

QUALITY ASSESSMENT FOR INTEROPERABLE QUANTITATIVE CT IMAGING (QA4IQI) - OPEN ACCESS TO STANDARDIZED QUANTITATIVE IMAGING

FINAL REPORT – OPEN DATA PROJECT CALL – HES-SO 2022

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I/ RESEARCH SUMMARY

This project aimed at making the data of the Swiss Personalized Health Network (SPHN) project entitled Quality Assessment for Interoperable Quantitative CT-Imaging (QA4IQI) publicly available. The goal of the QA4IQI project was to evaluate the variation of quantitative measurements (e.g. lesion size, density, texture and shape, also called “radiomics features”) in Computed Tomography (CT) images when various imaging equipments (e.g. scanners) and protocols are used. To this end, a radio-opaque 3D printed anthropomorphic phantom¹ was imaged with the clinical CT scanners of all University Hospitals and three additional imaging centers in Switzerland. This allowed to generate a unique and rich image collection representing and isolating the variations related to (i) imaging device (e.g. manufacturer) and (2) imaging parameters (e.g. tube current and voltage settings, pitch, rotation time, detector configuration), when compared to other variations that are related to the object that is imaged. The anthropomorphic phantom allowed to control and perfectly stabilize the object of interest to image and to be very close to true human tissue while avoiding excessive radiation dose to human subjects. Several other similar studies were already proposed, highlighting the importance of the topic. However, limitations consist of either a very small number of acquisitions with human subjects (e.g. test-retest [1]–[3], open dataset²) or with non-anthropomorphic phantoms resulting in inadequate representations of human tissue [4]–[6].

Phantom design and surveying CT scanners and protocols

Before starting the data acquisition, a survey was conducted on popular scanning protocols in Switzerland to determine the space of scanning parameters as well as phantom design. The protocol survey collected scan parameter of four different protocols. Three of the protocols are used for tumor search and infectious foci in thoracic, abdominal and thoraco-abdominal CT. The fourth protocol is the late arterial phase for hypervascular liver lesion assessment. The survey included 9 hospitals, 21 CT scanners of various age from 4 manufacturers. Scanning parameters and reconstruction parameters (slice thickness and increment, reconstruction algorithm and kernel) were collected, evaluated and summarized in tables. Significant differences in the acquisition protocols between hospitals were observed. For example, some hospitals use dual-energy protocols, while others do not.

Several phantom versions were created and tested. The last phantom version had the lowest air inclusions and the best fidelity in terms of Hounsfield Units (HU), i.e. the density of the imaged tissue (voxel values of CT images). HU fidelity means the agreement between the HU values of the original data sets (from which the phantom was manufactured) and the HU values determined in the phantom by a CT measurement. The phantom enables the simulation of a patient measurement with an outstanding level of detail in the acquired image data sets (see Fig. 1). This “final” version of the phantom comprises three separate sections: a half-mirrored lung tumour section, an abdominal section focusing on the liver and test patterns (e.g. Gaussian-distributed white noise, Siemens star) used mainly for calibration and quality insurance. The lung tumour section is derived from a non-small-cell lung carcinoma patient (PAT1) that was made publicly available to serve as radiomics phantoms [7], including for the Image Biomarker Standardisation Initiative (IBSI) [8]. The abdominal section was taken from a scanned patient at the University Hospital Basel and included Regions Of

¹ <https://phantomx.de/>, as of November 2022.

²

<https://wiki.cancerimagingarchive.net/display/Public/RIDER+Lung+CT#2251273204d01ce259734cd78f048b1666ceceee>, as of November 2022.

Interest (ROI) from normal liver tissue and 3 lesion types (benign cyst, hemangioma and one pathology proven liver metastasis from a colon carcinoma).

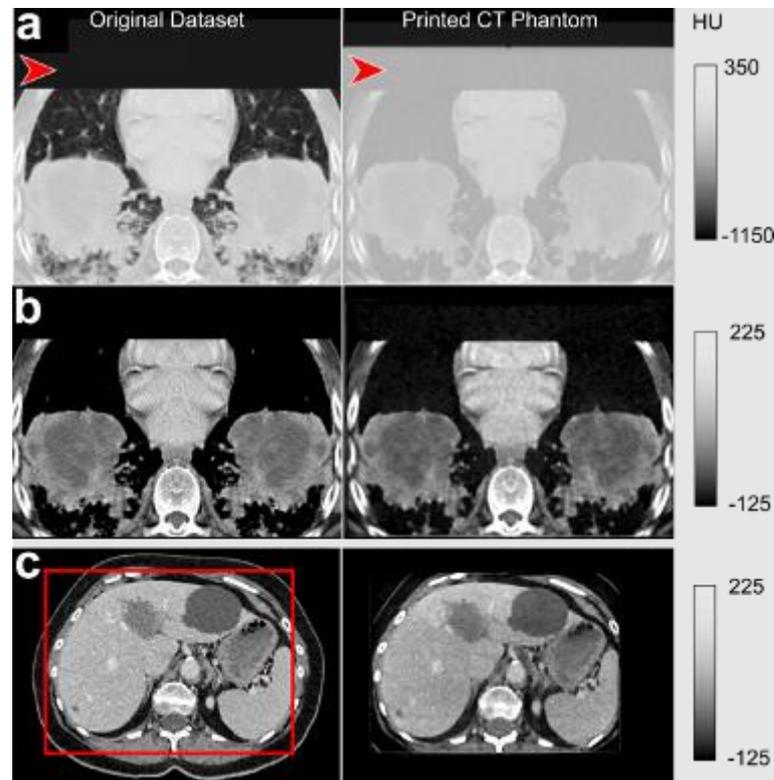


Figure 1: Original datasets (left) and corresponding CT phantom datasets (right). Left: original CT dataset that serves as a basis for the phantom production. Right: corresponding CT image of the phantom. The windowing is the same for both images. a) lung dataset, red arrows: in the original dataset the HU above the CT image marked with the red arrow is -1000. This region is represented by pure paper in the phantom. The HU value of the paper is around -100 and defines the minimum HU value that can be reproduced in the phantom. b) lung dataset shown in a soft tissue window. c) abdominal dataset. The printable area is restricted to 19 x 26 cm² and is marked by the red rectangle.

Data acquisition (phantom scanning)

After finalizing the design/printing of the phantom and defining the protocols' parameters to explore, data acquisitions started. The phantom measurements were performed by a trained physicist who visited the participating centers with the phantom. He was supported by the technicians on site. In this way, it was ensured that the phantom measurements were performed under the same conditions on all CT devices. In total, the phantom was scanned in 8 institutions (5 University Hospitals and 3 other imaging centers) and with 13 distinct CT machines from 4 different vendors. All common vendors are represented (Siemens, Philips, Canon/Toshiba, GE).

For data sharing internally to the project consortium, an instance of the web-based Kheops platform was deployed³ in HES-SO Valais. Kheops⁴ is developed at Campus Biotech in Geneva. It provides

³ <https://kheops.ehealth.hevs.ch/>, as of November 2022.

⁴ <https://kheops.online/>, as of November 2022.

a flexible and open image archiving solution. Kheops can also be queried via its API⁵, which allowed us to use it as a data source for our image analysis pipeline (see Section “Image analysis and quantitative feature computation” below).

Image analysis and quantitative feature computation

The development of the feature extraction pipeline was implemented and released as open source on GitHub⁶. PyRadiomics⁷ and other required libraries were implemented in Docker-containers. For DICOM image sharing, storage and management, a seamless integration with Kheops was realized. In particular, our cloud-based radiomics research platform QuantImage v2⁸ can directly analyse (e.g. feature extraction) image collections hosted in Kheops.

Feature stability assessment

Based on a first dataset (DS1, see Section “II / DATA DESCRIPTION”) based on one single scanner at the University Hospital Basel where the phantom was scanned 30 times for 8 parameter variations of reconstruction algorithms, reconstruction kernels, slice thickness, and slice spacing (238 scans in total), we showed that the 8 CT parameter variation pairwise group comparisons had statistically significant differences on average in 78/86 radiomics features. On the other hand, 84% of the univariate radiomics feature tests had a successful and statistically significant differentiation of the 4 classes of liver tissue. We concluded that the differences in radiomics feature values obtained from different types of liver tissue are generally greater than the intraclass differences resulting from CT parameter variations. This study is published in the Investigative Radiology journal [9]. We are currently finalizing the analysis of the multi-centric/multi-scanner dataset (DS2, see Section “II / DATA DESCRIPTION”) using a similar methodology and we plan to submit it to the Radiology journal⁹.

In parallel, we also used another approach to assess feature stability, which was based on simulated CT acquisitions¹⁰ as a potential surrogate of actual CT acquisitions [10].

Phantom quality assessment

We assessed the quality of the anthropomorphic phantom used [11]. We concluded that while some expected deviations in individual radiomics features between the original dataset and the phantom can occur, radiomics features can be reliably extracted in repeat phantom measurements and used for further analysis to differentiate tissue types. Limitations exist in terms of lesion size, shape, small residual air enclosures, and the fidelity of HU values and the use for dual-energy CT assessment.

II/ DATA DESCRIPTION

Two datasets were produced in the context of the QA4IQI project: a first dataset acquired in a single center and a single scanner to analyze variability across different CT acquisition protocols (denoted

⁵ <https://github.com/OsiriX-Foundation/KheopsAuthorization/wiki>, as of November 2022.

⁶ <https://qa4iqi.github.io/>, as of November 2022.

⁷ <https://pyradiomics.readthedocs.io/>, as of November 2022.

⁸ <https://medgift.github.io/quantimage-v2-info/>, as of November 2022.

⁹ <https://pubs.rsna.org/journal/radiology>, as of November 2022.

¹⁰ <http://www.astra-toolbox.com/>, as of November 2022.

as **DS1** from here on), and a second, larger dataset that studies variability across different scanners located at different centers (denoted as **DS2** from here on).

Below is a description of the details of both datasets. The two main data formats used for medical imaging are

- DICOM¹¹ (Digital Imaging and COmmunications in Medicine): Standard for the communication and management of medical imaging information and related data. In general, 3D image volumes are called “image series” and are composed of a stack of several 2D slice images. One DICOM image is one of these 2D slices, which results in a collection of ~50-500 files for one single volume/patient. An extensive collection of metadata is available describing image acquisition settings as well as information concerning patient and medical center.
- NIfTI¹² (Neuroimaging Informatics Technology Initiative): Data format for medical imaging information developed to facilitate inter-operation of medical data analysis software packages. One 3D volume is one NIfTI file and only few meta data are provided.

DS1

- **Data type** : The acquired data consists of CT scans of an anthropomorphic & radio-opaque phantom.
- **Data format** : All acquired CT images & regions of interest (ROIs) are stored in the standard DICOM file format. For the ROIs, the DICOM-SEG (DICOM Segmentation¹³) module was used.
- **Data quantity** : The dataset consists of CT scans of the phantom, acquired using 8 different protocols and repeated 30 times (apart from 2 exceptions), for a total of **238 DICOM series**. Each DICOM series consists of 343 DICOM slices and 6 DICOM-SEG files for the ROIs. The total number of files is ~80'000 and the space used by the dataset represents ~57GB.
- **Data sensitivity** : Since the project involved a phantom rather than human subjects, the data is not of a sensitive nature.

DS2

- **Data type** : The acquired data consists of CT scans of an anthropomorphic & radio-opaque phantom.
- **Data format** : All acquired CT images & ROIs are stored in the standard DICOM file format. For the ROIs, the DICOM-SEG (DICOM Segmentation) module was used.
- **Data quantity** : The dataset consists of CT scans of the phantom, acquired using 10 different protocols (5 dose levels & 2 reconstruction algorithms) and repeated 10 times in general. Some scanners also had Deep Learning reconstruction algorithms available, and in one instance only 9 repetitions were performed, leading to a total of **1378 DICOM series**. Most DICOM series consist of 343 DICOM slices (with the exception of one scanner which produces 275 DICOM slices) and 6 DICOM-SEG files for the ROIs. The total number of files is >470'000 and the space used by the dataset represents ~300GB.

¹¹ <https://www.dicomstandard.org/>, as of November 2022.

¹² <https://nifti.nimh.nih.gov/>, as of November 2022.

¹³ https://dicom.nema.org/medical/Dicom/2016e/output/chtml/part03/sect_C.8.20.html, as of November 2022.

- **Data sensitivity** : Since the project involved a phantom rather than human subjects, the data is not of a sensitive nature.

III/ RELATED WORK

Several data repositories exist in the medical imaging field, and also more generic data repositories could be considered to store the QA4IQI datasets.

Our requirements were that the data should be free to host and to access, the repository should allow for storing large datasets (~300GB) and ideally make it possible to easily find the data using various metadata.

Data repositories recommended by the Swiss National Science Foundation for their approach to the FAIR principles were analyzed, but had certain issues:

- Dryad¹⁴: Does allow for datasets up to 300GB, but charges a base fee of 120\$ per submission, plus excess storage fees for datasets larger than 50GB.
- Zenodo¹⁵: Is free to use, but has a general limit of 50GB for a dataset.
- Harvard Dataverse¹⁶: Is free and allows for up to 1TB of storage space per dataset, but is not specifically geared towards medical imaging data and doesn't directly offer rich search capability for DICOM header information.

Looking more in detail at medical image repositories, we also considered some possible options, that did not fully fit our needs:

- Image Data Resource¹⁷ is made for bioimaging (typically microscope images) and does not support DICOM, which limits its usefulness for our purposes.
- The SICAS Medical Image Repository¹⁸ is another platform, supporting DICOM files. It is also geared towards challenges (participant submissions, evaluation of results, etc.).
- The Coherent X-Ray Imaging Data Bank (CXIDB)¹⁹ is another data hosting platform in the medical field, but largely focused on X-Ray imaging, not other modalities such as CT or PET.
- The Cell Image Library²⁰ is yet another example of a medically-oriented data repository, but it is mostly focused on hosting microscopy images, not radiology data.

Finally, we identified The Cancer Imaging Archive (TCIA)²¹ as an interesting option for several reasons. It is free to use, does not impose any fixed size limit on datasets and generates Digital Object Identifiers (DOIs) for the uploaded datasets. Furthermore, it has an advanced retrieval system specifically geared towards medical images in the DICOM format, allowing users to find data by imaging modality: CT, Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI), etc.), examined body part (e.g. brain, abdomen, lungs) or disease and allows specifically to search for scans of phantoms as well. TCIA is also one of the most well-known platforms in the field,

¹⁴ <https://datadryad.org/stash/faq>, as of November 2022.

¹⁵ <https://help.zenodo.org/>, as of November 2022.

¹⁶ <https://dataverse.harvard.edu/>, as of November 2022.

¹⁷ <http://idr.openmicroscopy.org/about/>, as of November 2022.

¹⁸ <https://www.smir.ch/>, as of November 2022.

¹⁹ <https://www.cxidb.org/>, as of November 2022.

²⁰ <http://www.cellimagelibrary.org/home>, as of November 2022.

²¹ <https://www.cancerimagingarchive.net/>, as of November 2022.

containing widely-used data collections²² with thousands of patients for diseases such as lung cancer, breast cancer, COVID-19, etc. In our case, the ability to share the DICOM files was crucial since DICOM not only contains the images themselves but also an extensive collection of meta data (DICOM tags) that is related to the image acquisition protocol. Therefore keeping this information and being able even to search these tags was uniquely proposed in TCIA. In addition, TCIA is popular in the quantitative imaging community and officially recommended by the journals Nature Scientific Data²³, Medical Physics²⁴, Elsevier²⁵, which allows to further boost the visibility of our dataset and research contributions.

IV/ IMPLEMENTING THE FAIR PRINCIPLES

The aim of the QA4IQI project was to share the acquired data in an open manner to allow other researchers to benefit from the wealth of information created by the hundreds of scans performed with the printed phantom.

Identifying the correct platform to host the data was an important step and it was helpful to have the FAIR guiding principles to make our decision. The principles were considered in the following manner, both for DS1 and DS2:

FINDABLE

As mentioned in the previous section, TCIA creates a DOI for the dataset, ensuring a globally unique and persistent identifier. Additionally, a large amount of metadata included in the headers of the DICOM files is indexed and searchable (imaging modality, body part, scanner manufacturer, slice thickness, etc.).

ACCESSIBLE

Most collections on TCIA are open-access and can be downloaded without the need for signing any user agreement or authenticating using a login/password. Since datasets can be very large (several hundred GBs), an open-source download tool (programmed as a cross-platform Java application) called the NBIA Data Retriever²⁶ is provided to manage parallel downloads, pausing & resuming downloads, etc. Additionally, other methods of retrieving data are available, such as an Application Programming Interface (API)²⁷ that allows communicating with the platform through standard HTTP requests. There is also a new cloud-based data repository called the Imaging Data Commons²⁸ from the National Cancer Institute that is populated with TCIA datasets and allows to retrieve data using various tools.

²² <https://www.cancerimagingarchive.net/collections/>, as of November 2022.

²³ <https://www.nature.com/sdata/policies/repositories#imaging>, as of November 2022.

²⁴ <https://www.aapm.org/pubs/MPJ/policies/details.asp?id=465&type=MP>, as of November 2022.

²⁵ <https://www.elsevier.com/authors/tools-and-resources/research-data/data-base-linking>, as of November 2022.

²⁶ <https://wiki.cancerimagingarchive.net/display/NBIA/NBIA+Data+Retriever+FAQ#NBIADataRetrieverFAQ-IsNBIADataRetrieveropensource?>, as of November 2022.

²⁷ <https://wiki.cancerimagingarchive.net/display/Public/TCIA+Programmatic+Interface+REST+API+Guides>, as of November 2022.

²⁸ <https://datacommons.cancer.gov/repository/imaging-data-commons>, as of November 2022.

INTEROPERABLE

To ensure maximum interoperability, the standard DICOM format was used for all the acquired data. This was not an issue for the CT scans themselves, but proved to be challenging for the ROIs. Indeed, a typical workflow for segmenting and generating ROIs for medical images involves converting the DICOM images to the NIfTI format, and the created ROI files are therefore also created as NIfTI files. In order to upload the data to TCIA and harmonize the data formats, the NIfTI ROIs needed to be converted back to the DICOM Segmentation format.

After some research, we identified a library called `pydicom-seg`²⁹, which allows doing this conversion. It requires the original DICOM images, as it needs to inject references and values coming from the original scans into the generated DICOM SEG file.

REUSABLE

In terms of reusability, we wanted to provide the data in a manner that doesn't require additional steps for setting up or preparing the data. A challenging aspect related to this was that originally, the ROIs were created on the original data that was used to print the phantom itself. The initial approach was then to register/align all the acquired image series to the original data so that the ROIs would also be aligned.

This approach worked but meant that the DICOM images needed to be modified via slight affine transformations as well as image resampling with interpolation. The latter was particularly problematic since this dataset specifically focuses on image changes induced by scanning, which would have been difficult to separate from the effects of postprocessing. Therefore, we preferred providing the original raw data acquired by the scanners in the dataset. So as an alternative, the ROIs were instead aligned to the images, leaving the CT scans untouched and only adapting the ROIs to the slight changes in position caused by the scanning of the phantom in different scanners and centers. In this way, every DICOM series has its own ROI files directly attached, making the usage of the data more straightforward & convenient.

Additionally, we developed the code that allows to extract radiomics features from the acquired data, and provide this code in a GitHub³⁰ repository, to allow anyone to reproduce the same results. To further make our approach reusable, we developed the code as a Docker container which can be built and makes the code independent of the user's locally installed operating system, version of Python, libraries, etc.

Considering the above as well as the comparison of the available repositories in Section "III/ETAT DE L'ART", we decided to submit a proposal to TCIA for DS1 as a starting point, to understand the required information and the data submission process as well as opportunities to make the dataset visible and searchable. The DS1 collection was accepted by TCIA and the data is in the process of being uploaded. We expect DS1 to be fully released and available on TCIA by the end of the year. The same procedure will soon be repeated for DS2, for which we already started the discussions with TCIA. We are also in the process of writing a Nature Scientific Data journal paper describing the content but also initial image analyses, similarly to the ones we carried out on DS1, published in [9]. The full analysis of DS2 will be submitted to the Radiology journal, a paper led by our QA4IQI

²⁹ <https://github.com/razorx89/pydicom-seg>, as of November 2022.

³⁰ <https://github.com/QA4IQI/qa4iqi-extraction>, as of November 2022.

partner in the University of Basel³¹. The curation of DS2 is over and it is fully ready for submission to TCIA. We plan to submit the Nature Scientific Data paper in early 2023. The release of DS2 on TCIA was slightly delayed due to an embargo decision from the QA4IQI consortium that we wanted to first publish the Radiology paper before sharing this multicentric DS2 dataset to the scientific community. This was important since Nature Scientific Data requires to include initial experiments and data analyses to demonstrate how the dataset can be used, and we did not want to jeopardize our chances to publish in the Radiology journal first.

The amount of work hours and specific skills that were required to curate the DS1 and DS2 collections and make them FAIR compatible is difficult to quantify precisely. Two full time equivalents (Roger Schaer and Oscar Jimenez) worked together (asynchronously) for about a total of 3 full weeks each. Adrien Depeursinge worked about 2 full weeks for scientific and report writing. The main skills required are an extensive knowledge of medical imaging data formats and storage, CT physics, Python programming and image processing (registration, resampling, analysis via radiomics feature extraction) as well as the use of other tools and tasks (e.g. GitHub, scientific writing).

The lessons learned with TCIA in the context of this project are also relevant to publish another highly curated dataset from a parallel research effort funded by a Swiss National Science Foundation (SNSF, project number 205320_179069) in the context of the HECKTOR challenge³² that we organized for three consecutive years at the prestigious MICCAI conference [12], [13]. This dataset contains 883 patients with Head and Neck Cancer from 9 medical centers around the world. For each case, a PET/CT image is available along with tumor and metastatic lymph nodes delineated by experts, accompanying clinical data (e.g. age, gender, tobacco) as well as follow up of treatment failure events such as recurrence and death. We also plan to release the outputs of the participant's algorithms to enable meta-analyses. While the dataset has evolved and was downloaded/analyzed by all participants of the three editions of the challenge, we expect that making it publicly available on TCIA will push its scientific impact even further, e.g. similarly to the AutoPET challenge³³ [14].

V/ LEGAL AND ETHICAL ISSUES

The QA4IQI project luckily did not have many legal & ethical hurdles to overcome, as the phantom that was scanned is not a human subject, and therefore does not require the same level of anonymization, consent management, restricted access to the data, etc.

The lung section of the phantom is publicly available³⁴ [7] under the Non-Commercial CC BY-NC License. The liver section was gathered while respecting patient consent and ethics protocol at the University of Basel.

Some basic anonymization & pseudonymization was still performed on certain DICOM headers, i.e. to remove the name & location of the hospitals where the data was acquired (replacing it with names from A-H), and TCIA performs general anonymization of identifying DICOM tags, which again were not problematic in our case.

³¹<https://www.unispital-basel.ch/ueber-uns/departemente/theragnostik/kliniken/radiologie-und-nuklearmedizin/lehre-und-forschung/forschung/>, as of November 2022.

³² <https://hecktor.grand-challenge.org/>, as of November 2022.

³³ <https://wiki.cancerimagingarchive.net/pages/viewpage.action?pageId=93258287>, as of November 2022.

³⁴ <https://www.cancerdata.org/resource/doi:10.17195/candat.2016.08.1>, as of November 2022.

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