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Cardiac image analyser

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Executive Summary

In this deliverable, EuCanSHare presents the *Cardiac Image Analyzer*, the first open-source image analysis platform for cardiac magnetic resonance images (CMR). Automated CMR analysis is of paramount importance for accurate disease diagnosis and risk stratification. Adequate tools to perform the essential steps of a typical cardiac image analysis pipeline were developed by the University of Barcelona (UB). The tools were subsequently incorporated into the Virtual Research Environment (VRE) of euCanSHare, a platform developed by the Barcelona Supercomputing Center (BSC). The tools are offered as cloud-based services to the users, free of any charge. The deliverable is the series of open-source software/tools that comprise the euCanSHare *Cardiac Image Analyser* implemented in the VRE. The present document provides a description of the developed tools and their usage. The platform will be tested during 2020-2021 and any necessary adaptations according to the users' needs will be performed.

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Acronyms

CMR: Cardiac magnetic resonance

VRE: Virtual Research Environment

LV: Left ventricle

RV: Right ventricle

MYO: LV myocardium

DICOM: Digital Imaging and Communication On Medicine

NIFTI: Neuroimaging Informatics Technology Initiative

ES: End-systole

ED: End-diastole

3D: Three dimensions

4D: Four dimensions

UB: University of Barcelona

BSC: Barcelona Supercomputing Center

1. General objectives and overview of the offered solution

Cardiac magnetic resonance (CMR) is the reference modality for the assessment of heart function and structure. Traditionally, the analysis of CMR images is performed manually or in a semi-automatic way. This process is tedious, time-consuming, while it is prone to human errors. Moreover, the analysis is limited to a small number of parameters, such as ejection fraction and ventricular volumes, that can be extracted by current available means. To fully exploit the rich information present in CMR images and, thus, improve on-time disease diagnosis and risk stratification, fully automated CMR analysis tools are essential. Towards this aim, euCanSHare delivers the *Cardiac Image Analyser,* a series of tools enabling automated CMR analysis.

The euCanSHare *Cardiac Image Analyser* allows the user to automatically extract regions of interest (ROI) from CMR images, avoiding the need for any manual delineation. Subsequently, using the extracted ROI and the corresponding CMR, the user can obtain a high number of quantitative parameters, i.e. radiomics, to assess different aspects of the heart structure and function. Furthermore, the *Cardiac Image Analyser* offers the opportunity to convert between different medical image file formats. Lastly, the output of the *Cardiac Image Analyser* is envisioned to be used in conjunction with the *Machine learning toolbox (D4.5, UB, M36)* to build models that automatically distinguish between patients and healthy participants or different pathologies using state-of-the-art machine learning algorithms. An overview of a typical workflow involving CMR analysis to achieve diagnosis/risk stratification is provided in Figure 1. Thanks to the tools developed within euCanSHare, including the *Cardiac Image Analyser,* the platform's users will be able to apply such complete workflows to their data.

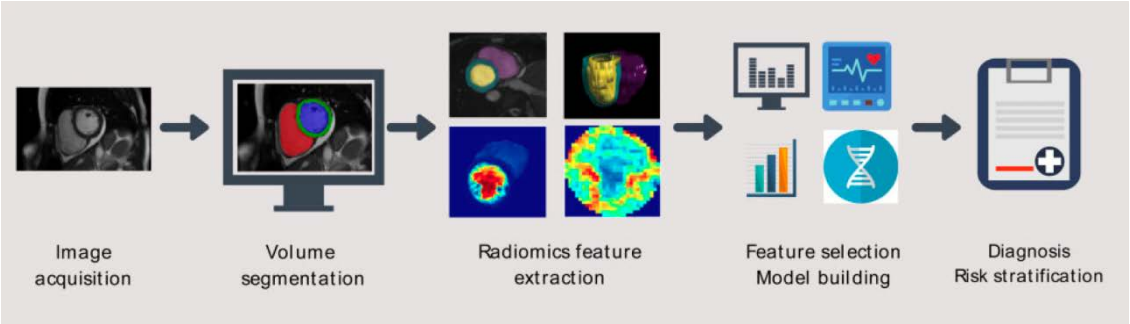

Figure 1: Overview of a typical workflow involving CMR analysis for model building with the aim of performing diagnosis/risk stratification. Figure reproduced from (Raisi-Estabragh, et al., 2020).

1. Overview of the components of the Cardiac Image Analyzer

To address the above steps, the *Cardiac Image Analyser* implemented in the VRE comprises of the following tools:

1. **DICOM 2 NIFTI Converter**: The tool is designed to convert CMR files from DICOM (Digital Imaging and Communication On Medicine) to NIFTI (Neuroimaging Informatics Technology Initiative) format in order to reduce storage requirements and facilitate subsequent analysis.
2. **Segmentation tool**: Automatic delineation/extraction of the ROI to study: (i) left ventricle (LV), (ii) right ventricle (RV), and (iii) LV myocardium (MYO).
3. **Radiomics analysis tool**: Extraction of a high number of quantitative features to characterize shape, intensity and texture of the ROI, known as radiomics.

Figure 2 provides an overview of the current state of the VRE homepage and the tools offered.

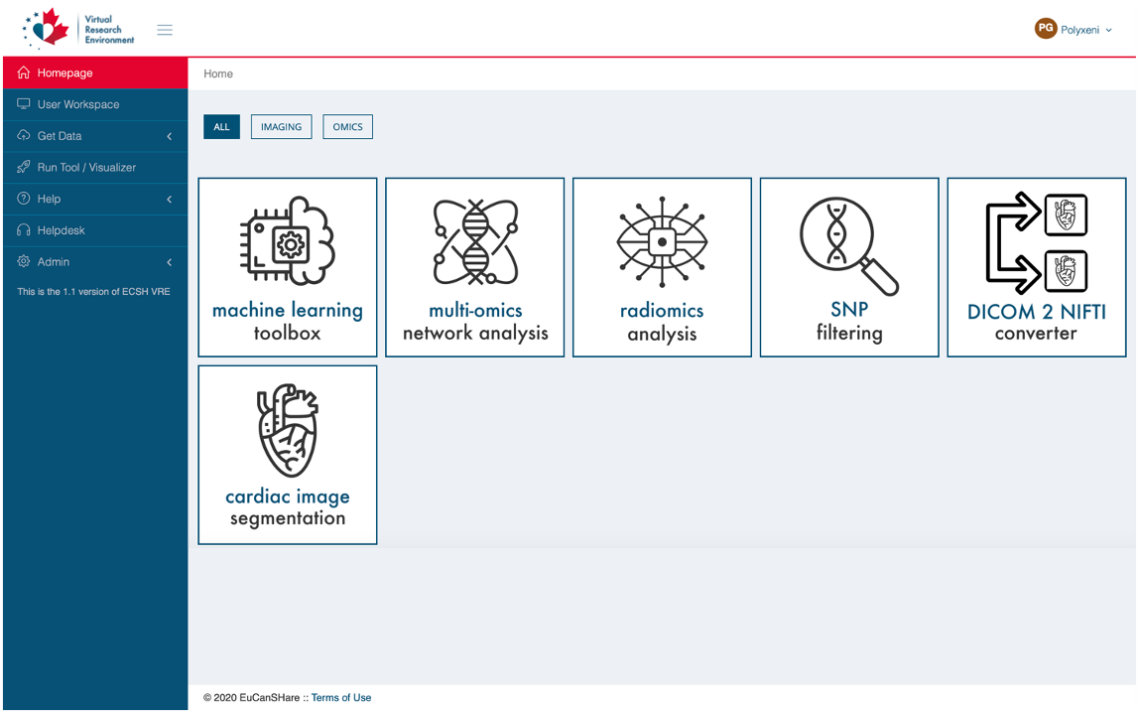

Figure 2: Homepage of the VRE. In this page, the available components of the Cardiac Image Analyzer (DICOM 2 NIFTI converter, cardiac image segmentation tool and radiomics analysis tool) are listed and can be assessed. Other available or under development tools can also been viewed.

The tools can be assessed by (i) the homepage as shown in Figure 2, (ii) the "User workspace" tab (Figure 3) if the appropriate file types are chosen, i.e. the file types that each tool accepts as input, and (iii) the "*Run Tool/Visualizer"* tab (https://vre.eucanshare.bsc.es/vre/launch/) (Figure 4). Each tool has its own front page where it can be configured (Figure 6, Figure 7 and Figure 9). Once the user provides the adequate input and presses the ¨Compute¨ button, he/she is redirected to the "User Workspace". On this page, it is possible to monitor the job until it finishes. When the job finishes, the result(s) appears under the given experiment name and can be downloaded from here.

It should be noted that in the "User workspace" page, apart from results, the files (e.g. CMR, segmentations, .csv etc) that the user has manually uploaded or imported from EuroBioimaging (https://www.eurobioimaging.eu/about-us/about-eubi) are also listed. These files can be downloaded or selected as inputs to the different tools. The uploading and/or importing process is performed in the "Get data" tab (Figure 5). The user can manually upload files to the VRE by dragging and dropping. Alternatively, he/she can import data from the EuroBioimaging to which he/she has been previously granted access.

A detailed description of the tools is provided in the following sections. In addition, this information regarding the tools and how to use them is provided in the documentation page of the VRE to facilitate the users.

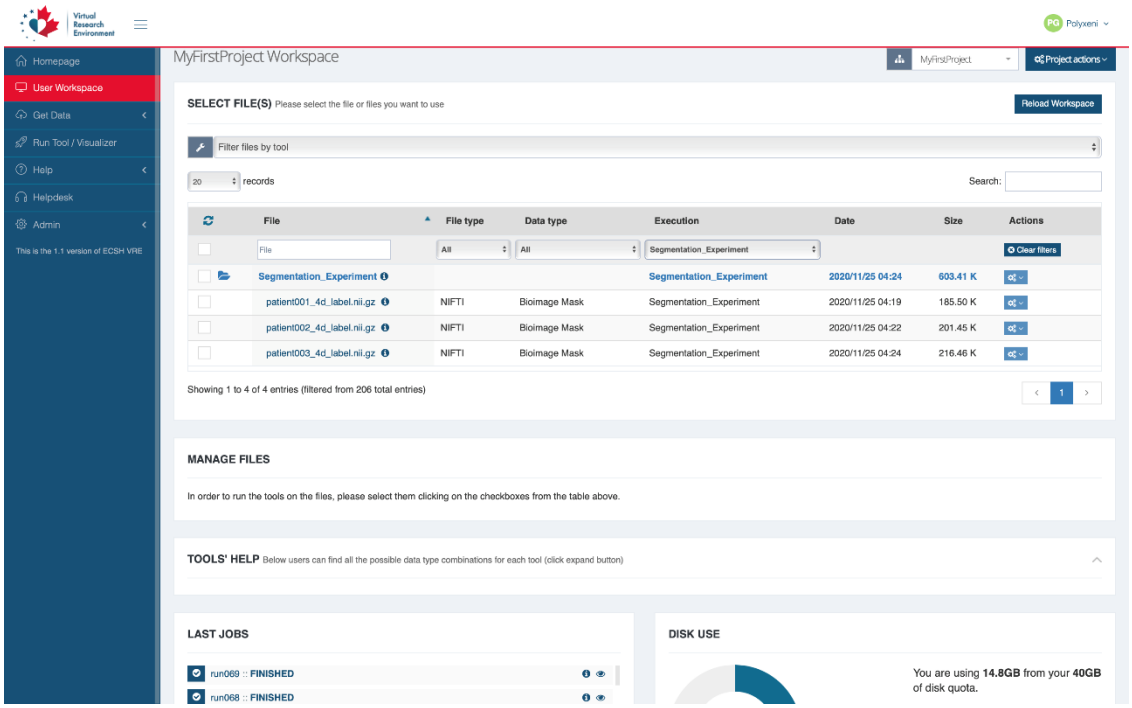

Figure 3: The "User workspace" tab. In this page the user can find the data he was uploaded/imported and the results of his/her experiments. In addition, he/she can select files and see available tools to process them. Lastly, he/she can monitor the running jobs.

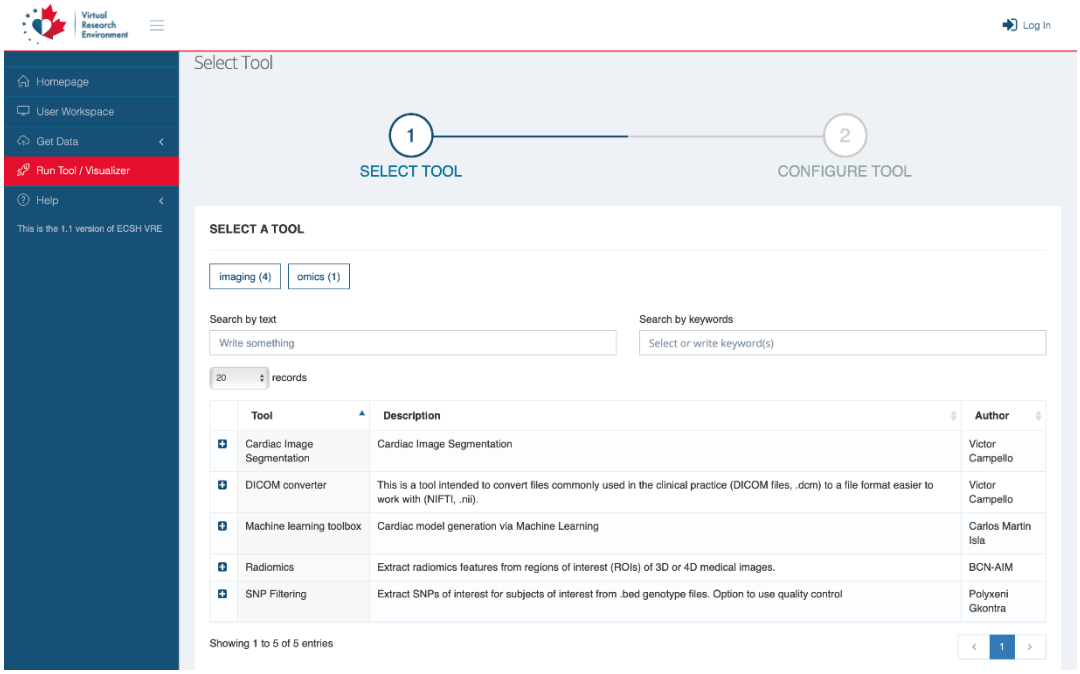

Figure 4: The Run tool/visualizer tab of the VRE. In this page, the available tools are listed and can be assessed, including those comprising the Cardiac Image Analyser.

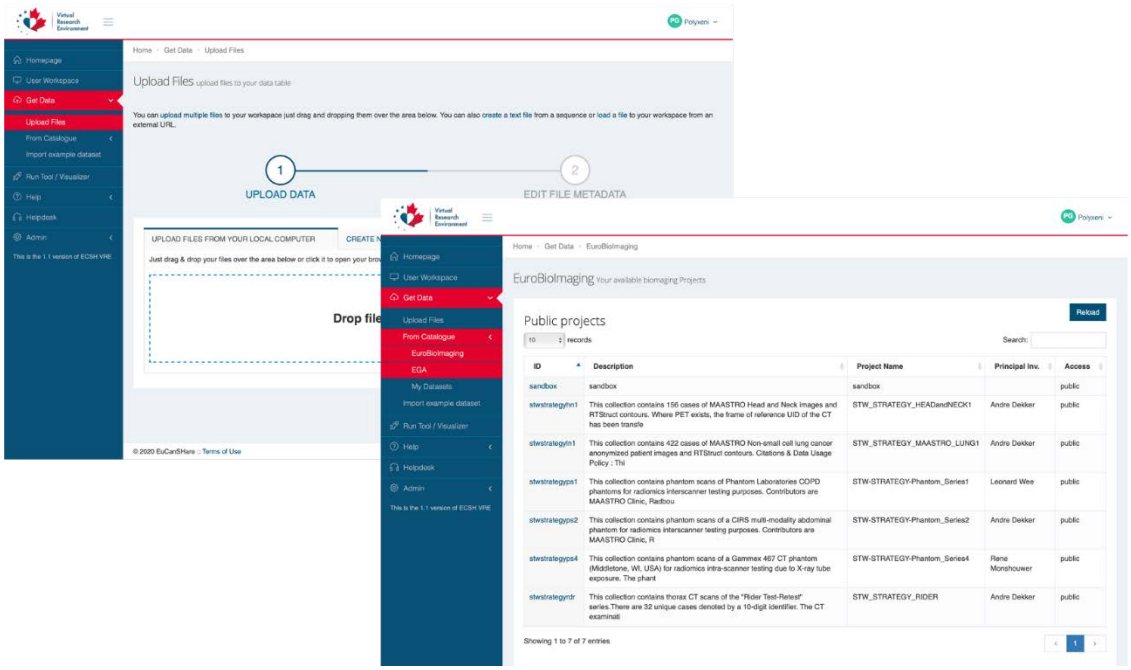

Figure 5: The "Get data" tab. In this page, the user can upload files by dragging and dropping (back figure) or import data from EuroBioimaging that he/she found through the euCanSHare catalogue and to which he/she has been granted assess.

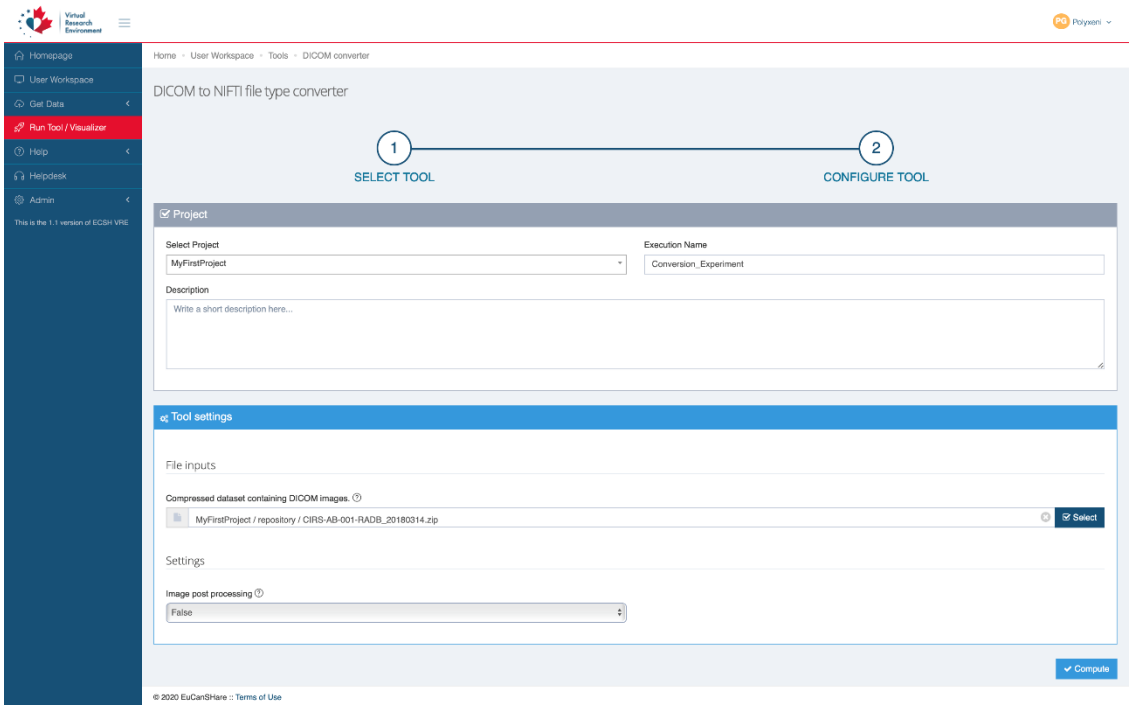

Figure 6: Main page and configuration settings for the DICOM 2 NIFTI converter. The zipped dataset must be selected and the option for the final image post-processing must be defined prior to its execution.

2. DICOM 2 NIFTI converter tool

In clinical practice, the common image format used is DICOM. In this format, each two-dimensional image is saved in a separate file and the information to build the whole study for a patient is contained in the file header. This configuration makes it difficult to analyse large patient cohorts where many files would be needed to move around. The NIFTI format is

designed to collect all images from a scan in one unique file and to reduce its size with dynamic compression, thus reducing up to ten times the dataset size.

Towards benefitting from these properties, a conversion tool has been implemented. The tool takes as input entire datasets with several studies and parses all files to extract NIFTI images. The output files are also enriched with metadata extracted from the original files header such as the organ scanned, the image modality or the scanner manufacturer.

2.1 Tool overview

Figure 6 shows the front page of the DICOM 2 NIFTI converter tool. Once the user selects the appropriate input and settings, he/she can run the tool by pressing "Compute" to perform the conversion.

2.1.1 Input

As input, the user must provide:

1. A **zip file** containing the scans that the user wants to convert. More in detail, this file contains:
    1. **DICOM files** for the patients scans.
    2. An optional file (in cvi42ws or cvi42wsx format) with **manual delineations** of important regions as detailed by an expert. This format follows the structure as provided by Circle cvi42 software (Circle Cardiovascular Imaging Inc., Calgary, Alberta, Canada).

    The input file should have been uploaded to the VRE or imported through EuroBioimaging using the "Get data" page, so that it is already available in the "User workspace", as detailed in the previous section.
2. Whether he/she wants the tool to post-process the resulting image. By default, this option is not considered. When the user selects this option, the tool chooses the most recent slices for each slice position, substituting therefore the repeated images.

2.1.2 Output

A NIFTI file with the CMR and adequate metadata is produced.

3 Segmentation tool

The first step after a successful acquisition of a short-axis CMR image is to delineate the contours for the different relevant areas in the functional assessment of the heart. The main regions considered in CMR are: (1) the left ventricle cavity (LV), (2) the right ventricle cavity (RV) and (3) the left ventricle myocardium (MYO). The *Cardiac Image Analyser* segmentation tool automates the delineation process by predicting these regions and generating a file containing this information.

3.1 Tool overview

Figure 7 shows the front page of the segmentation tool.

3.1.1 Input

As input, the user must provide the following arguments:

1. A collection of **NIFTI files/images** that need to be segmented. These may be static images (3 dimensions (3D)) or images containing an entire beat (4 dimensions (4D) – 3D

plus time). When the input images are 4D, the tool also estimates the location of the end-diastolic time frame (ED - time frame of maximum dilation) and of the end-systolic time frame (ES - time frame of maximum compression).

2. The **deep learning model** to use. The user will be able to choose different models from a dropdown menu, depending on the details of the input dataset. For example, if the user has a collection of studies from a Canon scanner, he/she would be able to select the model trained on multi-centre data as those available from the M&M Challenge (https://www.ub.edu/mnms/) organised recently by UB. Such models are expected to achieve high accuracy. Currently, the model selection is restricted to one U-net model (Ronneberger, Fischer, & Brox, 2015) and will be extended to a wide diversity of models, including robust models trained on multi-centre and multi-vendor studies.

3.1.2 Output

A NIFTI file with the segmentation mask of the ROI is produced per input CMR. The output file contains in its metadata the ES, ED frame and the correspondence between segmentation labels and ROI. In Figure 3, we can observe the three masks produced when running the tool for the three input CMR as shown in Figure 7.

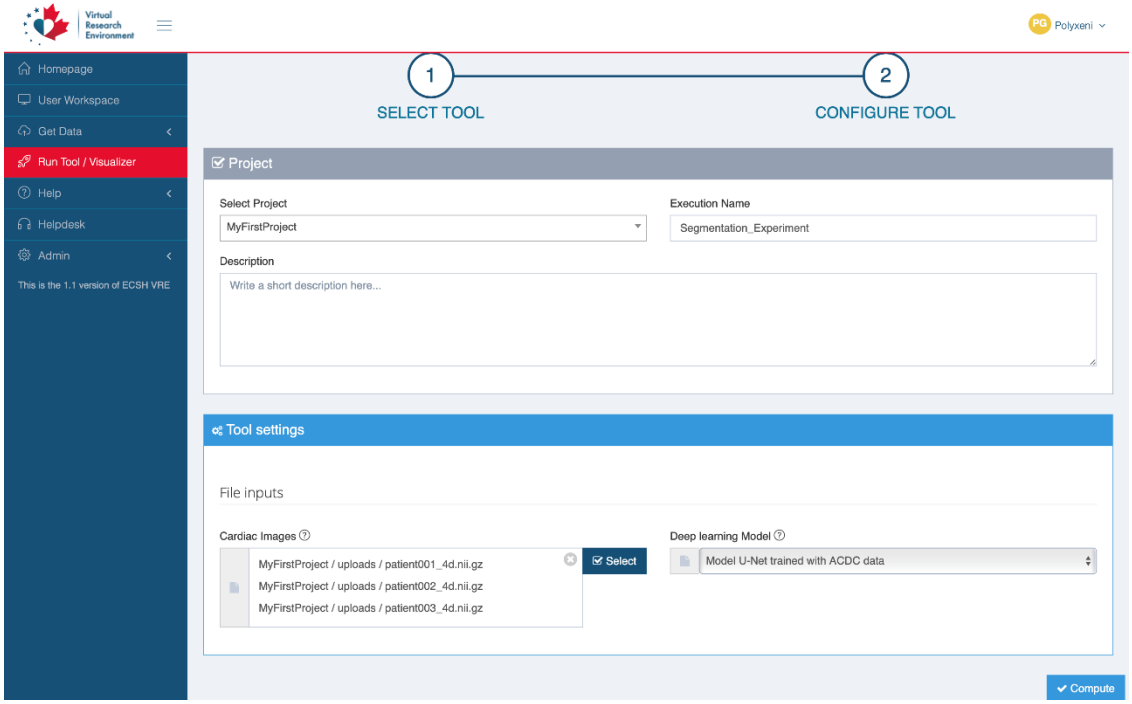

Figure 7: Main page and configuration settings of the Segmentation tool. A collection of NIFTI images must be attached and a deep learning model selected from the dropdown menu on the right.

4 Radiomics analysis tool

Following successful applications in oncology, radiomics analysis of CMR images has recently emerged as a novel image analysis technique for the assessment of the heart (Raisi-Estabragh, et al., 2020). The approach involves the extraction of a high number of features that quantify major properties of the structures of interest that could not be acquired manually or in a semi-automatic way.

The radiomics analysis tool of the euCanSHare *Cardiac Image Analyzer* has been based in the open-source python-based PyRadiomics platform version 2.2.0 and is developed in python. In

total, 105 features per ROI are extracted. The features can be divided in three categories (Figure 9):

1. **Shape radiomics**: features of this category characterize the morphology, size and geometry of the ROI. 13 features within this category are calculated for every ROI: volume, surface area, surface area to volume ratio, sphericity, maximum 3D diameter, maximum 2D diameter (slice), maximum 2D diameter (column), maximum 2D diameter (row), major axis length, minor axis length, least axis length, elongation, flatness.
2. **Intensity radiomics**: features that quantify the CMR intensity. 18 features are extracted for every ROI: energy, total energy, entropy, minimum, 10th Percentile, 90th Percentile, maximum, mean, median, interquartile range, range, mean absolute deviation, robust mean absolute deviation, root mean squared, skewness, kurtosis, variance, uniformity.
3. **Texture radiomics**: The texture features quantify relations in intensities between neighbouring voxels. In total, 74 features are extracted using five different matrices: grey-level co-occurrence matrix (GLCM, 23 features), grey level run-length matrix (GLRLM, 16 features), grey-level size-zone matrix (GLSZM, 16 features), neighbouring grey tone difference matrix (NGTDM, 5 features), and grey-level dependence matrix (GLDM, 14 features).

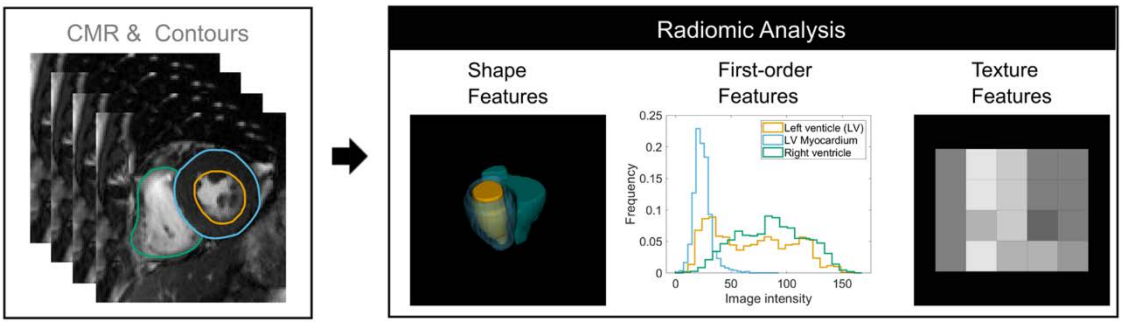

Figure 8: Overview of the three types of radiomics features extracted from CMR images. Figure reproduced from (Raisi-Estabragh, Harvey, Neubauer, & Petersen, 2020).

4.1 Tool overview

Figure 9 shows the front page of the radiomics analysis tool. The produced output file will be used in the future as input to the *Machine Learning Toolbox* to perform diagnosis and identify the most informative features for the task at hand.

4.1.1 Input

The tool accepts as input:

1. **3D/4D short-axis CMR in NIFTI format**: CMR to be used for radiomics calculation. The CMR file can be (i) 4D, i.e. CMR that contains multiple cardiac cycle phases, one 3D image per phase, or (ii) 3D, i.e CMR of only one cardiac phase. In the case of 4D CMR, radiomics are calculated for ES and ED phases.
2. **Segmentation mask in NIFTI format:** 4D or 3D depending on whether the CMR provided is 4D or 3D respectively. One segmentation per CMR should be provided.
3. **CSV with information regarding the masks (optional):** a .csv file that contains the information regarding (1) the ES and ED frames, and (2) the correspondence between ROI and the labels present in the segmentation mask. The .csv should contain at least the following columns: (1) id: CMR filename, (2) ES: frame of 4D CMR corresponding to end-systole, (3) ED: frame of 4D CMR corresponding to end-diastole, (4) LV: mask label corresponding to left ventricle, (5) MYO: mask label corresponding to myocardium, (6)

RV: mask label corresponding to right ventricle. If the CMR is 3D, the user can leave the columns ED, ES empty or add any random value. It should be noted that if the segmentations masks were created using the *Cardiac Image Analyser* segmentation tool, the required information is obtained automatically from the segmentation mask file metadata and the .csv is not necessary.

4. **Bin width (Optional)**: parameter for grey value discretization necessary used for radiomics calculation. If not specified by the user, the default value 25 (grey levels) is used.

It is worth mentioning that an unlimited number of CMRs and segmentations can be passed at the same time to the tool. The segmentation masks filename must be the same as that of the corresponding CMR with the addition of the suffix "_label".

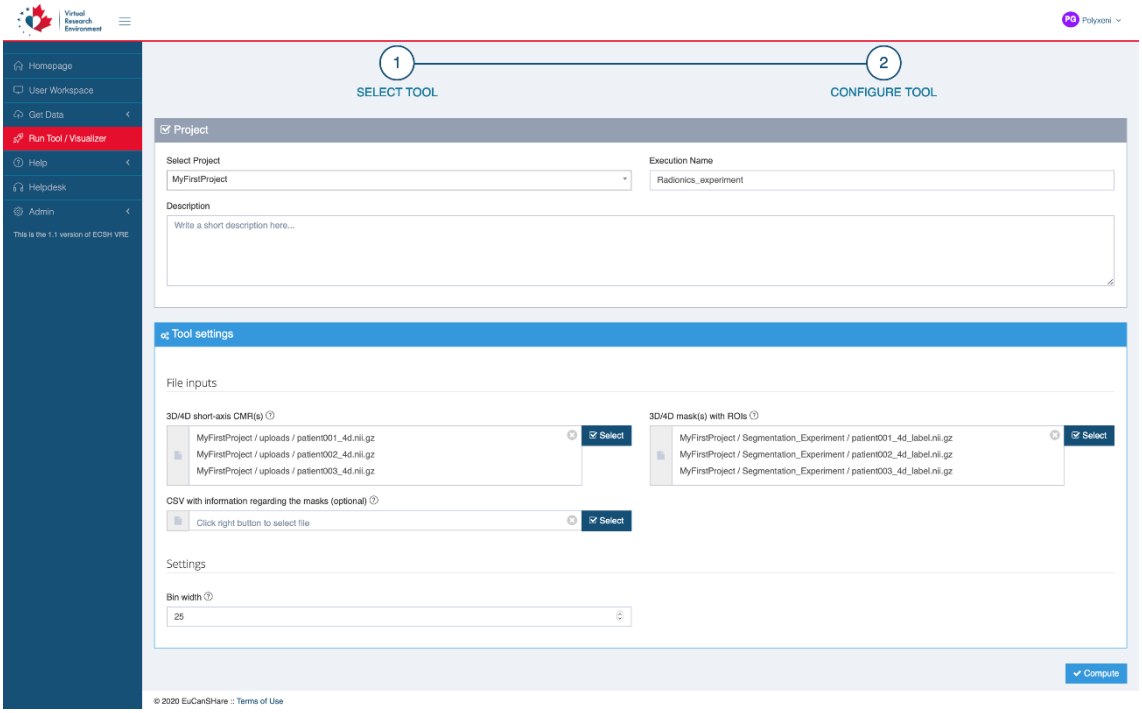

Figure 9: Main page and configuration settings of the radiomics tool. 3D/4D short-axis CMR(s) along with the corresponding segmentation mask(s) with different ROI can be selected to extract radiomics for every ROI.

4.1.2 Output

The output of the *Radiomics Tool* is a .csv file. Each row corresponds to a participant for which the CMR and ROI has been provided and each column to a radiomic feature. The features names are formatted as feature_name_region_phase, where phase is "ES" or "ED" in the case of 4D CMR otherwise is "", and region is one of the following: "LV", "RV", "MYO".

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5 Bibliography

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