PLOS Digital Health

RESEARCH ARTICLE

The deployment of ProKnow for cloud-based clinical research in radiotherapy

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Citation: Anagnostatou V, Knauer M, Maier SH, Winderl T, Reiner M, Thasler R, et al. (2026) The deployment of ProKnow for cloud-based clinical research in radiotherapy. PLOS Digit Health 5(7): e0001131. https://doi.org/10.1371/journal.pdig.0001131

Editor: Farima Safari, Shiraz University of Medical Sciences, IRAN, ISLAMIC REPUBLIC OF

Received: November 24, 2025

Accepted: June 5, 2026

Published: July 17, 2026

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Data availability statement: The data supporting the findings of this study are available from the Clinical Trial Center of the Department of Radiation Oncology at LMU University Hospital (Strahl.Studien@med.uni-muenchen.de).

Abstract

ProKnow is an archive and restore tool for radiation oncology and imaging data, peer review, distributed contouring, study of metrics and discovery of trends; it represents a common ground for plan analysis and comparison due to an integrated industry standard Dose-Volume Histogram (DVH) engine, which can be used for all patient datasets. The aim of this work is to present a deep and easy-to-use implementation of the Elekta ProKnow DS cloud-based Picture Archiving and Communications in Radiotherapy (RT-PACS) system within our department. Two de-identification workflows of the DICOM data are presented, the first one is accomplished via the ProKnow Dicom Agent (PDA) and the second one involves a trusted third-party service. We can access ProKnow not only through the user interface, but also through the Application Programming Interface (API) with scripts written in the Python language to extract information from the uploaded data, calculate and store metrics as well as upload clinical data. A drawback of the currently implemented de-identification process is that in a subsequent clinical data upload, matching the original and de-identified IDs is not possible. To mitigate this drawback, we collaborate with the MeDIC^{LMU}(Data Integration Center [DIC]) for development and implementation of an automated de-identification process via a trusted third party service. With this architecture, it will be possible to merge clinical data in local DIC databases with de-identified data in ProKnow at any point in time, facilitating the longitudinal outcomes analysis. We used ProKnow for a retrospective dosimetric feasibility study of an isotoxic dose-escalated radiotherapy proof-of-concept for glioblastoma. Furthermore, to ensure protocol-compliant irradiation planning for the preparation of a prospective dose-escalation trial, we conducted a dummy run with 10 collaborating institutes in Germany. RT-structures were automatically downloaded (via the API)

Access to the DICOM imaging files is restricted due to legal reasons.

Funding: This project has received funding from the Bavarian Cancer Research Center (BZKF, https://bzkf.de) and from Deutsche Krebshilfe (Project 70114648, https://www.krebshilfe.de)., VA has received partial funding from BZKF. The sponsors did not play a role in the study design, data collection, analysis, etc.

Competing interests: The authors have declared that no competing interests exist.

and the Dice Score and Hausdorff Distance were calculated and set as metric in ProKnow.

Author summary

We deem our work as noteworthy, because it highlights the benefits which can be gained in a radiation oncology department from the implementation of ProKnow DS for clinical research; Proknow allows us to perform a quality assurance strategy. Until now, it has been difficult to make scientific comparisons of treatments in radiation oncology because complex dose-volume distributions have to be examined rather than point doses at an isocentre, as is often thought. For the first time, ProKnow software enables the manufacturer-independent comparison of dose-volume distributions in tumour and normal tissue for large cohorts in comparison to alternative software, which often rely on native or standard dose grid resolution and may underestimate volumes at superior/inferior borders; The ability to correlate the individual treatment plan data with clinical data for large cohorts, such as side effects, life expectancy or other custom metrics, renders ProKnow an important data analysis tool for the assessment of a treatment plan. With the integration of ProKnow in the clinical routine, multicentre research with state-of-the-art, secure, cloud-based data flows becomes easy to use.

Introduction

With the expansion of cloud computing and cloud storage, Picture Archiving and Communications in Radiotherapy (RT-PACS) systems have become available as cloud-based solutions, especially not only for storage but also for viewing and analysis of data for clinical research. ProKnow DS (Elekta, Stockholm, Sweden) is a cloud-based software solution (SaaS) accessed from any device over a web browser and/or an Application Programming Interface (API) written in the Python language for archiving, restoring and managing of radiation oncology data, plan evaluation and "big data analysis". Software's build-in tools, such as the calculation of key radiation therapy metrics, the user's ability to define metrics and set scorecards, organize, analyze and explore cohorts of patients, enable research and outcome analysis anytime from anywhere in the world. Due to the additional ProKnow's vendor agnostic technology allowing its use with a variety of treatment planning systems render it an attractive tool for big data gathering, benchmarking of planning practices, standardization and clinical excellence. ProKnow was chosen by the NHS England for the above-mentioned capabilities and was deployed in 2019 in 49 radiotherapy providers to enable sharing and learning from radiotherapy plans. It is now populated with more than 26000 patients [1]

Potential in advancements of methodologies and techniques in radiation therapy can be identified in many study areas of radiation therapy in the literature; ProKnow provides a framework for benchmarking of planning practices (international, national,

local studies) [1–18] (see also Table 1), testing of segmentation algorithms [19–21], testing of automated treatment planning techniques [22], DVH evaluation [23–24], education training in radiotherapy for physicians and/or medical physicists [25–32], as well as TPS planning conversion validation and archival [33].

Since the acquisition of the software, we have focused our efforts to build an end-user friendly and individual configurable data pipeline of radiotherapy data (DICOM) from internal clinical databases and locally archived data storages into the ProKnow cloud-based RT-PACS system. The de-identification of the DICOM data, which is a prerequisite for uploading RT-Plans on any cloud-based RT-PACS system in Germany, is part of the dataflow pipeline.

Within our department, we have established ProKnow for internal and nationwide retrospective as well as prospective radiotherapy studies of various tumor sites; we have exploited its capability for remote peer-review, quality assurance in the preparation of a clinical trial (protocol compliance) [13] as well as treatment plan quality evaluation, during a prospective multicenter phase IIa trial [9]. Owing to ProKnow's API, we have developed scripts in Python, which run automatically on a virtual server following a patient upload to extract information from the uploaded data for calculation and storing of important metrics for plan evaluation and analysis, such as the Equivalent Uniform Dose (EUD), Dice Score and Hausdorff distance, adding value to the clinical decision.

Materials and methods

Pre-configuration of a Dicom Agent service

A dedicated virtual server (Windows Server 2022, CPU 2, RAM 8 GB, partition System: 100 GB, data: 260 GB) had been set up for the installation and configuration of the software tools required for the de-identification and upload of

Table 1. Literature summary on ProKnow usage in clinical research.

Year	Tumor Site	Study type	Country	Plans/Patients	Reference
2018	Craniopharyngioma	International	–	1	Whitaker et. al.
2020	Prostate	National	UK	102	Taylor et.al.
2020	Cervix	National	LatAm	1	Li et. al.
2022	Breast	Local	Minnesota, USA	35	Morris et. al.
2023	Adrenal Gland, Pancreas, Oligo metastasis (pelvis), Prostate	International	–	4	Bisgaard et. al.
2023	Pancreas	International	–	136	Parikh et. al.
2023	Breast	International	–	10	Tan et. al.
2024	Craniospinal	National	Turkey	2	Senkesen et. al.
2024	H & N	International	–	2	Selek et. al.
2024	Lung	International	–	2	Selek et. al.
2024	H & N	Local	Minnesota, USA	136	Pepin et. al.
2024	Lung	Local	Newcastle, UK	102	Stamp et. al.
2024	Lung, breast	National	UK	NA	Byrne et. al.
2024	Prostate, cervix, liver, lymph node	International	–	5	Murr et. al.
2024	Glioblastoma	National	Germany	10	Maier et. al.
2024	H & N	Local	Florida, USA	20	Cabrera et. al.
2024	Glioblastoma	National	Germany	10	Bodensohn et. al.
2024	Prostata	International	–	5	Sritharan et. al.

A literature summary of the international, national and local studies performed with ProKnow.

https://doi.org/10.1371/journal.pdig.0001131.t001

patients' DICOM data from clinical premises to ProKnow. It is important to note that ProKnow DS does not support any of the DICOM network services (transfer, query/retrieve, workflow management, print management), which is the reason why the workflow for transferring of DICOM data to ProKnow need to include other applications like the ProKnow Dicom Agent (PDA) or the API. The PDA is a local Windows application that supports network transfer of the standard DICOM SOP Classes, and it is recommended to install it on hardware equipped with device encryption to protect data, including protected health information (PHI) and personally identifiable information (PII); protection of data results from the fact that the information is encrypted into an unreadable format that can only be unlocked with a specific digital key. In addition to DICOM data transfer, the PDA provides de-identification of selected attributes, as defined, for example, in NEMA PS3 [34].

The PDA is installed on the virtual server and managed by a server administrator who pre-configures a so-called Dicom Agent de-identification service for each project. Since the PDA uses the API directly to upload DICOM files, the user is granted API permission which is encrypted within a.json file that can be download from the user interface. The pre-configuration of a Dicom Agent service includes loading the.json file, loading a user-defined.xml file with the DICOM attributes' de-identification rules (e.g., "Clear", "Remove", etc.), the "Watched" folder destination (original data), the local data storage destination (copies of the original and de-identified data), as well as the data destination in ProKnow (i.e., the ProKnow workspace). The original data reaching the "Watched" folder are de-identified based on the.xml file and are uploaded promptly to the ProKnow workspace, while copies of the original and de-identified data can be saved locally on the virtual server.

Transfer of DICOM data to ProKnow

De-identification via the Dicom Agent. The transfer of the DICOM data from the clinical databases (the treatment planning system Monaco and the patient database MOSAIQ) to the "Watched" folder (Process 2, Fig 1), is accomplished using the storescp application of the OFFIS' open source DICOM Toolkit DCMTK [35], which is installed and run on the virtual server.

The aforementioned application implements a Service Class Provider (SCP) for the Storage Service Class, listens on a specific TCP/IP port for incoming association requests from a Storage Service Class User (SCU) and can receive the patients' DICOM data within a user-defined local folder (in this case the "Watched" folder). On the other side, the clinical databases (SCU user) are configured to export data to the specified IP address and pre-configured TCP/IP port(s) on the virtual server. The transfer of the DICOM data could alternatively be processed directly from the clinical databases to the "Watched" folder, bypassing the use of the DCMTK toolkit; the AE entity and TCP/IP port defined within the PDA de-identification service (SCP user) should be identical to the AE entity and port defined within the export configuration settings of the clinical databases (SCU user).

DICOM data saved within a local folder of the clinical network, can be transferred to the "Watched" folder of the virtual server via network drive mapping; write/read access should be given to the users (e.g., physicians) involved in a project, who can thereafter copy the data to the mapped "Watched" folder (Process 1, Fig 1).

The data reaching the "Watched" folder are automatically handled by the pre-configured PDA service, de-identified and uploaded to a ProKnow workspace, while the generated log.txt files, containing the code list (key-list patient identification), are saved locally on the virtual server. The log files can be sorted and automatically converted to a csv/excel file (using scripting) which can be visible (to the project's involved users) within the "Watched" folder in case of a prospective study; in contrast to a retrospective study in which the key list is not allowed to be shared to the physicians, since the patient consent is often waived. Following the upload of the de-identified dicom data to ProKnow, the clinical data upload can proceed at any time (Fig 1, bottom), as long as the server administrator maps the original Patient IDs with the ProKnow patient IDs (i.e., the patient data should match the de-identified ids). The code list lies on the virtual server and only in prospective studies can be shared to project members. For this reason, the server administrator overtakes the task of the clinical data upload either via the ProKnow User Interface (https) using an excel file of a specified format (with the

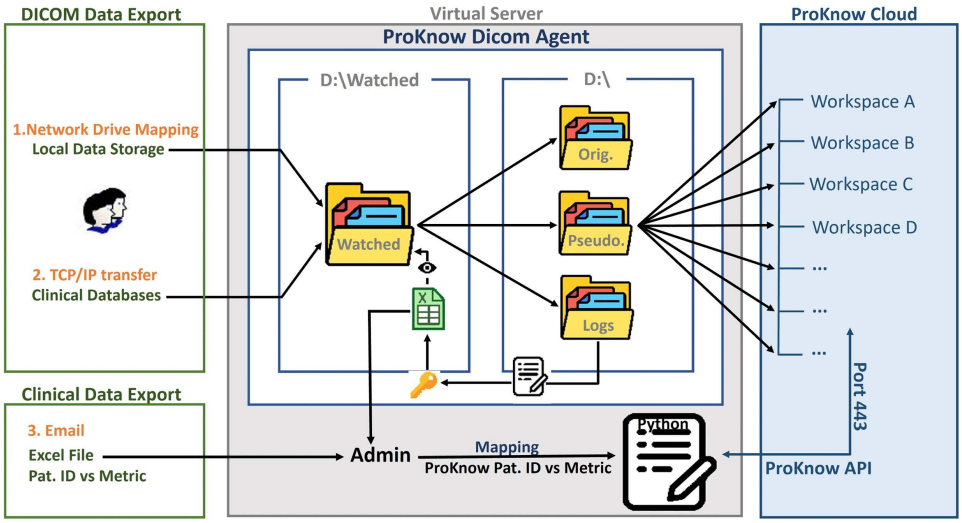


Fig 1. Dicom and Clinical Data de-identification and Upload to ProKnow (via the PDA). Graphical representation of the Dicom and Clinical Data Export routine and de-identification of Clinical DICOM data to ProKnow via the ProKnow Dicom Agent (PDA). Please note that the possibility for a key-list file generation (designated with the key and excel file symbol) visible on the "Watched Folder" can be applicable to prospective trials only (due to patient consent in such case). A "Python" script can be used to upload dicom and/or clinical data (bottom), "watch" a ProKnow workspace (such as EUD custom metric generation described in 'Use cases') or perform other API operations.

https://doi.org/10.1371/journal.pdig.0001131.g001

ProKnow Patient ID and custom metrics) or via the API using a Python script for the assignment and storage of the given metrics in ProKnow.

De-identification via a trusted third party. As an alternative to the PDA de-identification service, we are currently developing an automated de-identification and pseudonymization workflow in collaboration with the MeDIC^{LMU} (Data Integration Center) of the LMU University Hospital for the development and implementation of a de-identification process via a trusted third party service. Within this workflow the DICOM data can be transferred from the clinical databases (the treatment planning system Monaco and the patient database MOSAIQ) to a local folder on the virtual server following the processes explained in previous sub-section. As shown in Fig 2, the original patient's DICOM data are automatically zipped after reaching the local folder on the virtual server (via an automated Python script "watching" the input folder), and sent to the DIC SFTP Server for de-identification. The retrieval of the zipped output data to a "Watched" folder of the virtual sever (as well as unzipping) is undertaken by the automated Python script and is completed within 2–3 minutes. At this stage the Dicom Agent de-identification service is facilitated and can be pre-configured to upload the DICOM data to ProKnow without the use of a.xml de-identification file, since these are already de-identified data.

The MeDIC service results in retaining a code list in a trusted third party service (not known to any project member), that allows longitudinal data enrichment. Clinical Data retrieval could be done in parallel and mapped directly to the de-identified IDs. The data can be directly uploaded from MeDIC to ProKnow, through the ProKnow API, given the fact that DIC will be granted API rights; Nevertheless, a file upload (via https) could also be possible for physicians or other project members, which could be made available into the "Output" folder.

ProKnow data extraction

The ProKnow API can also be used for extracting information from the uploaded data (such as DVH data) for the calculation of important parameters, as well as storing of these parameters as custom metrics in ProKnow. The API requests in ProKnow (executed through Port 443, which is the standard default port for HTTPS (Hypertext Transfer Protocol Secure))

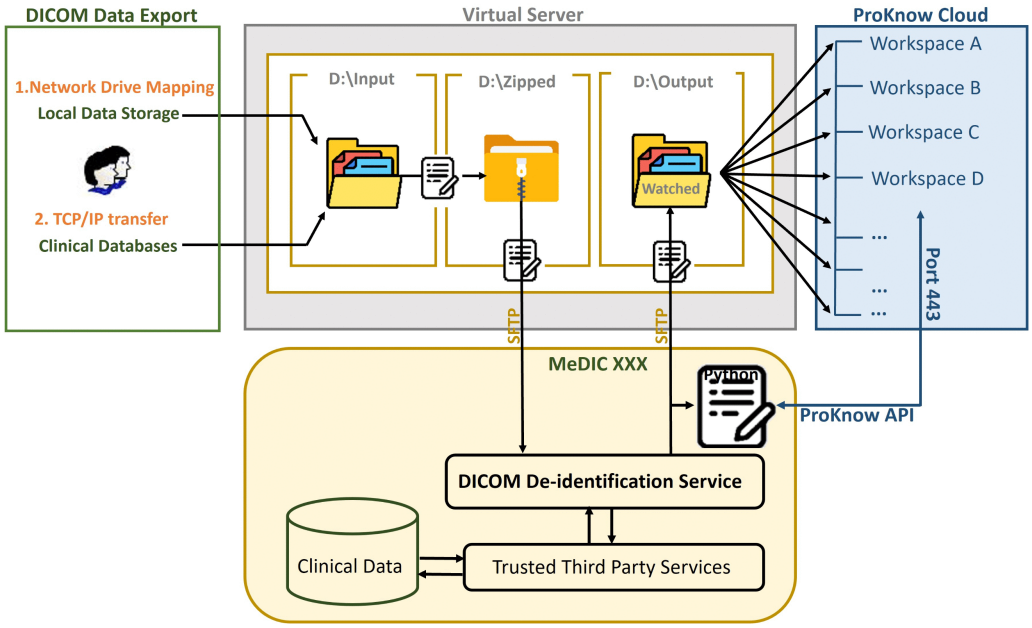


Fig 2. Dicom and Clinical Data de-identification and Upload to ProKnow via the MeDIC[LMU]. Graphical representation of the Dicom and Clinical Data Export routine and de-identification of Clinical DICOM data to ProKnow via the MeDIC[LMU] (Data Integration Center) and upload via the ProKnow Dicom Agent (PDA).

https://doi.org/10.1371/journal.pdig.0001131.g002

require the installation of the Python programming language [36], the installation of the "proknow" python library from PyPI [37], as well as a development environment for programming in Python. For the structure geometric similarity comparison in ProKnow and calculation of the Dice similarity coefficient (DSC) and Hausdorff Distance (HD, and 95th percentile HD95), the open-source software Plastimatch [38] was installed and initiated via a Python script.

Results

Implementation - EUD Calculation

A script (attached, S1 Python Script) written in Python running on the virtual server was used to access the information from the ProKnow DVH graphs for the calculation of the Equivalent Uniform Dose (EUD, introduced by Niemierko et al. [39]) of the brain and storing of the metric in ProKnow (via the ProKnow API), during a retrospective proof-of-concept study for the dosimetric feasibility of an isotoxic dose-escalated radiotherapy for glioblastoma. The EUD value, was compared to the ground truth EUD value calculated from the Monaco TPS. The percentage differences between the two methods (see S1 Table) were in very good agreement to each other (within the range of 0-0.4%) owed to the fact that the "EUD (ProKnow)" uses the ProKnow DVH engine, which provides smooth, high-resolution, and accurate DVH Curve and extracted points [40]. In more detail, The ProKnow DVH engine implements (1) a dose super-sampling implemented for small or complex volumes, and/or coarse dose grids, (2) 'end-capping' at superior and inferior borders, and (3) dose bin resolution (Gy) of at least 1000 (and up to 10,000) bins along the dose axis for each structure, i.e., from zero dose to the structure's max dose.

With regard to the sensitivity of the parameter "a" in the EUD formulation, parameter "a" was derived from the the previously published work by Niyazi et al. [41], (a = 9) where the corresponding modelling framework and confidence intervals are described. Given the explanatory nature of the dosimetric feasibility study, a formal sensitivity analysis was not performed at this stage, it however represents an important aspect for future investigation which is planned to be

addressed in the prospective clinical setting of the PRIDE trial ("Protective VEGF Inhibition for Isotoxic Dose Escalation in Glioblastoma", NCT05871021; NOA-28; ARO-2024-01; AG-NRO-06), where sufficient data will be available to support such analysis.

Implementation - DICE similarity coefficient and Hausdorff distance calculation

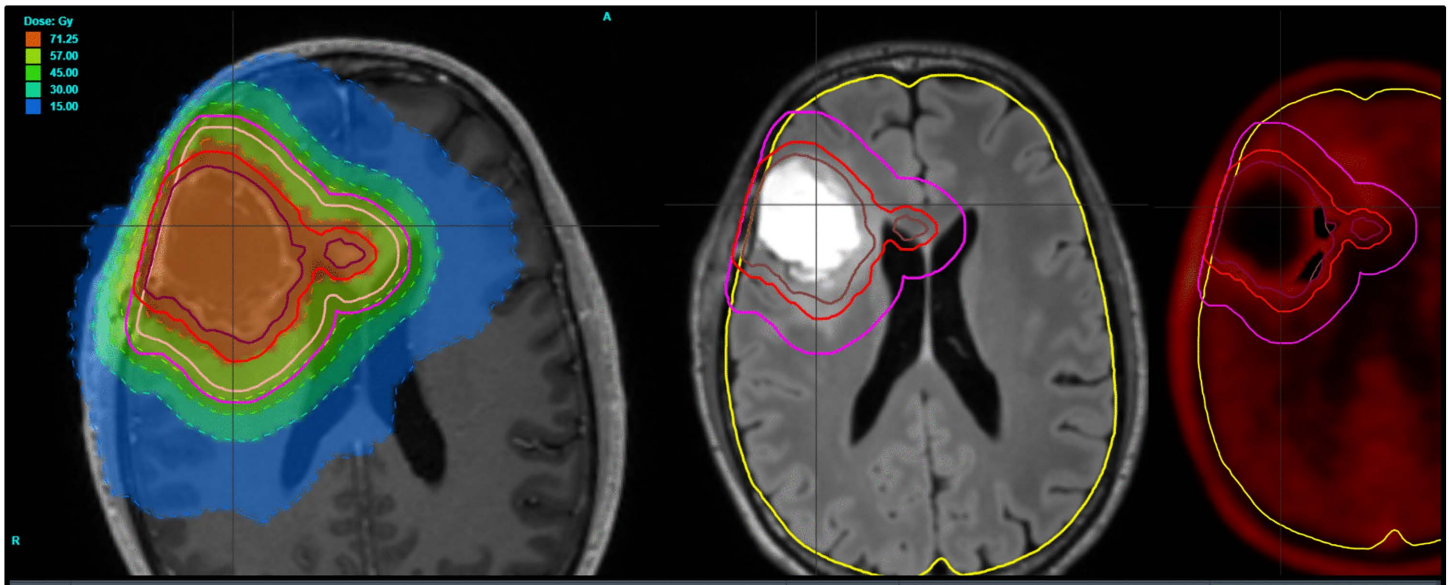
For a comparison of the geometric similarity between structures a Python Script (attached, S2 Python Script) was developed and run on the server for downloading the respective RT-Structures, initiating the calculation of the Dice similarity coefficient (DSC) and Hausdorff Distance (HD, and 95th percentile HD95), and storing the similarity metric computations in ProKnow. The similarity metric computations are then calculated using Plastimatch, while the downloading of the structures and storing of the metrics are performed via the ProKnow API. The script was used for the similarity comparison between the structures of the main study center and different study sites during the preparation of a prospective dose-escalation trial. The DSC/HD coefficients had been validated against those calculated via the Golden Rule software [42].The percentage differences between the two methods (plastimatch versus Golden Rule) were in the order of 0 and 6% (see S2 Table). The highest discrepancies of 6% were observed for small volumes, due to the calculation being highly sensitive to small spatial shifts when applied to small volumes.

Use cases

ProKnow was used for the assessment of the dosimetric feasibility of an isotoxic dose-escalated radiotherapy proof-of-concept study for glioblastoma [13], prior to its implementation in the PRIDE trial ("Protective VEGF Inhibition for Isotoxic Dose Escalation in Glioblastoma", NCT05871021; NOA-28; ARO-2024-01; AG-NRO-06). For the dosimetric analysis of the study, 10 patients, who had previously undergone treatment for glioblastoma, were selected from the internal database MOSAIQ for the comparison and analysis of the standard treatment approach and experimental treatment protocol which was going to be utilized in the PRIDE trial. The primary aim was to demonstrate the technical plausibility of achieving the proposed dosimetric criteria across a range of heterogeneous and clinically realistic glioblastoma geometries. To this end, the cases were deliberately selected to reflect variability in tumor size, shape, and location, rather than to represent a statistically representative cohort. The images, registrations, structure sets, and dose distributions of the reference and experimental plan (generated in Monaco TPS), were de-identified and uploaded in ProKnow (via the PDA, as described above). The review of the dose values of the target volumes for both plans, the dose exposure of organs at risk (OAR) as well as the dose-volume histograms (DVH graphs) were made available by ProKnow's dosimetric tools (Fig 3).

Based on the prescription and constraints for the study, scorecards were created in ProKnow enabling the assessment and comparison of plan quality. The EUD (see section 'Implementation – EUD Calculation') was used for the comparison of the reference and experimental treatment plans regarding the assessment of the risk of a radiation treatment-related toxicity, such as radiation necrosis. The key objective of this study, which was to show that the underlying concept can be implemented under diverse anatomical conditions, was consistently achieved in all selected cases. The overall concept of the dosimetric feasibility study is currently being evaluated within the PRIDE trial, where predefined inclusion criteria, endpoints, and statistical considerations are fully implemented.

ProKnow was also used for the preparation and quality management assurance of the PRIDE trial (Fig 3). To ensure protocol-compliant conduct of irradiation planning with all participating study centers, one benchmarking case (dummy run) from the test cohort from the dosimetric feasibility study was sent to the collaborating centers. The primary intention of this exercise was not to provide a definitive quantification of variability, such as the comprehensive assessment of inter-rater/inter-center variability, but rather to demonstrate feasibility and, importantly, the learning effect associated with protocol implementation across institutions. Each study site prepared a radiation plan for the standard as well as a dose escalated plan (according to the study's manual), including the relevant OAR. The de-identified DICOM plans and dose files were returned to the main study center (via databox – due to data security clearance delays in participating centers),



19	Dose (Gy) covering **0.03** (cc) of the **Pituitary**	17.310	40 54	IDEAL
20	Dose (Gy) covering **0.03** (cc) of the **Brainstem**	45.591	54 60	IDEAL
21	Dose (Gy) covering **0.03** (cc) of the **Brainstem_Centre**	31.628	54 56	IDEAL
22	Dose (Gy) covering **0.03** (cc) of the **Cochlea_L**	5.456	54 60	IDEAL
23	Dose (Gy) covering **0.03** (cc) of the **Cochlea_R**	6.984	54 60	IDEAL
24	Mean dose (Gy) to the **Cochlea_L**	5.123	45	PASS
25	Mean dose (Gy) to the **Cochlea_R**	6.617	45	PASS
26	Dose (Gy) covering **0.03** (cc) of the **Eye_L**	9.559	54	IDEAL
27	Dose (Gy) covering **0.03** (cc) of the **Eye_R**	36.077	54	IDEAL
28	Mean dose (Gy) to the **Brain-GTV**	19.101		
29	Volume (cc) of the **Brain-GTV** covered by **40.00** (Gy)	209.177		
30	Volume (cc) of the **Brain-GTV** covered by **45.00** (Gy)	187.409		

Custom Metrics

	Metric	Value	Objectives	Result
1	EUD	53.557		

Fig 3. Dosimetric tools in ProKnow. ProKnow Examples Views made visible for peer-review by the main investigator (PRIDE Dummy Run study [9]), showing MR and PET fusions overlayed over dose and structures in the upper part and a scorecard for a quick overview as well as the automatically calculated EUD.

https://doi.org/10.1371/journal.pdig.0001131.g003

which were uploaded to ProKnow via the PDA (Process 1, Fig 1). Similar to the dosimetric feasibility study, the EUD of the brain (for both standard and experimental plan) was calculated for each dummy run and set as a custom metric in ProKnow via the ProKnow API. Although each dummy run was planned in a different TPS we could rely on the ProKnow DVH engine to calculate the EUD, thanks to its vendor agnostic technology which can be used for all patient datasets, regardless of the TPS in which the dose was calculated. For an exact comparison of the geometric similarity between the structures of the main study center and different study sites, the Dice similarity coefficient and Hausdorff distance were calculated as described in section 'Implementation – DICE similarity coefficient and Hausdorff distance calculation'. A review process based on the specified parameters was performed by three radiation oncology specialists for all submitted plans, including examining registration, plan quality, and adherence to protocol. The dummy run could be therefore interpreted as an initial calibration and harmonization step embedded within a broader quality assurance strategy.

In the prospective PRIDE phase II trial, the first three plans of each center must be reviewed for quality assurance and approved by the leading study center prior to therapy initiation, which is inherently time-critical in order to avoid delays in treatment; this enables a more robust and clinically relevant evaluation of protocol adherence under real world conditions.

To support the plan review process, the Python script calculating the EUD continuously monitors the ProKnow workspace and automatically initiates the calculation whenever a plan is uploaded. Thanks to the drive-mapping functionality, the upload of a plan to ProKnow can be made from any individual granted access to the "Watched" folder, which automatically triggers the calculation of the EUD without the intervention of the server administrator. The script runs via the task scheduler on the virtual server every 5 minutes, ensuring that the EUD custom metric is generated automatically following a plan upload (Fig 1, bottom), thus allowing the main investigator to peer-review the case remotely, assess the plan quality and protocol-compliance, and grant permission for irradiation with the dose-escalated concept.

For the use cases presented in this paper, it was not required that we have an ethics approval since only retrospective data were used; In our region, the retrospective data can be used for a study, even without the use of an ethical agreement of a patient, as long as the data are fully anonymized (this was done with the use of PDA) and the key list is not made available. On the other side, the PRIDE trial which is a prospective study, as well as the consent to participate to the study, were both approved by the local ethics committee of the Ludwig-Maximillians-University Munich (application number: 23–0068 fed). The raw DICOM imaging datasets of the presented use cases cannot be provided due to missing de-facing which can result in potentially identifiable data (legal restriction). Data supporting the findings of this study are available from the Clinical Trial Center of the Department of Radiation Oncology at LMU University Hospital (Strahl.Studien@med.uni-muenchen.de).

Discussion

Uploading of clinical data is a strong feature of ProKnow, allowing to study trends and compare treatment outcomes by observing the correlations between clinical data and/or dosimetric parameters for a cohort of patients (via histograms or scatter plots); a limitation lies however on the fact that it requires, the processing of the non-standardized internal files containing the custom metrics as well as the correlation of the original Patient ID with the de-identified ProKnow ID before proceeding to the upload. The clinical data need first to be gathered from a physician or medical student out of many different clinical databases and manually typed into a file (usually an excel file), which is a time-consuming and prone to error procedure. Nonetheless, the data follow a non-standardized format, e.g., a long list of unnecessary for ProKnow PHP data, clinical data listed under the Patient IDs (in subsequent rows) or next to the Patient IDs (in subsequent columns), etc. Such format generates the laborious task of having to manually tailor the file to the ProKnow desired format (upload via User Interface) or update the Python script each time (upload via the API) to perform the correct assignment of the custom metrics to the de-identified patients in ProKnow (Fig 1, bottom). To overcome this issue completely, the solution we propose is the use of merged clinical data in a standardized data format with already de-identified Patient IDs. The Medical Informatic Initiative – Germany – has already established DIC centers in various hospital sites in Germany

who are responsible for the data integration, data quality and data protection [43]. For making such solution realizable we have started discussions with the MeDIC^{LMU} (Data Integration Center) of the LMU University Hospital, to undertake the tasks of merging the clinical data in local DIC databases, as well as the development and implementation of an automated de-identification and pseudonymization process via a trusted third-party service (E-PACS), depicted in Fig 2. The file containing the merged clinical data could be retrieved from the SFTP DIC Server via an automatic script or could be sent directly from DIC Server to ProKnow via the API. Within this standardized clinical data file, the de-identified Patient IDs match the ProKnow IDs (the uploaded DICOM data), hence no tailoring or processing of the given file would be necessary for the upload. Clinical or DICOM data can be added to the same patients at any point in time, since PDA keeps a Patient ID database ensuring uploads to the correct patient(s). The establishment of such workflow for the integration of radiotherapy data (DICOM RT) with clinical data and upload to ProKnow, aims to facilitate the discovery of trends and longitudinal outcomes analysis correlated with individual treatment plan data.

After an extended implementation phase, the advantages of deep implementation include shared network project folders for physicians, customisable access options, and project-specific semi-automated de-identification and data processing in the background. While the workflow was developed and tested at a single German institution, its core components are based on standard data formats and interfaces and are therefore, in principle, transferable to other institutions, provided that local infrastructure and vendor-specific configurations are appropriately adapted.

Limitations of use cases

The presented use cases were designed as a dosimetric feasibility/dummy run analysis rather than a hypothesis testing trial, which is why formal statistics were not the primary focus. Our calculated metrics (EUD, DICE) derived using a single, internally validated pipeline, which avoids inter-software bias, but for a feasibility/dummy-run type study, a consistent single pipeline is generally acceptable. We do frame this, however as a limitation, since using a multiple validation pipelines would certainly increase robustness.

We would also like to clarify, that we cannot provide any conclusions on safety (e.g., toxicity data), efficacy or outcome validation for the presented use cases, due to the early stage of the ongoing PRIDE trial; these are currently being evaluated and will be published following the completion of the PRIDE trial using ProKnow's statistical tools. Sufficient data will be then available to also support a parameter robustness analysis in the prospective clinical setting of the PRIDE trial.

Conclusions

We present an easy-to-use implementation of a highly efficient workflow solution that integrates ProKnow into the clinical environment, allowing for project-specific de-identification and post-processing. Once this has been achieved, the way is open for a larger-scale introduction into the radio-oncology study landscape. The possibility of quick, cloud-based processing of DICOM RT data for time-dependent multicentre studies, as well as semi-automated quality control even before the start of radiotherapy treatments during oncological studies, should enable us to take radiotherapy treatment and homogeneity in future studies to a new level. ProKnow, being an online big-data cloud-based discovery software can be used for the examination of data between any international sites or collaborative institutes, such as the sites in the Bavarian Cancer Research Center (BZKF), opening new opportunities for research and improved healthcare in radiotherapy.

Supporting information

S1 Python Script. EUD Calculation. Python script using the ProKnow API to access the DVH graphs for the calculation of the Equivalent Uniform Dose (EUD, [39]) of the brain and store the metric in ProKnow.
(TXT)

S2 Python Script. DICE similarity coefficient and Hausdorff distance calculation. Python script using the ProKnow API to download the dummy-run RT-Structures, initiate the calculation of the Dice similarity coefficient (DSC) and Hausdorff Distance (HD, and 95th percentile HD95), and store the similarity metric computations in ProKnow.
(TXT)

S1 Table. The EUD values for the dosimetric feasibility study calculated via the ProKnow API (using the ProKnow DVH Curves and the Niemierko et. al. formula) versus the EUD calculated from the Monaco TPS.
(DOCX)

S2 Table. Dice Coefficients calculated via Golden Rule versus Dice coefficients calculated via Plastimatch for 2 example dummy run cases.
(DOCX)

Acknowledgments

We would like to thank Rahul Kashyap (Applications Specialist ProKnow, Elekta) and the ProKnow Community Team for their support. The authors would like to acknowledge the use of graphical vector assets from Freepik (www.freepik.com) in the preparation of Fig 1 and Fig 2.

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