


Integration and Optimization of XNAT-Based Platforms for the Management of Heterogeneous and Multicenter Data in Biomedical Research

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Abstract: The rise of data-driven analysis methods in biomedical research has led to the need for proper data management. Organizing large datasets of heterogeneous biomedical data can be challenging, especially in multi-centric studies, with the need to ensure data integrity, quality, and privacy compliance with laws. In this work, we report and discuss two solutions that we are starting to implement: a platform for collecting Computed Tomography imaging data of phantoms and associated metadata in a multi-centric study focused on radiomics, and a platform for gathering, sharing, and analyzing diverse data acquired in a project focused on FLASH radiotherapy. Both platforms will be built on top of the XNAT technology. Our goal is to establish a secure and collaborative medical research environment that promotes data sharing, customized workflow analysis, and stores data and results for subsequent studies. The key innovation is the creation of a personalized platform system that currently does not exist. This is essential from a scientific point of view to enable advanced statistical analysis and reveal non-trivial relationships among heterogeneous data. This cannot be achieved with disorganized data collection. The platforms will also integrate analysis tools and quality control pipelines executable directly from the platform on stored data.

1 INTRODUCTION

The management of multicentric and heterogeneous data is a longstanding problem in the biomedical research field (Ismail et al., 2020; Brancato et al., 2024). The advancements in data acquisition technologies and the increasing development of data-driven analysis methods, such as Artificial Intelligence (AI), are now requiring more attention in the steps of collection, storage, and processing of data. This is particularly true when there is the need to merge data from different domains or institutions, where variations in acquisition, format, and collection can occur. In fact, having a well-organized dataset in experimental biomedicine is not obvious, especially when various protocols, extensive metadata, and large datasets are involved. However, properly integrating datasets with different characteristics is crucial to ensure re-

producibility and prevent the loss of information or to avoid any bias in the successive data analysis. The introduction of FAIR principles, a set of guidelines to ensure the Findability, Accessibility, Interoperability, and Reusability of the data, emphasized the urgent need for improved scientific data management (Wilkinson et al., 2016; Jansen et al., 2017), in order to facilitate data usability by both machines and individuals.

One of the open-source software platforms developed to support the FAIR principles and facilitate medical data management is the Extensible Neuroimaging Archive Toolkit (XNAT), <https://www.xnat.org/>. It was designed to be efficient for neuroimaging data storage and sharing (Marcus et al., 2007; Redolfi et al., 2023). However, over time it was extended to other medical imaging domains (Herrick et al., 2016; Timón et al., 2017; Wahle et al., 2013). What makes XNAT preferable to other

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software platforms for medical data storage is its high customizability. It can be configured in different ways to support any data and project management needs. XNAT relies on a three-tiered software architecture: a PostgreSQL database back-end, a Java-based middleware tier, and a web-based user interface. With an XNAT-based platform, it is possible to upload, organize, share, view, and download the data while securing and managing access. It allows searching and exploring large datasets through the web interface and also running complex processing (HPC) on the data. The access settings and user permissions can be customized and updated as needed. The data model can be expanded infinitely, and new data types can be created in addition to the existing ones. It is also possible to configure different project types based on specific data sharing and usage requirements. All these specifications allow the storing and sharing of heterogeneous and interconnected data among different experiment groups, making the XNAT technology highly suitable for facilitating the integration of multicentric and heterogeneous data.

This study aims to describe the following two parallel solutions of integrated XNAT-based platforms that we are starting to implement.

- A platform for collection and sharing of multicenter Computed Tomography (CT) imaging data of phantoms, with the integration of a quality control pipeline to ensure consistency of the data for successive radiomics analyses.
- A platform for collection, sharing, and analysis of heterogeneous data acquired in different types of experiments (dosimetry, radiobiology, and simulations) in the context of a project focused on FLASH radiotherapy.

In the following sections, we discuss the rationale behind the need for these platforms, the description of the intended architecture, the novelty of the tool, and the similarities between the two projects.

2 XNAT PLATFORM FOR MULTICENTER PHANTOM IMAGING DATA

2.1 Background and Objectives

Radiomics is a quantitative analysis approach that consists in extracting quantitative information from medical images. These can be then employed by Machine Learning (ML) algorithms to obtain automated predictions. However, changes in the image acquisition and reconstruction protocols can affect the values

of extracted radiomics features impeding the generalization of radiomics-assisted models.

Phantoms are physical models that reproduce the properties of the biological tissues involved in the realization of medical images. They represent an adequate test environment for both medical quality assurance and research since they can offer the possibility of repeating acquisitions several times even with imaging techniques involving ionizing radiation such as CT. There are numerous types of phantoms, from simple geometric to sophisticated human-like models (Wegner et al., 2023), whose choice depends on the task to fulfill. More complex and customized phantoms are needed to address specific research questions, and in-house-produced phantoms can be preferred to commercially available ones.

We developed a preliminary study using CT images of phantoms to characterize image quality and investigate a potential upstream harmonization based on image appearance matching with the objective of improving the robustness of radiomics features. Phantom data from different centers can represent a valuable source of information to conduct reproducibility and harmonization analyses across multiple scanners and protocols. Reproducibility is a prerequisite to increase the trust of stakeholders in AI decision systems based on the analysis of radiomics features. In fact, the lack of robustness and generalization ability represents the major bottleneck to validating the many published models and establishing their clinical added value. A pilot study with a phantom involving different clinical centers can help in defining a common protocol for reproducibility improvement. Our objective is to perform this multi-center study to evaluate the impact of different image acquisition parameters on the robustness of radiomics features.

The first strategy for image quality characterization was defined by using a commercial phantom, the Catphan-500. Then, the Radiomik phantom model, specifically designed for radiomics (Pallotta et al., 2020), has been utilized to test for repeatability and robustness of radiomics features. The analysis concluded that in multi-centric studies, the image quality-based harmonization strategy could improve the robustness of radiomics features, but it is necessary to follow a standardized process for both image acquisition and feature extraction to enhance the validity of radiomic models.

To address this, a dedicated platform for data collection and sharing is necessary. This can help the remote collaboration between centers located in an extended territory. This open-access platform will be designed to contain CT images of different phantom models acquired in the different centers with all

Subject	Phantom_name	Scanner	CTDIvol	ReconstructionAlgorithm	IterativePercentage	PixelSpacing	SliceThickness	ConvolutionKernel
CAT_fc18_2_aidrSTD	Catphan	TOSHIBA	2	AIDR3D	40	0.428	1	FC18
CAT_lung_2_asir10	Catphan	GE	2	ASIR	10	0.406	1.25	LUNG
RAD_lung_4_FBP	Radiomik	TOSHIBA	4	FBP	0	0.781	1	LUNG
RAD_lung_7_asir10	Radiomik	GE	7	ASIR	10	0.703	1.25	LUNG

Figure 1: Example of list of subjects within the project focused on phantoms, with the associated searchable parameters.

the related acquisition and reconstruction parameters. Moreover, the idea is to integrate analysis tools that can be automatically executed from within the platform.

2.2 Architecture and Implementation

The platform will support the direct upload of CT images of phantoms in the DICOM standard format by the clinical centers where they will be acquired. Different acquisition and reconstruction parameters must be used to test for protocol variations for reproducibility and harmonization studies. The DICOM format allows the storage of these parameters in the DICOM header associated with the image. However, we want some of these parameters to be directly searchable from the platform database to make specific queries and retrieve a particular subset of data on which to perform the successive analysis. Specifically, among the parameters that are useful to store and be available for queries, are: the phantom used, the scanner, the reconstruction kernel, the dose level, the reconstruction algorithm, and the voxel dimension. Within the XNAT Project, the Subject entity will correspond to an ID that identifies the CT acquisition at a specific center, with a particular scanner and phantom and a specific set of acquisition and reconstruction parameters (Figure 1). Each subject will include the CT session experiment, i.e. the CT series associated with those parameters, and each series will contain the CT scans acquired as a repetition with the same set of parameters (Figure 2). This is because for radiomics repeatability studies more images acquired with the same protocol are necessary to perform a statistically significant analysis. In Figure 3, we show an example of a CT slice of the Catphan phantom, used to characterize image quality (Mail, 2013; Samei et al., 2019; Barca et al., 2018a; Barca et al., 2018b; Fantacci., 2024), visualized in XNAT.

The added value of our platform with respect to other existent XNAT collections of multicenter CT phantom datasets (Kalendralis et al., 2019) will be the integration of an automated data quality control pipeline within the platform. Also, we will integrate innovative plugins to perform external analysis on the data within the project with the possibility to store the output of the analysis process as additional metadata associated with the subject.

Subject Details: RAD_lung_4_FBP

Details
Projects

Accession # XNAT_S00003

Date Added 2024-03-25 16:30:49 (camilla)

Birth year --

Gender

Handedness

Group radiomik Phantom

Custom Variable Sets

Parameters used to reconstruct the image	
ReconstructionAlgorithm	FBP
IterativePercentage	0
PixelSpacing	0.781
SliceThickness	1
ConvolutionKernel	LUNG

Parameters used for the acquisition	
Scanner	TOSHIBA
CTDIvol	4
kVp	120

Details on the phantom models	
Phantom_name	Radiomik

Experiments

Date	Experiment	Project	Label
2023-10-31	CT Session	Toy Platform Phantom	999999-003

Figure 2: Example of subject opened in XNAT with the associated custom variables and experiments. The CT Session experiment includes different scans acquired with the same set of variables.

2.2.1 Detectability Index Plugin

One of these plugins will be based on a Python script to automatically compute an index that quantifies image quality in CT images, the detectability index (Samei et al., 2019). Some open-access software exists for this index evaluation, such as imQuest (Duke University, Durham, NC, USA) (Solomon, 2018). However, they require a time-consuming manual ROI positioning step before the computation. Moreover, another disadvantage of the software is the lack of documentation for some functions and parameters. For this reason, we developed a Python script for the automated computation of the detectability index. We plan to integrate this script as an XNAT plugin so that it can be launched directly from the platform to evaluate this index on the stored images, with the possibility of storing this output index as another parameter

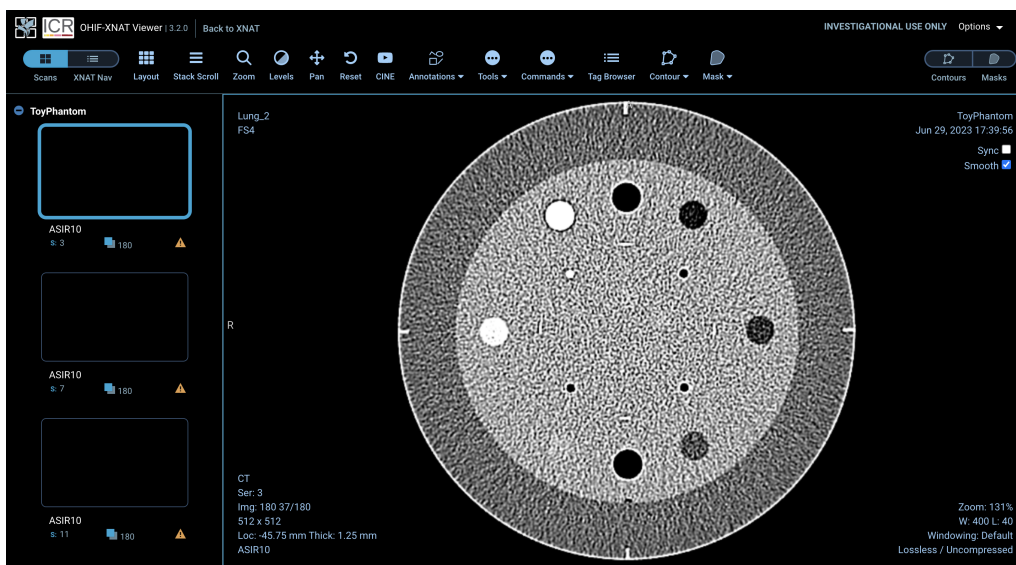


Figure 3: Example of direct visualization of a CT scan of the Catphan phantom with the OHIF-XNAT Viewer plugin.

associated with the image session.

2.2.2 Quality Control Pipeline

Inconsistencies in data acquisition and collection methodologies could compromise the validity of reproducibility and radiomic studies. Integrating datasets with varying characteristics needs meticulous consideration to prevent loss of information or misinterpretation during the integration process.

The CT acquisitions conducted for our pilot study in a single center already highlighted possible inconsistencies at the acquisition and storage levels that can affect the subsequent analysis. It may happen that when the scanner is set to acquire more subsequent acquisitions of the phantoms, some of the parameters manually set by the operator before starting the scanning, e.g. the reconstruction kernel, can accidentally change between two subsequent acquisitions. Also, the positioning of the phantom and the Field Of View (FOV) of the image, meaning the voxel size and the centering of the exact number of slices, should be checked once the acquisition is completed. Moreover, it may be the case that fewer or different numbers of scans are made or saved than expected. This can be a problem when it is necessary to have a specific number of repetitions under identical conditions for the significance of the subsequent analysis.

We experienced that these errors can be quite frequent, thus a pipeline to check for these eventual faults, i.e. an automated quality control on the CT acquisition uploaded on the platform, could be very useful. The pipelines in XNAT are powerful mini-applications that can be run on the project data and

the output can be saved back into XNAT as assessor data. We aim to set a pipeline for the automated quality control to auto-run as a CT session is archived. The result will be a positive/negative response to the quality check. The response will be uploaded as an additive variable associated with the CT session. This allows the operator to have immediate feedback on the quality, hence, in case of a negative response, he could try to retrieve the raw file in the scanner or PACS memory if the error is related to image reconstruction or otherwise repeat the acquisition. This can help save time in the acquisition and storage steps, a fairly important thing if the CT scanner is in clinics and can be left available for phantom acquisitions only for a short time.

The quality check flowchart that we aim to follow is summarized in the pseudocode of Algorithm 1.

3 PLATFORM FOR THE COLLECTION OF HETEROGENEOUS BIOMEDICAL DATA

3.1 Background and Objectives

In oncological radiotherapy, a new effect has been observed since the 1960s and a recent interest emerged in preclinical studies to translate this therapy in clinics. This is the so-called “FLASH effect” (Lin et al., 2021), consisting in administering the therapeutic radiation dose in a single session and in a very short

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Data: Uploaded CT session
Result: Quality check response (
    positive/recover raw file/repeat
    acquisition)
upload DICOM file on XNAT project;
while CT session = specific label do
    read number of scans;
    if number of scans  $\neq$  expected number
    then
        response = repeat the acquisition;
    else
        read dicom header of each scan;
        if reconstruction dicom tags  $\neq$ 
        custom variables then
            response = recover raw file from
            pacs;
        end
        if acquisition dicom tags  $\neq$  custom
        variables then
            response = repeat the acquisition;
        end
        if all dicom tags = custom variables
        then
            read dicom image;
            if phantom is not centered then
                response = repeat the
                acquisition;
            else
                response = positive;
            end
        end
    end
end

```

Algorithm 1: Steps for automated quality control.

time. The advantage is to lead to equivalent effects on the tumor, but much reduced damage to healthy tissues. This could enable radiotherapy to be effective also against tumors characterized, to date, by unfavorable prognosis. This potential paradigm shift could lead to great clinical, economic, and social benefits. However, the radiobiological mechanisms responsible for the FLASH effect have not been fully understood and new devices to deliver ionizing radiation with these characteristics must be defined.

We are involved in a project that aims to study new tools and methods to translate this advanced radiotherapy technique from the models to the clinics, performing fundamental studies to understand the radiobiological mechanism underlying the FLASH effect. This involves a multidisciplinary team, different research groups and centers with different expertise dedicated to dosimetry, radiobiology, simulations, and preclinical studies to investigate the different aspects of the FLASH effect.

Since from the different and parallel experiments conducted for the diverse tasks of the project, heterogeneous data are being collected, we aim to develop an informatics software platform to store, organize, share, and analyze these heterogeneous data. It is essential to have a common database to avoid disorganized and sporadic data organization and to compare the different kinds of data. Moreover, studying the mechanisms underlying the biological effects due to irradiation in this new FLASH effect requires grasping complex relationships and associations among data of different origins and typologies. Only through an IT platform based on an organized and well-indexed database, it is possible to perform advanced statistical analysis that can reveal complex emergent properties, associations, and relationships among data from experiments of different kinds.

The purpose of the platform is to enhance collaboration and data exchange among project partners efficiently. Moreover, since it is an open-source software, it is expected to be maintained even after the completion of the project. This is aimed to provide a foundation for future developments. The ultimate goal is to establish a data platform that can be easily accessed and utilized by a wide range of research teams. This will help standardize data, formats, parameters, and definitions that are currently missing in the field of the FLASH effect study.

3.2 Architecture and Implementation

Due to its high level of extensibility, with the possibility to create new data types, XNAT is an ideal choice for this project. In fact, the platform should have the capability to upload a wide range of data, from DICOM images with associated metadata, to other formats produced by the devices used in the project (e.g., microscopy images), raw formats, and user-defined configuration files. The three main areas of experiments that produce data to store in this common platform are dosimetric experiments for beam characterization, radiobiological experiments, modeling and simulations. The data related to these different areas must be interconnected in order to study the dependence of the radiobiological effect on radiation parameters and other data produced by experiments of different kinds.

In particular, the dosimetric quantities used for sample irradiation, such as, among the others, the delivered dose or the dose rate (Di Martino et al., 2023), usually recorded in Excel files, should be linked to the data related to the specific radiobiological experiment. Various radiobiological experiments, both in vivo and in vitro, involve storing heterogeneous types

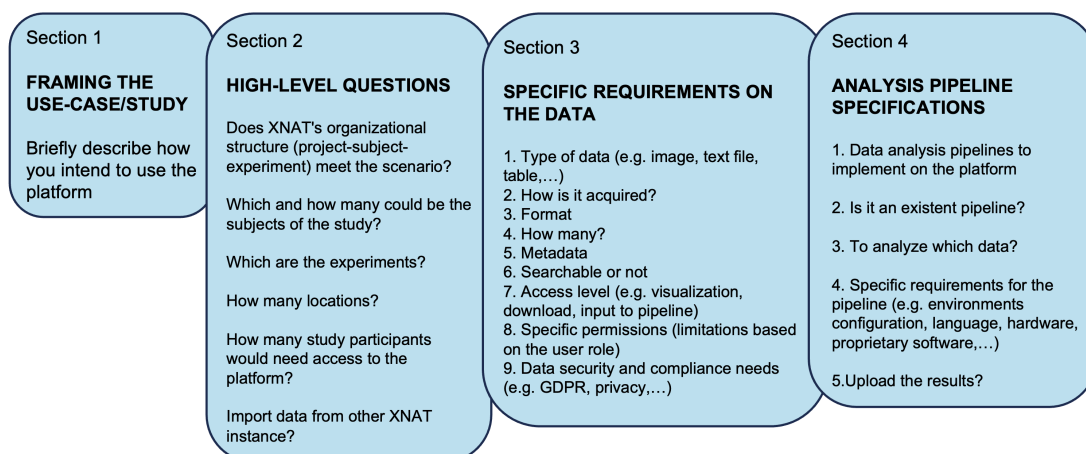


Figure 4: Questionnaire form required to be filled out by the various experimental groups in the project focused on FLASH therapy to define the platform specifications.

of data, including details on the subject irradiated (organism, organ, tissue, etc.) and the measured endpoint (cell survival, ROS assessment, etc.). These data types range from microscopy imaging data with associated metadata in XML files to high-throughput, histological, staining, and gene expression data in tabular or text format and raw data in proprietary format. Moreover, for modeling and performing multi-scale simulations (“in silico”), scientists need to use experimental data to optimize the parameters of kinetic network models that describe processes within various radiobiological effects. Additionally, the large amount of simulation data produced using different software must be stored as raw data, trajectory files, etc., describing the quantities along simulations, and labeled with input parameters.

As evident, a basic XNAT configuration is not sufficient to manage these heterogeneous and interconnected data (Figure 5). We will proceed with defining the project type and personalized data model, organization, and indexing that can meet the needs of the various experimental groups, trying to identify the entity in common at the lowest level among the experiments, to create an extremely personalized database.

Moreover, the platform will offer the possibility of integrating analysis pipelines and workflows, as well as simulating processes and AI tools, for the direct analysis of the data with related results uploaded on the platform itself.

To understand how to manage data heterogeneity, the reconnaissance of the specific requirements for each research group collaborating on the project is being conducted by sharing a questionnaire form among the researchers to grasp their intended use of the platform. The questions posed in the form are summarized in the four sections in Figure 4.

What resulted from the collected answers is that the project needs to build and configure a platform with very specific and unique characteristics. Even though the XNAT core functionalities have been already expanded for supporting data management in other use cases different from medical imaging, such as preclinical imaging (Zullino et al., 2022), to the best of our knowledge, there is no other example of an IT platform designed to store and connect the heterogeneous typology of data related to a new radiation therapy investigation.

The method that we want to adopt for extending the XNAT functionality and creating a platform with these specific characteristics is via plugins. A plugin is a compiled, self-contained package installed into XNAT through which it is possible to add and configure new XNAT data types, create new user interface elements, create new services as analysis tools, etc.

4 COMMON INFRASTRUCTURE

On a technical level, we will host the above-discussed platforms on a common infrastructure. An XNAT server has already been installed in a dockerized container at the Data Center of our research institute. It serves as a pilot project structured with incremental multi-phase deployment and feasibility valuation step-by-step. In particular, we created a new Virtual Machine (VMware cluster) on top of that we deployed the XNAT instance as a dockerized container with configurable dependencies. Then, we set up the storage (GPFS cluster membership), customized the authentication plugin (LDAP), and configured the user notification system (SMTP) and the SSL certificate. The next steps we plan are the configuration of

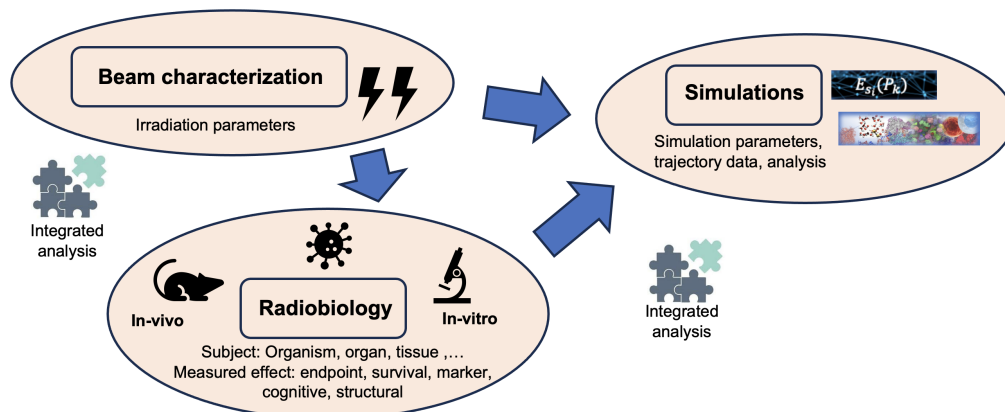


Figure 5: General schema of the experimental areas with the related data to be stored and how they must be interconnected within the platform.

the OpenID plugin for multi-institution authentication (IDEM) and an integrated way to run batch job data analysis workflow.

These steps will enable the realization of a medical research environment to promote data sharing and collaboration between multidisciplinary groups, preserving input data privacy, custom workflow analysis, and storing results for future applications.

5 CONCLUSIONS AND PERSPECTIVES

It has been a long-standing practice for researchers to organize their data into directories, with meta-data stored within the directory and/or the filenames. However, this approach proves to be particularly inadequate in biomedical research as the number of datasets and experiments grows. Especially, with the advent of AI, there is an increasing need for appropriate data management and administration systems. In particular, in multi-centric studies, collecting and organizing large datasets of medical imaging data presents several challenges. Therefore, it is recommended that we adopt more scalable and efficient data management practices to meet the demands of our expanding research endeavors. This is the objective for the two XNAT-based platforms we aim to realize.

The innovativeness of this project is in the realization of an XNAT-based platform for the storage and analysis of extremely heterogeneous data, with the possibility of having multi-centric access. The main novelty of the phantom imaging data project will be the integration of the described automated quality control pipeline, built on top of the experienced issues on data collection in our preliminary work, useful to both save time and ensure the usability of the stored

data for subsequent radiomic analyses. The platform for FLASH radiotherapy-related data, will improve the sharing of the data among various research groups and partners and allow advanced statistical analysis that can reveal nontrivial emergent properties, associations, and relationships among heterogeneous data and experiments. Such a personalized product is not already available and is considered essential from a scientific point of view to make progress in understanding the FLASH effect.

Research centers engaged in medical research projects often face an IT gap due to the absence of adequate IT tools enabling them to share everything they need at all process stages: input data collection, analysis methods and models, and storing results for future use. The two XNAT projects will be designed on top of a common infrastructure in our institution in order to meet all these requirements, definitely bringing specific benefits to biomedical research from the implementation of both platforms.

Moreover, by leveraging structured and organized prior data, research efforts can be streamlined, thereby reducing the need for experimentation on already explored strands. This approach will make data readily available and searchable for future research, as well as directly usable by analysis software, including those based on the latest Artificial Intelligence technologies. The proposed data infrastructure will also be compliant with the General Data Protection Regulation (GDPR) and FAIR (Findable, Accessible, Interoperable and Reusable) data principles and data quality standards, offering high computational performance, and achieving interoperability.

In conclusion, the proposed project aims to create a unified structured platform that can help achieve this goal by integrating data of multiple types and supporting the scientific analysis of these data and their connections in multi-centric studies.

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