A European Cancer Image Platform Linked to Biological and Health Data for Next-Generation Artificial Intelligence and Precision Medicine in Oncology

Deliverable D6.3: Adapted In-silico platform for EuCanImage

Reference	D6.3_ EuCanImage_UM_v1
Lead Beneficiary	UM
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Dissemination level	Public
Type	Report
Official Delivery Date	31 March 2023
Date of validation of the WP leader	30 March 2023
Date of validation by the Project Coordinator	30 March 2023
Project Coordinator Signature	

1. Version log

Issue Date	Version	Involved	Comments
28/03/2023	v0.1	Zohaib Salahuddin, Nuwan Udawatte	First Draft
29/03/2023	v0.2	Henry Woodruff, Philippe Lambin	Feedback
30/03/2023	V1	Anais Emelie & Karim Lekadir	Revised and corrected final version.

2. Executive Summary

In recent years, the use of artificial intelligence tools for medical imaging analysis has shown significant potential in improving the accuracy and efficiency of diagnoses. However, it can take years to carry out prospective validation of the developed AI tools in the clinical scenario and quantitatively determine the added value of these tools in clinical practice. As an alternative, virtual in-silico trials can be used to carry out prospective validation using available retrospective data. In this deliverable, we report the detailed functionality and specifics of the first version of the in-silico platform as a web application. After analysing and discussing with clinicians and AI researchers, it was determined that Volview's interface and capabilities are better suited for EuCanImage as compared to OpenCVT. As a result, it was adapted to develop an in-silico platform. This in-silico platform will be used to carry out three types of trials: a trial of clinical performance, a trial of AI vs. a combination of AI and physician, and a trial of AI vs. a combination of AI, physician, and explanations.

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Acronyms

Name	Abbreviation
In-silico trial platform	IST
Machine Learning	ML
Computed Tomography	CT

1 Introduction

Medical imaging plays a critical role in the diagnosis and treatment of a wide range of diseases and conditions. In recent years, the use of artificial intelligence (AI) tools for medical imaging analysis has shown significant potential in improving the accuracy and efficiency of diagnoses. However, it is difficult to carry out prospective validation of the developed AI tools in the clinic, and it can take many years to determine the added value of AI tools in the clinic. Alternatively, in-silico trials can be carried out using retrospective data in a prospective fashion to benchmark clinical performance as well as measure the added value of the AI tool in quantitative terms.

The in-silico trial for AI tool's prospective validation is as rigorous as a real-life clinical trial. It needs to be pre-registered on online platforms such as clinicaltrials.gov and osf.io. To avoid exploratory research, question trolling, cherry picking, and HARKing, the in-silico trial should only test an a priori hypothesis that is pre-documented. HARKing leads to irreproducibility or replication crises [1]. A sample size calculation needs to be performed beforehand.

A study published in Nature Communications by Maastricht University conducted a prospective in-silico trial to demonstrate that their proposed method is faster and more reproducible than clinicians for the automated detection and segmentation of non-small lung cancer using computed tomography images [2] This trial was registered on clinicaltrials.gov (NCT04164186). A prospective in-silico trial was also conducted to compare proposed methods with two radiologists and one pulmonologist for idiopathic pulmonary fibrosis and interstitial lung disease classification [3].

Figure 1: (a) The in-silico platform used in [2] for measuring the preference of participants for manual or automatic contour. (b) The in-silico platform used in [3] for comparing the performance of radiologists and pulmonologists for idiopathic pulmonary fibrosis and interstitial lung disease classification.

Figure 1 (a) and (b) show in-silico platforms with limited capability to conduct in-silico trials for different endpoints. These in-silico platforms were improved with better visualization capabilities, integration of non-imaging parameters, incorporation of explanations, and converted into a web application for seamless integration into the EuCanImage platform.

The developed in-silico trial platform will facilitate three types of trials. The two pilot trials will be conducted as indicated in the proposal for diagnostic questions regarding the accuracy and robustness of AI models: a trial of AI vs. physicians and a trial of AI vs. a combination of AI and physician. As the explainability of the AI models is integral for synergistic collaboration between the AI tool and clinicians, an additional clinical trial will be conducted to determine the efficacy of the explainability interface: a trial of AI vs. a combination of AI, physician, and explanations. These in-silico trials will be conducted using real imaging and clinical data as a gold standard and using a mix of real data and synthetic data as a silver standard.

In this document, we describe the various functionalities of the current version of the *in-silico* trial platform. The current version of the *in-silico* platform will be adapted for different use cases in the EuCanImage.

2   In-silico platform

The user interface of this tool has been developed using Vue.js, a JavaScript-based framework that runs entirely on any modern web browser. To interact with non-imaging data, we have used the Python Flask API. Additionally, we have extended an open-source viewer called Volview, which was developed by Kitware [4] and is also based on Vue.js.

This is a simple tool where the user only needs to log in and set the main folder structure path. Figure 2 shows the folder structure that needs to be populated with the dataset. This can be done automatically from XNAT or set manually for local use.
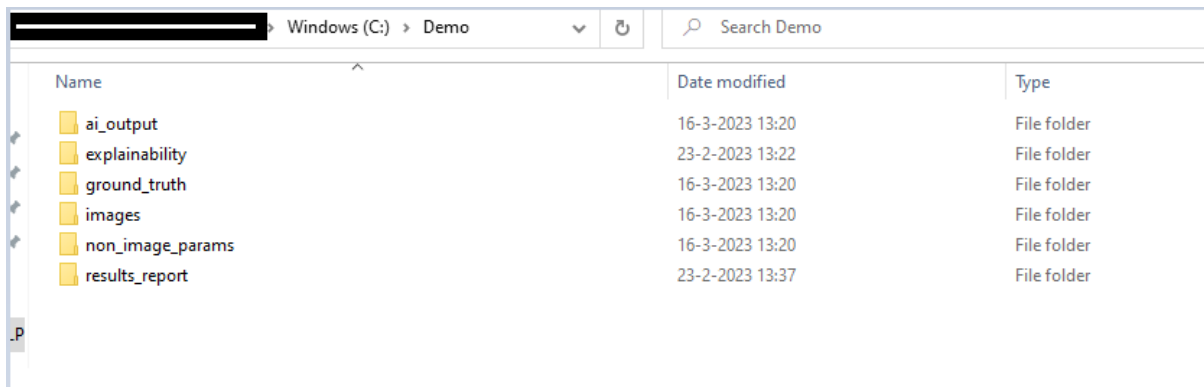

Name	Date modified	Type
ai_output	16-3-2023 13:20	File folder
explainability	23-2-2023 13:22	File folder
ground_truth	16-3-2023 13:20	File folder
images	16-3-2023 13:20	File folder
non_image_params	16-3-2023 13:20	File folder
results_report	23-2-2023 13:37	File folder

Figure 2: Arrangement of the folder structure for using the tool.

2.1 Type of In-silico Trials

The current version of IST features a login page that users encounter when accessing the tool. Once the login is successful, users can choose from three available trial options: evaluating the performance of clinicians, evaluating the performance of the combination of AI tool output and physician, and evaluating the performance of the combination of AI tool, clinicians, and explainability interface. Figure 3 shows the interface that users can use to make one of these three choices. Depending on the user's selection, the IST tool will display a different interface.

Figure 3: User will be redirected to the above screen after a successful login. Here the user has three options to choose from. Depending on the choice the user made, the tool will provide the appropriate viewer.

2.1.1 Clinicians Only

Figure 4 displays the clinical-only interface. In Figure 4(a), the red box indicates the non-imaging parameters for the particular image, while the green box shows the location where the doctor selects the appropriate option for the diagnostic question.
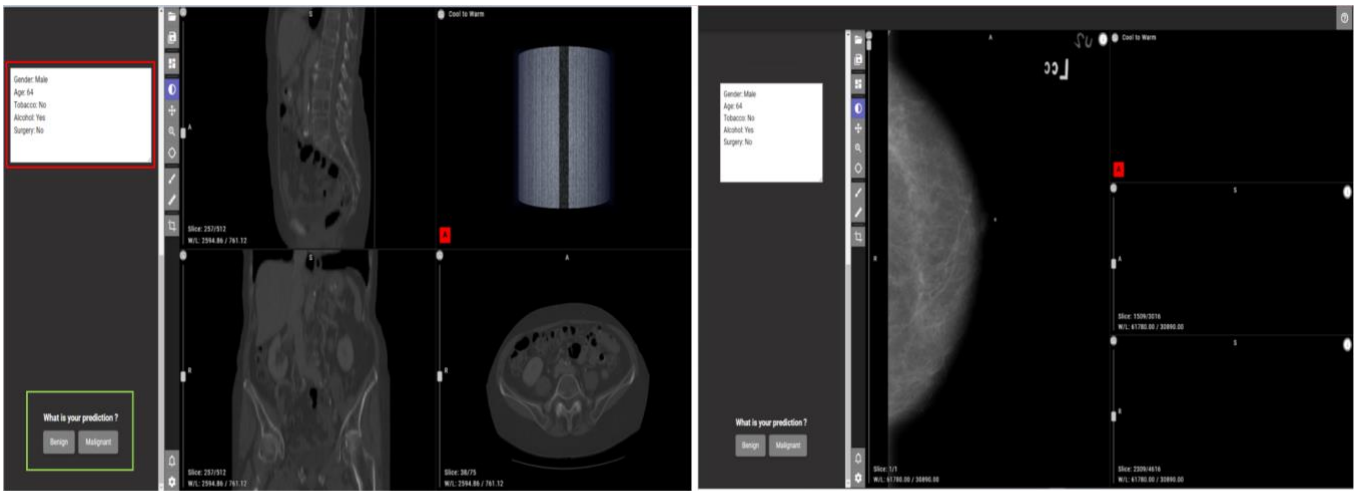
(a)   (b)

Figure 4: Above screens are from the "Clinical Only" view. The viewer supports many different file types such as nfti files,DICOM files etc. Image (a) is a nifti image and (b) is a DICOM file.

2.1.2 Clinicians + AI

Figure 5 displays the AI + Clinicians interface, which allows clinicians to view the output of the AI tool, examine the image, and then make their final choice.
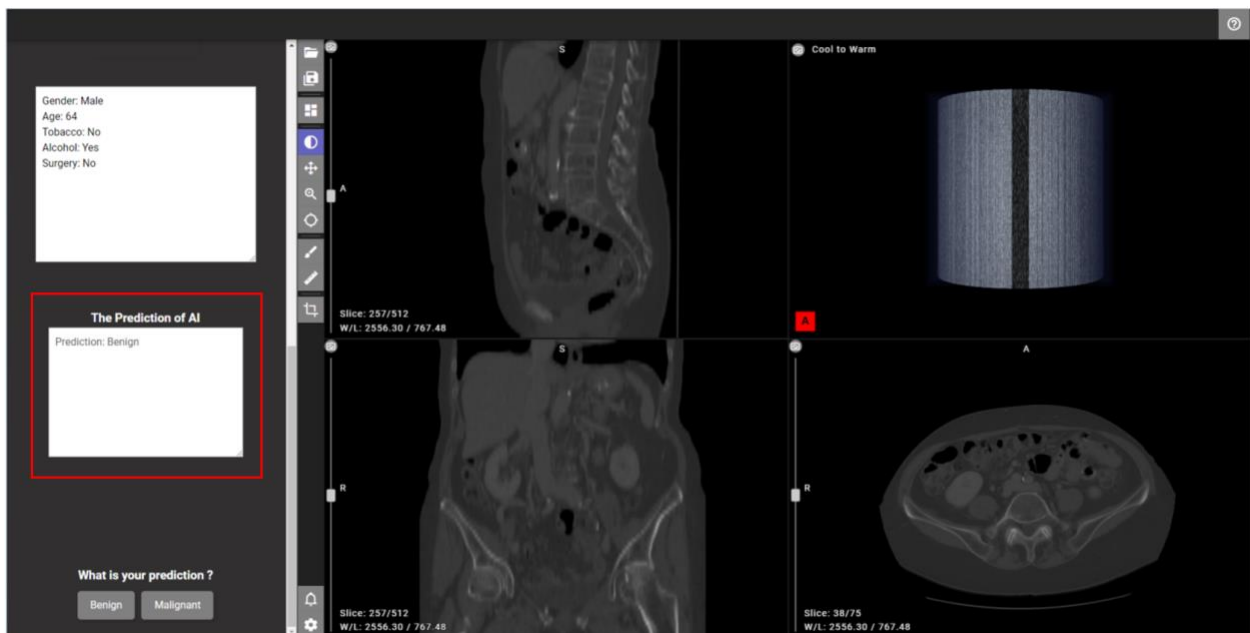

Figure 5: User will be redirected to the above screen when clicked on "AI + Clinical". In this screen there is an additional text area (outlined in red box)to show the AI prediction. The users can get an insight on the AI prediction before making their decision.

2.1.3 Clinicians + AI + Explainability

Figure 6 displays the interface that users will see if they select the "AI + Clinicians + Explainability" option. In comparison to the "AI tool + Clinicians" option, IST displays an additional button for viewing explainability. Once clicked, a new window opens, showing explanations for that particular image.
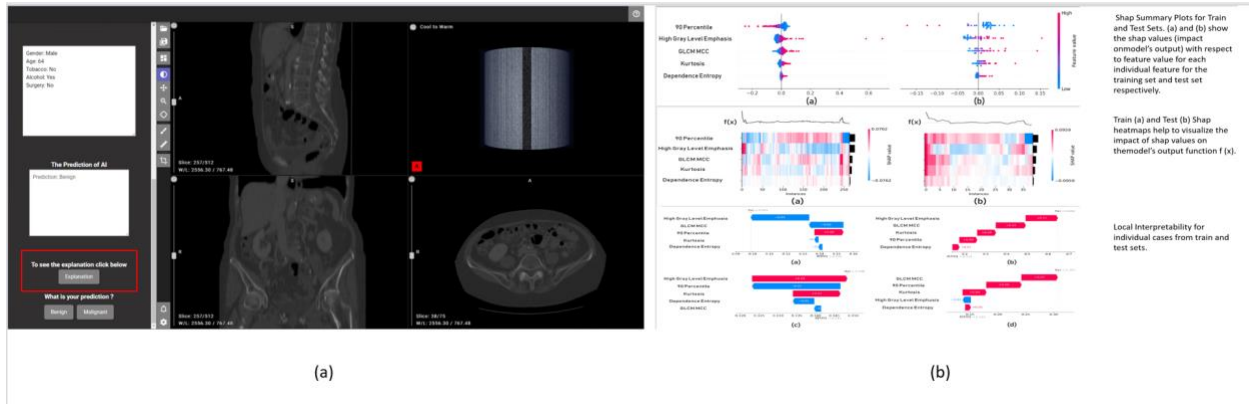

Figure 6: User will be redirected to the above screen(a) when clicked on "AI + Clinical+Explainability". In this screen there is an additional button, when clicked a new tab will open and display the screen(b). These explanations are saved in the folder structure mentioned in Figure 2.

2.2 Functionalities for Visualization

The in-silico platform inherits strong visualization capabilities from the VolView web viewer. Figure 7 demonstrates the different buttons available for interacting with medical images, and we describe some of the visualization capabilities that are available to clinicians.

Figure 7: This is the tool strip available in the viewer. It has many options and capabilities.

2.2.1 Layout Schemes

Clinicians can select from different layout schemes while interacting with the IST tool, as shown in Figure 8. In Figure 8(a), the axial plane is the primary column, while the coronal, sagittal, and 3D views are displayed in a smaller dimension. However, in Figure 8(b), the IST tool is in quad mode, and all four different views have the same size.
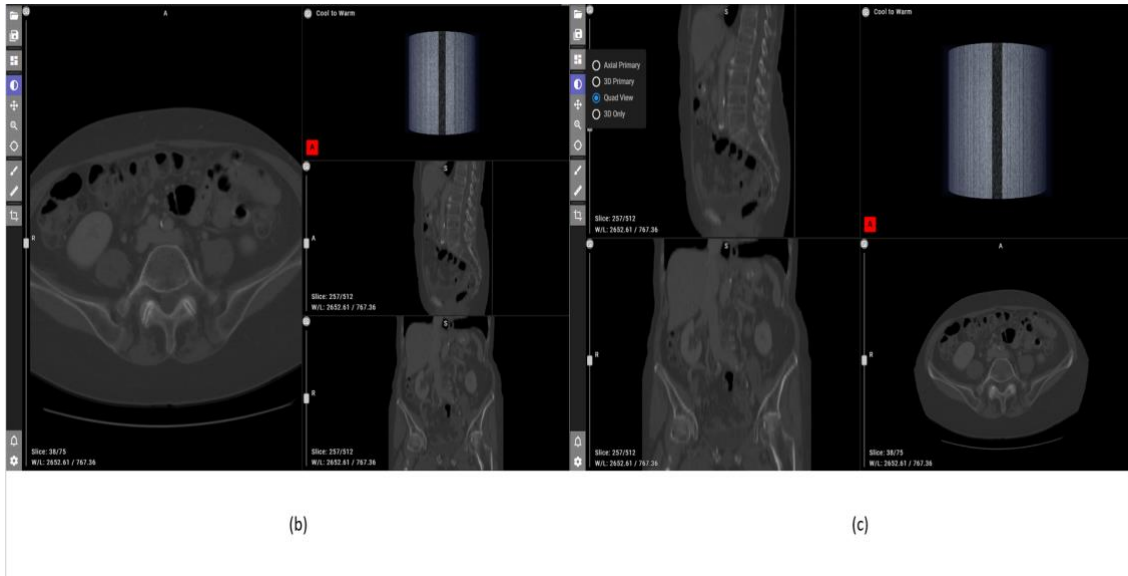

Figure 8: Images (a) and (b) show different layouts for the viewer.

2.2.2 Windows and Levels

Clinicians use different windows for different organs of interest, specifically in computed tomography images. IST has the ability to apply different windows to the images and adjust the levels using the tool in Figure 9(a). Figure 9(a) and (b) demonstrate the effect of using different windows on the images.

(a)
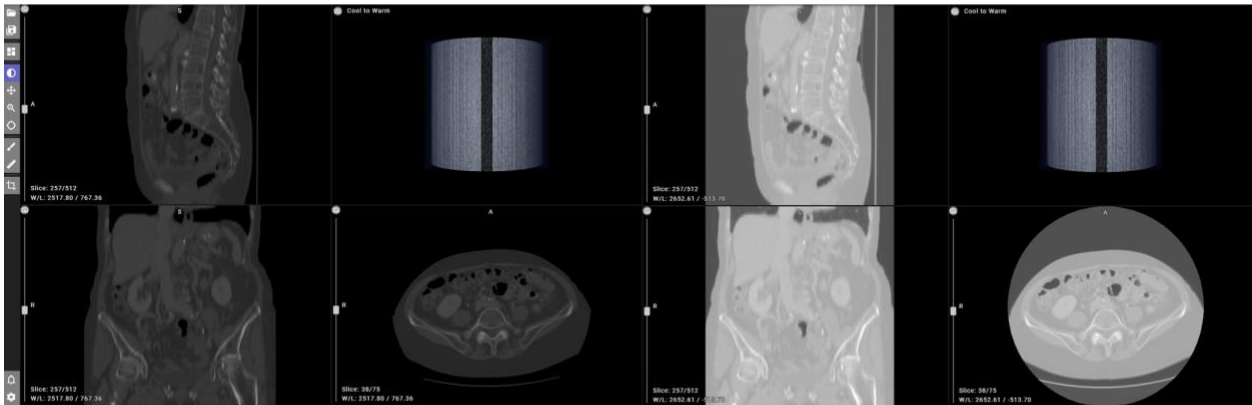
(b)   (c)

Figure 9:Window/Level Controller as shown in (a) and images (b) and (c) shows the different effects on the images. This function helps to change the level(color) of the viewer. Simply after selecting this tool drag your mouse while clicking the left mouse button for the effects.

2.2.3   Zooming

During radiological assessments, clinicians need to zoom into different areas of interest on different views of the images. IST inherits the ability to zoom in on different planes from Volview. Figure 10(a) shows the zoom in/out tool. Figure 10(b) shows the original image, and Figure 10(c) demonstrates how different views can be zoomed in to investigate different areas of the image.

(a)
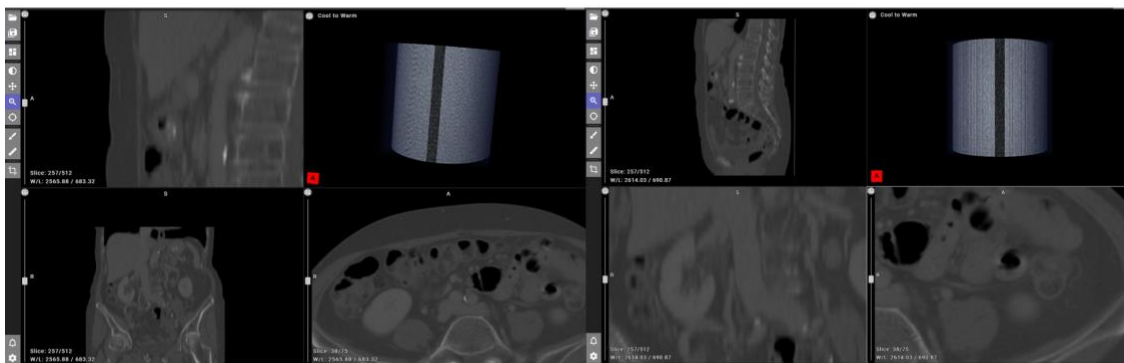
(b)   (c)

Figure 10:Zoom In/Out controller (a). After selecting this functionality the user can zoom in and out of the image. Zoom works separately in each quadrant of the viewer as you can see in the images (b) and (c)

2.2.4 Cross Hair Tool

Figure 11(a) shows the crosshair tool that clinicians can use to investigate the voxel intensity values. The crosshair tool in Figure 11(b) is represented by the yellow line.
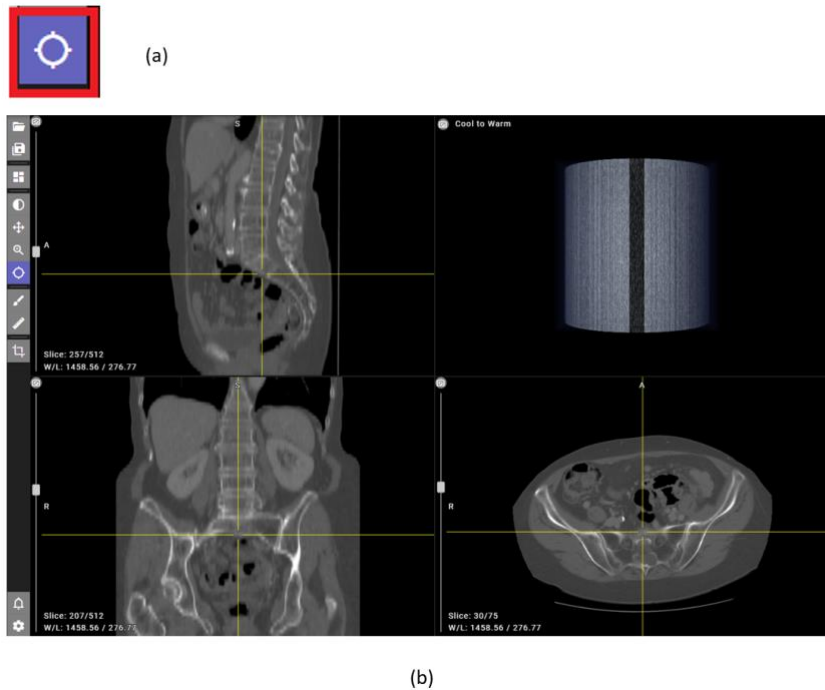

(a)

(b)

Figure 11:Crosshair (a).Using this function user can pinpoint an area of the image and it will indicate that point in each quadrant as shown in image(b)

2.2.5 Paint Brush Tool

The IST platform also supports a paintbrush tool that clinicians can use to make marks on the image during analysis. In the future, it will be investigated whether this paintbrush tool can be used to perform annotations on the IST platform and evaluate inter-observer variability for segmentation tasks among different clinicians.

(a)

(b)

(c)

Figure 12: Annotations (a).Using this functionality user can able to create/draw annotations on the viewer as show in image(c).It is also possible to select a desired color and brush thickness of the lines user want to draw as shown in (b)

2.2.6   Ruler Tool

In some medical imaging tasks, the size of the lesion and the distance from important organs are important clinical variables used during diagnosis. Figure 13(b) shows the ruler tool that can be used to measure the distance between any two points in the axial, coronal, or sagittal planes.

(a)

(b)

Figure 13: Ruler Functionality(a). When the ruler is selected , the left mouse button is used to place and adjust ruler end-markers. This gives the lengths of two selected points in the viewer as shown in (b)

2.3   Results from In-silico trial platform

The IST platform records the time taken by clinicians to arrive at a diagnosis for each image. These three types of trials, with a washout period, will allow benchmarking of the time taken for decision-making and recording of observations made by the clinicians. Figure 14 shows the results from a user who selected diagnoses for five images in a trial. The trial

results can then be fed into the OpenEBench platform from BSC to quantitatively compare the performance of clinicians, clinicians + AI, and clinicians + AI + explainability with the AI tools.

	User	Image ID	Start Time	End Time	Time Taken(s)	Result
	A	B	C	D	E	F
	User1	Image_3	Tue Mar 28 2023 14:04:36 (	Tue Mar 28 2023 14:04:42 GMT	6	Malignant
	User1	Image_14	Tue Mar 28 2023 14:07:00 (	Tue Mar 28 2023 14:07:09 GMT	9	Benign
	User1	Image_2	Tue Mar 28 2023 14:15:10 (	Tue Mar 28 2023 14:18:25 GMT	195	Benign
	User1	Image_19	Tue Mar 28 2023 14:09:16 (	Tue Mar 28 2023 14:10:36 GMT	79	Benign
	User1	Image_7	Tue Mar 28 2023 15:08:26 (	Tue Mar 28 2023 15:10:29 GMT	123	Malignant

Figure 14: Results of the sample use cases that are obtained using the tool.

3   Future Work

The current version of the in-silico trial platform will be adapted and tested for various use cases. Additionally, support for simultaneous visualization of multiple image modalities will be added to the tool. The in-silico platform will also be integrated into the EuCanImage platform.

4   References

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