.

(D): Scripts will use the comment function to explain each analysis step. Data sets and .xlsx documents will have a clear document name and row/column description; if needed for understanding, further metadata (.txt/.docx) will be created

(F): Radiotherapy plans will be exported from the clinical database (ARIA) and uploaded to the Onco Place platform (Aquilab) after pseudonymisation

Will a metadata standard be used? If so, describe in detail which standard will be

Will a metadata standard be used? If so, describe in detail which standard will be used. If no, state in detail which metadata will be created to make the data easy/easier to find and reuse.

- Yes

The data will be structured according to the different data types (i.e. folder structure as follows: data/scans; data/behaviour; data/questionnaires). This folder structure will be defined in the abovementioned codebook. For organizing and storing medical imaging data, a standard structure for medical imaging will be used (BIDS, see above). A considerable portion of the meta-data is included in the header information of the original MR DICOM images. The header contains information regarding the acquisition settings (acquisition time, flip angle, bandwidth, TE, TR, matrix, field of view, slice thickness) and some patient characteristics at the time of the scan, such as height and weight

5. Data storage and backup during the FWO project

Where will the data be stored?

1. The time-stamped master copy of the data will be kept on the the local hospital's facility (e.g. UZ Leuven). Pseudonymized copies can be made and kept on password protected work computers/drives if needed for analyses/transfer.

2. Since we will be working with sensitive personal data, data will be pseudonymized as soon as possible. Only one record that is linking the pseudonym to the personal data ('Participant identification list') will be kept on a second separate drive, that will be password secured. Access will be granted to researchers directly involved in the maintenance of this database and be kept as limited as possible.

3. MR imaging data will be stored on an external hard drive, and reconstructed files will be transferred to the hospital PACS system and uploaded on the Oncolopace platform. Since we will collaborate with researchers from other research units and groups, we will use both the Aquilab Oncoplace platform as well as the REDCap platform for active use of the data during the project.

How is backup of the data provided?

The data will be stored on the university hospital's servers with weekly back-up procedures. The involved researcher of the local study team will perform the backup and recovery on a secured OneDrive (e.g Cumulus UZ Leuven) storage and on an external backup drive.

Pseudonymous data will be stored on the Redcap en Aquilab Onco Place platform.

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

- Personal data: UZ Leuven server, UZ Leuven cumulus OneDrive

- Pseudonymous data: Redcap and Aquilab Onco Place platform (secured), external back-up hard drive of 6TB

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

The external back-up on 2 external hard drives will cost approximately 400euros.

The Redcap licence costs 40 euros per year, which is funded by Stand Up To Cancer.

The Aquilab Oncoplace platform costs 41 000 euro for 4 years, which is funded by Stand Up To cancer.

Data security: how will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?

1. The identifiable data files from this study will be managed, processed, and stored in a secure environment of the local hospital (e.g. UZ Leuven). Access will be controlled by PI determined access rights mediated by password protection and customised read/write permissions

2. The access to the pseudonymised data on the REDCap and Aquilab oncoplace platform will be limited to researchers of the local studyteam only. Only the studyteam of UZ Leuven will have access to all pseudonymised data.

6. Data preservation after the FWO project

Which data will be retained for the expected 5 year period after the end of the project? In case only a selection of the data can/will be preserved, clearly state the reasons for this (legal or contractual restrictions, physical preservation issues, ...).

All data will be retained for at least 10 years years after the end of the project (policy KU Leuven).

Where will the data be archived (= stored for the longer term)?

The data will be archived on the university hospital servers only. After the end of the study, also the external drives (including the high capacity back-up drive) containing the pseudonymized data will be saved in the hospital.

What are the expected costs for data preservation during the retention period of 5 years? How will the costs be covered?

There will be no additional costs after the end of the project.

7. Data sharing and reuse

Are there any factors restricting or preventing the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)?

- Yes. Specify:

We've signed a contract with Aquilab restricting the data to be shared beyond the project collaborators. After the project, data will be downloaded and stored in a secured enviroment in UZ Leuven. The data will be destroyed on the Aquilab Onco Place platform.

Which data will be made available after the end of the project?

The full pseudonymized behavioural dataset will be made available after publication of the data, upon request with the PI, for clearly defined research purposes and after signing a data sharing agreement. Because of the nature of medical imaging data that does not allow for full anonymization, even when removing all personal information from the files and defacing the images, this will be kept restricted.

Where/how will the data be made available for reuse?

- Upon request by mail

As explained above, medical imaging data is rather sensitive personal data. Therefore, re-use within or outside of the research group will be provided if requested via mail. In this case, only the necessary pseudonymized information will be shared. In case of data sharing outside of the study team, the universities' privacy and legal experts will be consulted prior to data sharing to conform with all current privacy standards and regulate the data sharing process.

When will the data be made available?

- Upon publication of the research results

Data will only be made available to other researchers after publication of the research results.

Who will be able to access the data and under what conditions?

Sharing of pseudonymized data will be considered after a request is submitted explaining the planned reuse. Only uses for research purposes will be allowed and commercial reuse will be excluded. All participants will have signed the informed consent, containing the agreement to share pseudonymized data with other researchers inside or outside KU Leuven (open data). Data will only be shared if the research is approved by the ethical committee and participants will be informed regarding this secondary use. Publications relating to the study will be provided in open access via Lirias.

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

No costs for data sharing are expected. If any occur, they will be covered by the requesting Parties.

8. Responsibilities

Who will be responsible for data documentation & metadata?

Maarten Lambrecht, MD PhD
Applicant: Laurien De Roeck

Who will be responsible for data storage & back up during the project?
- UZ Leuven; Maarten Lambrecht, MD PhD (PI) and Laurien De Roeck, MD
- UZ Gent: Tom Boterberg, MD PhD (PI)
- GZA: Katrien Erven, MD (PI)
- Platforms: Aquilab (Onco Place) & REDCap

Who will be responsible for ensuring data preservation and reuse ?
Maarten Lambrecht, MD PhD
Applicant: Laurien De Roeck

Who bears the end responsibility for updating & implementing this DMP?
The PI bears the end responsibility of updating & implementing this DMP.