1127523N - Optimization of staging and treatment in pregnant patients with cervical cancer

A Data Management Plan created using DMPonline.be

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Project abstract:

Cervical cancer (CC) complicates 1-12 in 100.000 pregnancies. This co-existence is highly challenging since the cervix is both the primary site of the malignancy and an essential factor in maintaining the pregnancy. Management is currently hampered by a lack of robust evidence and several questions remain. Whether pregnancy might lead to diagnostic delay and higher stage at diagnosis is still a point of discussion. Both the impact of pregnancy-preserving management on survival of pregnant compared to nonpregnant CC patients, as well as the impact of the mode of delivery on oncological outcomes remain unknown. In addition, lymph node staging, which is vital in guiding treatment decisions in early-stage CC, is highly challenging during pregnancy. In this research project, I will investigate the impact of pregnancy on CC diagnosis and the influence of obstetric management on cancer recurrence and survival in the largest cohort of pregnant CC patients to date. In addition, I will perform a pilot study in a prospective cohort of pregnant CC patients to assess indocyanine green-guided sentinel lymph node biopsy as a minimally invasive surgical staging method. Lastly, I will evaluate whether the application of advanced MRI techniques such as radiomics could be a viable non-invasive alternative to surgical lymphadenectomy for lymph node staging during pregnancy. With this, I aim to contribute to clinical guidelines and improve management and outcome of pregnant CC patients.

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Questionnaire

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

For this research project, we will reuse exsisting data and generate new data.

In WP1, the following clinocopathological data of 40 pregnant patients with cervical cancer, who underwent an T2 and/or diffusion weighted MRI pelvis and/or whole body will be retrospectively collected from the International Network on Cancer, Infertility and pregnancy (INCIP) registry (established and chaired by the promotor of the current FWO project prof. dr. Frédéric Amant): date of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, histopathological subtype, follow-up data (relapse yes/no, site of relapse, treatment of relapse, date of relapse, date of death if applicable), status of lymph nodes after lymphadenectomy, lymphovascular space invasion (LVSI) status, MRI image system, acquisition sequence, maximal tumor diameter on MRI, MRI-reported lymph node status, region of lymph node metastasis (LNM), gravidity, parity, date of primary diagnosis, gestational age at diagnosis, gestational age at lymphadenectomy, gestational age at delivery, type of delivery, neonatal parameters (birth weight and according percentile, sex). MR images and anatomopathological reports will be requested in the different participating INCIP centers. Centers participating in the INCIP network will be requested to transfer T2W, DWI and/or ADC MRI whole body and/or pelvis of elegible patients participating in the INCIP registration study part I.IA. Images transfer will occur using standard DICOM format to the secured environement and secured servers of the medical imaging research center (MIRC) of the UZ Leuven. Servers are not accessible outside the University Hospitals Leuven. Image data will immediately be anonymized. Clinical data will be pseudonymized (coded) and compiled in the encrypted REDCap database as the MIRCCaP study.

In WP2, the following clinocopathological data of 15 pregnant patients with early-stage cervical cancer who will go indocyanine-green guided sentinel lymph node biopsy, will be prospectively collected in the the International Network on Cancer, Infertility and pregnancy (INCIP) registry (established and chaired by the promotor of the current FWO project prof. dr. Frédéric Amant): date of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, diagnostic procedures, histopathological subtype, tumor size, gravidity, parity, date of primary diagnosis, gestational age at diagnosis, neonatal outcome and mode of delivery. Surgical variables (i.e operation time, complications (bleeding, neurovascular injury, infection) and post-operative complications will be recorded, in combination with surgery outcome of the sentinel lymph node mapping characteristics (SLN detection rate, side-specific detection rates, median number of SLNs and SLN locations. Clinical data will be will be pseudonymized (coded) and compiled in an encrypted Excel database.

In WP3, the following clinocopathological data of 350 pregnant patients with cervical cancer will be retrospectively collected in the the International Network on Cancer, Infertility and pregnancy (INCIP) registry (established and chaired by the promotor of the current FWO project prof. dr. Frédéric Amant): date of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, histopathological subtype, follow-up data (relapse yes/no, site of relapse, treatment of relapse, date of relapse, date of death if applicable), type of therapy during pregnancy, gravidity, parity, date of primary diagnosis, gestational age at diagnosis, gestational age at lymphadenectomy, gestational age at delivery, type of delivery, neonatal parameters (birth weight and according percentile, sex). Additionally, the following information will be collected from 700 controls: each case will be matched to 2 nonpregnant controls, matchin will be based on 2009 FIGO stage, center, histological tumor characteristics and age (+/- 5 years). Clinical data for the 350 pregnant patiens will be pseudonymized (coded) and compiled in the encrypted REDCap database, clinical data for the nonpregnant controls will be will be pseudonymized (coded) and compiled in an encrypted Excel database.

For WP1 and WP3, the REDCap database is hosted on dedicated KU Leuven data servers at Campus Heverlee. At the clinical database level only study team members, monitors and auditors/inspectors for whom the Coordinating or Principal Investigator (as applicable) has requested project-specific eCRF access, are granted data access. Upon successful training completion each user is centrally assigned a user role, associated with predefined system/data privileges, in accordance with CR DM-WI-001. The gatekeeper for UZL REDCap is UZL CTC (ctc.datamanagement@uzleuven.be).

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

The PI (Prof. Dr. F. Amant) is responsible for ensuring data preservation and reuse of the research data.

Pseudonymized clinicopathological data will be stored for 20 years in accordance with the research protocol (s25470) on the UZ Leuven servers and the data will be transferred to the online REDCap database.

Since we will be working with sensitive personal data that will be pseudonymized, clinicopathological data will be stored at the UZ Leuven's secure environment and the REDCap database during the research project. All other data (imaging, experimental) will be retained on the central servers of the UZ Leuven, without storage limit and with automatic daily back-up procedures. After the research, clinicopathological patient data (encrypted) are preserved in the online REDCap database, for use in other research projects in accordance with the study protocol s25470, approved by the Ethics Committee Research UZ/KU Leuven.

During the research and after termination of the research, only members of the lab group 'gynaecological oncology' that have permission to access the files will have the ICT permission to do so. (e.g. students won't be granted access to sensitive data).

Costs for storage on the central servers of UZ Leuven are taken by the Department of Oncology. The cost for the 'INCIP registry' REDCap database is €80/year, which will be covered by the 'Fonds voor onderzoek naar kanker tijdens de zwangerschap'.

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)

All the data generated will be retained for minimally 20 years after the end of the FWO project, in accordance with the research protocol s25470, which was approved by the Ethics Committee Research UZ/KU Leuven 20 January 2022. Since the creation of the International Network on Cancer, Infertility and Pregnancy in 2005, clinical (oncological and obstetric data from more than 3200 patients in 75 centers worldwide have been collected, resulting in the largest database concering this rare toppic, but further research questions arrise with the development of new oncological treatment techniques. The preservation of clinicopathological data for minimally 20 years after the ending of the FWO project provides the opportunity of reuse of the data for future research projects conducted by INCIP. The informed consent includes a clause that permits later reuse of the obtained data.

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)

Yes, human subject data will be collected during this research project.

- The INCIP study (S25470) obtained ethical approval by the Ethics Committee Research UZ/KU Leuven on 20th January 2022.
- The MIRCCaP study (S67391) obtained ethical approval by the Ethics Committee Research UZ/KU Leuven on ###.

GDPR questionnaires were filled in and submitted for all studies above with the Ethics Committee Research UZ/KU Leuven.

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

None

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DPIA

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

- Not applicable

1127523N - Optimization of staging and treatment in pregnant patients with cervical cancer GDPR

GDPR

Have you registered personal data processing activities for this project?

- Not applicable

1127523N - Optimization of staging and treatment in pregnant patients with cervical cancer FWO DMP (Flemish Standard DMP)

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	
WP1: Clinicopathological data MIRCCaP	Clinicopathological features of 40 pregnant patients with cervical cancer with MRI imaging, available in the REDCap database for the CIP-study (s25470)	Reuse existing data	Digital	Observational	.cvs, .xls, .pdf	< 100 MB	
WP1: Subject identification log MIRCCaP	Subject identification log connecting participating patients with study number	Generate new data	Digital	Observational	.xls, .pdf	< 100 MB	
WP1: Imaging data MIRCCap	T2 and/or DWI whole body MRI images of 40 pregnant patients with cervical cancer: retrieval of existing imaging in the participating centers	Generate new data	Digital	Observational	DICOM	< 1 GB	
WP1: Radiomic features MIRCCap	List of first and second order MRI features per patient, extracted according to IBSI guidelines	Generate new data	Digital	Experimental	.xls, .pdf	< 100 MB	
WP2: Informed consent SLN-ICG	Signed informed consents of 15 pregnant patients with early-stage cervical cancer participating in WP2	Generate new data	Physical Digital (stored on the UZ Leuven server)	Experimental	.pdf	< 100 MB	1 binder in the closed cabinet of the lab of Gynecological Oncology, KU Leuven
WP2: Clinicopathological data SLN-ICG	Clinicopathological features of 15 pregnant patients with early-stage cervical cancer undergoing sentinel lymph node biopsy using indocyanine green	Generate new data	Digital	Observational	.cvs, .xls	< 100 MB	
WP2: Subject identification log SLN-ICG	Subject identification log connecting participating patients with study number	Generate new data	Digital	Observational	.xls, .pdf	< 100 MB	
WP2: Surgical information SLN-ICG	Surgical variables (i.e operation time, complications (bleeding, neurovascular injury, infection) and post-operative complications	Generate new data	Digital	Observational	.cvs, .xls	< 100 MB	
WP2: Surgical images SLN-ICG	Peroperative photos charting the location of sentinel lymph nodes using indocyanine green per patient	Generate new data	Digital	Observational	.jpg	< 1 GB	
WP3: Clinicopathological data INCIP cervix - cases	Clinicopathological features of 350 pregnant patients with cervical cancer, available in the REDCap database for the CIP-study (s25470)	Reuse existing data	Digital	Observational	.cvs, .xls, .pdf	< 100 MB	
WP3: Clinicopathological data INCIP cervix - controls	Clinicopathological features of 700 matched non-pregnant controls with cervical cancer, matched on 2009 FIGO stage, center, histological tumor characteristics and age (+/- 5 years)	Generate new data	Digital	Observational	.cvs, .xls, .pdf	< 100 MB	

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:

Since the creation of the International Network on Cancer, Infertility and Pregnancy (INCIP) in 2005, clinical, oncological and obstetric data from more than 3200 patients in 75 centers worldwide have been collected, resulting in the largest database concering this rare toppic. The INCIP registry is available via REDCap, hosted on dedicated KU Leuven data servers at Campus Heverlee.

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

The project is a combination of research studies that were approved by the Ethics Committee Research UZ/KU Leuven: S25470, S67391 and S67253.

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

Short description of the kind of personal data that will be used:
WP1: year of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, histopathological subtype, follow-up data (relapse yes/no, site of relapse, treatment of relapse, date of relapse, date of death if applicable), status of lymph nodes after lymphadenectomy, lymphovascular space invasion (LVSI) status, MRI image system, acquisition sequence, maximal tumor diameter on MRI, MRI-reported lymph node status, region of lymph node metastasis (LNM), gravidity, parity, date of primary diagnosis, gestational age at diagnosis, gestational age at lymphadenectomy, gestational age at delivery, type of delivery, neonatal parameters (birth weight and according percentile, sex).
WP2: year of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, diagnostic procedures, histopathological subtype, tumor size, gravidity, parity, date of primary diagnosis, gestational age at diagnosis, neonatal outcome and mode of delivery, surgical variables (i.e operation time, complications (bleeding, neurovascular injury, infection), post-operative complications; sentinel lymph node mapping characteristics (SLN detection rate, side-specific detection rates, median number of SLNs and SLN locations).
WP3: year of birth, age, body mass index, presenting symptoms, FIGO stage at diagnosis, histopathological subtype, follow-up data (relapse yes/no, site of relapse, treatment of relapse, date of relapse, date of death if applicable), type of therapy during pregnancy, gravidity, parity, date of primary diagnosis, gestational age at diagnosis, gestational age at lymphadenectomy, gestational age at delivery, type of delivery, neonatal parameters (birth weight and according percentile, sex).
All clinical data will be pseudonymized and compiled in an encrypted REDCap database. A separate password-encrypted MS Excel file linking the electronical medical record file (EAD) to the unique research-specific patient identification code used in the subsequent data analysis and research-dedicated records will be kept seperately from the other data. Only researchers will have access to the data files which will be kept on computers linked to the UZ Leuven network server and secured with a password.

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.

- Yes

The proposed project is an extension of an existing multicentric study (WP1) and a substudy within an existing multicentric study (WP3) with collaboration within the INCIP network. In agreeance with the legal department of the CTC of the University Hospitals Leuven (communication with Aernout De Raemaeker), data transfer will initially work trough protocol for both study S25470 and S67391. All aspects related to data transfer in accordance with GDPR are regulated through the protocol. If certain centers require a separate agreement, an adapted DTA has be provided for the site(s) in question.
All publications from the INCIP study (S25470) will be done according to the INCIP Publication Policy. The described publication policy applies to all articles resulting from WP1, WP2 and WP3. (https://www.cancerinpregnancy.org/sites/default/files/guidelines_for_authorship_for_studies_run_within_incip.pdf

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).

For documentation purposes, we will make use of:
At project level:
- A README file will be provided for each of the WPs. We will use KU Leuven's template.
- For each WP, a protocol is provided, describing the methodology used to collect the data in detail. Details about patient selection and study design are reported in the study protocol.

At data level:
- For each WP, a data dictionary codebook from REDCap will be provided, describing labels for all variables, variables types, units of measurement and key identifiers.
All relevant documentation will be stored in a seperate, restricted acces folder on the UZ Leuven server.

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

For each workpackage, metadata concerning the clinicopathological information will be stored in a REDCap datadictionary, a specifically formatted .csv spreadsheet containing the metadata used to construct data collection instruments and fields.
For WP1, metadata concerning the MRI images will be extracted and stored from the DICOM files.

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

Where will the data be stored?

Since we will be working with sensitive personal data that will be pseudonymized, clinicopathological data will be stored at the UZ Leuven's secure environment and the REDCap database during the research project. All other data (imaging, experimental) will be retained on the central servers of the UZ Leuven, without storage limit and with automatic daily back-up procedures.

How will the data be backed up?

The data will be stored on UZ Leuven's central servers with automatic daily back-up procedures.
The REDCap database is hosted on dedicated KU Leuven data servers at Campus Heverlee, the gatekeeper for UZL REDCap is UZL CTC. Data using UZL REDCap is backed up as follows:

- The web server backup regime is specified below:
  - An hourly backup, the last 6 versions of which are saved
  - A daily backup, the last 7 versions of which are saved
  - A weekly backup, the last 6 versions of which are saved
- The database backup regime is specified below:
  - A nightly cold backup of all databases
  - One month's storage of the nightly cold backups

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, data will be stored on the central server of the UZ Leuven and the KU Leuven servers for REDCap, which have no storage limit.

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

During the research and after termination of the research, only members of the lab group 'gynaecological oncology' that have permission to access the files will have the ICT permission to do so on the secure UZ Leuven servers. (e.g. students won't be granted access to sensitive data). Documents containing personal information, e.g. informed consents, subjects identification log, etc, will receive additional password protection.
The REDCap database is hosted on dedicated KU Leuven data servers at Campus Heverlee. At the clinical database level, only study team members, monitors and auditors/inspectors for whom the Coordinating or Principal Investigator (as applicable) has requested project-specific eCRF access, are granted data access. Upon successful training completion each user is centrally assigned a user role, associated with predefined system/data privileges, in accordance with CR DM-WI-001. The gatekeeper for UZL REDCap is UZL CTC (ctc.datamanagement@uzleuven.be).

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

Costs for storage on the central servers of UZ Leuven are taken by the Department of Oncology. The cost for the 'INCIP registry' REDCap database is €80/year, which will be covered by the 'Fonds voor onderzoek naar kanker tijdens de zwangerschap'.

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 the clinicopathological data generated in this research project, will be retained for minimally 20 years after the end of the FWO project, in accordance with the research protocol S25470, which was approved by the Ethics Committee Research UZ/KU Leuven 20 January 2022. The preservation of clinicopathological data for minimally 20 years after the ending of the FWO project provides the opportunity of reuse of the data for future research projects conducted by INCIP. The informed consent includes a clause that permits later reuse of the obtained data.

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

Clinical data (encrypted) will be stored according to legal recommendations for 20 years after termination of the project on the UZ Leuven server and the data will be transferred to the online REDCap database.
Imaging data will be retained on the central servers of UZ Leuven, more specifically the secured environement and secured servers of the medical imaging research center (MIRC) of the UZ Leuven for 25 years according tot legal recommendations.

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

All data will remain on the central servers of UZ Leuven, the costs are taken by the Department of Oncology.

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 a restricted access repository (after approval, institutional access only, …)

Data can be shared upon request, with the exeption of personal data, which will never be made available, under any circumstance, Given that we deal with sensitive data, a data access

committee (UZ Leuven) will go over the request and decide wheter data can be shared with a third user.

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

Not applicable

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
- Yes, Ethical aspects

Participants of the study can indicate wheter they agree with potential usage of data for subsequent other research purposes in the informed consent form. Data can be shared upon request, with the exception of personal data, which will never be made available under any circumstance.

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

Data will be shared in coded form, upon request, after approval by a data access committee (UZ Leuven).

When will the data be made available?

Upon publication of the research results.

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

In agreeance with the legal department of the CTC of the University Hospitals Leuven (communication with Aernout De Raemaeker), data transfer will initially work trough protocol for both study S25470 and S67391. All aspects related to data transfer in accordance with GDPR are regulated through the protocol. If necessary or if the request for data sharing is made by an investigator not already involved within the INCIP network, an addition data sharing agreement can be drafted upon request.

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

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

Cost of data sharing would be negotiated upon request.

6. Responsibilities

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

Charlotte LeJeune, PhD researcher, and PI, prof. dr. Frédéric Amant, will be responsible for verifying data is accurate and records are up to date.

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

UZ Leuven IT is responsible for the central UZ Leuven servers. REDCap is hosted on dedicated KU Leuven data servers at Campus Heverlee, the gatekeeper for UZL REDCap is UZL CTC.

Who will manage data preservation and sharing?

The PI (prof. dr. Frédéric Amant) is responsible for ensuring data preservation and sharing.

Who will update and implement this DMP?

The PI (prof. dr. Frédéric Amant) bears the end responsibility of updating and implementing this DMP.