Data preparation for artificial intelligence in medical imaging: A comprehensive guide to open-access platforms and tools

Oliver Diaz^{a,*}, Kaisar Kushibar^a, Richard Osuala^a, Akis Linardos^a, Lidia Garrucho^a, Laura Igual^a, Petia Radeva^a, Fred Prior^b, Polyxeni Gkontra^a, Karim Lekadir^a

^a Faculty of Mathematics and Computer Science, University of Barcelona, Barcelona, Spain

^b Department of Biomedical Informatics, University of Arkansas for Medical Sciences, Arkansas, USA

ARTICLE INFO

Keywords:

Artificial intelligence
Medical image datasets
Data curation
Annotation
Segmentation
Image storage
Open access
Image quality assessment

ABSTRACT

The vast amount of data produced by today's medical imaging systems has led medical professionals to turn to novel technologies in order to efficiently handle their data and exploit the rich information present in them. In this context, artificial intelligence (AI) is emerging as one of the most prominent solutions, promising to revolutionise every day clinical practice and medical research. The pillar supporting the development of reliable and robust AI algorithms is the appropriate preparation of the medical images to be used by the AI-driven solutions. Here, we provide a comprehensive guide for the necessary steps to prepare medical images prior to developing or applying AI algorithms. The main steps involved in a typical medical image preparation pipeline include: (i) image acquisition at clinical sites, (ii) image de-identification to remove personal information and protect patient privacy, (iii) data curation to control for image and associated information quality, (iv) image storage, and (v) image annotation. There exists a plethora of open access tools to perform each of the aforementioned tasks and are hereby reviewed. Furthermore, we detail medical image repositories covering different organs and diseases. Such repositories are constantly increasing and enriched with the advent of big data. Lastly, we offer directions for future work in this rapidly evolving field.

1. Introduction

The term artificial intelligence (AI) was first coined in 1956 [1], but it was only recently that AI technologies showed their potential to reach or even surpass human performance in clinical practice. Roughly speaking, AI is a wide concept that refers to a set of computer algorithms that can perform human behaviour tasks, such as learning. On the other hand, machine learning is a sub-area of AI that covers machines with the ability to learn a given task by learning from past experience or past data, without the need for specific programming. Currently, AI has become a prominent topic in the healthcare sector [2], particularly in medical imaging [3,4]. By leveraging the latest innovations in computing power (e.g. Graphics Processing Units (GPU)), emerging AI technologies are expected to increase the quality and reduce the costs of medical imaging in future healthcare. This includes delivering enhanced image reconstruction [5–7], automated image segmentation [8–10], quality assurance approaches [11,12] and adequate image sequence selection [13], as well as by developing advanced image quantification

for patient diagnosis and follow-up [14,15].

The development of AI solutions that are reproducible as well as transferable to clinical practice will require access to large scale data for model training and optimisation [16–18] (otherwise known as big data, and also referred to as the "oil" of the 21st century [19]). However, despite the acquisition of large volumes of imaging data routinely in clinical settings, access to big data in medical imaging poses significant challenges in practice. Hence, many researchers and developers have dedicated focused on the development of methods, tools, platforms and standards to facilitate the process of providing high-quality imaging data from clinical sites for technological developments, while complying with the relevant data regulations. To this end, data preparation pipelines [20] should cover a number of key steps as described in Fig. 1, including (i) image acquisition at clinical sites, (ii) image de-identification to remove personal information and protect patient privacy, (iii) data curation to control for image and non-image information quality, (iv) image storage and management, and finally (v) image annotation.

* Corresponding author.

E-mail address: oliver.diaz@ub.edu (O. Diaz).

<https://doi.org/10.1016/j.ejmp.2021.02.007>

Received 30 November 2020; Received in revised form 27 January 2021; Accepted 15 February 2021

Available online 5 March 2021

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

In more detail, after getting approval from the corresponding ethical committees at the clinical sites, data de-identification is key to obtain anonymised images and to comply with local data protection regulations (e.g. GDPR, HIPAA). Subsequently, data curation is required to ensure that the associated data, e.g. metadata included in the image headers, are correct. For data storage and management, the FAIR guiding principles [21] recommend that data should be Findable, Accessible, Interoperable and Reusable (FAIR). Last but not least, medical annotations, including anatomical boundaries and lesion descriptions, are highly important not only for training, but also for testing the AI algorithms.

The purpose of this article is to provide a comprehensive guide to the main image data preparation stages, tools and platforms that can be leveraged before and during the design, implementation and validation of AI technologies. More precisely, we review existing solutions for image de-identification, data curation, centralised and decentralised image storage, as well as medical image annotation. We focus this survey on open-access tools that can benefit both clinical researchers and AI scientists at large scale, thus enabling community-wide and standardised data preparation and AI development in the medical imaging sector. Furthermore, we provide examples of medical imaging datasets and open-access data platforms that already cover different anatomical organs, diseases and applications in medical imaging.

2. Image de-identification tools

Tools in this category are also regarded as patient privacy preserving tools. Patient privacy is arguably of value by itself, but also ensures further values considered as fundamental such as dignity, respect, individuality and autonomy. More practically, privacy, and guarantees of such, enable patients to provide complete disclosures of their conditions, hence, enabling effective communication, trust, and constructive relationships between patients and their health providers [22].

Consensus exists to consider patient data as a highly sensitive resource with a need for privacy protection and secure communication. Legal regulation imposed by data protection authorities determine distribution, ownership and usage rights of such patient-specific data. Apart from legal considerations, organisations and individuals responsible for the collection and distribution of such data are encouraged to also apply ethical reasoning [23] to ensure a morally solid decision-making process guiding their actions of sharing or using these sensible data resources.

We consider sensitive patient data resources as any Protected Health Information (PHI) and Personally Identifiable Information (PII) linked to patient health information. The latter may include data from Electronic Health Records (EHR), medical images, clinical and biological data, and any other data collected by health providers that can add towards identifying a subject.

There are four major file formats in medical imaging [24]. DICOM (Digital Imaging and Communication On Medicine) format [25] is the international standard in this domain and covers all imaging modalities and organs, and it is supported by all vendors of clinical imaging

systems. DICOM images contain a header, often referred to as metadata, with information regarding the image sequence, hospital, vendor, clinician or patient information among other information.

Despite the widely spread of DICOM, alternative (imaging or non-strictly-imaging) formats (developed specifically for neuro imaging) are also available, such as NIFTI, MINC and ANALYZE (first version of NIFTI). More recently, the format BIDS is rapidly replacing NIFTI.

Such patient data are an essential resource not only inside their natural environment, i.e. clinical site, but also outside. For example, patient data can be used for clinical trials and teaching [26], for research, and for training and validating AI solutions. Before using such data in these scenarios, they must comply with aforementioned data protection regulations such as HIPAA [27] or GDPR [28]. Techniques such as de-identification, anonymisation and pseudo-anonymisation can be applied to make the data available while simultaneously preserving patient privacy by removing all personal information which could identify an individual from medical images [29] before they leave the clinical centre. However, as expanded later in this document, there are several AI strategies that can be used to train AI models locally (federated learning) or extract key pathological information to generate synthetic images (generative adversarial network) without leaving the clinical centres.

The process of de-identification consists in removing or substituting all patient identifiers such as name, address, hospital identification number, from the patient data, i.e. the image metadata in the DICOM header, according to the local data protection regulation body. Anonymisation removes all patient identification data, thus they cannot be identified. The name, address, and full postcode must be removed, together with any other information which, in conjunction with other data held by or disclosed to the recipient, could identify the patient. Pseudonymisation is a procedure in which the PII is key coded using a unique identifier (i.e. a pseudonym). Such identifiers do not have relation with the individual, but could be traced back (if needed) through a well-secured and separately stored re-identification table. ISO 25237 [30] exemplifies one of several existing common standards for privacy preservation methods.

Apart from sensitive image metadata, the pixel/voxel data of the images also needs to be de-identified if it contains burned in PHI/PII data annotations or if it illustrates body features that can aid to identifying a patient such as for example facial features as depicted in Fig. 2.

In the DICOM Information Object Definitions (IODs) such facial features are referred to as recognisable visual features if they allow the identification of a patient from an image or from a reconstruction of images [31]. Schwarz et al. [32] showed that computer vision algorithms could be used to identify individuals from their cranial MRIs. Their study, hence, demonstrated that patient identification via facial features poses a significant threat to patient privacy in clinical datasets. For 70 out of 84 participants (83%), they were able to match a photograph of the participant with the reconstructed facial image from the participant's MRI using publicly available face-recognition software. Defacing tools address this issue by de-identifying a patient's facial

Fig. 1. Data preparation pipeline prior developing and/or evaluation of AI solution.

Fig. 2. Before (top) and after (bottom) de-identification of facial features using pydeface [34] on a brain magnetic resonance NIfTI image example ('MRHead') from 3D Slicer v4.10.2 [37].

features by removing the pixels/voxels in an image that correspond to the facial features of the patient. However, defacing tools contain trade-offs between the facial feature removal and the respective information loss and, thus, cannot guarantee perfect de-identification nor usability of the resulting images. It is recommended to visually inspect the results from defacing tools and to be aware of edge cases and limitations i.e. no defacing algorithm can handle head/neck cancers when the lesions are on the face. Examples of defacing tools include FreeSurfer's `mri_deface` [33] command line tool, `pydeface` [34] and `mrdefacer` [35], both Python libraries under MIT license for defacing of MRI, and `Quickshear` [36], a Python library under BSD-3-Clause license for defacing of neuroimages.

As illustrated in Table 1, different tools exist for applying privacy preserving methods to medical imaging datasets. Gonzalez et al. [38] provide a list of requirements for data de-identification tools that are to be considered when selecting and applying such a tool for personal or professional use. Sampling from this list, we encourage the prospective user to consider the following recommendations and to incorporate them in decision-making processes when evaluating de-identification tools:

- Refrain from de-identifying the data in a place different from its natural environment (clinical site).
- Apart from DICOM header anonymisation, also handle and validate the de-identification of burned in annotations and of identifying facial features (i.e. deface brain magnetic resonance images (MRI) as demonstrated in Fig. 2) when feasible. Note that, in selected cases (e.g. radiation therapy or radiosurgery treatment planning, head and neck cancers with lesions on the face), facial features information is necessary for the AI model.
- Actively evaluate your tool's compliance with DICOM standards, i.e. by validating conformance with DICOM Application Level Confidentiality Profile Attributes [25].
- Define concrete privacy preservation requirements for the specific use-case and data at hand.
- Ensure traceability and audit compliance i.e. by keeping a record of software, version, affected data portion, results, etc, for every usage event.

For further analysis of a selection of tools highlighted in Table 1, we point to the analyses provided by Lien et al. [47], Aryanto et al. [48], and Gonzalez et al. [38] that may further assist the interested reader to match specific tool requirements with specific tool capabilities.

Moreover, with notable advances in AI research in recent years, novel approaches have appeared in the development of AI solutions that avoid and circumvent patient identification. These approaches compete with or complement the tools and techniques described in Table 1 and include federated learning [49] and synthetic data generation, i.e. using generative adversarial networks [50]. For example, Abadi et al. [51] demonstrated how to generate synthetic COVID CT images while Alyafi et al. [52] produced synthetic breast lesions from mammography images. Federated learning is a privacy-preserving approach, where AI models are trained at the clinical site, hence eliminating the requirement of transporting sensitive clinical data out of their natural environment. The resulting models from different sites are combined in a centralised location.

3. Curation tools

We define data curation as the entirety of procedures and actions after data gathering that refer to data management, creation, modification, verification, extraction, integration, standardisation, conversion, maintenance, quality assurance, integrity, validation, traceability and reproducibility. According to this broad definition, multiple tools and applications could arguably be serving the goal of data curation. To provide a concise yet comprehensive list of curation tools, we, hence, focus on tools with broad application that cover the most frequent use-cases of curation in medical imaging such as DICOM conversion, modification and validation. Table 2 illustrates the list of curation tools. Many of these tools are platform-independent and support various different technologies and integration options. It is to be noted that de-identification tools and processes could be seen as part of the data curation workflow, as they, for instance, modify and standardise the gathered data. It is in this regard that de-identification tools of Table 1 may also be found in Table 2, in particular if such tools offer additional curation capabilities alongside their de-identification or anonymisation features.

Data curation tools are important due to their function of investigating, detecting, preventing and solving issues in the datasets. Thus, in the absence of data curation processes, various issues are prone to arise in the later stages of AI development such as errors stemming from unreliable data or introduction of bias and uncertainty of the validity of prediction results. For instance, prediction results on the test dataset lack validity in case of non-curated image duplicates, where one image is added to the training dataset and its duplicate to the test datasets [40].

Bennett et al. [40] present further examples that highlight the

Table 1
List of patient privacy preserving tools.

Name	Core features	Documentation/ verification	Reference
DicomCleaner™	Java-based web UI, header cleaning blackout burned in annotations	detailed website, open source code	https://www.pixelmed.com/cleaner.html
Posda Tools	perl tool, de-identification in accordance with DICOM Standard PS3.15 2016a [39]	readme, open source code, publication [40]	https://posda.com/
DicomAnonymizer	Python library, cleaning of headers DICOM standards, BSD 3-Clause license	readme, open source code	https://github.com/KitwareMedical/dicom-anonymizer
DVTk DICOM Anonymizer	C# library with GUI, de-identification, DICOM standards, configurable header modification	open source code, publication [41]	https://github.com/151706061/DVTk
Niffler	Python3 library, DICOM header cleaning real-time PACS receiver, BSD-3-Clause license	readme, open source code, publication [42]	https://github.com/Emory-HITL/Niffler
DICOM Anonymizer	GUI tool for Mac OS, configurable DICOM anonymisation, GPLv3 license	simple website	https://dicomanonymizer.com/
MIRC CTP	Java tool, DICOM header and burned in annotation anonymisation	detailed wiki, publications [43,44]	https://mircwiki.rsna.org
DCMTK (DICOM Toolkit)	ANSI, C, C++ library, DICOM standards bsd-3-clause license	website, wiki, code, publication [45]	https://www.dcmkt.org/
PrivacyGuard	Java library, flexible and extensible de-identification, Apache V2.0 license	website, open source code, publication [38]	https://sourceforge.net/projects/privacyguard/
Dicomanon	Matlab library, DICOM header cleaning	detailed website	https://www.mathworks.com/help/images/ref/dicomanon.html
Horos	GUI tool for Mac OS, DICOM viewer with anonymisation option, LGPL-3.0 license	detailed website	https://horosproject.org
GDCM/Gdcmanon	C++ library, anonymisation burned in annotation removal, BSD license	detailed wiki	http://gdcm.sourceforge.net
PET/CT viewer	Plugin for FIJI, Orthanc DICOM anonymisation and sharing	detailed website with user manual	http://petctviewer.org/index.php/dicom-operations
Conquest	Web server for Windows and	detailed website with forum	

Table 1 (continued)

Name	Core features	Documentation/ verification	Reference
	Linux DICOM anonymisation		https://ingenium.home.xs4all.nl/dicom.html
De-identification Toolbox	Java tool, header anonymisation de-identification audit and validation	simple website, publication [46]	https://www.nitrc.org/projects/de-identification
Pydicom Deid	Python library, configurable header and pixel data anonymisation, MIT license	detailed website, open source code	https://pydicom.github.io/deid

importance of data curation in medical imaging. This includes issues such as spatial information loss due to separate frame of reference unique identifiers of associated image slices, and DICOM inconsistencies in shared attributes across a given entity such as a patient, study or series. They also report problems with data normalisation, missing change reproducibility that causes uncertainty, and the need for verifying DICOM metadata conformity to enable interoperable data exchange.

The efforts of standardising the DICOM format is reflected in the development and progress of DICOM curation tools such as DCMTK [45]. For instance, DCMTK's DCMCHECK [53] and dcm4che/dcmvalidate test the adherence of DICOM files to DICOM Information Object Definitions[54,55]. Alongside offering standardised implementation of medical imaging formats such as DICOM or BIDS [56], curation tools provide further standardisation aiding methods. These include conformity, inconsistency and referential integrity tests as implemented in Posda [40], as well as attribute, multiplicity, consistency and encoding validation available in dicom3tools, and in DVTk's DICOM Validation Tool (DVT) [41].

A further distinctive feature of curation tools is accessibility, which is characterised by the capability of a tool to inclusively enable prospective users to access its functionality. Accessibility, hence, determines whether broad and heterogeneous user groups can readily adopt a tool into their workflows. Facilitating user interaction, a graphical user interface (GUI) can improve accessibility and simplifies adoption for users not familiar with a tool's backbone technologies. Curation tools providing a GUI for user interaction include Posda, DVTk, dcm4che, BrainVoyager, LONI Debabeler, and dcm2niix via its GUI MRICroGL. Despite providing a user interface or in absence thereof, some curation tools require user to be familiar with underlying technologies such as command line tools (dicom3tools), docker (dcmqi) or programming languages such as Java (Java DICOM Toolkit) or ruby (ruby-dicom). These tools are less accessible to a broad user population, but arguably equally or more accessible to a specialised sub-population of prospective users such as software engineers. Also, access to the backbone technologies allows such specialised user groups to reproduce, configure, or extend the functionality of the respective tool. Optimally, a curation tool provides accessibility to both, specialised user groups and broad heterogeneous user populations, through suitable user interaction channels. For example, Posda, DVTk and dcm4che provide users with the option to choose between using web-based GUIs or programming language interfaces such as perl [40], C# [41] and Java [55], respectively.

Given a rapid technological progress, software upgrades are needed to provide users with the benefits of the latest technological advancements. The absence of such upgrades reinforces the risk of technological obsolescence of curation tools. Obsolescence is either caused by outdated methodology within a software tool (technological obsolescence) or by an outdated modality targeted by a software tool (functional obsolescence) [61]. Awareness of technological changes and paradigm shifts enables responding in time to a shift in demands to avoid

Table 2

List of curation tools.

Name	Core features	Documentation/verification	Reference
Posda Tools	perl tool, revision tracking, roll-back, bulk edits duplicate, inconsistency and conformity tests	readme, open source code, publication [40]	https://posda.com/
dicom3tools	Command line tool, DICOM conversions validation, attribute modification, BSD License	website, open source code	http://www.dclunie.com/dicom3tools.html
DCMTK	ANSI C C++ library, DICOM standards converting, network, bsd-3-clause license	website, wiki, code, publication [45]	https://www.dcmk.org
DVTk	C# library with GUI, DICOM standards, edit, validate, compare, network analysis	open source code, publication [41]	https://github.com/151706061/DVTk
dcm4che	Java tool with web UI, production-ready DICOM standards and conversions	website, detailed wiki, publication [55]	https://www.dcm4che.org
dcmqi	C++ library, DICOM conversions, querying, format for sharing, 3-clause BSD license	website, open source code, publication [57]	https://qiicr.gitbook.io/dcmqi-guide
dcm2niix	C library, extension of dcm2nii, DICOM to Nifti conversion	website, open source code, publication [58]	https://www.nitrc.org/plugins/mwiki/index.php/dcm2nii:MainPage
LONI Debabeler	Java tool with GUI, configurable conversions metadata extraction	website, publication [59]	https://resource.loni.usc.edu/resources/downloads/loni-debabeler
BIDS Tools	Tools for neuroimaging dataset standardisation DICOM to BIDS conversion	website, open source code, publication [56]	https://github.com/bids-standard
BrainVoyager	C++ neuroimaging tool with GUI, analysis normalisation, coregistration	detailed website, publication [60]	http://www.brainvoyager.com
ruby-dicom	Ruby library, editing, writing, network support for DICOM, GPL-3.0 license	readme, open source code	https://github.com/dicom/ruby-dicom
Java DICOM Toolkit	Java stand-alone tool, write, validate, query DICOM network support, BSD license	website, javadoc, user guide	http://www.pixelmed.com/dicomtoolkit.html

obsolescence. Signals of changing demands are prone to be provided by users requesting new features or reporting limiting design decisions or missing functions, issues, and bugs. The organisation, objectives and community driving the development of a curation tool differs across tools and, as a correlate, so does the prioritisation and response to feature requests and reported issues by users. A suggested causal relationship between obsolescence and the quality and continuity of the response to user reports and feature requests motivates continued development, issue tracking and regular maintenance. For instance, dcm4che's publicly accessible agile project management boards, DCMTK's bug and feature tracker, or the issues pages of dcmqi and BIDS Tools contribute to transparent tracking, prioritisation, and response to reported issues and requested features.

Apart from problem prevention and standardisation, data curation

also allows AI researchers and developers to convert medical imaging data to desired formats. For instance, complex formats such as DICOM can be transformed to simpler formats such as Nifti that are suitable and more common in AI development. Also, a configurable or standardised automated transformation can improve the consistency of the resulting imaging dataset and reduce its size. Curation tools also allow users to visually inspect the data before and after applying curation procedures. Often, this will enable users to detect inconsistencies and issues of the gathered data [58].

Additionally, data curation is a suitable part of AI development to introduce fairness evaluation according to the FAIR Guiding Principles. As previously stated, a fair dataset has been assembled once the datasets fulfil the FAIR requirements comprising findability, accessibility, interoperability, and reusability. Among others, following the FAIR principles includes providing well-described, searchable, uniquely identifiable and standardised image metadata, a data usage license, alongside creation, version and attribute details of the dataset [21].

4. Image storage

To address the limitations of hard-copy based medical image management, the first basic form of Picture Archiving and Communication Systems (PACS) was developed [62]. The first large scale installation of PACS took place in 1982 at the University of Kansas, Kansas City, USA [62,63]. At its core, PACS is an environment that facilitates the storage of multi-modal medical images (MRI, computerised tomography CT, positron emission tomography PET, etc) in central databases and their communication through browser-based formats (i.e. DICOM) that are easily accessible within entire hospitals as well as across multiple devices and locations. Furthermore, PACSs interface with other medical automation systems, including Hospital Information System (HIS), Electronic Medical Record (EMR) and Radiology Information System (RIS).

The PACS workflow (Fig. 3) begins with the packaging of multi-modal images to DICOM format which is then sent to a series of devices for relevant processing. The whole pipeline is summarised as follows:

- Quality Assurance (QA) workstation: verifies patient demographics and any other important attributes to the study. Note that this step might not be a common practise in some countries such as the USA.
- Archive (central storage device): stores the verified images along with any reports measurements and other relevant information relating to them.
- Reading Workstations: the place where a radiologist reviews the data and formulates their diagnosis.

An important extra step that one has to take with PACS is backup, i.e. ensuring facilities and means to recover images in the event of an error or disaster. As any critical data storage and management system, PACS data should be protected by maintaining them in several locations while adhering to privacy regulations. Traditionally, this has been done by transferring data physically through removable media (e.g. hard drives) off-site. However, with the advent of cloud computing, an increasing number of centres is migrating to a Cloud-based PACS paradigm [64]. That means that rather than a central storage device, image data are safely stored within the cloud, whose physical storage spans multiple servers, often in multiple locations.

The PACS revolution has sparked a boom in the production of commercial tools for image storage overcoming the limitations of this clinically-focused tool. Apart from commercial solutions, there also exist several open source solutions that require minimal investment from researchers and clinicians to follow. All of these open source solutions are frameworks from which to build your own server, but do not maintain a free storage service which would be costly to maintain. However, they are expandable and offer a variety of plugins, allowing

Fig. 3. PACS workflow.

one to store medical images in the cloud through a separate provider which can comply with the data protection regulations.

Dcm4che (<https://www.dcm4che.org>) [55] is the most popular tool for clinical data management with Kheops (<https://docs.kheops.online/>) gaining ground rapidly. On the other hand, the Extensible Neuroimaging Archive Toolkit (XNAT) <https://www.xnat.org/> [65] is arguably the leading open source solution for management and storage of large heterogeneous data in research. It is a highly extensible Java web application that runs on an Apache TomCat server. It is able to support many kinds of data, but engineered with a focus on imaging and clinical research data. Project owners have complete control to grant data access and user rights. Data can be stored indexed, searchable in a Postgres database or as resource files on a file system. With an extensible XML-based data model, it can support any kind of tabular data. The core is the RESTful API which can be used for handling data (requesting, displaying, uploading, downloading, removing) and is tied to the same user permission model providing the same level of access as the front end assuring the security of the stored data. XNAT contains rich documentation and a video series 'XNAT Academy'. A wide range of institutes are using XNAT and most prominently the Human Connectome Project [66].

Dicoogle is an extensible, open source PACS archive. It has a modular architecture that allows for pluggable indexing and retrieval mechanisms to be developed separately and integrated in deployment. Storage, indexing and querying capabilities are entrusted to plugins. Therefore, Dicoogle does not offer a database of its own, but rather abstractions over these resources. Documentation for its functionalities includes a learning pack for getting started and developing with comprehensive examples and snippets of code.

Orthanc provides a lightweight standalone server and, similarly to XNAT and Dicoogle, it is expandable through plugins. It has an extremely detailed guide, the "Orthanc Book", including guides for both users and developers as well as useful information on plugins, working with DICOMs, integrating other software and more. Orthanc also includes a professional version with extended capabilities.

The reader may refer to Table 3 for more open source solutions. For commercial solutions some examples include ORCA, iQ-WEB, Post-DICOM and Dicom Director.

5. Image annotations

In order to train and validate AI algorithms, image annotations are pivotal. Image annotation corresponds to the process of labelling the images with essential information (e.g. spatial location, classification), and are often refereed as ground truth. This data is often contained inside the same DICOM file or in a separate text report and should be converted to a more readable and standard format, such as JSON or CSV, for later processing and AI development.

Medical image annotations depend on the type of image (2D, 3D, 4D) and the image technology used (e.g. MRI, US, CT). Therefore, there is a need for tools that are able to handle and annotate different image modalities and formats. More precisely, the type of image annotation will vary depending on the task to be performed by the AI algorithm.

For example, in cases where solely localisation information is needed, bounding boxes or contours (e.g. circles, ellipses, polygons) are typically used to depict the spatial location of an object of interest. If the AI task requires pixel-wise labels, then more detailed contours are

Table 3

List of open source image storage (PACS) solutions. They are all cross-platform except for JVS DICOM which runs only on Windows. Some include premium options.

	Programming language/API	Documentation	Application	Reference
XNAT	Java, RESTful API	XNAT Academy: video series	Research	https://www.xnat.org/about/
Kheops	RESTful API	API resources documented, includes user guide.	Clinical	https://kheops.online/
Dicoogle	Java, RESTful API	Learning pack, snippets and examples	Research	https://www.dicoogle.com/
Orthanc-Server	C++, RESTful API	Orthanc Book, rich documentation	Both	https://www.orthanc-server.com/
OHIF	JavaScript (Meteor)	Detailed guide including deployment instruction	Clinical	https://ohif.org/
JVS DICOM	C++	Lacking	Research	https://wsiserver.jilab.fi/old-jvsmicroscope-software/
EasyPACS	Java, dcm4che API	One github page	Research	https://mehmetesen80.github.io/EasyPACS/
PacsOne Server	MySQL, RESTFUL DicomWEB	PDF manual may be downloaded	Research	https://www.pacsone.net/solutions.htm?
Dcm4Che	Java	One github page	Clinical	https://www.dcm4che.org/
NeurDICOM	Python, (plugins also in C, C++), RESTful	One github page	Research	https://github.com/reactmed/neurdicom

created to segment the image into the regions or volumes of interest. However, obtaining such detailed segmentation masks is more challenging and time-consuming (Fig. 4).

Manual medical image annotation is a tedious task, especially on 3D images. Semi-automated or automated image annotation tools can alleviate the workload of human observers, i.e. clinicians, and increase the number of available annotations necessary for the development of AI solutions in the field of medical imaging.

In addition of image localisation information, annotations can also include lesion descriptions, cancer diagnoses and stages, patient outcomes and other clinical data of interest (Fig. 5).

Although previous works have also provided a detailed list of tools for data annotation [69,70], this section provides a selection of open-source, user-friendly and medical image oriented tools and platforms, as described in Table 4. A description of the most common tools is provided below. 3D Slicer [37] is a well known open source software platform widely used for medical image informatics, image processing, and three-dimensional visualisation. 3D Slicer capabilities include handling a large variety of imaging formats (e.g. DICOM images),

Fig. 4. ITK-SNAP workspace. Brain MRI with corresponding brain structure segmentation masks from MICCAI 2012 Grand-Challenge is shown as an example [67].

Fig. 5. Sample GUI (ImageJ) where observers are requested to evaluate the realism of a (real or simulated) breast lesion [68].

Table 4

List of open access tools for medical image annotations.

Name	3D visualisation	Medical imaging oriented	Open-source	Web-based	Annotations	Reference
3D Slicer	✓	✓	✓		manual, auto	www.slicer.org
ePAD	✓	✓		✓	manual	epad.stanford.edu
Horos Viewer	✓	✓	✓		manual, semi-auto	www.horosproject.org
ImageJ/ FIJI	✓	✓	✓		manual, auto	fiji.sc
InVesalius	✓	✓	✓		manual, auto	invesalius.github.io
ITK-SNAP	✓	✓	✓		manual, semi-auto	www.itksnap.org
MedSeg	✓	✓		✓	manual, auto	www.medseg.ai
MeVisLab	✓	✓			manual, auto	www.mevislab.de
MITK	✓	✓	✓		manual, auto	www.mitk.org
ParaView	✓	✓	✓	✓	manual	www.paraview.org
Seg3D	✓	✓	✓		manual, semi-auto	www.sci.utah.edu/cibc-software/seg3d
Crowdsourcing Platforms						
CMRAD	✓	✓		✓	manual	www.cmrاد.com
Crowds Cure	✓	✓		✓	manual	www.crowds-cure.org

interactive visualisation of 3D images, and manual and automated image segmentation features, among others. It is a powerful tool with a large user community with a complete documentation including a wiki page, a discussion forum, and user and developer manuals. Slicer supports different types of modular development and has extensions for improved segmentation, registration, time series, quantification and radiomic feature extraction available on their web page. As an example, the EMSegment Easy module performs intensity-based image segmentation automatically.

ITK-SNAP [71] is the product of a collaboration between the universities of Pennsylvania and Utah, and focuses specifically on the problem of image segmentation offering a user friendly interface. ITK-SNAP provides tools for manual delineation of anatomical structures. Labelling can take place in all three orthogonal cut planes (axial, coronal and sagittal) and visualised as a 3D rendering. ITK-SNAP also provides automated segmentation using the level-set method [72] which allows segmentation of structures that appear homogeneous in medical images using little human interaction. This tool has been widely applied in many several areas such as cranio-facial pathologies and anatomical studies [73], carotid artery segmentation [74], diffusion MRI analysis [75], prenatal image analysis [76] and virtual reality in Medicine [77], among others. A screenshot of ITK-SNAP is shown in Fig. 4.

The Medical Imaging Interaction Toolkit (MITK) [78], developed by the German Cancer Research Center, is an open-source software focused on the development of interactive medical image processing. MITK combines the Insight Toolkit (ITK) and the Visualization Toolkit (VTK) within an application framework. The leading GPU manufacturer NVIDIA has created the NvidiaAnnotation plugin for MITK Workbench which can be used to leverage the power of an NVIDIA AI-Assisted Annotation Server and perform automated segmentation.

Horos Viewer is a free, open source medical image viewer. The goal of the Horos Project is to develop a fully functional, 64-bit medical image viewer for Mac OS X. Horos is based upon OsiriXTM and other open source medical imaging libraries.

Another popular tool in the medical imaging field is ImageJ [79], a Java-based image processing and analysis tool developed at the National Institute of Health and the Laboratory for Optical and Computational Instrumentation (LOCI, University of Wisconsin). ImageJ has built-in support for reading DICOM files. However, Fiji (Fiji Is Just ImageJ) [80], which is an image processing distribution of ImageJ, bundles a lot of plugins to facilitate scientific image analysis, including DICOM support. Fiji plugins useful for medical image annotation include, among others:

- Bio-Formats: an open source solution for converting proprietary microscopy image data and metadata into standardised, open formats.
- SciView: 3D visualisation and virtual reality capabilities for images and meshes.
- MaMuT: combines TrackMate and BigDataViewer for browsing, annotating, and curating annotations for large image data.
- Trainable Weka Segmentation: a tool that combines a collection of machine learning algorithms with a set of selected image features to produce pixel-based segmentation.

All the tools described above are typically used locally to annotate images. However, there are crowd-sourcing portals, such as Crowds Cure and CMRAD platform, which allow experts to collaboratively annotate medical images on the cloud across sites.

One of the main challenges of AI in medical imaging is the lack of consensus on image annotations across clinicians and clinical sites (i.e. intra- and inter-observer variability). Thus semi-automated and automated tools with little supervision from clinicians can be a potential tool to reduce the time dedicated to this task.

6. Medical image repositories

The previous sections have shown tools to prepare data before they are used for developing or evaluating AI solutions, or to create an image repository. However, there exists many medical imaging repositories, often open-access or controlled-access, which can be used to enrich datasets (e.g. multicentre, multi-vendor, multi-disease) or directly develop own solutions.

Due to the data-driven nature of ML algorithms – in particular, DL approaches – there have been some initiatives that significantly advanced the data collection and availability for the research community. Table 5 summarises various sources of open-access medical imaging databases categorised by target organ and disease. Note that while some sources are open-access, with online registration being required in some cases, the others require permission to access the data. The latter is often attainable via an online request.

One of the well-known resources is the TCIA data repository [81], which offers a variety of curated imaging collections for multiple organs specifically oriented towards cancer imaging. Recently, X-ray and Computed Tomography (CT) images for COVID-19 patients were added to the resource. The images from this repository can be downloaded as collections grouped by a common disease or imaging modality. The primary data format used in TCIA is DICOM. However, as detailed in Table 2, there are different open-access tools that could be used to convert into other different data formats such as NIfTI, which store an image in a single compressed file. Moreover, TCIA also provides clinical data for some of the cases such as patient outcomes, treatment details, genomics and expert analyses. TCIA uses the National Biomedical Imaging Archive (NBIA) software (<https://imaging.nci.nih.gov>) as a backbone and extends its utilisation by providing more curated datasets, user support, and wiki-guides.

UK Biobank is another resource that achieved an outstanding impact in medical data collection and research. Apart from a wide variety of clinical data such as EHR, it hosts imaging collections of more than 100,000 participants including scans of brain, heart, abdomen, bones and carotid artery.

Over the past few years, several challenges have been organised on different medical imaging topics as part of the Medical Image Computing and Computer Assisted Intervention (MICCAI) conference. These challenges are organised by different institutions, which provide a dataset to solve a particular medical imaging problem. These datasets often become benchmarks for evaluating novel AI approaches, which is crucial in terms of reproducibility and comparison with the state-of-the-art approaches. The Grand-Challenges repository provides a compilation of references to the original resources where the datasets can be downloaded or requested from the challenge organisers. Moreover, starting from 2018, MICCAI organisation developed an online platform for challenge proposal submissions with structured descriptions of challenge protocols (<https://www.biomedical-challenges.org/>). This allows more transparent evaluation, reproduction, and adequate interpretation of the challenge results [82].

While the MICCAI challenges are yearly organised events, Kaggle offers ongoing challenges on different ML topics including Medical Imaging. Recently, Kaggle introduced a dataset usability rating for each available challenge, which indicates how easy-to-use is its data. Datasets with high usability rating are often processed and curated for the participants to download and immediately proceed with their experiments. This is particularly important for the newcomers to AI in the Medical Imaging field.

The aforementioned imaging repositories host datasets for multiple organs and various medical conditions. However, there are other data collection initiatives that focus on a specific organ. For example, large sets of neuroimaging datasets could be accessed from IDA, OASIS, NITRC, and CQ500 [83] repositories (see Table 5) that include imaging data for healthy young, adult, ageing, and patient data for various neurological disorders. Most of the datasets from these collections are

Table 5

List of medical image repositories for different anatomical organs and diseases. Open Access (OA) and Review Committee (RC) datasets are shown. Letters ‘s’, ‘f’, ‘d’ before MRI indicate structural, functional, and diffusion, respectively. TBI stands for Traumatic Brain Injury.

Organ	Disease	Name	Access	Images	Reference
Multiple	Cancer	The Cancer Imaging Archive (TCIA)	OA/RC	Radiology, histopathology	https://www.cancerimagingarchive.net
Multiple	Multi	National Biomedical Imaging Archive (NBIA)	OA/RC	Radiology	https://imaging.nci.nih.gov
Multiple	Multi	UKBiobank	RC	MRI, DXA	https://www.ukbiobank.ac.uk
Multiple	Multi	Grand-Challenges	OA	Multi-domain	https://grand-challenge.org
Multiple	Multi	Kaggle	OA	Multi-domain	https://www.kaggle.com
Multiple	Multi	VISCERAL: Visual Concept Extraction Challenge in Radiology	RC	Multi-domain	http://www.visceral.eu/benchmarks
Multiple	Multi	Medical Segmentation Decathlon	OA/RC	CT, MRI	http://medicaldecathlon.com
Brain	Multi	OpenNeuro	OA/RC	Multi-domain	https://openneuro.org
Brain	Multi	Image and Data Archive (IDA)	OA/RC	s/f/dMRI, CT/PET/SPECT	https://ida.loni.usc.edu
Brain	Normal, dementia, Alzheimer's	OASIS Brains Dataset	OA	MRI	https://www.oasis-brains.org
Brain	Multi	NITRC: NeuroImaging Tools and Resources Collaboratory	OA	s/fMRI	https://nitrc.org
Brain	TBI	The Federal Interagency TBI Research (FITBIR)	RC	MRI, PET, Contrast	https://fitbir.nih.gov
Brain	TBI, Stroke	CQ500	OA/RC	CT	http://headctstudy.qure.ai/dataset
Brain	Multi	NDA	RC	MRI	https://nda.nih.gov
Brain	Multi	Connectome	RC	sMRI, fMRI	https://www.humanconnectome.org
Breast	Cancer screening	MIAS mini-database	OA	MG, US	http://peipa.essex.ac.uk/info/mias.html
Breast	Cancer screening	BCDR	RC	MG, US	https://bcdre.eu
Breast	Cancer	DDSM	OA	MG	http://www.eng.usf.edu/cvprg/Mammography/Database.html
Breast	Cancer	OMI-DB	RC	MG	https://medphys.royalsurrey.nhs.uk/omidb
Breast	Cancer	INbreast	OA/RC	MG	http://medicalresearch.inescporto.pt/breastresearch/index.php/Get_INbreast_Database
Cardiac	Clinical routine care	EchoNet-Dynamic	OA/RC	Echocardiogram videos	https://echonet.github.io/dynamic
Cardiac	Multi-abnormal	CAMUS project	OA/RC	Echocardiogram	https://www.creatis.insa-lyon.fr/Challenge/camus
Cardiac	Multi	EuCanShare	RC	MRI	http://www.eucanshare.eu
Cardiac	Multi	Cardiac Atlas Project	OA/RC	MRI	http://www.cardiacatlas.org
Full body	Healthy, unknown	Visible Human Project (VHP)	OA	CT, MRI	https://www.nlm.nih.gov/research/visible
Lung	Thorax	NHS Chest X-ray NIHC	OA	X-ray	https://nihcc.app.box.com/v/ChestXray-NIHCC
Lung	Multi	Cornell Engineering: Vision and Image Analysis lab	OA	CT	http://www.via.cornell.edu/databases
Lung	COVID19	MosMedData	OA	CT	https://mosmed.ai/en
Lung	COVID19	COVID-19 CT segmentation	OA	CT	http://medicalsegmentation.com/covid19
Lung	COVID19	BIMCV COVID-19	OA	CT, CXR	https://github.com/BIMCV-CSUSP/BIMCV-COVID-19
Lung	COVID19	COVID-19 Image Data Collection	OA	CT, CXR	https://github.com/ieee8023/covid-chestxray-dataset
Lung	COVID19	Fig. 1 COVID-19 Chest X-ray Dataset Initiative	OA	CXR	https://github.com/agchung/Figure1-COVID-chestxray-dataset
Retina	Multi	STARE:Structured Analysis of the Retina	OA	Retinal fundus	http://cecas.clemson.edu/~ahoover/stare
Retina	Diabetes	CHASE_DB1	OA	Retinal fundus	https://blogs.kingston.ac.uk/retinal/chasedb1
Retina	Diabetes	High-Resolution Fundus (HRF) Image Database	OA	Retinal fundus	https://www5.cs.fau.de/research/data/fundus-images
Skin Imaging Collaboration (ISIC)	Lesion OA	International Skin Digital images	https://www.isic-archive.com		

benchmarks to evaluate AI-based approaches for image segmentation or disease classification. Similarly, STARE, DRIVE (part of Grand-Challenges), and HRF [84] datasets are commonly used to evaluate automatic methods for retinal fundus image segmentation as they provide expert annotations for human eye disease studies, just to mention a few. The International Skin Imaging Collaboration (ISIC) provides a collection of digital images of skin lesions for teaching and to promote development of automated diagnostic tools by organising public

challenges.

OPTIMAM (OMI-DB) is an on-going project collected over 2.5 million breast cancer screening mammography images [85]. EchoNet-Dynamic is another resource with over 10 K echocardiography videos with corresponding labelled clinical measurements and human expert annotations [86]. In addition, euCanShare – a joint EU-Canada project funded by European Horizon 2020 programme – is establishing a cross-border data sharing and multi-cohort cardiovascular research platform.

NHS Chest X-ray [87] provides annotated X-ray images of 14 common thorax diseases. Also, collections of diagnosed lung CT images of pulmonary diseases are obtainable from the Cornell-Engineering: Vision and Image Analysis lab repository. Moreover, the worldwide impact of the recent COVID19 pandemic on healthcare systems required an immediate reaction to develop automated diagnosis methods. Thus, open-source initiatives accumulated a vast amount of crowd-sourced Chest X-ray and CT images of COVID19 along with healthy and other pulmonary cases. Examples of such datasets include BIMCV COVID19 [88], COVID-19 Image Data Collection [89]. As of 2020, these datasets are continuously expanding (see Table 5) and the images are aggregated from different sources, hence, some overlapping cases may occur. Nonetheless, it is an enormous effort that the research community has put together in battling against the pandemic. Additionally, a more curated dataset with CT images could be requested from a MICCAI endorsed COVID19 lesion segmentation challenge in <https://covid-segmentation.grand-challenge.org> as well as in TCIA.

Although listed in the Grand-Challenges, it is worth mentioning the medical image segmentation decathlon challenge that provides expert annotated images for ten different tasks: brain tumour (BraTS) [90], heart (LASC) [91], and liver (LiTS) [92] compiled from previous MICCAI challenges and TCIA databases; and brain hippocampus structure, prostate [93], lung [94,95], pancreas [96], hepatic vessel [97], spleen [98], and colon datasets were acquired from various healthcare institutions [99]. In addition, detailed CT and MRI full body post-mortem scans of a male and a female subjects are available in the Visible Human Project to study human anatomy as well as to evaluate medical imaging algorithms.

7. Discussion

As confirmed by many healthcare professionals [100–104], AI is revolutionising the field of medicine in general and medical imaging in particular. For instance, AI is suggested to be included in the Medical Physics Curricular and Professional Programme [105]. Although there are still several open issues to be addressed, AI has already demonstrated significant potential to overcome human performance in selected tasks, such as image segmentation. Moreover, AI provides key information in the clinical decision-making process. Without AI, this information would have been extremely difficult, if not infeasible, to extract and combine in an optimal way.

The success of AI is in part thanks to the increasing number of (open-access) medical image datasets becoming available. The images are used by AI networks to extract the most informative features for identifying the boundaries of anatomical structures or for predicting the presence of a disease. However, prior to this step, medical images need to be adequately prepared in order to be safely used and to maximise their potential in the AI development or assessment.

7.1. Remaining challenges of data preparation

As shown in this paper, a wide range of open access image repositories and open source tools have been developed over the last decade to promote standardised best practices for data preparation in medical imaging. However, there are still many challenges that will require further attention and research, as discussed below.

7.1.1. Anonymisation

Image anonymisation (or de-identification) is key to preserving patient privacy. In the last years, several international regulatory environments (e.g. GDPR, HIPAA) have been updated and such changes must be regularly reflected within the image de-identification tools. Therefore, mechanisms should be put in place to automate this process (currently performed in a semi-automated way), and more importantly, to demonstrate that these anonymisation tools actually meet regulatory requirements. Special emphasis should be put into synthetic data

generation and validation procedures, which can overcome many of the current limitations.

As previously discussed, a 3D reconstruction of the head should not identify a person, thus certain spatial information should be also removed (image defacing). However, the challenge is to remove identifiable facial features while preserving essential scientific data without distortion. This is difficult for several diseases such as head/neck cancers, or radiation therapy planning where currently key data is destroyed.

Although all anonymisation efforts are focused on the image, anonymisation strategies should also consider the associated clinical data, annotations and other forms of labelled data.

7.1.2. Curation

Data curation is another important step to ensure the data is properly organised and structured. Once the data collection is defined in a fair way, our efforts should focus on improving the quality of the data. This can be achieved by setting standards and guidelines in the entire process of medical image preparation from the de-identification step to the data annotation step and specially in the data curation step. Initiatives in the data collection and availability are also crucial for AI research in medical imaging because they allow to create benchmarks for multi-centre and multi-scanner AI evaluation.

Automated tools and standards for measuring image quality, particularly for quantitative analyses, are greatly needed. Furthermore, approaches to automatically detect and correct image artefacts will be vital to guarantee certain quality in the images used to train AI algorithms. Similar efforts (quality standards and tools) should be also promoted to assure the quality of annotations, labels and image derived features.

7.1.3. Annotation

Image annotations are also pivotal to ensure a correct training of AI algorithms and they should be performed with care. However, having accurate delineations or annotations is challenging as well as very time consuming, especially in 3D imaging modalities. Annotators (typically clinicians) do not have the time to annotate the hundred or thousand images needed to train AI algorithms. At the same time, despite the advances made with the advent of deep learning, automated segmentation tools that can be robustly applied across varying imaging protocols and clinical sites are still lacking, in particular as open-source. As an illustration, our experience in the EuCanImage Horizon 2020 project, focused on the annotation of liver, colorectal and breast cancer images, suggests that additional research is needed to develop the next generation of open-access image segmentation tools for the wide benefit of the community. Current and future crowdsourcing and collaborative annotation platforms will be of high value to capture the heterogeneity of annotation based on several clinicians.

7.1.4. Storage

Since most of the image datasets are scattered in the web, large scale integration of distributed data repositories are needed to centralise its access and to reuse the image derived features. This opens new questions as to whether researchers should process their data on the cloud (typically a paying option) or if they should download the data to work on their own computing environment. The availability of such platforms should also allow the cross-linkage and semantic integration of radiology/pathology/clinical/-omics data with the images.

Furthermore, data accessibility is very important to promote a good standardisation of AI development. This is already covered by the FAIR principles [21] and it is a requirement for open science, open access to de-identify data. A key component to enhance data accessibility (currently adopted by the TCIA, the largest cancer imaging archive), is the use of a digital object identifier (DOI) to each data collection so that collection can be cited and directly accessed from the DOI.

From the image standardisation point of view, the DICOM format

already provides an international standard for image data, although other image formats have appeared in the last years (mostly for neuro imaging). However, in order to facilitate the distribution of AI models, standardised containers could be of great benefits for the field. Once developed, AI tools should be made open source to facilitate their distribution. In addition, the development of an open source community that supports that software is pivotal to guarantee its maintenance and upgrade.

7.2. Future research in AI

In addition to data preparation, which is the focus of this paper, it is worth discussing future directions for AI in medical imaging: (i) Data augmentation and synthesis, (ii) Federated learning, (iii) ethical issues of AI, and (iv) Uncertainty estimation.

Data augmentation has shown promise in AI and to enrich the data preparation stage. State-of-the-art data augmentation techniques range from basic strategies using feasible geometric transformations, flipping, colour modification, cropping, rotation, noise injection and random erasing [106] to other more advanced techniques that involve the creation of new synthetic images, such as generative adversarial networks [50].

Recently, new privacy-preserving approaches, known as Federated learning [49,107], have been promoted in clinical research for privacy-preserving AI and, somehow, to enrich the datasets used by the AI technology. These techniques train an algorithm across multiple decentralised clinical sites holding local data samples, without exchanging them. Therefore, locally-trained AI results are later combined in a centralised location. Such novel paradigms should enable larger and more representative samples while also assisting in protection of patient privacy [108,109].

Ethical use of AI tools in medicine is a major concern. The statement presented in [110] highlights the consensus of several international societies that ethical use of AI in radiology should promote well-being, minimise harm, and ensure that the benefits and harms are distributed among stakeholders. Important issues of ethics, fairness and inclusion can arise from the pitfalls and biases during data preparation. Routine clinical data collected by clinical sites can be deficient, biased (e.g. gender imbalance [111]), or prone to noise (e.g. presence of image artefacts [112]). Several advancements can be achieved by defining algorithms that can track these issues efficiently [113]. However, in order to generalise the AI-generated results to the human population, large-scale, multi-centre training and test datasets of sufficient quality are often required [18].

As shown in this paper, there are many parameters that affect the data preparation and the quality of the data compiled for AI training. As a result, in addition to accuracy, AI models for medical image analysis should be assessed on the level of confidence in the predictions. Uncertainty estimation is of particular importance since data preparation is imperfect. If the uncertainty is too high, the clinicians should be notified in order to take this information into account in the final decision-making process.

Kendall and Gal [114] have demonstrated two types of uncertainties in computer vision that are also applicable in medical image analysis: the epistemic uncertainty caused by lack of knowledge in the AI model (reduced training data) and the aleatoric uncertainty (inherent to the data such as acquisition artefacts, patient movement, radiofrequency spikes, etc.).

Uncertainty estimation in deep learning scenarios is often obtained by approximating Bayesian posterior using neural networks [115–117], although non Bayesian approaches have also been addressed [118]. The uncertainties are usually represented as a heat map defined by certain uncertainty measures such as entropy, variance, and mutual information.

Overall, the predictive model uncertainty should be always considered in making critical decisions which is always part of common

clinical routines. We believe that this emerging research topic will improve the applicability of AI towards practical scenarios by increasing the trustworthiness of such methods that are currently considered as black-box.

8. Conclusions

In this article, we reviewed open access tools and platforms for the different steps of medical image preparation. This process is essential before starting the design or application of any AI model. More precisely, the steps comprising a typical medical image pipeline are: de-identification, data curation, centralised and decentralised medical image storage, and data annotations tools. The presented structured summary provides users and developers a comprehensive guide to choose among the plethora of currently available tools and platforms to prepare medical images prior to developing or applying AI algorithms. Furthermore, we provided a detailed list of medical imaging datasets covering different anatomical organs and diseases.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 952103, from the Spanish Ministry (grant RTI2018-095232-B-C21) and Catalan government (grant SGR1742).

References

- [1] Andresen SL. John McCarthy: father of AI. *IEEE Intell Syst* 2002;17(5):84–5.
- [2] Patel VL, Shortliffe EH, Stefanelli M, Szolovits P, Berthold MR, Bellazzi R, et al. The coming of age of artificial intelligence in medicine. *Artif Intell Med* 2009;46(1):5–17.
- [3] Giger ML. Machine learning in medical imaging. *J Am College Radiol* 2018;15(3):512–20.
- [4] Savadjiev P, Chong J, Dohan A, Vakalopoulou M, Reinhold C, Paragios N, et al. Demystification of ai-driven medical image interpretation: past, present and future. *Eur Radiol* 2019;29(3):1616–24.
- [5] Teuwen J, Moriakov N, Fedon C, Caballo M, Reiser I, Bakic P, et al. Deep learning reconstruction of digital breast tomosynthesis images for accurate breast density and patient-specific radiation dose estimation. *arXiv preprint arXiv:200606508* 2020;.
- [6] Wang G, Ye JC, De Man B. Deep learning for tomographic image reconstruction. *Nat Mach Intell* 2020;2(12):737–48.
- [7] Singh R, Wu W, Wang G, Kalra MK. Artificial intelligence in image reconstruction: The change is here. *Phys Med* 2020;79:113–25.
- [8] Agarwal R, Diaz O, Lladó X, Gubern-Mérida A, Vilanova JC, Martí R. Lesion segmentation in automated 3d breast ultrasound: volumetric analysis. *Ultrason Imag* 2018;40(2):97–112.
- [9] Kushibar K, Valverde S, González-Villà S, Bernal J, Cabezas M, Oliver A, et al. Automated sub-cortical brain structure segmentation combining spatial and deep convolutional features. *Med Image Anal* 2018;48:177–86.
- [10] Apte AP, Iyer A, Thor M, Pandya R, Haq R, Jiang J, et al. Library of deep-learning image segmentation and outcomes model-implementations. *Phys Med* 2020;73:190–6.
- [11] Kimura Y, Kadoya N, Tomori S, Oku Y, Jingu K. Error detection using a convolutional neural network with dose difference maps in patient-specific quality assurance for volumetric modulated arc therapy. *Phys Med* 2020;73:57–64.
- [12] Olaciregui-Ruiz I, Torres-Xirau I, Teuwen J, van der Heide UA, Mans A. A Deep Learning-based correction to EPID dosimetry for attenuation and scatter in the unity MR-Linac system. *Phys Med* 2020;71:124–31.
- [13] Wang Y, Wang M. Selecting proper combination of mpMRI sequences for prostate cancer classification using multi-input convolutional neuronal network. *Phys Med* 2020;80:92–100.
- [14] Lekadir K, Galimzianova A, Betriu À, del Mar Vila M, Igual L, Rubin DL, et al. A convolutional neural network for automatic characterization of plaque composition in carotid ultrasound. *IEEE J Biomed Health Inf* 2016;21(1):48–55.
- [15] Cetin I, Raisi-Estabragh Z, Petersen SE, Napel S, Piechnik SK, Neubauer S, et al. Radiomics signatures of cardiovascular risk factors in cardiac MRI: results from the UK Biobank. *Front Cardiovascular Med* 2020; 7.

- [16] Syeda-Mahmood T. Role of big data and machine learning in diagnostic decision support in radiology. *J Am College Radiol* 2018;15(3):569–76.
- [17] Morris MA, Saboury B, Burkett B, Gao J, Siegel EL. Reinventing radiology: big data and the future of medical imaging. *J Thoracic Imag* 2018;33(1):4–16.
- [18] Prior F, Almeida J, Kathiravelu P, Kurc T, Smith K, Fitzgerald T, et al. Open access image repositories: high-quality data to enable machine learning research. *Clin Radiol* 2020;75(1):7–12.
- [19] Cao L. Data science: a comprehensive overview. *ACM Comput Surveys (CSUR)* 2017;50(3):1–42.
- [20] Willemink MJ, Koszek WA, Hardell C, Wu J, Fleischmann D, Harvey H, et al. Preparing medical imaging data for machine learning. *Radiology* 2020;295(1):4–15.
- [21] Wilkinson MD, Dumontier M, Aalbersberg LJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding Principles for scientific data management and stewardship. *Sci Data* 2016;3(1):1–9.
- [22] Gostin LO, Levit LA, Nass SJ, et al. Beyond the HIPAA privacy rule: enhancing privacy, improving health through research. National Academies Press; 2009.
- [23] Larson DB, Magnus DC, Lungren MP, Shah NH, Langlotz CP. Ethics of using and sharing clinical imaging data for artificial intelligence: a proposed framework. *Radiology* 2020;192536.
- [24] Larobina M, Murino L. Medical image file formats. *J Digital Imag* 2014;27(2):20–6.
- [25] ISO 12052:2017. Digital Imaging and Communications in Medicine (DICOM) Standard. Standard; National Electrical Manufacturers Association; Rosslyn, VA, USA; 2017. <http://medical.nema.org/>.
- [26] Noumeir R, Lemay A, Lina JM. Pseudonymization of radiology data for research purposes. *J Digit Imag* 2007;20(3):284–95.
- [27] The Health Insurance Portability and Accountability Act (HIPAA). <http://purl.fdlp.gov/GPO/gpo10291>; 2004. [Online; accessed 26-November-2020].
- [28] European Parliament and Council of European Union (2016) Regulation (EU) 2016/679. <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32016R0679>; 2016. [Online; accessed 26-November-2020].
- [29] Noumeir R, Lemay A, Lina JM. Pseudonymization of radiology data for research purposes. *J Digit Imag* 2007;20(3):284–95.
- [30] ISO 25237:2017. Health informatics — Pseudonymization. Standard; International Organization for Standardization; Geneva, CH; 2017. [Online; accessed 26-November-2020]; <https://www.iso.org/standard/63553.html>.
- [31] DICOM PS3.3 2020e. DICOM PS3.3 2020e - Information Object Definitions. Standard; DICOM Standards Committee, National Electrical Manufacturers Association (NEMA); 2020. [Online; accessed 24-January-2021]; <http://dicom.nema.org/medical/dicom/current/output/chtml/part03/PS3.3.html>.
- [32] Schwarz CG, Kremers WK, Therneau TM, Sharp RR, Gunter JL, Vemuri P, et al. Identification of anonymous mri research participants with face-recognition software. *New England J Med* 2019;381(17):1684–6.
- [33] Bischoff-Grethe A, Ozyurt IB, Busa E, Quinn BT, Fennema-Notestine C, Clark CP, et al. A technique for the deidentification of structural brain MR images. *Human Brain Mapp* 2007;28(9):892–903.
- [34] pydeface: defacing utility for MRI images. <https://github.com/poldracklab/pydeface>; 2019. [Online; accessed 30-November-2020].
- [35] mrdefacer: Helper to aid de-identification of MRI images (3D or 4D). <https://github.com/mih/mrdefacer>; 2018. [Online; accessed 24-January-2021].
- [36] Schimke N, Kuehler M, Hale J. Preserving privacy in structural neuroimaging. In: IFIP annual conference on data and applications security and privacy. Springer; 2011. p. 301–8.
- [37] 3D Slicer: a multi platform, free and open source software package for visualization and medical image computing. www.slicer.org; 2020. [Online; accessed 26-November-2020].
- [38] González DR, Carpenter T, van Hemert JJ, Wardlaw J. An open source toolkit for medical imaging de-identification. *Eur Radiol* 2010;20(8):1896–904.
- [39] DICOM PS3.15 2016a. DICOM PS3.15 2016a - Security and System Management Profiles. Standard; DICOM Standards Committee, National Electrical Manufacturers Association (NEMA); 2016. [Online; accessed 24-January-2021]; <http://dicom.nema.org/medical/Dicom/2016a/output/chtml/part15/PS3.15.html>.
- [40] Bennett W, Smith K, Jarosz Q, Nolan T, Bosch W. Reengineering workflow for curation of DICOM datasets. *J Digital Imag* 2018;31(6):783–91.
- [41] Potter G, Busbridge R, Toland M, Nagy P. Mastering dicom with dvt. *J Digital Imag* 2007;20(1):47–62.
- [42] Kathiravelu P, Sharma A, Purkayastha S, Sinha P, Cadrin-Chenevert A, Banerjee I, et al. A DICOM Framework for Machine Learning Pipelines against Real-Time Radiology Images. *arXiv preprint arXiv:200407965* 2020.
- [43] Freymann JB, Kirby JS, Perry JH, Clunie DA, Jaffe CC. Image data sharing for biomedical research—meeting HIPAA requirements for de-identification. *J Digital Imag* 2012;25(1):14–24.
- [44] Erickson BJ, Fajnwaks P, Langer SG, Perry J. Multisite image data collection and management using the RSNA image sharing network. *Transl Oncol* 2014;7(1):36–9.
- [45] Eichelberg M, Riesmeier J, Wilkens T, Hewett AJ, Barth A, Jensch P. Ten years of medical imaging standardization and prototypical implementation: the DICOM standard and the OFFIS DICOM toolkit (DCMTK). In: Medical imaging 2004: PACS and imaging informatics, vol. 5371. International Society for Optics and Photonics; 2004. p. 57–68.
- [46] Song X, Wang J, Wang A, Meng Q, Prescott C, Tsu L, et al. Deid—a data sharing tool for neuroimaging studies. *Front Neurosci* 2015;9:325.
- [47] Lien CY, Onken M, Eichelberg M, Kao T, Hein A. Open source tools for standardized privacy protection of medical images. In: Medical imaging 2011: advanced PACS-based imaging informatics and therapeutic applications, vol. 7967. International Society for Optics and Photonics; 2011. 79670M.
- [48] Aryanto K, Oudkerk M, van Ooijen P. Free DICOM de-identification tools in clinical research: functioning and safety of patient privacy. *Eur Radiol* 2015;25(12):3685–95.
- [49] McMahan B, Moore E, Ramage D, Hampson S, y Arcas BA. Communication-efficient learning of deep networks from decentralized data. In: Artificial intelligence and statistics. PMLR; 2017. p. 1273–1282.
- [50] Goodfellow I, Pouget-Abadie J, Mirza M, Xu B, Warde-Farley D, Ozair S, et al. Generative adversarial nets. In: Advances in neural information processing systems. 2014. p. 2672–2680.
- [51] Abadi E, Paul Segars W, Chalian H, Samei E. Virtual imaging trials for coronavirus disease (COVID-19). *Am J Roentgenol* 2020:1–7.
- [52] Alyafi B, Diaz O, Martí R. DCGANs for realistic breast mass augmentation in x-ray mammography. In: Medical imaging 2020: computer-aided diagnosis; vol. 11314. International Society for Optics and Photonics; 2020a. p. 1131420.
- [53] Hewett AJ, Grevenmeyer H, Barth A, Eichelberg M, Jensch PF. Conformance testing of DICOM image objects. In: Medical imaging 1997: PACS design and evaluation: engineering and clinical issues; vol. 3035. International Society for Optics and Photonics; 1997. p. 480–487.
- [54] dcm4che.org: Open Source Clinical Image and Object Management. <https://www.dcm4che.org/>; 2021. [Online; accessed 21-January-2021].
- [55] Warnock MJ, Toland C, Evans D, Wallace B, Nagy P. Benefits of using the DCM4CHE DICOM archive. *J Digital Imag* 2007;20(1):125–9.
- [56] Gorgolewski KJ, Auer T, Calhoun VD, Craddock RC, Das S, Duff EP, et al. The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. *Sci Data* 2016;3(1):1–9.
- [57] Herz C, Fillion-Robin JC, Onken M, Riesmeier J, Lasso A, Pinter C, et al. DCMQI: an open source library for standardized communication of quantitative image analysis results using DICOM. *Cancer Res* 2017;77(21):e87–90.
- [58] Li X, Morgan PS, Ashburner J, Smith J, Rorden C. The first step for neuroimaging data analysis: DICOM to NIFTI conversion. *J Neurosci Methods* 2016;264:47–56.
- [59] Neu SC, Valentino DJ, Toga AW. The LONI Debabeler: a mediator for neuroimaging software. *Neuroimage* 2005;24(4):1170–9.
- [60] Goebel R. Brainvoyager—past, present, future. *Neuroimage* 2012;62(2):748–56.
- [61] Bradley M, Dawson RJ. An analysis of obsolescence risk in IT systems. *Software Qual J* 1998;7(2):123–30.
- [62] Huang HK. PACS and imaging informatics: basic principles and applications. John Wiley & Sons; 2004.
- [63] Bick U, Lenzen H. PACS: the silent revolution. *Eur Radiol* 1999;9(6):1152–60.
- [64] Silva LAB, Costa C, Oliveira JL. A PACS archive architecture supported on cloud services. *Int J Comput Assisted Radiol Surg* 2012;7(3):349–58.
- [65] Marcus DS, Olsen TR, Ramaratnam M, Buckner RL. The extensible neuroimaging archive toolkit. *Neuroinformatics* 2007;5(1):11–33.
- [66] Van Essen DC, Smith SM, Barch DM, Behrens TE, Yacoub E, Ugurbil K, et al. The wu-minn human connectome project: an overview. *Neuroimage* 2013;80:62–79.
- [67] Landman, B., Warfield, S. Miccai 2012 workshop on multi-atlas labeling. In: Medical image computing and computer assisted intervention conference. 2012.
- [68] Alyafi B, Diaz O, Elangovan P, Vilanova JC, del Riego J, Martí R. Quality analysis of dcgan-generated mammography lesions. In: 15th International workshop on breast imaging (IWBI2020); vol. 11513. International Society for Optics and Photonics; 2020b. p. 115130B.
- [69] Rebinth A, Kumar SM. Importance of manual image annotation tools and free datasets for medical research. *J Adv Res Dyn Control Syst* 2019;10:1880–1885.
- [70] Hanbury A. A survey of methods for image annotation. *J Visual Lang Comput* 2008;19(5):617–27.
- [71] ITK-SNAP. www.itksnap.org; 2014. [Online; accessed 26-November-2020].
- [72] Osher S, Sethian JA. Fronts propagating with curvature-dependent speed: algorithms based on hamilton-jacobi formulations. *J Comput Phys* 1988;79(1):12–49.
- [73] Kauke M, Safi AF, Grandoch A, Nickenig HJ, Zöller J, Kreppel M. Image segmentation-based volume approximation—volume as a factor in the clinical management of osteolytic jaw lesions. *Dentomaxillofac Radiol* 2019;48(1):20180113. PMID:30216090.
- [74] Spangler EL, Brown C, Roberts JA, Chapman BE. Evaluation of internal carotid artery segmentation by InsightSNAP. In: Pluim JPW, Reinhardt JM, editors. Medical imaging 2007: image processing, vol. 6512. International Society for Optics and Photonics; SPIE; 2007. p. 1164–71.
- [75] Corouge I, Fletcher PT, Joshi S, Gouttard S, Gerig G. Fiber tract-oriented statistics for quantitative diffusion tensor mri analysis. *Med Image Anal* 2006;10(5):786–798. The Eighth International Conference on Medical Imaging and Computer Assisted Intervention – MICCAI 2005.
- [76] Addario V, Rossi A, Pinto V, Pintucci A, Cagno L. Comparison of six sonographic signs in the prenatal diagnosis of spina bifida. *J Perinatal Med* 2008;36:330–4.
- [77] Rizzi SH, Banerjee PP, Luciano CJ. Automating the extraction of 3D models from medical images for virtual reality and haptic simulations. In: 2007 IEEE international conference on automation science and engineering. IEEE; 2007. p. 152–157.
- [78] MITK. www.mitk.org; 2014. [Online; accessed 26-November-2020].
- [79] Rueden CT, Schindelin J, Hiner MC, DeZonia BE, Walter AE, Arena ET, et al. ImageJ 2: ImageJ for the next generation of scientific image data. *BMC Bioinf* 2017;18(1):529.
- [80] Schindelin J, Arganda-Carreras I, Frise E, Kaynig V, Longair M, Pietzsch T, et al. Fiji: an open-source platform for biological-image analysis. *Nat Methods* 2012;9(7):676–82.

- [81] Clark K, Vendt B, Smith K, Freymann J, Kirby J, Koppel P, et al. The Cancer Imaging Archive (TCIA): maintaining and operating a public information repository. *J Digital Imag* 2013;26(6):1045–57.
- [82] Maier-Hein L, Eisenmann M, Reinke A, Onogur S, Stankovic M, Scholz P, et al. Why rankings of biomedical image analysis competitions should be interpreted with care. *Nat Commun* 2018;9(1):1–13.
- [83] Chilamkurthy S, Ghosh R, Tanamala S, Biviji M, Campeau NG, Venugopal VK, et al. Deep learning algorithms for detection of critical findings in head ct scans: a retrospective study. *The Lancet* 2018;392(10162):2388–96.
- [84] Budai A, Bock R, Maier A, Hornegger J, Michelson G. Robust vessel segmentation in fundus images. *Int J Biomed Imag* 2013;2013.
- [85] Halling-Brown MD, Warren LM, Ward D, Lewis E, Mackenzie A, Wallis MG, et al. Optimam mammography image database: a large scale resource of mammography images and clinical data. *arXiv preprint arXiv:200404742* 2020;.
- [86] Ouyang D, He B, Ghorbani A, Yuan N, Ebinger J, Langlotz CP, et al. Video-based AI for beat-to-beat assessment of cardiac function. *Nature* 2020;580(7802):252–6.
- [87] Wang X, Peng Y, Lu L, Lu Z, Bagheri M, Summers RM. ChestX-ray8: hospital-scale chest X-ray database and benchmarks on weakly-supervised classification and localization of common thorax diseases. In: *Proceedings of the IEEE conference on computer vision and pattern recognition*; 2017. p. 2097–106.
- [88] Vayá MdI, Saborit JM, Montell JA, Pertusa A, Bustos A, Cazorla M, et al. BIMCV COVID-19+: a large annotated dataset of RX and CT images from COVID-19 patients. *arXiv preprint arXiv:200601174* 2020;.
- [89] Cohen JP, Morrison P, Dao L, Roth K, Duong TQ, Ghassemi M. COVID-19 Image Data Collection: Prospective Predictions Are the Future. *arXiv 200611988* 2020;.
- [90] Bakas S, Reyes M, Jakab A, Bauer S, Rempfler M, Crimi A, et al. Identifying the best machine learning algorithms for brain tumor segmentation, progression assessment, and overall survival prediction in the BRATS challenge. *arXiv preprint arXiv:181102629* 2018;.
- [91] Tobon-Gomez C, Geers AJ, Peters J, Weese J, Pinto K, Karim R, et al. Benchmark for algorithms segmenting the left atrium from 3D CT and MRI datasets. *IEEE Trans Med Imag* 2015;34(7):1460–73.
- [92] Bilic P, Christ PF, Vorontsov E, Chlebus G, Chen H, Dou Q, et al. The liver tumor segmentation benchmark (lits). *arXiv preprint arXiv:190104056* 2019;.
- [93] Litjens G, Debats O, van de Ven W, Karssemeijer N, Huisman H. A pattern recognition approach to zonal segmentation of the prostate on mri. In: *International conference on medical image computing and computer-assisted intervention*. Springer; 2012. p. 413–420.
- [94] Napel S, Plevritis SK. NSCLC radiogenomics: initial Stanford study of 26 cases. *Cancer Imag Arch* 2014.
- [95] Bakr S, Gevaert O, Echegaray S, Ayers K, Zhou M, Shafiq M, et al. A radiogenomic dataset of non-small cell lung cancer. *Sci Data* 2018;5(1):1–9.
- [96] Attiye MA, Chakraborty J, Doussot A, Langdon-Embry L, Mainarich S, Gönen M, et al. Survival prediction in pancreatic ductal adenocarcinoma by quantitative computed tomography image analysis. *Ann Surg Oncol* 2018;25(4):1034–42.
- [97] Pak LM, Chakraborty J, Gonen M, Chapman WC, Do RK, Koerkamp BG, et al. Quantitative imaging features and postoperative hepatic insufficiency: a multi-institutional expanded cohort. *J Am College Surgeons* 2018;226(5):835–43.
- [98] Simpson AL, Leal JN, Pugalenth A, Allen PJ, DeMatteo RP, Fong Y, et al. Chemotherapy-induced splenic volume increase is independently associated with major complications after hepatic resection for metastatic colorectal cancer. *J Am College Surgeons* 2015;220(3):271–80.
- [99] Simpson AL, Antonelli M, Bakas S, Bilello M, Farahani K, Van Ginneken B, et al. A large annotated medical image dataset for the development and evaluation of segmentation algorithms. *arXiv preprint arXiv:190209063* 2019;.
- [100] Pinto dos Santos D, Giese D, Brodehl S, Chon SH, Staab W, Kleinert R, et al. Medical students' attitude towards artificial intelligence: a multicentre survey. *Eur Radiol* 2019;29:1640–6.
- [101] Gong B, Nugent JP, Guest W, Parker W, Chang PJ, Khosa F, et al. Influence of artificial intelligence on Canadian medical students' preference for radiology specialty: a national survey study. *Acad Radiol* 2019;26(4):566–77.
- [102] Lai M, Brian M, Mamzer M. Perceptions of artificial intelligence in healthcare: findings from a qualitative survey study among actors in france. *J Transl Med* 2020;18:14.
- [103] van Hoek J, Huber A, Leichtle A, Härmä K, Hilt D, von Tengg-Kobligh H, et al. A survey on the future of radiology among radiologists, medical students and surgeons: students and surgeons tend to be more skeptical about artificial intelligence and radiologists may fear that other disciplines take over. *Eur J Radiol* 2020;121:108742.
- [104] Diaz O, Guidi G, Ivashchenko O, Colgan N, Zanca F. Artificial intelligence in the medical physics community: an international survey. *Phys Med* 2021;81:141–6.
- [105] Zanca F, Hernandez-Giron I, Avanzo M, Guidi G, Crijs W, Diaz O, et al. Expanding the medical physicist curricular and professional programme to include artificial intelligence. *Phys Med* 2021;83:174–83.
- [106] Shorten C, Khoshgoftaar TM. A survey on image data augmentation for deep learning. *J Big Data* 2019;6(1):60.
- [107] Kaissis GA, Makowski MR, Rückert D, Braren RF. Secure, privacy-preserving and federated machine learning in medical imaging. *Nat Mach Intell* 2020;2(6):305–11.
- [108] Chang K, Balachandrar N, Lam C, Yi D, Brown J, Beers A, et al. Distributed deep learning networks among institutions for medical imaging. *J Am Med Inf Assoc* 2018;25(8):945–54.
- [109] Sheller MJ, Edwards B, Reina GA, Martin J, Pati S, Kotrotsou A, et al. Federated learning in medicine: facilitating multi-institutional collaborations without sharing patient data. *Sci Rep* 2020;10(1):1–12.
- [110] Geis JR, Brady AP, Wu CC, Spencer J, Ranschaert E, Jaremko JL, et al. Ethics of artificial intelligence in radiology: summary of the joint european and north american multisociety statement. *Can Assoc Radiol J* 2019;70(4):329–34.
- [111] Larrazabal AJ, Nieto N, Peterson V, Milone DH, Ferrante E. Gender imbalance in medical imaging datasets produces biased classifiers for computer-aided diagnosis. *Proc Nat Acad Sci* 2020;117(23):12592–4.
- [112] Antun V, Renna F, Poon C, Adcock B, Hansen AC. On instabilities of deep learning in image reconstruction and the potential costs of ai. *Proc Nat Acad Sci* 2020.
- [113] Swinger N, De-Arteaga M, au2 NTHI, Leiserson MD, Kalai AT. What are the biases in my word embedding? *arXiv preprint arXiv:181208769* 2019;.
- [114] Kendall A, Gal Y. What uncertainties do we need in bayesian deep learning for computer vision? *arXiv preprint arXiv:170304977* 2017;.
- [115] MacKay DJ. A practical bayesian framework for backpropagation networks. *Neural Comput* 1992;4(3):448–72.
- [116] Gal Y, Ghahramani Z. Dropout as a bayesian approximation: Representing model uncertainty in deep learning. In: *International conference on machine learning*. PMLR; 2016. p. 1050–1059.
- [117] Blundell C, Cornebise J, Kavukcuoglu K, Wierstra D. Weight uncertainty in neural network. In: *International conference on machine learning*. PMLR; 2015. p. 1613–1622.
- [118] Lakshminarayanan B, Pritzel A, Blundell C. Simple and scalable predictive uncertainty estimation using deep ensembles. *arXiv preprint arXiv:161201474* 2016;.