PapAI

user interface of the diagnostic system

user manual

ver. 2.0, system ver. at: 2023-03-28

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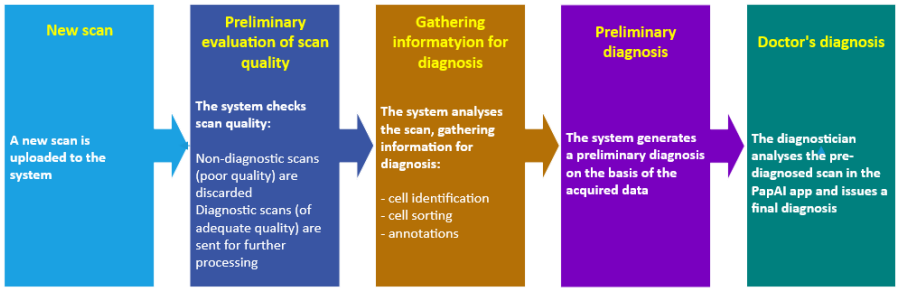
What is PapAI?

The **PapAI** application is part of a digital pathology diagnostic system to automate the process of cervical cancer diagnosis.

PapAI is a user interface, an application used by diagnostic physicians.

Scans of cytological samples, pre-processed by other parts of the system, are transferred to the application: divided into boxes (tiles), with cells containing dysplasia of a certain type marked and described, and a preliminary diagnosis suggested by the system.

PapAI allows the diagnostician to view the scan and all information related to the scan (boxes, annotations) edit them and add new ones. Based on this, the diagnostician gives a final diagnosis - either confirms the system's initial diagnosis or changes it, issuing his own.

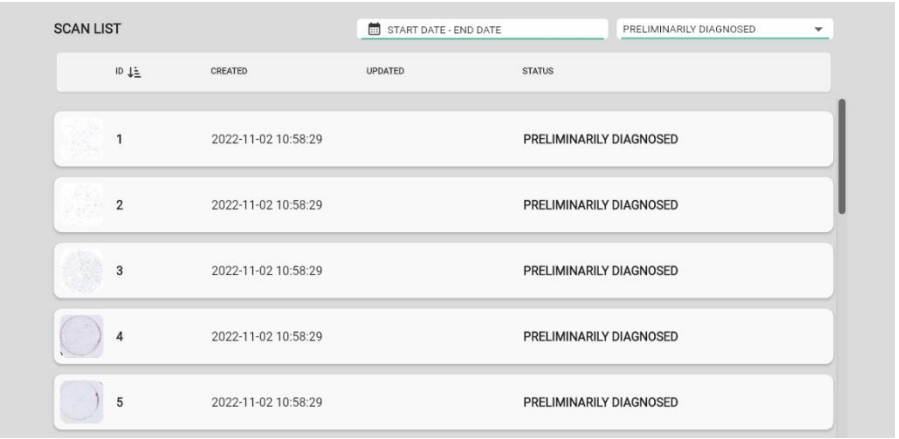


Select a scan

First you need to select the scan you want to work with.

A list of available scans can be found in the **Scan List** window.

By default, the list shows scans with a status of **Preliminarily Diagnosed**, that is, scans with a preliminary diagnosis, issued by the system.

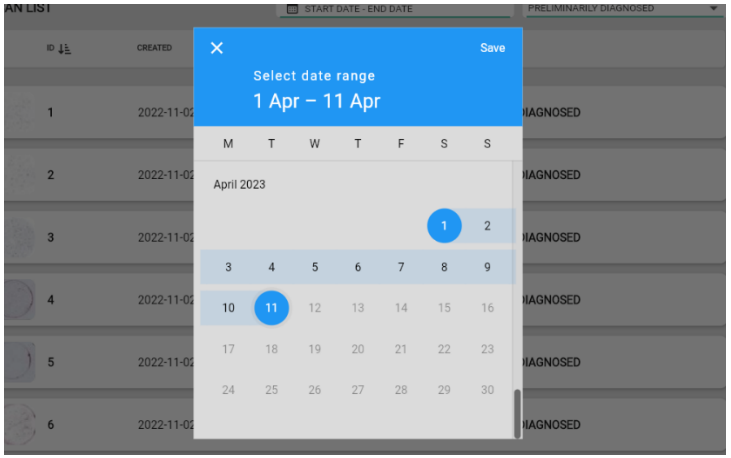


Filter the scans in the list

You can filter the scans in the list **by their creation dates**.

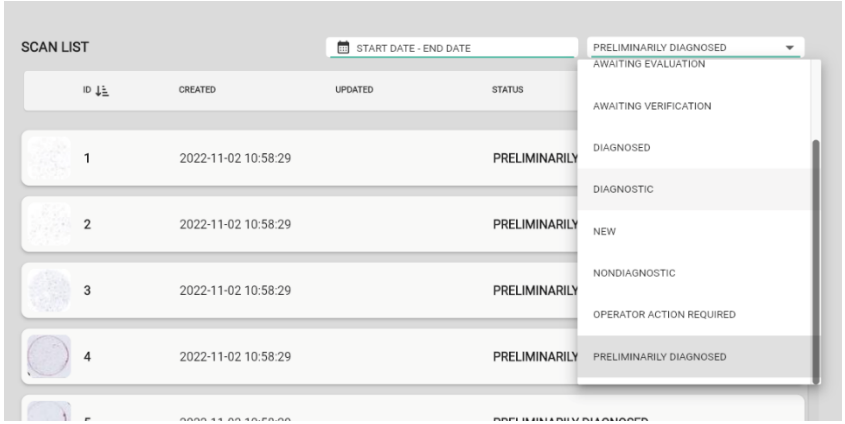
Click the calendar box, visible above the list.

The system will open a calendar where you define a period: its start date and end date. One can go through the months in the list by scrolling with the mouse: up and down.



You can also view scans with a status other than **Preliminarily Diagnosed**.

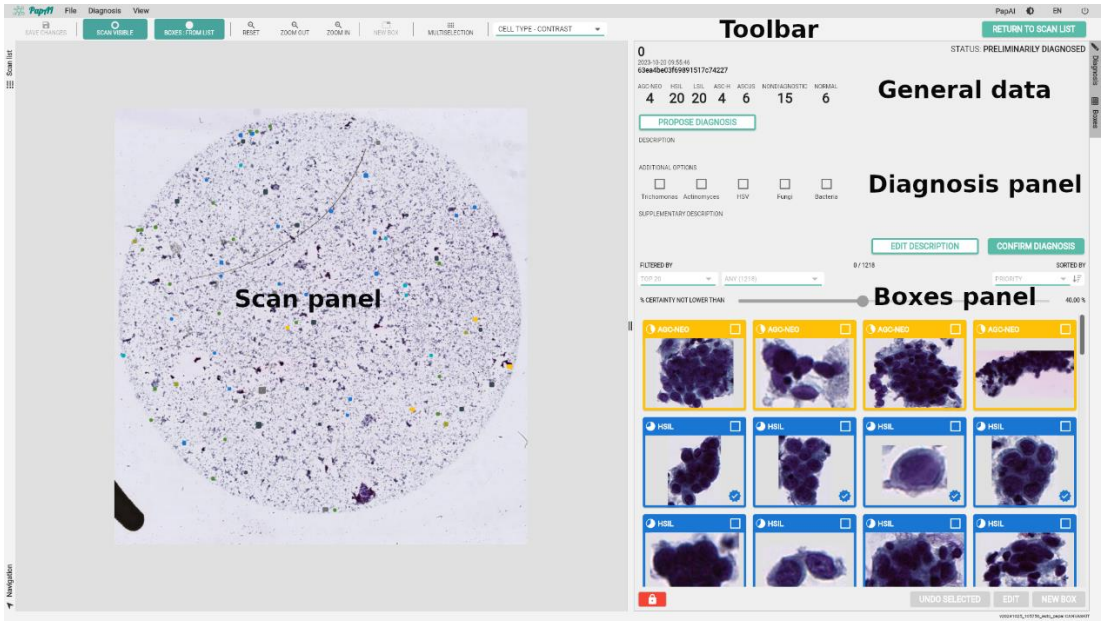
Click the field with the name of the status and select the required scan status from the list of values.



Scan window

The scan detail view consists of 5 elements:

1. Scan image panel.
2. Toolbar
3. General data
4. Diagnosis panel
5. Boxes panel



The **scan window** shows a preview of the entire scan together with groups of marked cells (boxes). The **toolbar** contains shortcuts to the most frequently used actions. The **General Data** section contains basic information about the scan itself: scan ID, date and time of creation, source file name (optional), scan status, and counts of marked cells, grouped by type. The **Diagnosis Panel** contains general information relating to the diagnosis. The **Boxes Panel** contains a list of labelled cell groups (boxes), which can be filtered and sorted according to selected criteria.

The **General Data** panel is visible when at least one of the main panels on the right-hand side of the screen is visible: **Diagnosis Panel** or **Boxes Panel**. You can close the **Diagnosis Panel** and the **Boxes Panel** to get additional space to preview the entire scan. Simply click the **Diagnosis** or **Box** button, visible on the right-hand side of the screen. The buttons act like

toggles - they show and hide the corresponding panels.

You can obtain the same effect by selecting from the View menu the options: **Diagnosis Panel** and **Boxes Panel**.

You can also change the amount of space occupied by the panels on the right-hand side of the screen: click and hold the left edge of the panels, then drag it to the desired location.

Scan window

The scan image is displayed in the window on the left of the screen.

Note that some cells on the scan are marked in color, and their thumbnails in the box panel are also marked in the same color. These are highlighted, identified groups of cells - dysplastic cells by type, cells identified as normal, or described as non-diagnostic.

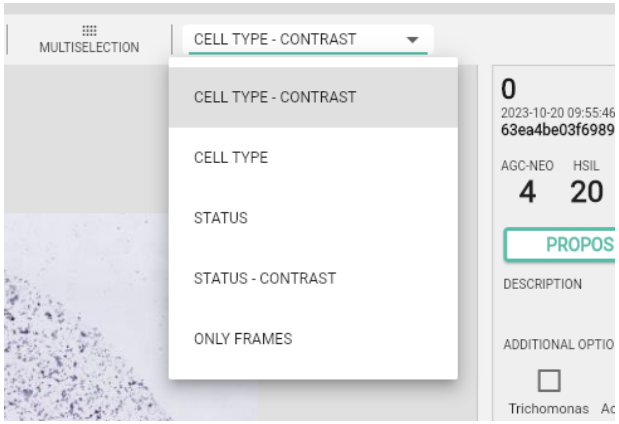
By default, the system only shows cells, visible in the **Boxes panel**. You can change the visibility of the boxes using the switch on the toolbar:

- **Boxes: from** list (or menu option **View** - **Boxes**: **from list**) - the system will only show boxes that match the filters of the **Boxes panel** (default setting).
- **Boxes: all (**or menu option **View** - **Boxes: all**) - the system will show all boxes.
- **Boxes: none** (or menu option **View** - **Boxes**: **none**) - the system will not show any of the marked boxes.

Błąd! Nie można odnaleźć źródła odwołania.

Box color scheme

The scheme for displaying cell colours is selected from the list of values at the top right of the scan window.



The default scheme is **Cell Type - Contrast**, which is a scheme where a high contrast colour indicates a specific cell type: blue is cells identified as HSIL, red is ADCA cells, green is LSIL, etc.

The **Cell Type** scheme shows the same information but uses a different colour palette.

In the **Status** and **Status - Contrast** schemes, boxes that have been modified during the current diagnostic session (before saving the changes) are highlighted in colour. Modification means changing the cell type, adding/editing/deleting a comment, or marking the box as *'verified'*.

After saving the changes, the status of the boxes is reset (all boxes are marked as 'unchanged').

In the **Only Frames** scheme, only the frames of the boxes in the **Boxes panel** are marked with the cell type colour.

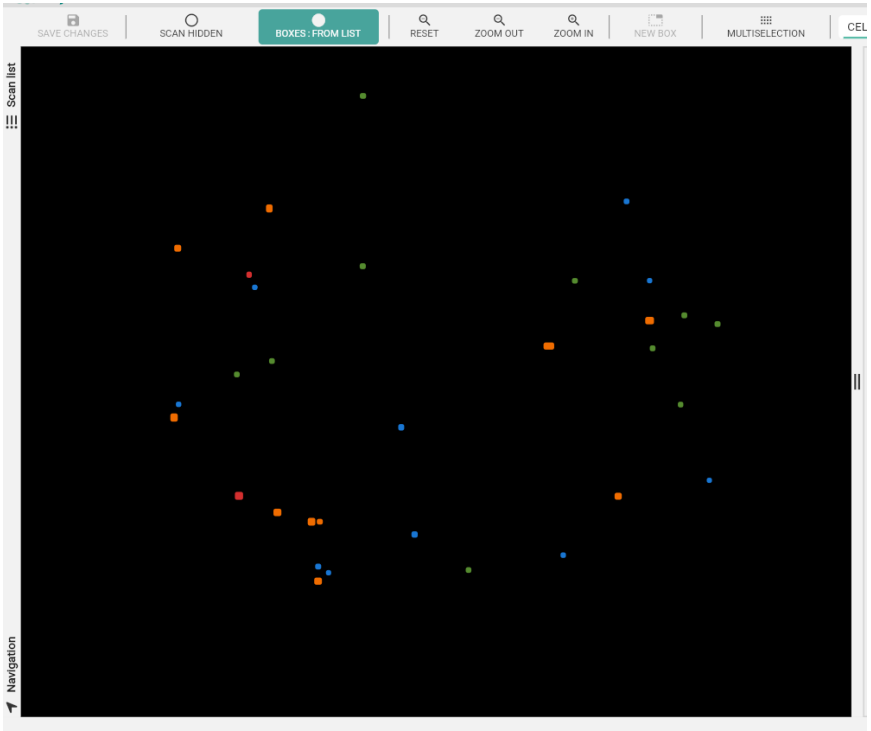
Hide scan so that only marked cells / groups of cells remain in the image

Click the **Scan Visible** button to hide the scan.

Only cells or groups of cells, marked as dysplastic, normal, or non-diagnostic, will remain on the screen.

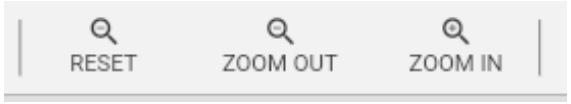
Which boxes are visible is determined by the state of the box visibility switch on the toolbar. The available options are **'none'** (boxes hidden), '**from list**' (only boxes from the list in the **Boxes panel** /with active filters/ visible), and '**all**' (all boxes visible).

Clicking the **Scan Hidden** button again restores the scan. Changing the visibility of the scan is also possible from the **View** menu (**View** – **Scan visible**).



Scale the scan

By default, the system shows the full scan image, fitted to the size of the window. You can zoom in and out of the image.



Click **Zoom In** (or press the '**=**' key - equal sign) or **Zoom Out** (the '**-**' key - minus sign) to - respectively - enlarge or reduce the image. You can also scale the image manually: hover the mouse cursor over the image and use the wheel to scroll up or down.

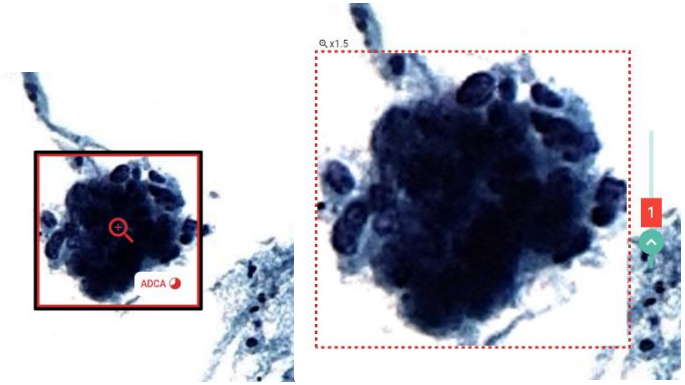
The **Reset** button (or the '**0**' - zero key on your keyboard) restores the default full scan image, fitting the window size.

You can also use the menu by selecting the appropriate option: **View** - **Zoom Out**, **View** - **Zoom In** or **View** – **Zoom reset**.

Additional box magnification and gamma value editing (brightness)

PapAI allows you to analyse in more detail and change the brightness level of the selected box. When you place the cursor over a box when the image is maximally zoomed in, a loupe icon appears inside the box .

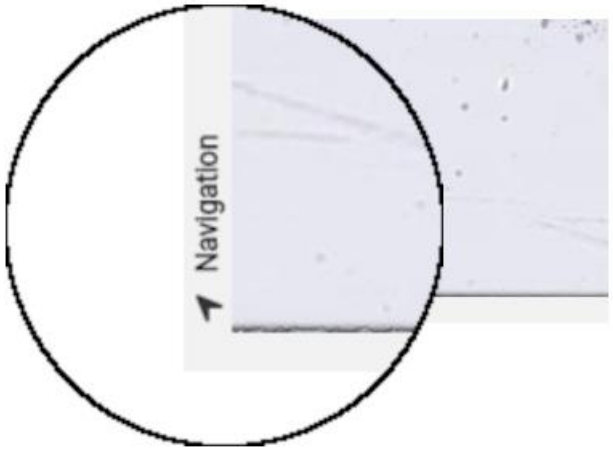
Clicking anywhere in the box will display the contents of the box with a 1.5-fold magnification, and allow you to change the gamma value, which is responsible for the brightness of the image. This is done using the green slider visible to the right of the box. While holding down the left mouse button, move the button with the green arrow up or down to brighten or darken the image. The current gamma value is shown in the red box above the button. Click the enlarged section of the scan again with the mouse to deactivate gamma editing mode. This mode will also be disabled when you change the zoom settings (zoom out of the image using the mouse wheel, toolbar buttons, or one of the **View** menu options).



Quick navigation

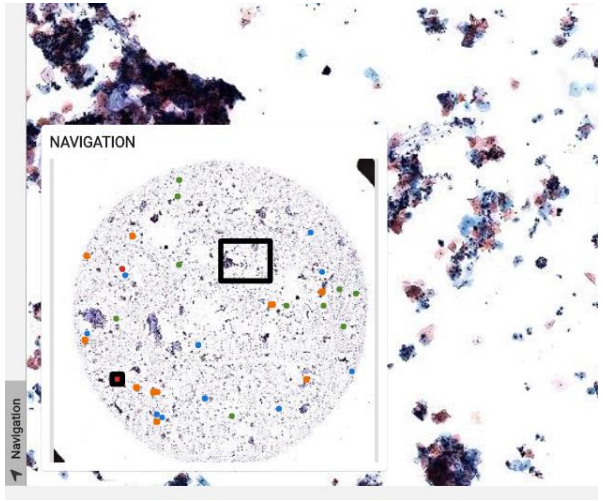
Viewing the zoomed in image you can, of course, move it in all sides. However, if you want to quickly see a part of the scan that is a little further away, you can use the quick image navigation.

Click on the **Navigation** field, visible in the bottom left-hand corner of the image.



On the thumbnail, click on the area you are interested in - the system will automatically show the selected part of the scan. The visible area is marked with a black frame, the size of which depends on the zoom setting.

You can also toggle the visibility of the **Navigation** window using the menu option **View** - **Navigation panel**.

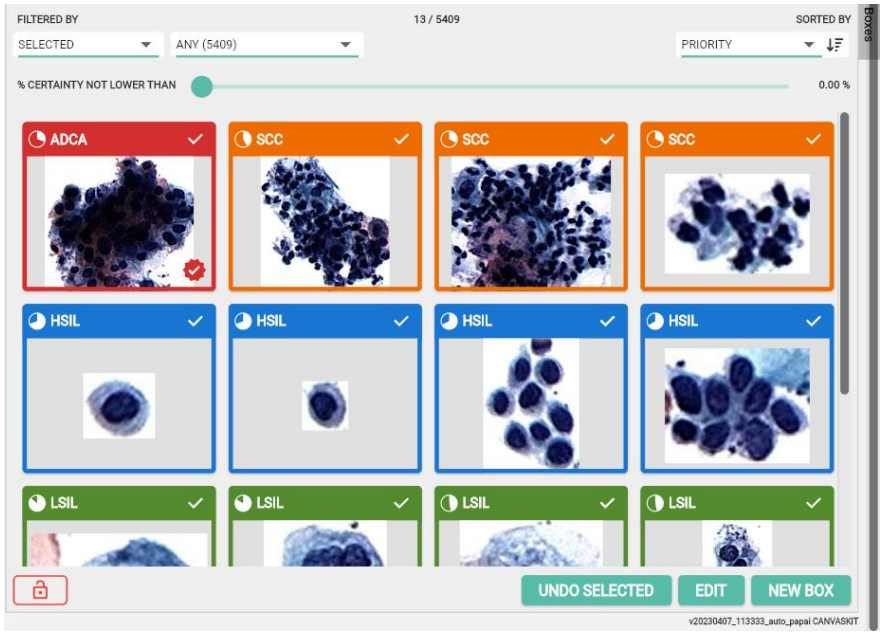


Boxes

The **Boxes panel** shows thumbnails of the boxes containing the selected cells / groups of cells.

The thumbnails preserve the proportions of the boxes and are scaled to the size of the tile only if necessary (if the box is larger than the tile, it will be shrunk with the original proportions; if it is smaller, its dimensions will remain the same).

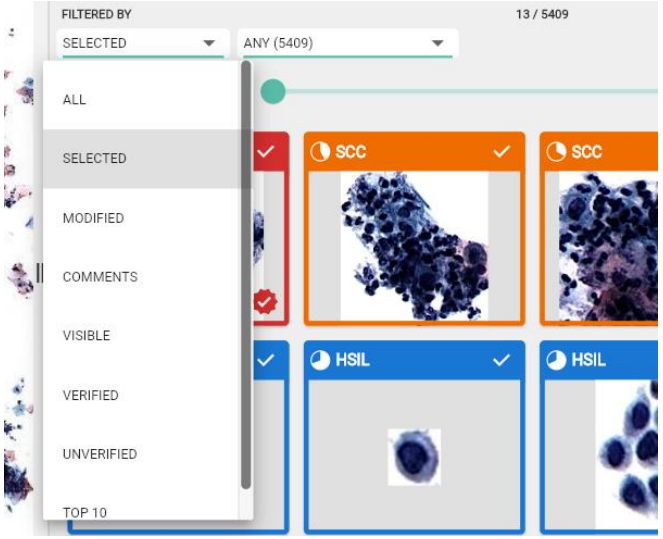
The colours of the boxes in the **Boxes panel** and the **Scan panel** depend on the colour display scheme selected from the list in the toolbar. The default is the **Cell Type - Contrast** scheme, where the colour of the box indicates the specific cell type.



Filter boxes

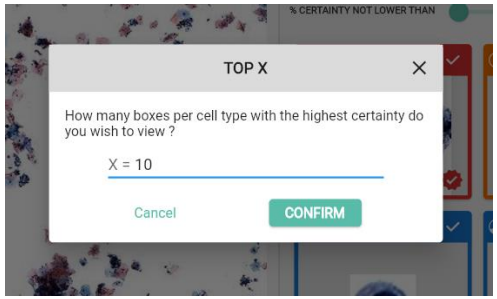
You can **filter** boxes by:

- **Condition** of the box:
  - **All** - show all boxes.
  - **Selected** - show only selected boxes.
  - **Modified** - show only modified boxes.
  - **Comments** - show only boxes with comments.
  - **Visible** - show only the boxes visible in the scan window (moving the scan and changing the zoom changes the list content).
  - **Verified** - show only boxes marked as verified.
  - **Unverified** - show only boxes without the 'verified' flag set.
  - **Top X** - show X boxes with the highest degree of certainty from each category (the value of the X parameter can be set from 1 to 50). The default value of the X parameter is 10.



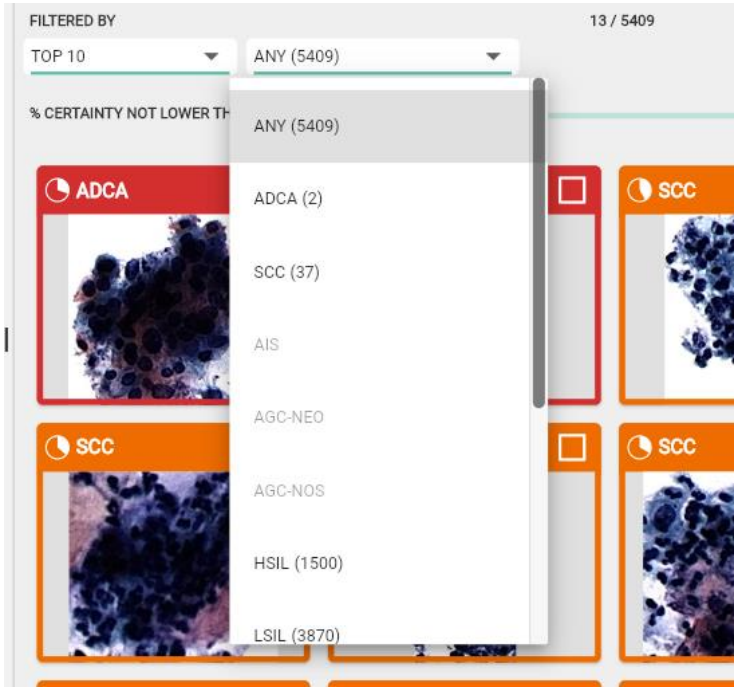
How do you set the value of the **Top X** filter parameter?

Select **Top X** as the active filter from the list and the system will display a window where you can specify the value of the X parameter.



- **Cell** type

The number in brackets next to the cell type name is the number of all cells / groups of cells of that type identified in the scan image. If the type name is greyed out, there are no identified cells / groups of cells of this type in the image.

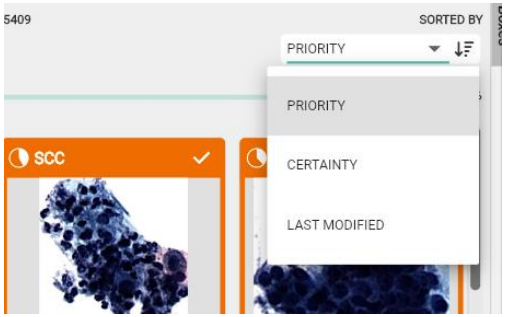


Box sorting

You can also sort the boxes by **priority**, **degree of certainty**, or **date of modification**.

The **priority** determines the degree of malignancy of a cell: cells with higher malignancy have a higher priority. Boxes with the same priority are additionally sorted in descending order of degree of certainty.

In addition to priority, you can also choose to sort the boxes according to the **degree of certainty** with which the cell / group of cells has been identified. Boxes with a cell type manually set by the diagnostician (icon Ⓜ



in place of the certainty indicator in the box header) are treated as boxes with 100% certainty.

The last option is to sort the boxes by **modification date**.

Regardless of the selected criterion, you can sort the boxes in ascending or descending order - use the button to the right of the list of sorting criteria to change the order.

Box list lock

Below the list of boxes, there is a button with a padlock sign (/)to toggle the box list lock on and off.

The lock stops the list from refreshing - if you change a box's data (e.g. by changing the cell type, editing a comment, or setting a validation flag), the change will not affect the order of the boxes, nor will it remove the box from the list.

The list lock also blocks the ability to filter and sort boxes, and you cannot add new boxes to the list.

Deactivating the lock removes these restrictions and automatically refreshes the list of boxes.

When the lock is disabled, the list of boxes is refreshed automatically after each modification, so if, for example, the list contains modified boxes and you withdraw changes to a selected box, it will be removed from the list - according to the currently set filter.

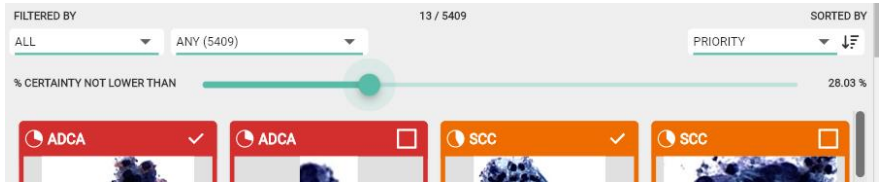
Certainty of cell type identification

The box header shows the type of cell(s) identified, and an icon indicating the degree of certainty with which the system has made the identification (HSIL). The more the circle is filled in, the higher the degree of certainty.

If a box is described with the letter M (e.g. M HSIL), it has been manually marked by the operator (diagnostician). This is equivalent to specifying a degree of certainty of 100%, which is important when sorting boxes in a list

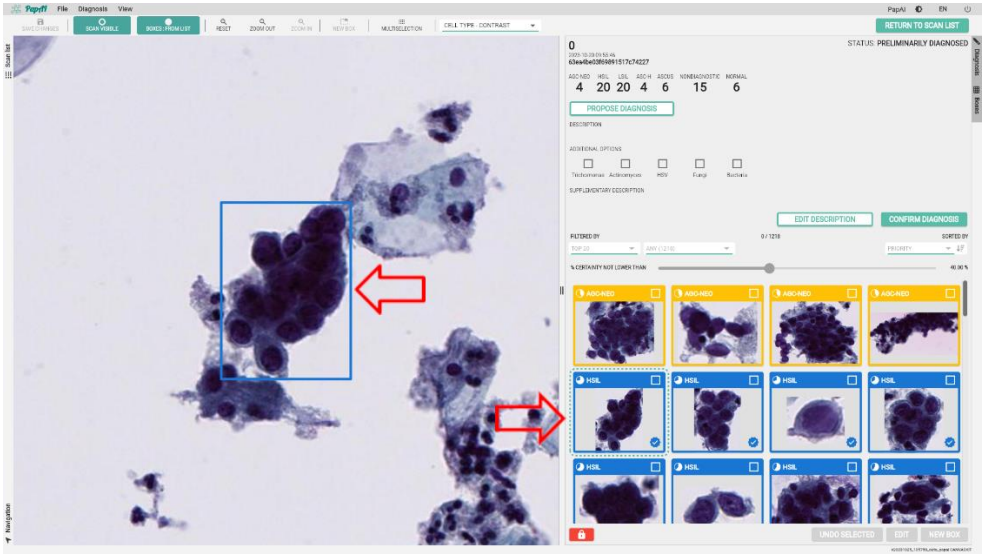
To remove boxes with a degree of certainty below a certain threshold from the list, you can use the slider above the list of boxes.

Double-click the slider to set the default value (50%).



Show cell on scan

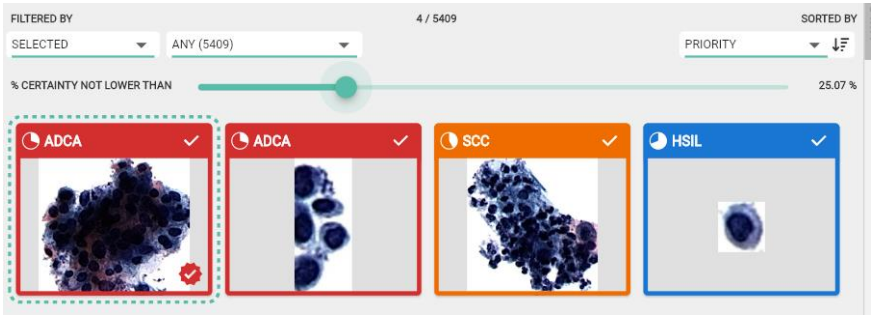
Click a box in the list to view it in the scan window at maximum zoom.



Note that when you hover the mouse cursor over an identified cell / group of cells in the scan image, a tooltip is displayed with complete information (cell type, identification confidence level, verification status, and comment - if added).

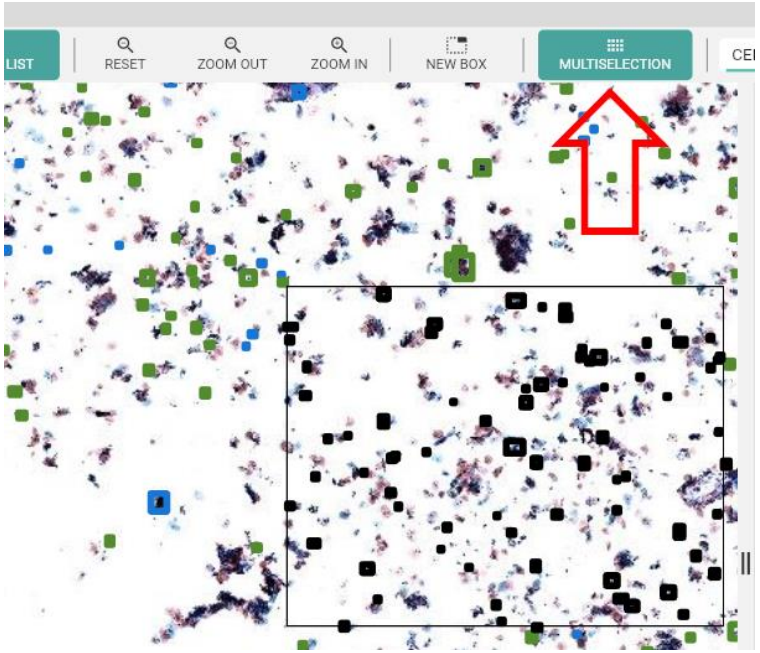
Selection of boxes

Select one or more boxes to edit data, or to undo changes you have previously made. You can do this in two ways:



1. In the **Boxes panel**: click the checkbox in the top right corner of the box. You can select entire groups of boxes - select the first box, press the Shift key, and hold it down to select the last box; all boxes between the first and last will be selected (the order of the beginning and end of the interval in the list does not matter). You can also use the keyboard shortcut Ctrl + A or the menu option **Diagnosis** - **Change selection of visible boxes** to enable/disable the selection of all boxes in the list.

2. In the **Scan window**: click the **Multiselection** button on the toolbar (or use the M key), and while holding down the left mouse button, select the rectangle containing the selected cells on the scan. Selecting boxes in this way requires multiselection mode to be activated each time.



This process can be simplified using keyboard shortcuts and one of the 2 'ad hoc' addition modes: by holding down the Ctrl key you can use the mouse to add more boxes to the selection list, while the Shift key allows you to replace the contents of the list. Using the Ctrl key, you can also remove individual boxes from the list by clicking on them or by surrounding them with a frame. The cells you have selected will be shown in the **Scan window** with a black border. Above the **Boxes panel** you will find a counter that shows the number of boxes selected and the number of all boxes.

You can quickly uncheck the boxes by pressing the Escape key or by selecting the menu option **Diagnosis** – **Deselect selected boxes**.

Editing of boxes

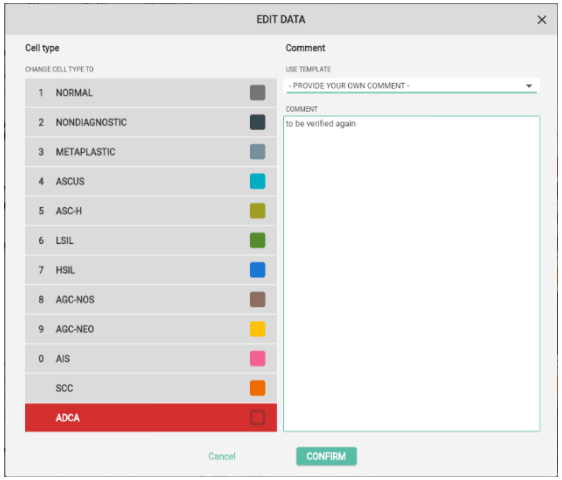
Double-click a box header in the list or a cell in the scan window to start editing box data. If you want to edit the data of several boxes, select them and click the **Edit** button under the list of boxes (you can also use the E key or select the menu option **Diagnosis** - **Edit selected boxes**). A data editing window will appear.

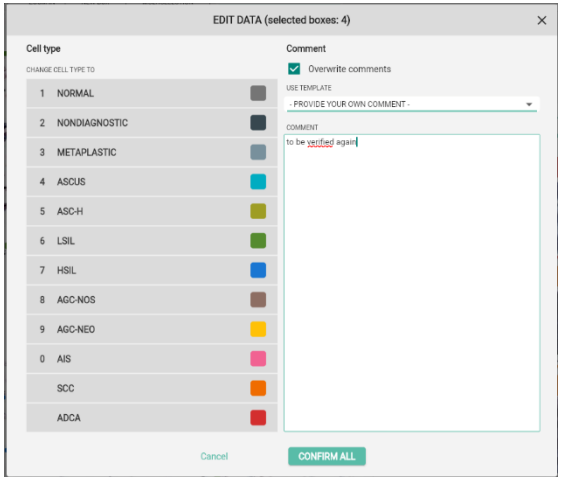
If you have selected one box, the system will show the current data. You can change the **Cell Type** and edit the **Comment** (verbal description). You can enter the comment manually or select from a list of available templates.

If you have selected several boxes, you will find the number of boxes in the title of the window. In the edit window you will not find the current cell type or comment, because the selected boxes may contain cells of different types, and have different comments.

The edit window allows you to set a single cell type and comment for all selected boxes (if you edit several boxes, overwriting comments requires the '**overwrite comments**' box to be checked; only after it is checked is it possible to edit a comment or select a template from the list).

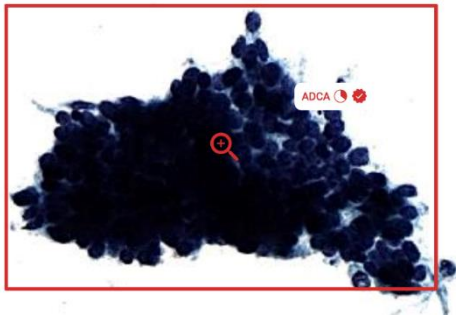
Confirming the changes with the **Confirm** / **Confirm all** button automatically sets the "*verified*" flag on the edited box(es).





Verification of boxes

Verification means that the application user (diagnostician) has looked at the box(es) in question, and either agreed with the designation proposed by the system or changed it by entering their own.



How to verify the box(es):

1. In the scan window, point the mouse cursor at the selected box and right-click on it. An icon will appear on the tooltip with box information to indicate that the box has been verified by a diagnostician. The same icon will appear in the bottom right corner of the box in the list in the **Boxes panel**.

2. Verification of one or more boxes is also possible via the box editing window described above. Confirming the changes with the **Confirm** / **Confirm all** button sets the verification flag - even if the cell type and comment have remained unchanged.

Box reset

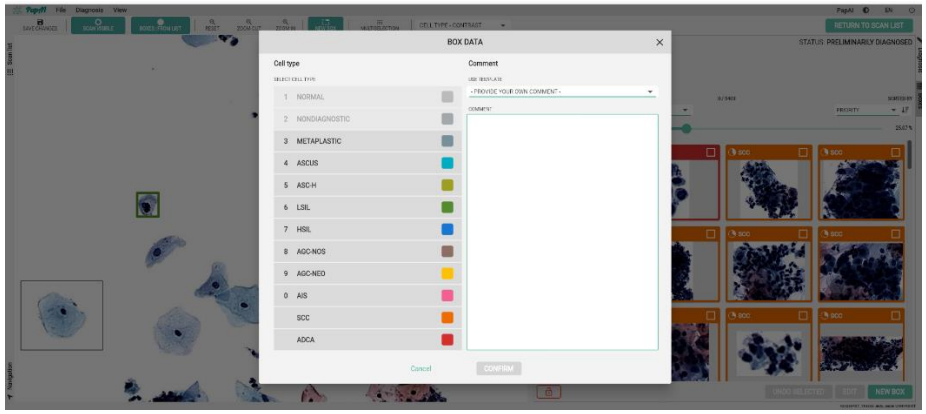
You can reset the boxes, i.e. change the cell type of the selected boxes to Normal:

1. Select 1 or more boxes.
2. From the **Diagnosis** menu, select **Reset selected boxes** or press the Delete key.
3. Confirm your decision by clicking the **Reset** button in the confirmation window.

New box

In addition to editing existing boxes, you can also define your own boxes:

1. Click the **New Box** button on the toolbar or at the bottom of the Boxes panel (you can also use the N key or select the **Diagnosis** - **Add new box** menu option).
2. In the scan window, select the desired area.
3. When you release the left mouse button, the system displays the **Box Data** window, where you should select the **Cell Type**. You can also enter a **Comment** or select one from the list of templates.



Undoing changes

If you change the box data (cell type, comment, or verification status) while working with the scan, the **Save Changes** button on the toolbar will be active and an asterisk will appear in the **General data** section - next to the scan **ID** - to indicate unsaved changes.

If you wish to undo the changes you have made:

1. Select the box or boxes for which you want to undo changes (you can search for them by selecting **Changed** in the filter box by box status).
2. Click the **Undo Selected** button and confirm your decision in the confirmation window by clicking the **Undo** button.

Diagnosis

The **Diagnosis panel** shows the basic elements of the diagnosis.

The **Propose Diagnosis** button starts the procedure for the system to issue an preliminarily diagnosis. Below this you will find **Description** of the main diagnosis for the scan, the **Additional Option** tags (if any), and the **Supplementary Description**.

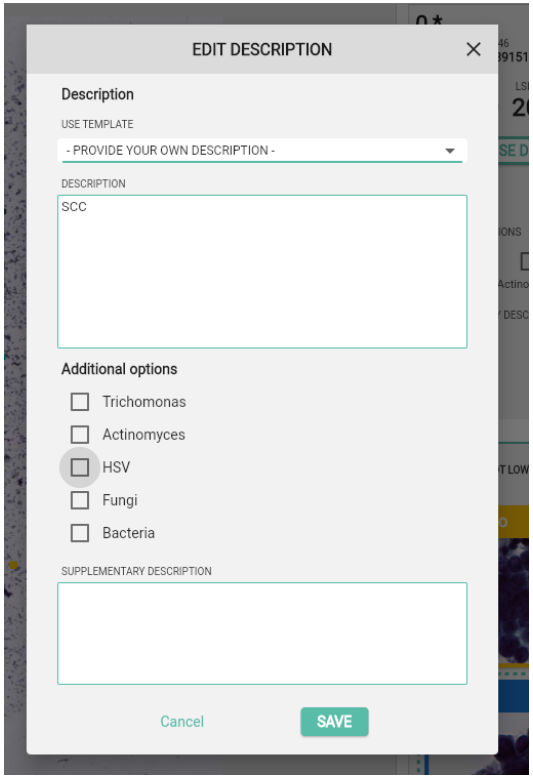
Proposed diagnosis

Click on the **Propose diagnosis** button to start the system's procedure for issuing an preliminarily diagnosis. The system will analyse the information it has about the scan and display its proposal for an preliminarily diagnosis in the **Diagnosis proposal** window. A verbal description will appear in the **Diagnosis** field, while in the **Certainty** field the system will show the degree of certainty with which it has formulated the diagnosis.

Acceptance of the diagnosis proposal will cause it to appear in the **Diagnosis panel** in the **Description** field.

Edit diagnosis

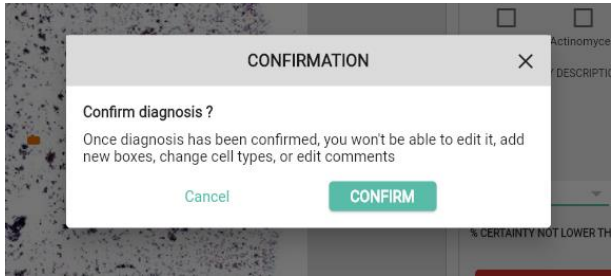
Click **Edit Description** to edit the diagnosis. You can also select the menu command **Diagnosis** - **Edit description**.



Confirmation of diagnosis

To confirm the diagnosis, click the **Confirm diagnosis** button or select the **Diagnosis** - **Confirm diagnosis** menu option.

All unsaved changes will be automatically saved and the scan will be set to **Diagnosed** status. This status means that the diagnosis has been finally validated and no further changes are possible.

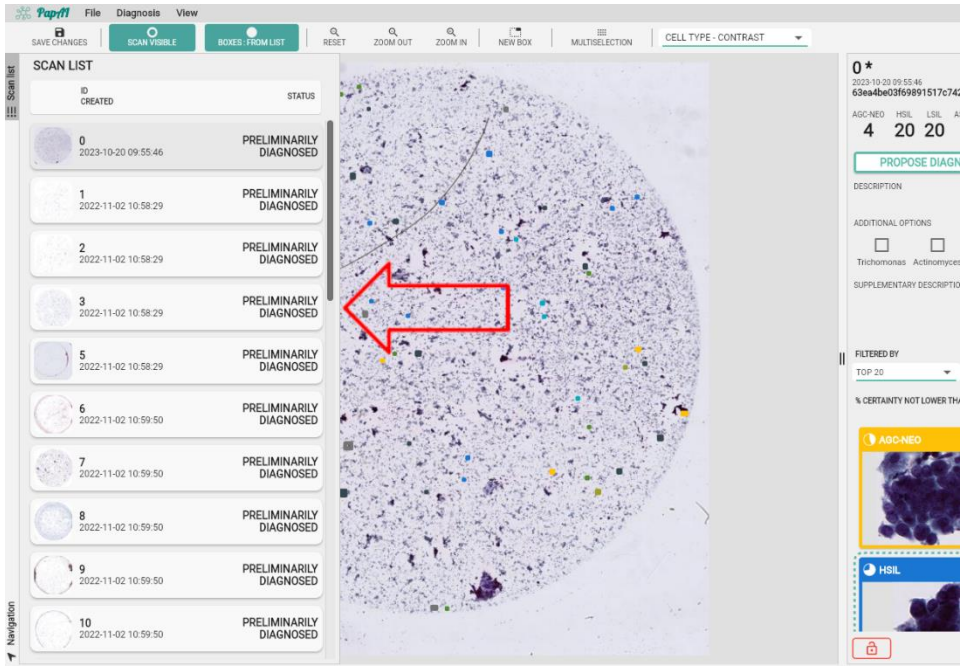


Return to scan list

Click the **Return to scan list** button at the end of the toolbar to return to the scan browser. Closing the current scan (**File** menu option - **Close** or Backspace key) also returns you to the scan browser; if you have any unsaved changes, the system will display a window asking you whether to save or discard them.

Scan list preview

To get a quick overview of the scan list, use the **Scan List** button, visible on the left side of the screen - below the toolbar (you can also use the **View** menu option - **Scan list panel**). This will open a quick handy list that allows you to quickly move between scans - without having to return to the search engine. The list only contains the scans that were visible in the search engine, i.e. it takes into account the active filters.



Annex

Technology

The service leverages the Ray v.2 technology to provide an end-to-end solution for an ML-based pipeline for the preliminary classification of digitalized samples.

Ray AI Runtime (AIR) (HTTPS://DOCS.RAY.IO/EN/LATEST/) is a scalable framework for creating ML workflows, facilitating the deployment of AI and Python applications and enabling the scaling of individual workloads.

The solution supports:

- **Retrieval of a digitalized sample from a DSA instance (Digital Slide Archive)**.
- **Conversion of a large image (digitalized sample) into the input format of the YoloR model (multiple rectangular images - tiles)**. the system divides the image into tiles. The system then checks with the help of the colorfulness metrics methodology, which measures color saturation, that there are cells on all tiles. Tiles with no cells will be discarded, tiles where the system has detected cells will be directed for further processing. The system also counts the ratio of the number of tiles sent for further processing to the total number of tiles. This ratio indicates whether the image scan was performed correctly (e.g. whether only a fragment of the specimen was scanned).
- **Feeding input images to a fine-tuned YoloR model for detection of all cells**. Based on the number of all cells identified in the image, the system evaluates whether the preparation is diagnostic. Bethseda system criteria for liquid cytology identify a preparation as valid when the cell count is over 20000 cells.

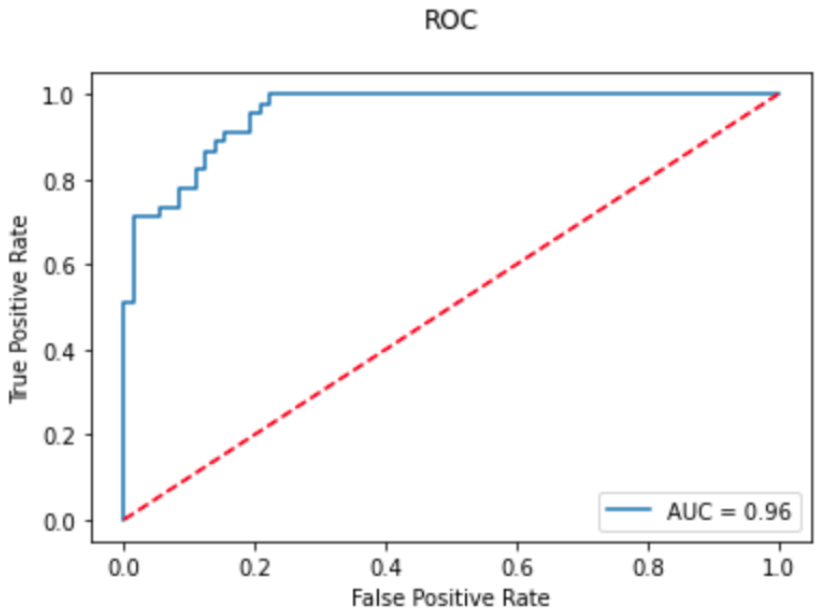
  All comments regarding the scan (whether it is diagnostic and correctly performed) are reported to the user, who decides on further processing of the scan.

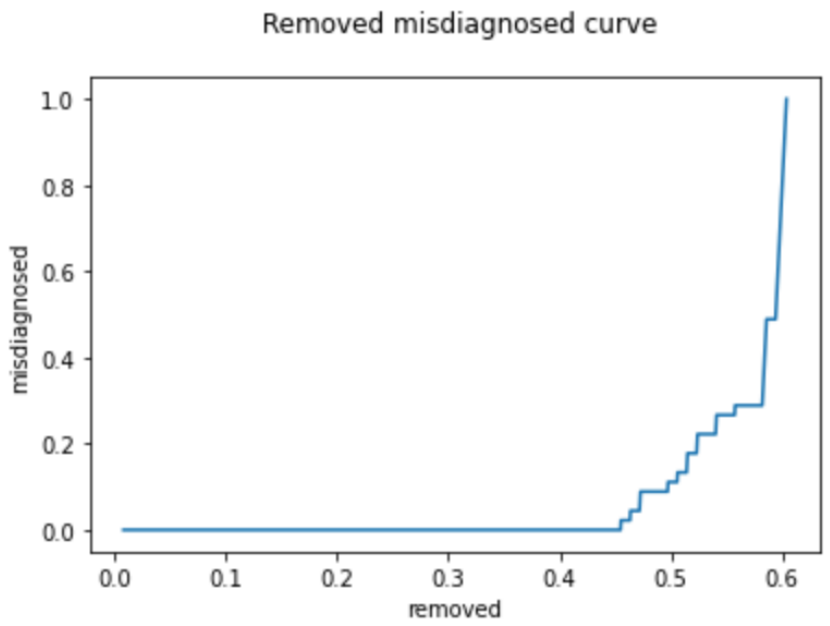
- **Feeding input images to a fine-tuned YoloR model for detection of abnormal cells of selected categories**.
- **Saving abnormal cell detection results to a DSA archive**.
- **Identification of normal samples, i.e., samples with a low probability of containing abnormal cells**.

  Proposed diagnosis:

  Based on the abnormal cells found, a set of features was prepared for training model of gradient boosting algorithm on decision trees.

  The results of the model for classifying whole slides into two classes – normal and cancer: **ROC curve with 0,96 AUC** and **removed-misdiagnosed curve** (see images below).





Requirements

All you need to use **PapAI** app is a web browser:

- **Chrome 84 & above**
- **Firefox 72.0 & above**
- **Safari on El Capitan & above**
- **Edge 1.2.0 & above**