Brain MRI Images Pre-processing of Heterogeneous Data-sets for Deep Learning Applications

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Abstract: Automatic segmentation of tissues and lesions is a very important step in any Artificial Intelligence pipeline designed to analyze medical images (especially MRI). This is particularly true for brain MRI images of patients affected by neurological pathologies like Multiple Sclerosis (MS). To perform well, cutting edge Artificial Intelligence approaches like Deep Learning need a huge amount of training data. Unfortunately, available data-sets of MRI medical images often lack annotations, standardized acquisition protocols, formats and dimensions. This heterogeneity in the data-sets makes it often very difficult to use and integrate different data-sets in the same pipeline. Available image pre-processing tools have specific requirements and might not be adequate for extensive usage with heterogeneous data-sets. This paper presents an on-going work on a comprehensive and consistent brain MRI images pre-processing pipeline for Deep Learning applications enabling the creation of a congruous data-set. The pipeline was tested with the public available ISBI2015 data-set.

1 INTRODUCTION

Magnetic resonance imaging (MRI) is a non-invasive and fundamental diagnostic and monitoring tool for many of the existing neurological conditions. Among them, Multiple Sclerosis (MS) is a chronic autoimmune disease for which MRI is particularly important as the disease needs to be carefully monitored with at least one MRI per-year. The progression of MS is variable between patients and a good monitoring is crucial for correct therapeutic choices: MRI is a support during disease diagnosis and follow-up, together with others indicators of disease status (Inojosa, 2021). MRI allows to visualize different brain tissues depending on the chosen acquisition sequence and acquisition protocol. The modalities that allow MS monitoring are the T1-weighted (T1w), that allows easy annotation of healthy tissues, and T2-weighted (T2w) and FLAIR images that are used for detecting inflammatory lesions, indicators of disease activity. Images are typically visually examined by neuro-radiologists that fill a written clinical report that in many cases is affected by intra-and-inter reader variability; therefore, a lot of attention is now being paid to tools and methodologies for the automatic segmentation of tissues and lesions (Kaur, 2021) (Zeng, 2020). The current problem with Deep Learning pipelines, is that not only they require very large training sets, but also they enforce strict requirements in the input data-sets' format, size, and image quality. This makes it often impossible to use different data-sets as inputs for the same pipeline because the differences in the data-sets can be easily result in biases in the segmentation results.

The purpose of this paper is to present a comprehensive pre-processing pipeline able to prepare raw MRI brain images data-sets (with the corresponding lesions masks, if present) so that they can be directly fed into Deep Learning architectures. The pipeline has been implemented entirely in Python and particular attention has been paid in giving the possibility to directly access each functions' parameters to allow further customizations/optimizations (see 3.1).

2 PROBLEMS DEFINITION

Several issues can negatively influence the performances of a segmentation strategy: not only non-brain tissues are a source of errors and need to be

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removed, but MS lesions come in different locations and sizes. Moreover, brain MRI images suffer the presence of noise artifacts, non-uniformities, and are affected by the intrinsic differences in the anatomy of human brains; the lack of annotated data (MRI images without a corresponding lesion mask) is also serious limitation that can cause misclassification problems, and result in a reduction of performances in lesion identification, both in Machine Learning and Deep Learning approaches. To overcome these problems, Artificial Intelligence requires very large training sets to correctly ”learn” to identify the relevant features (tissues/lesions) on the image. Unfortunately, on top of the physiological variability of the human brains and MS lesions, different data-sets also come in different formats, have been generated by different equipment that introduce different artifacts, have different dimensions, number of slices, file formats. On the other hand, Deep learning methods require, as input, images with a certain standard images' file format (such as PNG), so it is not possible to feed a deep learning architecture directly with an image stored in a typical medical image format (such as NIfTI or DICOM). Existing software and tools for image pre-processing have some limitations. Firstly, they are often maintained by separated groups: when updating to a new version of one of these tools, versioning problems and inconsistencies may occur if such update is not supported by the other tools or plugins, such as CBS Tools, JIST, TOADS-CRUISE, and BrainSuite. Secondly, they lack in easy customization, and have often strict requirements in terms of settings, making it difficult to simply obtaining homogenous and weel structured data-sets. All the mentioned problems often force scientists to rely on a single data-set, hopelessly affecting the quality of the Machine Learning or Deep Learning pipeline performance.

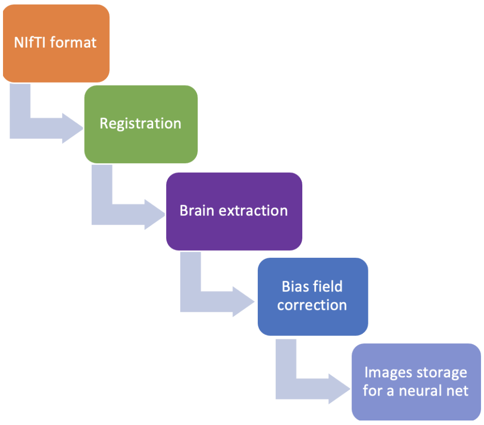


Figure 1: Steps of the proposed pipeline.

3 MATERIALS AND METHODS

Pre-processing is crucial for any data-analysis pipeline, and this is particularly true for medical images. The proposed pipeline (summarized in Figure 1) includes the following typical pre-processing steps for brain MRI images (which are usually performed by separate and independent tools):

- MRI sequence selection: consists in selecting the MRI modality that will be processed. Our pipeline focuses on T2w images, as MS lesions are mostly visible in such modality;
- Image registration: registering an image means, in this case, matching it with a reference model. It is a key step and a prerequisite for all applications that want to compare data-sets among subjects or across time (Toga, 2019); raw MRI images are not registered and may have different spacing and slice resolution (Alam, 2016). The registration step consists in a set of transformation of the raw image that optimises a similarity index with the reference image. The registered image is obtained linearly interpolating the initial image domain into the new domain, as image files consist of a variable number of slices, each slice corresponding to a different longitudinal brain section: when the number of slices in the original image is not consistent with the number of images in the atlas, the missing slices are interpolated. Our pipeline registers each MRI image and then saves it back as NIfTI files; moreover, this step makes sure the MRI image contains the same number of slices as the reference image by (if necessary) interpolating missing slices;
- Brain-extraction: also known as skull-stripping, it is a step which removes tissues that are not of interest, such as skull and dura mater. Including non-brain tissues is a known source of errors (Rehman, 2020); there are several possible brain-extraction methods, for instance relying on deep learning techniques or on traditional morphological operations (Kalavathi, 2016). The brain-extraction method proposed in this paper is an adaptation of the method proposed by Gambino et al. (Gambino, 2011), and uses a combination of morphological operations;
- Bias field correction and noise reduction: it corrects the bias field, that is a low frequency intensity nonuniformity present in the image data as inhomogeneity and illumination nonuniformity.
- Final data-set creation: images (and corresponding masks) are saved back as NIfTI files and as

PNG files in the correct format required by the chosen neural network pipeline.

The pipeline was tested on the raw longitudinal T2w images of the public avaiable ISBI2015 data-set that consists in MRI (acquired at 1 to 4 different time points) images of 5 subjects diagnosed with different MS subtypes. Lesions masks of two independent readers are also given. The data-set includes, besides the raw images, the images that were processed when creating the ISBI2015 data-set with the MIPAV software, integrated with several plugins such TOADS-CRUISE plugins. We used the latter images as a comparison to evaluate the results of our pipeline. The MIPAV package, as many others such as CBS Tools, JIST, and TOADS-CRUISE, are maintained by separate groups: when a new version of one is released, instabilities may occur if such update is not supported by the other tools or plugins.

The proposed pipeline addresses this limitation by using only stable Python libraries, chosen based on the clarity of their documentation and on their performances:

- ANTsPy for Registration, Brain extraction, and Bias Field Correction;
- Dicom2nifti for DICOM to NIfTI conversion;
- SimpleITK for NIfTI files storage.

As previously pointed out, using different data-sets acquired with different purposes and in different centers, is fundamental for developing accurate and efficient automatic segmentation methods based on Deep Learning.

3.1 Pipeline Description

ANTsPy library was chosen for implementing the most important steps of the pipeline because of its good performances and extensive documentation. To give the reader an idea, Table 1 shows the NIfTI to NumPy (NumPy Python library) conversion times of three common libraries on a MacBook Pro laptop. This time is important because in each MRI data-set there are thousands of images to be converted.

Table 1: Libraries performances.

ITK time	4.375 seconds
NIBABEL time	2.902 seconds
ANTS time	1.713 seconds

It is possible to easy access specific parameters as shown in Table 2 thus allowing the pipeline steps to be customized as well as optimized. Such parameters directly affect the core points of the processing functions.

Image Conversion

Image format conversion is fundamental to improve the ability to generalize and work with more diversified data. The present pipeline supports, if needed, the conversion from a series of DICOM images belonging to a single scan into a single NIfTI file, as the DICOM format is another widespread medical image format.

Table 2: Pipeline parameters.

Registration	Transform, atlas
Brain extraction	Iterations, kernels
Bias field correction	Correction parameters

Image Registration

Images were registered to a reference atlas that was chosen accordingly to the registration step proposed by the ISBI data-set guidelines as a matter of consistency: as they performed manual segmentation on FLAIR images with the help of T1w and T2w images, and as there is no matching standard atlas for FLAIR images, we rigidly registered T2w images to the corresponding reference T2 standard atlas in the MNI space [1], so that the correspondence between images and lesion masks was obtained. For the purposes of this paper and its future implementations for the development of segmentation via deep learning, only T2w images are considered at this point (Abderrahim, 2020). The atlas that was used is the ICBM Average Brain linearly transformed to Talairach space, adapted for use with the MNI Linear Registration Package. The pipeline is designed to easily choose to use different atlases too, as it is sufficient to download and import the desired file. Registration is done by determining the transformation needed to match the source image with the target atlas, optimizing the similarity index between them. The registered image is then obtained linearly interpolating the initial image domain into the new domain. The registration step is particularly important when different images are put together in a comprehensive set. Due to different acquisition parameters and settings, the number of slices (being each slice a section of the brain) between different image files can vary: registration makes it possible to uniform the number of slices to an atlas, consequently matching the resolution of the image to atlas resolution (in this case with a resolution of 1mm^3) via interpolation, so that the different scans match each other in terms of anatomical references and in terms of number of images per-scan. This step is extremely

[1] http://nist.mni.mcgill.ca/icbm-152lin/

important to reduce the input variability, which is fundamental in the development of neural networks. As an example, the original ISBI2015 T2w NIfTI files contain 70 slices, while the registered image consists of 181 slices.

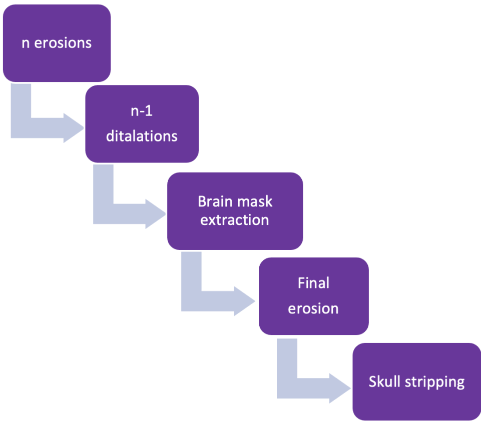


Figure 2: Brain extraction steps.

Brain Extraction

The steps that compose the brain extraction are briefly summarized in Figure 2. Such steps were implemented adapting the findings of Gambino et al. (Gambino, 2011). Skull-stripping is usually implemented on T1w images, but in our pipeline it is adapted to work directly on T2w images, without requiring intermediate steps that would need to further register T2w images to T1w images, in order to apply the brain mask obtained with the T1w images to the T2w scan. Brain extraction develops in five simple steps; again all parameters such as the number of iterations or the features of morphological operators can be easily customized (see Table 2):

1. n (n=3) erosions with a cross kernel,
2. n-1 dilatations with a cross kernel,
3. brain mask extraction,
4. final erosion,
5. the original image is multiplied by the brain mask, in order to obtain the brain.

Such parameters can be adapted in order to obtain better performances as future implementations, and most of them can be adapted in order to be able to work independently from the MRI image modalities. This is not true, for example, for tools such as MIPAV MP2RAGE that, in order to obtain the skull stripping of T2w images, require both T1w images and T2w images as input.

Bias Field Correction

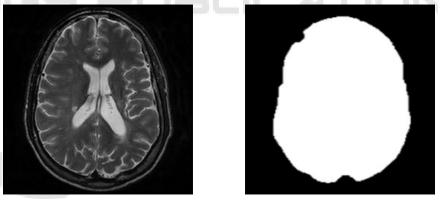
The N4 Bias Field Correction method (Tustison, 2010) was applied for estimating and correcting the bias, giving as output the corrected image.

Deep Learning Data-set Creation

Once the images are processed, it is possible to convert them into PNG files that can be then organised in folders, and directly fed to a neural network. As not all the images might be needed (for example, those for which the pre-processing has failed, or those that only partially show the cerebellum), the pipeline also allows to store only images of interest, selecting their corresponding identification number. Particular attention was paid to preserve image orientations during the creation of the data-set, as multiple conversions between formats is needed for the pipeline itself to work.

3.2 Working Example

The steps previously described are exemplified in Figure 3 and in Figure 4 where an image from the ISBI2015 data-set was processed and then saved as .png file for later use.

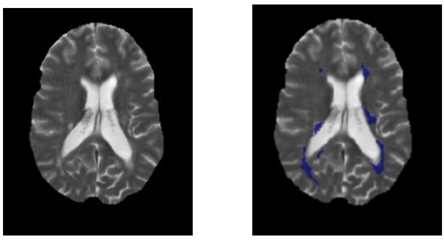


(a) Original image. (b) Brain mask.

Figure 3: Extraction of the brain.

Figure 3 shows a slice of the image that is fed to the pipeline for the pre-processing: the brain mask represents the result of the brain-extraction step. Such mask is then multiplied to the initial slice, giving the desired brain-stripped result.

In Figure 4 the lesion mask (coloured in blue) is superimposed over the skull-stripped brain, and such mask will serve as ground truth for a segmentation algorithm. The masks were given together with the ISBI2015 dataset, and they were obtained by two expert readers that annotated the MRIs previously pre-processed with the MIPAV software. The correspondence of such lesion masks with the brain images processed with our pipeline indicates that it works as expected and gives comparable results.



(a) Processed. (b) With lesions.

Figure 4: Skull-stripping.

3.2.1 Processing Time

We report here the processing times of the execution of the pipeline to the data-set. The processing times [2] of the registration step and of the rest of the process are separately reported, as the registration is performed on the original raw image, while brain-extraction and bias field correction are done on the registered image.

Table 3: Performances with 1 MRI scan.

Registration	4.5 sec.
Processing	143.52 sec.

Values in Table 3 refer to the processing of a single NIfTI file that corresponds to a T2w MRI scan of a subject. Each NIfTI file contains, once it is registered with the atlas, 181 images.

4 DISCUSSION

Deep Learning pipelines require large training sets, and have strict requirements in the input format, size, and image quality. Moreover, Deep Learning performances benefit from homogenous and weel structured data-sets. This makes it often impossible to use different data-sets directly as inputs because their differences can be easily result in biases in the segmentation results, affecting performances. This paper presents a comprehensive pre-processing pipeline able to prepare raw MRI brain images data-sets so that they can be directly fed into deep learning architectures. The pipeline has been implemented entirely in Python and it guarantees the possibility to directly access each functions' parameters to allow further customizations/optimizations. Several other approaches recommended for MRI images processing have strict constrains in terms of the images that they can process: some are limited to 3D images, and some require specific MRI modalities to function properly. The presented pipeline differs from other existing software as it incorporates, with flexibility and customizability, all the steps that are needed when preparing heterogenous data-sets for deep learning application, from the raw MRI scan (in different image formats) to the image that will be the input of a deep learning algorithm. Furthermore, it differs from other known tools such as BrainSuite as it can be directly and easily incorporated into the development of any automatic medical images analysis systems based on Deep Learning architectures, without limiting itself to a processing or visualising tool for MRI images and, above all, relying on stable Python libraries without depending on many plug-ins that can cause inconsistencies and versioning problems. This approach can help with the task of data preparation and image pre-processing, that cannot be ignored or underestimated when constructing data-sets for Machine Learning (and in particular Deep Learning) pipelines. Future implementations will include an optimization of the performances to include as input more MRI modalities and formats, increasing its versatility, and the incorporation of the pipeline as the backbone of an innovative Deep Learning architecture targeted for application in real clinical practice.

5 CONCLUSIONS

Handling the variability of MRI medical images needs an efficient pre-processing pipeline aimed at solving practical issues that include but are not limited to raw images format and dimensions, physiological differences, image artifacts. This paper introduces a pipeline to fill the gap between heterogeneous data-sets and their practical integration and usability in the same Artificial Intelligence pipeline. We successfully tested the pipeline to show how it helps filling the gap between heterogeneous data-sets and their practical use. Future work will include extensive comparative evaluations of the pipeline, and an optimization of the performances to include as input more MRI modalities and formats.

Finally, it is important to point out that the proposed approach is not necessarily strictly related to brain MRI images, but could be easily adapted to other MRI scans, such as chest imaging.

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APPENDIX

The code of the presented pipeline can be downloaded from GitHub at the following address: https://github.com/aSofworkOrange/BrainMRI-preproc