N4 BIAS FILTER
(FORTH)

Summary: The state-of-the-art N4ITK method is used for bias field correction of the MR images. Two main options are offered: (1) Apply N4 filter to image/images (either with the default parameters values or with parameters values defined by the user) (2) Find the optimal configuration of the N4 filter for specific image/images by measuring the Full Width at Half Maximum (FWHM) of the periprostatic fat distribution.

Status : Containerized

Contacts : dovrou@ics.forth.gr; nikiforakik@gmail.com;

Table of Contents

I. Purpose

The N4 bias filter tool aims to correct the bias field using the N4 filter and identify the optimal configuration of the N4 filter on prostate MR T2W images.

II. Tool description for its conceptual validation

The conceptual validation aims to ensure that a tool is aligned in its purpose and functionality with the pre-processing tools specified in EUCAIM T5.3. For this, the following documentation will detail **the necessity of the tool and its functioning**.

An oral presentation has been given on April 27th 2023 during a Task Force group meeting dedicated to data processing, for partners to understand the tool better as well as to provide feedback.
Link to the presentation of the tool :
https://docs.google.com/presentation/d/1eihlC9lz_EP4u24Tlk-CIbvPnbCT4Oh1/edit?usp=drive_link&ouid=111541155881395093632&rtpof=true&sd=true
Link to the video of the oral presentation :
https://drive.google.com/file/d/1IDCkWTfvhii6XXbHuufTBZHsxSCR_NE_/view?usp=drive_link

1. Name:

N4 Bias Filter

2. Contributor:

FORTH

3. Area:

Imaging data curation

4. Tool description:

The tool is designed to perform image pre-processing to reduce the bias field effect, improving the quality of the image. Two main functionalities are offered: (1) Apply N4 filter to image/images (either with the default parameters values or with parameters values defined by the user) (2) Find the optimal configuration of the N4 filter for specific image/images by measuring the Full Width at Half Maximum (FWHM) of the periprostatic fat distribution.

5. Data:

Magnetic Resonance Imaging (MRI) T2 weighted (T2W) prostate images.

6. Methodology/performance:

The bias field correction is performed using the state-of-the-art method for bias field correction, N4ITK filter. The values of the parameters of the N4ITK filter can be either the default or can be specified by the user. The default values of the parameters of the N4 filter are the values that were identified as optimal through our exploratory analysis performed on 4 publicly available prostate datasets. More specifically, the default values of the parameters are: convergence threshold 0.001, shrink factor 2, fitting level 5, number of iterations 25 and the use of default mask (i.e., the non-zero voxels of the image). For the identification of the optimal configuration, an exploratory analysis examining 240 different configurations is performed for each image. For each examined configuration, the periprostatic fat distribution is identified and the Full Width at Half Maximum (FWHM) of this distribution is calculated. The filter configuration that results in the minimum FWHM for each patient is considered as optimum, indicating homogeneous tissue representation.

7. Use: brief description of the tool's functioning (if it applies).

The tool can be used for bias field correction of MR T2W prostate images. It aims to improve the quality of the image by reducing the intensity inhomogeneities caused by

the low-frequency variation. Furthermore, it can be used to identify the optimal configuration (i.e. optimal values for each parameter) of the N4 filter for an T2W MR image or a batch of images. Thus, it can be used as a preprocessing step to reduce the bias field or identify the optimal configuration of N4 filter for MR T2W prostate images.

8. Input/output formats: description of the input/output of the tool at the validation stage (will help if some adaptation is needed).

Input : The input of the tool is a path with the raw images, which should be in DICOM format.

Output : For the first functionality (apply N4 filter), the output is the N4 filtered images, which are saved to a path specified by the user with the same format. For each patient, a folder will be created and the N4 filtered image in DICOM format will be stored within the folder. For the second functionality (identify optimal configuration), a text or excel file containing the optimal configuration(s) is saved to a path specified by the user.

9. Quantitative results: performance obtained during training of the tool (if applies)

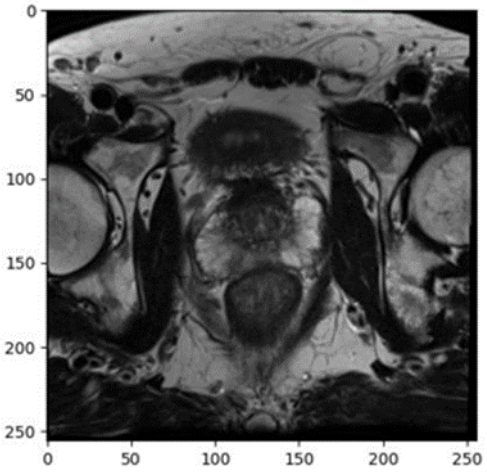
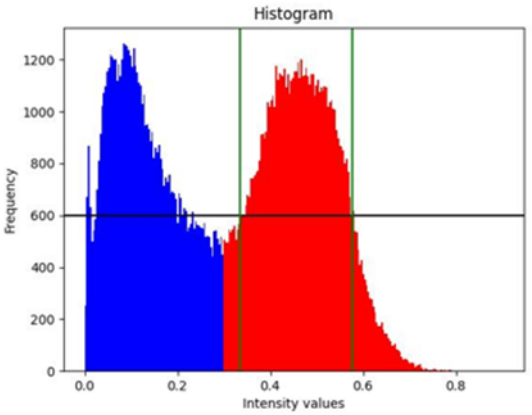
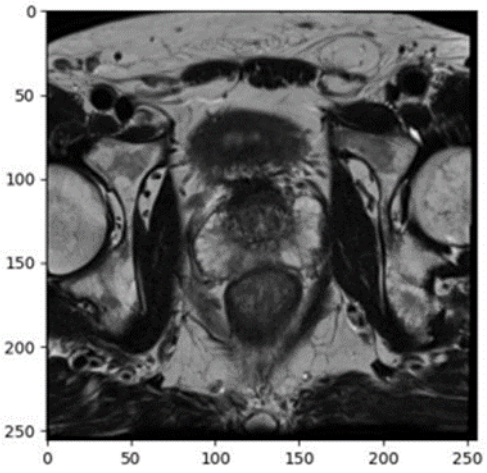
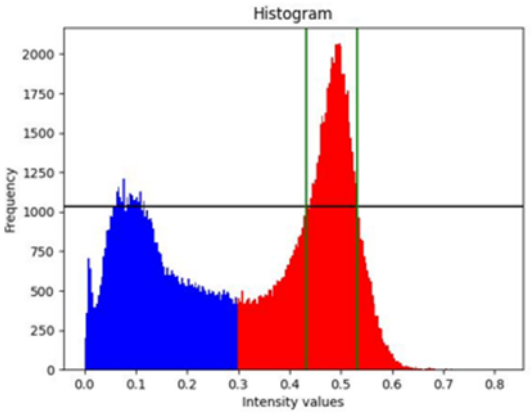
The results show that the set of N4 parameters, converging to optimal representations of fat in the image, were : convergence threshold 0.001, shrink factor 2, fitting level 6, number of iterations 100 and the use of default mask for prostate images acquired by a combined surface and endorectal coil at both 1.5T and 3T.

The corresponding optimal N4 configuration for MR prostate images acquired by a surface coil at 1.5T or 3T was: convergence threshold 0.001, shrink factor 2, fitting level 5, number of iterations 25 and the use of default mask.

Even for the patients that their minimum FWHM was obtained with different setting, the difference in the FWHM values between the derived optimal configuration and the setting with the minimum FWHM was small (< 20%).

10. Qualitative results: Provide some visual results (if available) of applying such tools.

The original and the N4 filtered image are presented, indicating that the image becomes brighter after applying the N4ITK filter as the low-frequency variation has been reduced. The corresponding histograms of the original and the N4 filtered image, respectively, show that the periprostatic fat distribution (indicated with red color) becomes narrower after applying the N4ITK filter. Thus, the FWHM of the periprostatic fat distribution becomes smaller after the N4ITK filter, indicating the reduction of the intensity inhomogeneities in the image.

	Image	**Histogram**
Original		
N4 filtered		

11. Additional information: successful use cases, external resources (open code, papers...) licence, certification … (if they apply).

Successful use cases: The tool was successfully applied to MR T2W series of 4 publicly available prostate datasets: PROSTATEx, PROSTATE-DIAGNOSIS,

Prostate-MRI and PI-CAI dataset. Furthermore, the tool was successfully applied to T2W series from the ProCAncer-I project as a pre-processing step.

Publication link :
https://www.sciencedirect.com/science/article/pii/S0730725X23000589?via%3Dihub#bb0075

ProCancer-I

Keywords for searching in databases: N4, N4ITK, bias field correction, bias field, T2W, MRI, preprocessing, prostate, prostate imaging

III. Technical specifications

This part of the documentation is dedicated to providing all relevant technical specifications to prepare for the tool's integration into the EUCAIM test environment.

It is possible that the tool's integration will require, among others, some modifications in the input/output, or the inclusion of monitoring mechanisms.

1. Data: In depth description of the data used to train the tool.

Magnetic Resonance Imaging (MRI) T2weighted (T2W) prostate images. Four publicly available datasets were used to train and validate the tools. The PROSTATE-DIAGNOSIS dataset contains 89 prostate cancer T2W MR images acquired on a 1.5T Philips Achieva scanner using combined surface and endorectal coil. The PROSTATEx contains 204 prostate T2W MR images that were acquired on two different types of Siemens 3T MR scanners with surface coil, the MAGNETOM Trio and Skyra. Two more datasets, the Prostate-MRI and the PI-CAI dataset, were used to validate the results. The Prostate-MRI dataset consists of 26 prostate T2W MR images acquired on a 3T Philips Achieva scanner using combined phased-array surface and endorectal coil. The PI-CAI dataset contains prostate T2W MR images acquired on Siemens Healthineers or Philips Medical Systems-based MR scanners at 1.5 T or 3 T using surface coils. Two subsets of T2W images from the PI-CAI dataset were selected based on the two different magnetic field strengths, i.e., 1.5T (59 patients) and 3T (80 patients).

2. Methods: in depth description of the methodology used for its development including all data preprocessing.

To apply the N4ITK filter, only the values of its parameters are required to be used as input to the filter's algorithm.

The parameters of the N4ITK filter are :

- the convergence threshold
- the shrink factor
- the fitting level
- the number of iterations
- the use of mask

To identify the optimal configuration of the filter, 240 different configurations are being examined. For each configuration, the original and the N4 filtered image are cropped to include only the periprostatic region by keeping the middle part of the image and removing the heterogeneous prostate gland and the area distant from the prostate. The mask of the prostate gland was derived automatically by using a deep learning model that extracts a cubic box around the estimated position of the whole prostate gland. The K-means algorithm (with K=2) is used to identify the periprostatic fat distribution with the high intensity signal. Then, the Full Width at Half Maximum (FWHM) of the periprostatic fat distribution is calculated. The filter configuration that results in the minimum FWHM for each patient is considered as optimum.

3. Specific Technical information:

    a. CPU
    b. Programming language : python 3.8.13
    c. Expected RAM usage : at least 8GB (depends on the amount of input data)
    d. Running mode : batch-based docker
    e. Software version : 1.7
    f. Libraries : docker
    g. Security measures: The tool does not require admin rights to execute and does not require privileged execution mode.

4. Traceability and monitoring mechanism.

Informative messages are displayed on screen when running the docker in interactive mode (specifying -it). If an error occurs, the corresponding error message will be displayed to inform the user what the source of the error was. Corresponding

messages for the start and the completion of the tool's execution are also displayed on screen.

5. Unitary tests: description of the tests implemented to verify the correct functioning of the tool.

Tests were performed in order to ensure the proper functionality of the tool. All possible functionalities were tested, i.e. applying the N4 bias filter with the default values, applying the N4 bias filter with values defined by the user, applying the pipeline to identify the optimal configuration for 1 image, and applying the pipeline to identify the optimal configuration for a batch of images.

6. Access restriction: Do you have any access restriction to the source code or to the binaries of your tool?

No.

7. Additional information for tool integration.

The tool is compatible with any operating system as it is dockerized. A comprehensive documentation is provided for the users.

IV. Integration specifications

1. Communication channel for the helpdesk, technical support channel

For any inquiries: dovrou@ics.forth.gr, nikiforakik@gmail.com

2. Most common errors

The most common errors are:

- No functionality selected (available functionalities: -N or -P)
- Empty directory
- Not valid input format (valid formats: DICOM)
- Lack of slice location information on the DICOM header
- Invalid image dimensions (the image should be represented by a 3D array of shape [SLICES, WIDTH, HEIGHT])
- Dimension mismatch error between image and corresponding mask

3. FAQs

Q: What is the purpose of the tool?

A: The tool can be used as an image pre-processing step to reduce the bias field effect on prostate images. It aims to improve the quality of the image by reducing the intensity inhomogeneities caused by the low-frequency variation. Furthermore, it can be used to identify the optimal configuration (i.e. optimal values for each parameter) of the N4 bias filter for an image or a batch of images.

Q: Which are the functionalities of the tool?

A: The tool offers two main functionalities:

a. Apply N4 filter to image/images (either with the default parameters values or with parameters values defined by the user) to reduce the bias field.
b. Find the optimal configuration of the N4 filter for specific image/images by performing the exploratory analysis using 240 different configurations and measuring the Full Width at Half Maximum (FWHM) of the periprostatic fat distribution for each configuration. The smaller the FWHM value, the better the bias field correction.

Q: In which data can the tool be applied?

A: The tool can be applied only for Magnetic Resonance (MR) T2weighted (T2W) prostate images.

Q: Are there any specific requirements for the execution of the tool?

A: The tool can run in any operating system, as it is containerized in order to ensure compatibility. However, the execution of the tool is time-consuming due to the iterative process of the N4 bias field correction algorithm. The process for the identification of the optimal configuration of the N4 filter requires much time due to the experimentation on 240 different configurations for each image. For example, it requires approximately 25 seconds to apply the N4 bias filter with the default parameter values to one image and 10 minutes to identify the optimal configuration of the N4 filter for one image.

4. User Manual

a. Installation/configuration instructions (only for downloadable tools)

Not applicable.

b. Usage instructions

The tool is dockerized.

1. Download the latest version of the docker image (image_batch_n4filter_v1.7.tar)
2. Load the docker image by running the following command (assuming you are in the same directory as the tar file):
   - udocker load -i image_batch_n4filter_v1.7.tar
3. Run the following command in order to create a container and instantiate the docker image:
   - udocker run --rm

     -v "your_input_path:/home/chaimeleon/datasets"

     -v "your_output_path:/home/chaimeleon/persistent-home"

     image_batch_n4filter:1.7

     [-h] [-i] [-N] [-t T] [-s S] [-f F] [-l l] [-m] [-c] [-P]

where *your_input_path* is the path that contains the folders with the original DICOM image of each patient

your_output_path is the path where the N4 filtered image of each patient will be saved

available arguments:

-h, --help: show this help message and exit

-i, --interactive: Execution in interactive mode

-N, --n4filter: Performs N4 bias field correction method

-t T, --threshold T: Convergence threshold

-s S, --shrinkFactor S: Shrink factor

-f F, --fittingLevel F: Fitting level

-I I, --Iterations I: Number of iterations

-m, --masks: If specified, the N4 algorithm uses masks

-c, --custom-masks: the path that contains the corresponding DICOM mask of the prostate gland of each patient. If specified, custom masks are used. If not specified, the masks will be extracted automatically by the algorithm

-P, --pipeline: Apply the whole pipeline to identify the optimal N4 configuration

The two main options are:

1) Apply N4 filter to image/images, by specifying -N

2) Find the optimal N4 configuration, by specifying -P

c. Additional considerations : Input/output description, if any preprocessing is needed, mandatory/optional data, cases in which the tool should not be used

Input/Output description:

Input : The input of the tool is a path with the dataset. The dataset should contain raw unnormalized images, which should be in DICOM format. In each dataset directory, an index.json file should be contained in order to walk through the contents of the dataset.

Examples of the required format of the input path:

```
-- patient_level (folder)
   -- study_level (folder)
      -- series level (folder)
         -- DICOM files (files)
…
-- index.json (file)
```

Output : For the first functionality (apply N4 filter), the output is the N4 filtered images, which are saved to a path specified by the user with the same format. For each series, a folder will be created and the N4 filtered image in DICOM format will be stored within the folder. For the second functionality (identify optimal configuration), a text or excel file containing the optimal configuration(s) is saved to a path specified

by the user.

No preprocessing is needed.

Mandatory/optional data: The original T2W MR image for each patient is required to run the tool.

Cases in which the tool should not be used: The tool should not be used in any organ/anatomy other than prostate. Furthermore, the tool should not be used in any sequence other than T2W. The tool is developed only for T2W MR axial prostate images.

5. Integration tests : Description of tests for assessing the correct integration of the tool

Tests were performed in order to ensure the proper integration of the tool in the platform.

6. Results of non-functional tests

Not applicable.