



VisionArray
Analysis Package MultiScan

REF E-4070-1

 1 Piece

For the simultaneous analysis of hybridization signals on up to 6 VisionArray Chips



In vitro diagnostic medical device
according to EU directive 98/79/EC

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1. Introduction

The VisionArray Analysis Package MultiScan stands for a simple visualization and a quick analysis of the VisionArray Chip data. The analysis of up to 6 chips simultaneously and the report of the results can be achieved in just a few minutes. Due to its *Wizard* format, the program navigation is easy and intuitive for the user. The scans are stored including all sample and chip data in an integrated database on the enclosed external hard drive.

2. Intended use

The software is intended to be used for the simultaneous detection and analysis of hybridization signals on up to 6 VisionArray Chips in combination with the corresponding VisionArray Chip File. When properly used, the presence or absence of the examined target sequences in a sample can be evaluated. In addition to the initial amount of the target sequences, further factors can influence the system. It is therefore not possible to access quantitative data on the basis of signal intensities. Depending on the chip type, the specific capture sequence for every dot is stored in the corresponding chip file and allows a qualitative evaluation of the sample. The identification of the dots is fully automated due to algorithms for pattern recognition.

For the rare case of damage or pollution of the glass slide, a tool for manual correction is implemented. The result of the dot identification is monitored by 3 control mechanisms.

This product is designed for *in vitro* diagnostic use (according to EU directive 98/79/EC).

Interpretation of results must be made within the context of the patient's clinical history with respect to further clinical and pathologic data of the patient by a qualified pathologist.

3. Clinical relevance

Please refer to the instructions for use of the respective chip.

4. Test principle

Sequence-specific DNA fragments in a pool of DNA fragments are detected by DNA/DNA hybridization with immobilized DNA catchers on a glass chip. First, the target sequences in this material have to be amplified via PCR and simultaneously marked with biotin molecules. Subsequently, the amplified sequences hybridize with the complementary DNA catchers on the glass chip. After the hybridization, unspecifically bound DNA fragments are removed by short and stringent washing steps. The specifically bound and biotinylated sequences are visualized by secondary marking with a streptavidin-peroxidase conjugate and a staining with tetramethylbenzidine (TMB).

5. Safety Precautions and Disposal

- ✓ Read the operating instructions prior to use!
- ✓ Do not alter any components of the VisionArray Analysis Package MultiScan (including hardware and software)! For repairs, contact your local distributor!
- ✓ Use an adapter for the local power line!
- ✓ Do not attempt to disassemble any components of the VisionArray Analysis Package! There is danger of an electrical shock! Opening your scanner will void your warranty!
- ✓ Do not subject the scanner to excessive vibration! It may damage the internal components!
- ✓ Your scanner operates best in temperatures between 10° C to 35° C!
- ✓ Do not use the scanner in rooms with high humidity ($\geq 80\%$)!
- ✓ Operate the system only after you have been advised by a qualified person!
- ✓ For disposal, send the hardware back to ZytoVision GmbH!

6. The VisionArray System

6.1 Terminological Conventions and Symbols

Following terminological conventions and symbols are used in the instruction for use:

<i>Italic</i>	specific terms (e.g. <i>Wizard</i>); terms that occur in the software itself (e.g. <i>Save Changes</i>); and trade names (e.g. <i>VisionArray</i>)
Framed, bold	buttons that occur in the software (e.g. Scan)
	critical steps that should be performed with particular care

6.2 Components and Accessories

The VisionArray Analysis Package MultiScan consists of the components and accessories displayed in Figure 1:



Figure 1: Components of the VisionArray Analysis Package MultiScan: 1) Scanner V600 Photo; 2) PC with preinstalled VisionArray Analyzer Software MultiScan; 3) External Hard Drive; 4) Computer Mouse; 5) USB-Hub

The provided PC runs under an English Windows operating system. The software is preinstalled on the computer and can be put into operation immediately.

6.3 Assembly

The VisionArray Analysis Package MultiScan should be assembled by a sales representative in order to ensure the proper operation.

1. Connect the laptop with the enclosed power supply to a 220-250 Volt power outlet.
2. Connect the Scanner V600 Photo to a 100-240 Volt power outlet.
3. Plug the enclosed USB-Hub into a free USB 3.0 socket of the laptop and connect it to a 220-250 Volt power outlet. Mind the USB 3.0 symbol  for a faster data transfer.



Enclosed adaptors for the local power line might be necessary for step 1, 2 and 3.

4. Plug the enclosed USB cable with the USB type B plug into the USB type B port at the back of the Scanner V600 Photo and connect it to any free USB port of the USB-Hub.
5. Plug the USB 3.0 cable of the external hard drive into a free USB port of the USB-Hub.



The external hard drive is mandatory for the proper operation of a VisionArray analysis. Use only the enclosed product.



Do not install other hardware or software from 3rd party manufacturers, except printer driver.

6. A printer can be added to the system via the USB-Hub. If a Driver has to be installed use the driver CD of the manufacturer.
7. The mouse dongle can be plugged into a free USB port on either the USB-Hub or the laptop.
8. Prior to the first scan unlock the transport latch on the back of the scanner.



Whenever unexpected problems occur, please contact helptech@zytovision.com or your local distributor.



Figure 2: Left: Scanner V600 Photo closed; Right: Scanner V600 Photo open with Slide Holder MultiScan;

Switch on the Scanner V600 Photo by pressing the power button. Afterwards switch on the PC with the VisionArrayAnalyzer Software MultiScan. Restart the PC if you have started the scanner after the PC and the scan does not work. The software opens automatically when the system has started.

The VisionArrayAnalyzer Software runs under Windows as operating system. The Windows components are hidden for an easier handling and only the VisionArray Analyzer Software is visible in full screen mode. The windows button  gives access to the system functions.

Please note that it is not possible to make changes that influence the system in user mode.

All data are stored on an external hard drive in order to ensure security of personal data.

6.4 Test Material

The VisionArrayAnalyzer Software is delivered preinstalled on a laptop together with the Scanner V600 Photo. A smooth chip analysis can only be assured in combination with the matching components.

The VisionArray Analysis Package MultiScan should only be used for the analysis of VisionArrayChips. The corresponding VisionArrayChip File information needs to be present in the VisionArrayAnalyzer Software in order to be able to scan. New chip files can be imported if required.

6.5 Important Information

The following should be kept in mind:

- ✓ The VisionArray Chips and the Scanner V600 Photo have to be kept dust-free at all times! Dust particles and other foreign objects may damage the unit.
- ✓ The enclosed external hard drive must be used and be connected to the system at all times! Otherwise, the system will malfunction.
- ✓ Each new chip type has its own characteristic chip file that has to be installed prior to use!

7. Quick Guide Scanning

- 1) Turn on the Scanner V600 Photo.
- 2) Turn on the PC.
- 3) Select a user  on the starting screen and press **Scan**.
- 4) Place up to 6 chips into the slide holder of the Scanner V600 Photo and press **Detect Slide IDs**.
- 5) Enter data and press **Save** to submit preliminary information to the database. Alternatively, press **Scan** directly to save and scan all positions without entering advance data.
- 6) Check scan of each chip. Ok: Check the OK box and proceed by pressing **Analysis**
 Not Ok: press **Rescan**
- 7) Check scan analysis. Ok: press **Next** to generate the respective report
 Not Ok: Edit in expert mode 
- 8) Close view (data are stored automatically) or press **Print Report**.

8. Starting Screen

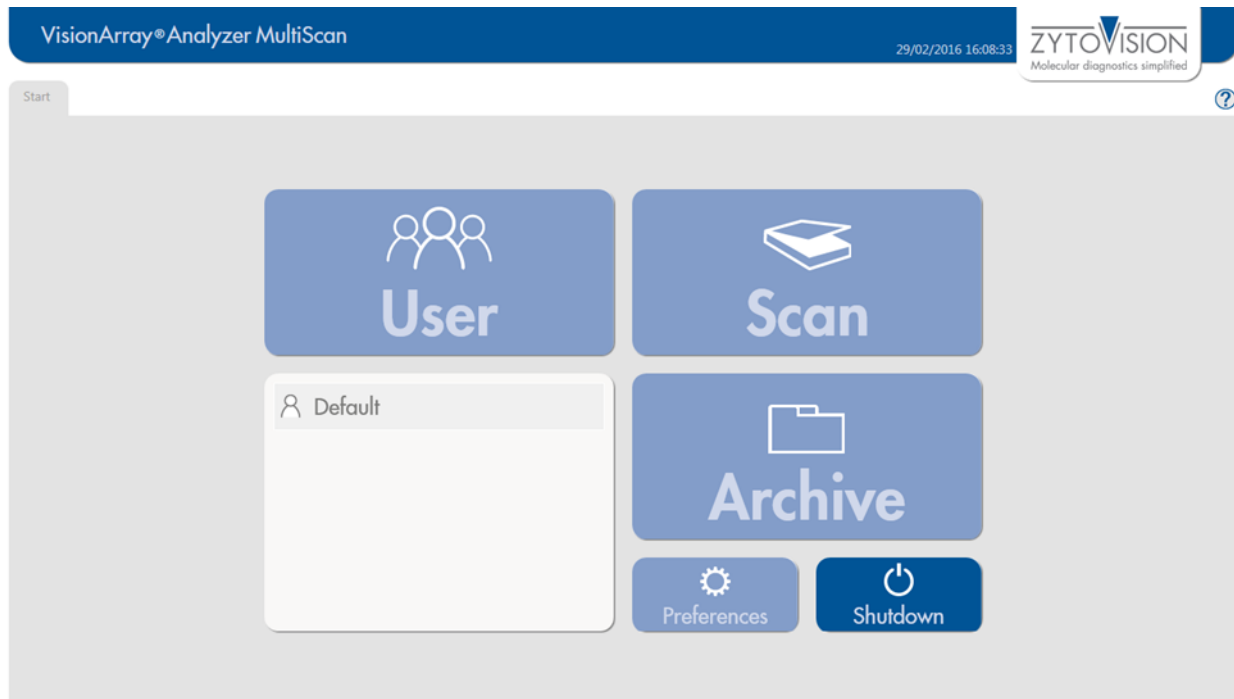


Figure 3: Starting Screen, no user logged in

The starting screen (Figure 3) of the VisionArray Analyzer Software gives access to all main control elements of the software. A user has to be logged in to be able to activate all control elements. Under **Preferences** a new user can be created.

Regardless of the login status the button **Shutdown**, which closes the program and shuts down the PC, and the Help-Function , can always be selected.

For the first setup of the system, select the preinstalled default user by double clicking.

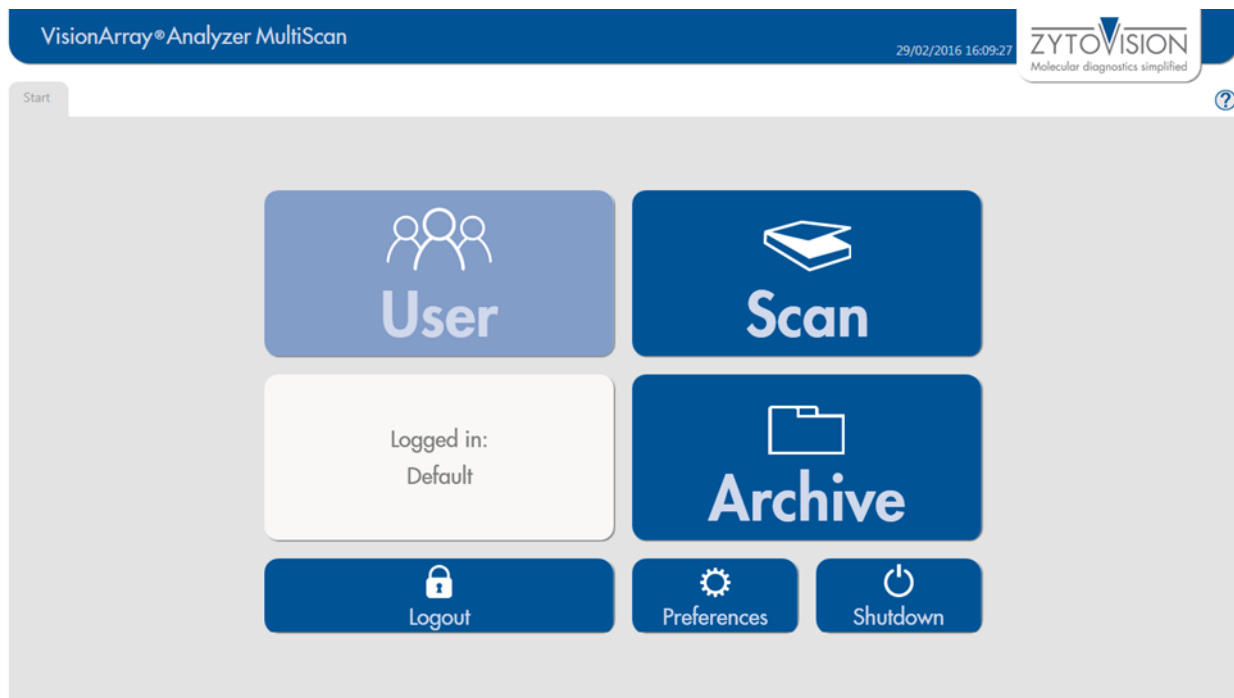


Figure 4: Starting Screen, user logged in

When a user has logged in, all functions of the starting screen are accessible (Figure 4). All subsequent steps are saved under the logged in user.

Scan enables the scanning of a VisionArrayChip. The data are stored automatically into a searchable **Archive** on the provided external hard drive and can be opened or edited if necessary.

Logout logs out the active user, but does not close the program.

Preferences leads to all program information of the installed software version. Additionally, new chip files can be imported, new users can be edited, and a backup can be produced and restored under this tab.

Shutdown closes the program and shuts down the PC.

9. Preferences

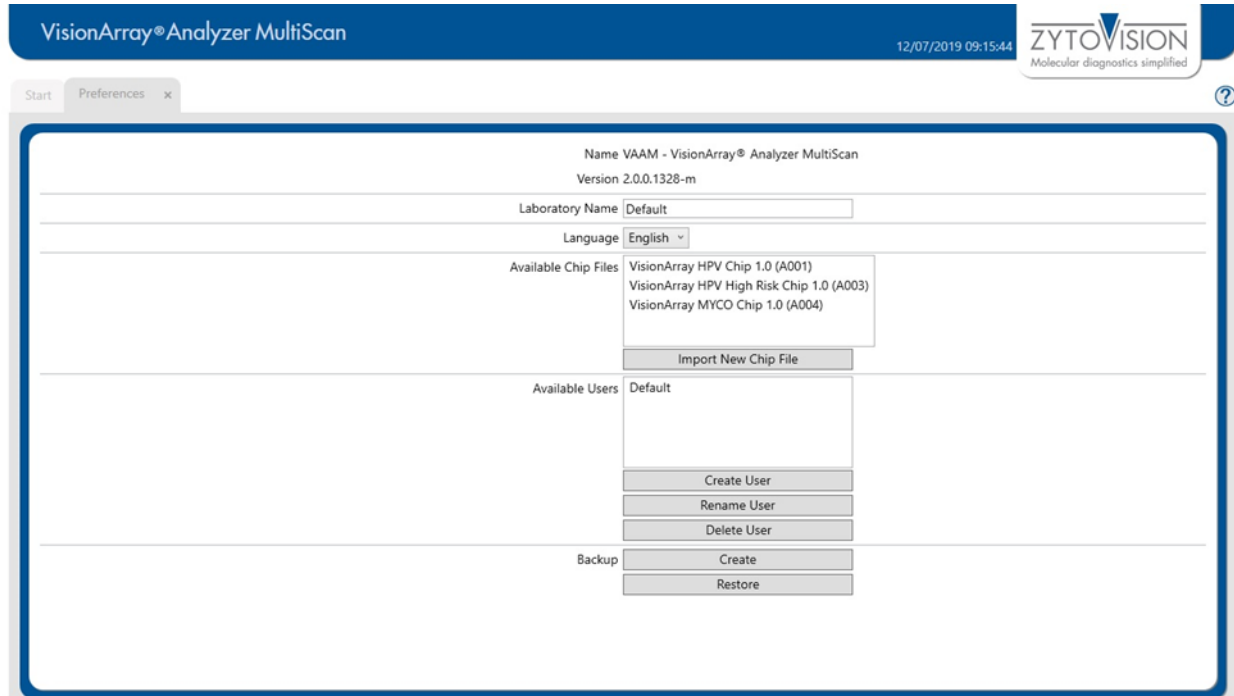


Figure 5: Preferences tab

The Preferences tab (Figure 5) gives an overview of the implemented program information such as version number, installed chip files and users. It is also possible to import new chip files, to create new users, to change the name of the laboratory, or to change the language. The default language is English.

Chip Files

Import New Chip File imports the VisionArray Chip File of a new type of chip. The button opens an explorer window in which the chip file can be selected and imported from an external device.

New chip files can be downloaded as a .zip file on the ZytoVision Homepage:

<https://www.zytovision.com/products/visionarray>



The Chip file has to be unpacked before it can be imported.

After the import, the new chip file appears in the list and can be used immediately.

User

Below the section with the installed chip files the users created for the program are listed. The buttons **Create User**, **Rename User** and **Delete User** are also located in this section.

Backup

Furthermore, it is possible in the Preferences tab to backup all saved data via **Create** or to **Restore** saved data from a secondary external device. The recovery process overwrites the database entirely with the recovery file.



All data in the database that are not saved will be lost during this process. We recommend creating backup files on a secondary external device periodically in order to minimize the risk and amount of data loss due to computer problems.

Changes will be saved by closing the Preferences tab.

10. Scan of an Array

The slide holder of the Scanner V600 Photo includes 6 slide slots that can be used simultaneously for scanning up to 6 arrays. The VisionArrayChip has to be placed in the holder with the labelling (QR code) facing downward and the label field on the left (Figure 6). Before starting the scan, close the lid of the Scanner V600 Photo.

Poor positioning in the scanner may result in irregular scans, or the scanner may not recognize the array field and the scan may need to be repeated.

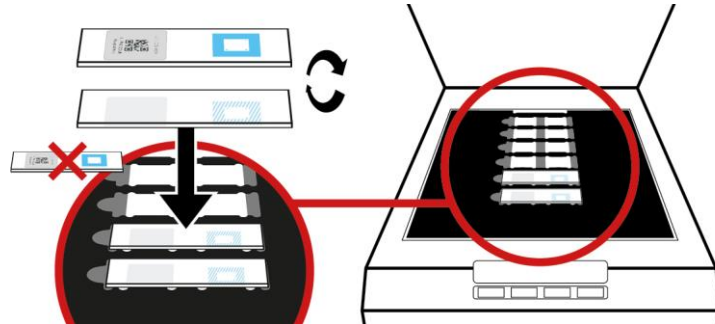


Figure 6: loading of VisionArrayChips in the slide holder of the Scanner V600 Photo

11. Enter Data and Start a Scan

11.1 Scan tab

Scan on the starting screen opens a tab for data entry (Figure 7). All individual data about the cases/patients and the chip can be entered and saved here in advance before starting array detection in the laboratory. Alternatively, data can also be entered later after the arrays have been detected. In this case, you may omit this data entry step and directly proceed by clicking the green **Scan** button.

Figure 7: Scan tab

The upper part of the Scan tab shows the 6 scan areas. The numbering indicates the position in the slide holder of the scanner (from top to bottom). In this tab the data of each chip can be entered. The *Slide ID* of the chips can either be read in automatically by clicking on **Detect Slide IDs**, or entered manually. Please note that an automatically detected Slide-ID cannot be edited and that any additional data can only be entered once a valid Slide-ID is present at the respective position. Further patient data for each specific slide may be entered afterwards in the detailed view by clicking on the magnifying glass symbol (see 11.2).

Save saves all entries made and converts to **Close** allowing you to close the Scan tab, while **Scan** saves all entries and immediately proceeds to scanning of the detected slides. For the scan to proceed, all other opened tabs but the scan tab will be closed.

Reset All clears all positions allowing you to start over.



Cancel closes the view and all entered data about patient/sample and chip are lost.

11.2 Detailed Scan tab

Figure 8: Detailed Scan tab

Slide (chip-information)

In the upper right section of the detailed Scan tab all relevant data for the chip type are entered. The information can be entered manually or quick and easy by clicking **Detect Slide ID**. The chip information is collected automatically.

Case (sample and/or patient data)

In the lower right section of the detailed Scan tab case/patient data may be entered. The completion of the field is optional and not necessary for conducting a scan. The date of birth entry will only be stored if a patient name has been entered. The entered preliminary data are stored in the archive. Editing or completion of the data is still possible at a later time in the preview tab after the scan has been performed. We recommend a detailed entry of all essential data in order to make the assignment as easy as possible.

Reset clears all entries of the detailed scan tab allowing you to start over.



Close closes the detailed view. Any data added is directly mirrored at the respective position and can be saved by clicking the **Save** button of the main scan tab.

12. Preview tab

In the Preview tab that opens after a scan has been performed, a greyscale image of each chip is shown (Figure 9). This tab can be used to check whether all chips have been scanned accurately. Additionally, case/patient data can be added or amended. To ensure integrity of data, Slide-IDs may not be added or edited manually on this screen. A rescan of all slides can be performed by clicking **Rescan All**, while a rescan of an individual position can be performed by clicking its distinct rescan button. Please note that clicking rescan resets any unsaved data entered.

Reset All clears all entries of the detailed scan tab allowing you to start over.



Cancel closes the view and all scanned images as well as any newly added or amended data are lost.

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Start Preview x

1. Slide-ID: A001-SF04-237 Case No. *: 242 Description *: HPV Test ☒ OK

2. Slide-ID: A001-SF04-236 Case No. *: 243 Description *: ☒ OK

3. Slide-ID: A001-SF04-235 Case No. *: 244 Description *: ☒ OK

4. Slide-ID: A001-SF04-234 Case No. *: 245 Description *: ☒ OK

5. Slide-ID: A001-SF04-233 Case No. *: 246 Description *: ☒ OK

6. Slide-ID: A001-SF04-232 Case No. *: Description *: ☒ OK

* optional

Cancel Reset All Rescan All Uncheck All Analysis

Figure 9: Preview tab

The detailed Preview tab displays the performed scan of the selected chip as a greyscale image (Figure 10). This tab can be used to check whether the chips are inserted correctly (using the 3 guide dots on each VisionArray Chip) or whether there is major pollution on the array field. If necessary, corrections can be made by adjusting the position of the chip or removing the pollution. Data can be added or amended in detail. A new scan of the slide can be performed by clicking **Rescan**, while **Reset** clears the position.

Any changes made in the detailed Preview tab are directly mirrored in the overview of the Preview tab. Return to the Preview tab by pressing **Close**.

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Start Preview x Position 1 x

Slide-ID: A001-SE06-195
Chip File: A001 (VisionArray HPV Chip 1.0)
Chip-Lot: SE06

Case No. *:
Description *:
Last Name *:
First Name *:
Date of Birth *:

* optional

Reset Rescan Close

Figure 10: Detailed Preview tab

If the performed scan is correct, check the OK box for each scan individually or the Check All button to automatically check all positions with valid Slide-IDs. The automated evaluation of the scan can be started by pressing **Analysis** in the Preview tab. After the analysis is finished, a separate Analysis tab opens for each scanned chip.

13. Analysis Screen

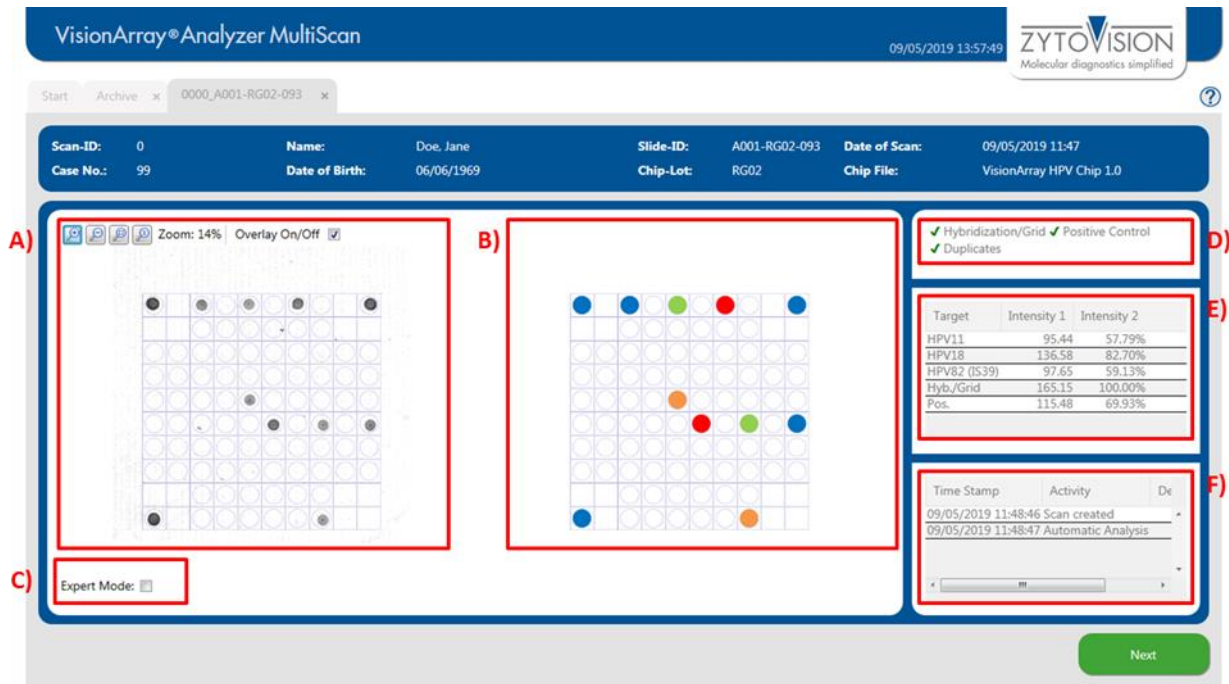


Figure 11: Analysis screen; A) Original Scan; B) Schematic view of the detected dots; C) Expert mode; D) Control mechanisms; E) Signal intensities; F) Analysis Protocol

13.1 Overview of the Analysis Screen

The analysis screen is divided into 3 parts (Figure 11):

On the left side the original greyscale scan is displayed (Figure 11 A). A grid can be toggled on/off by checking the box *Overlay On/Off*. The grid is toggled on per default. The visualization of the signals of the chip can be adjusted with the and buttons (see chapter 13.4). The automated evaluation of the array is performed based on the preview. The scan and all corresponding data are now saved in the database and cannot be edited anymore.

The centre of the analysis screen (Figure 11 B) shows a schematic view of the dots that have been detected by the software. The signals depend on the chip type. The associated information is stored in the corresponding chip file. The signals are color-coded depending on the chip type (see manual of the VisionArrayChip).

On the right side of the screen the control mechanisms, the signal intensities, and the analysis protocol are located (Figure 11 D,E,F).

13.2 Control mechanisms

The VisionArrayAnalyzer Software has 3 different control mechanisms (Figure 11 D).

Hybridization/Grid-control:

This control mechanism is based on the 3 guide dots in the corners of the array field that the software uses for orientation. The software spans the grid based on these 3 dots and allocates the positions to the signals. Additionally, the presence of the guide dots shows successful hybridization, labelling and staining. If the guide dots are too weak (intensity 1 < 150), a warning appears at this point. This may indicate poor hybridization.

Positive control

The positive control on the VisionArray Chips is used for assessment of the quality of the used PCR-template and of the PCR.

Duplicates

The third control mechanism implements a check by duplicates. This control is based on the fact that all capture molecules are applied in duplicates at different positions on the chip. A positive signal is therefore always visualized by 2 dots.

A green checkmark indicates the correct sequence of checks for each test. Irregularities are displayed by a red cross. Weak guide dots are highlighted by a yellow exclamation mark. The software evaluates the data even if the positive control or duplicates fail. The user has to assess the validity of the data by himself.

13.3 Signal Intensities and Analysis Protocol

The signals with corresponding intensities are listed below the control mechanism tab (Figure 11 E). Since all dots are applied as duplicates (triplicates for the guide dots) the intensity value of the dots is the result of the mean.

Intensity 1 shows the arithmetic mean of the grey value of the dots.

Intensity 2 shows the percentage signal of the guide dots. The guide dots are set as 100% intensity for an optimal hybridization result.

Below is a list of all actions that were performed after saving in the analysis protocol (Figure 11 F).

13.4 Zoom Level

The original scan and the schematic view are originally shown as an overview of the chip (Figure 11 A). A section of the chip can be enlarged by pressing the  or by clicking into the overview and scrolling the mouse wheel up (Figure 12). In order to zoom out it is possible to either use the  or to scroll the mouse wheel down after clicking on the scan.

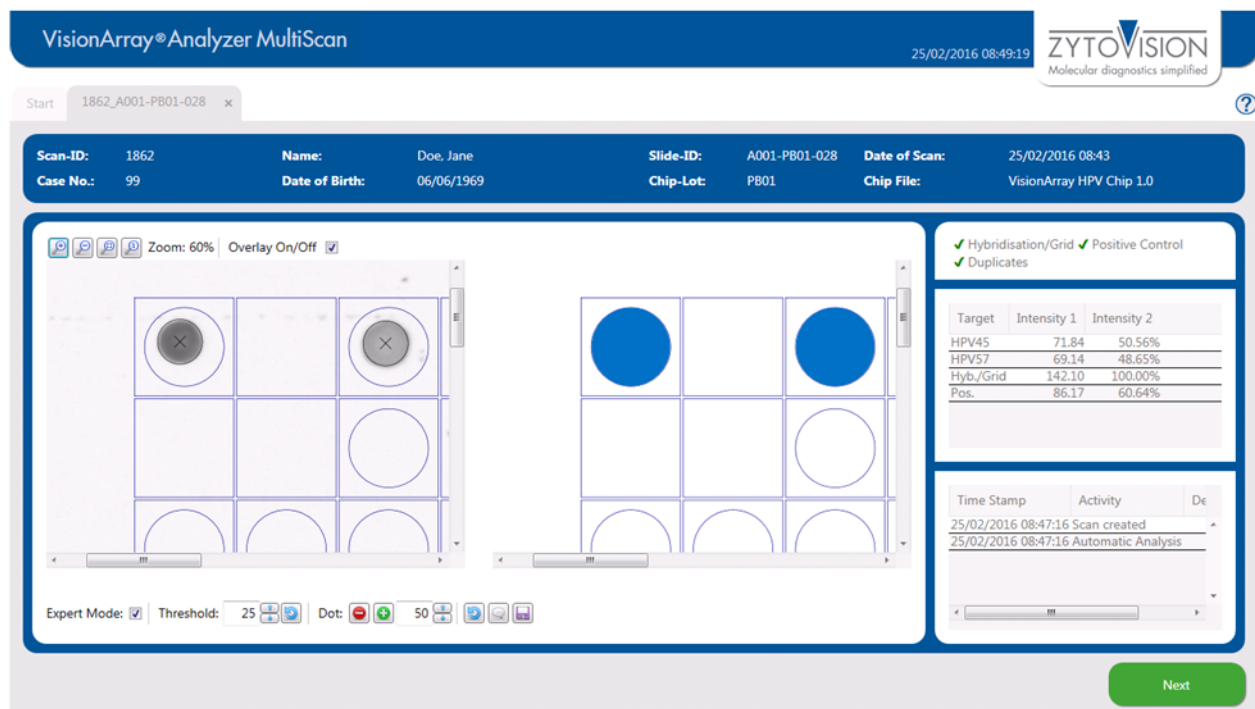


Figure 12: Analysis screen - zoomed in

13.5 Expert Mode

If it is necessary to make manual changes during chip analysis, the Expert Mode can be toggled on (Figure 11 C). All tools in the Expert Mode are visible when the box in the lower left corner is checked (Figure 13).



Figure 13: Active Expert Mode

13.5.1 Change Threshold

The threshold describes the negligible background on the chip (Figure 14). The threshold is predefined for each chip type. All dot signals that are stronger than the threshold are visualized in the schematic view and the table. Weaker signals are neglected and are not used for the evaluation.



Figure 14: Expert Mode - Threshold

13.5.2 Add/Delete Dots

If the software does not correctly detect a weak dot or a dot with an unusual morphology, it is possible to add it manually via Dot: + (Figure 15). It is possible to either add a dot with a preset size or set the size with the radius indicator. The added dot is displayed in the scan and the schematic view, respectively.



Figure 15: Expert Mode – Add/ Delete Dots

In rare cases, pollutions on the array field can be wrongly interpreted as positive dots. Via Dot: -, false positive dots can be removed in the Expert Mode (Figure 15). After clicking - the dot of interest can be selected and removed. The affected grid field is marked with an "X" to indicate a deleted dot. The changes are visible immediately in the schematic view, the detection status, and the listing table (Figure 16). The changes appear in the protocol only after changes have been saved by clicking the save symbol.

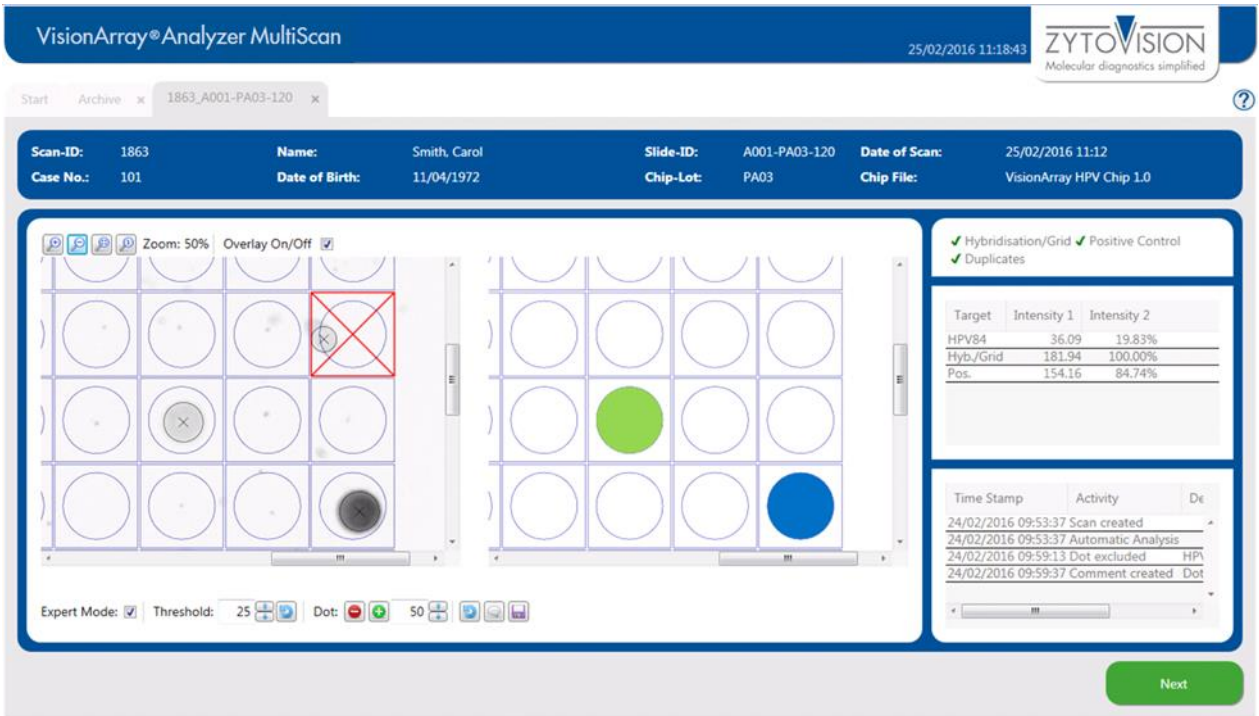


Figure 16: Analysis screen - excluding a dot

Addition or deletion of dots can be repeated infinitely. A deleted dot can be added again for the analysis by pressing + and vice versa.

13.5.3 Reset and Saving Options

All changes that have been made manually can be reset to the state of the automated scan by pressing the  button.

The changes can be saved by clicking the floppy disc symbol  or by closing the Expert Mode. After saving, all changes are listed in the analysis protocol.

13.5.4 Comments

The speech bubble icon  enables a comment field, where remarks can be made by the user. The comments will be displayed in the analysis protocol. Note that comments are also displayed in the anonymous reports. Personal data should therefore not be included in the comments.

14. Report

All information about a chip analysis can be printed or saved as a PDF-report (Figure 17).

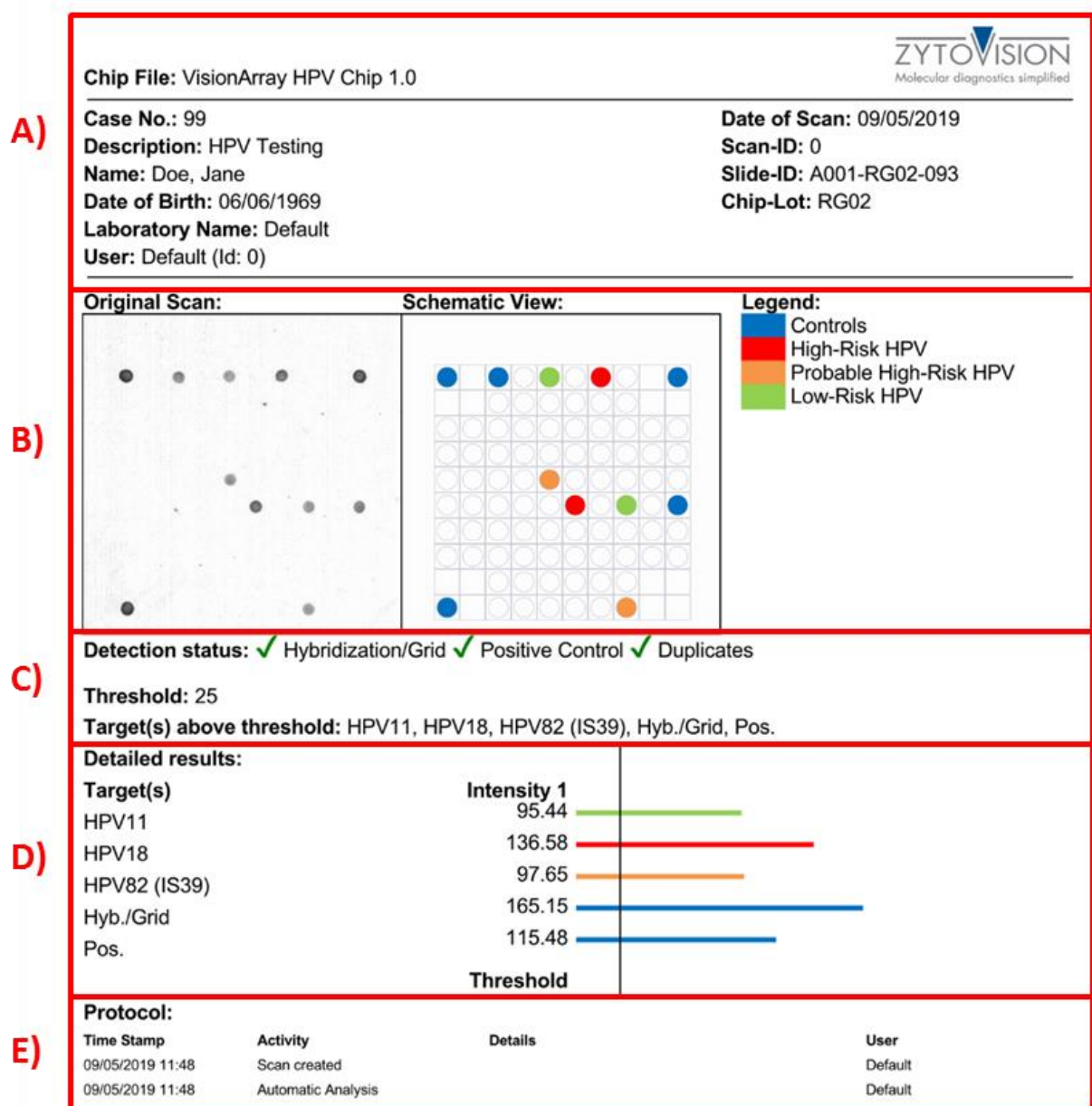


Figure 17: PDF-Report: A) Sample, patient, and chip information; B) Original scan and schematic view of the scan including legend; C) List of all controls, of the threshold, and of the detected signals; D) List and graphical display of the signal intensities; E) Protocol with detailed listing of all performed actions.

15. Data Export

In addition to the report of the data, it is possible to export the scan and the calculated signal intensities (Figure 18). Two common data and graphic formats are available under *Advanced Export*. To ensure data protection, the reports can be printed or exported anonymously by activating the anonymous report checkbox.

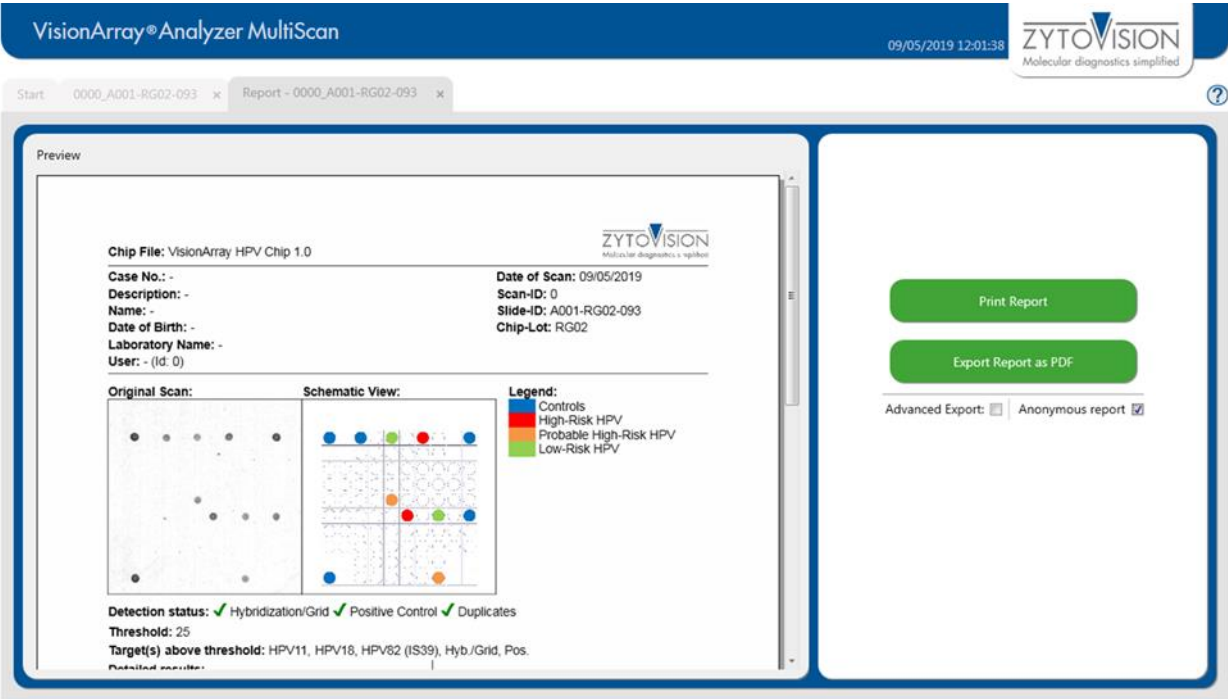


Figure 18: Possible export options

16. Archive

The Archive tab can be accessed from the start screen of the program. All chip files and the collected data of the VisionArrayAnalyzer software are automatically stored in the database on the supplied external hard drive and are accessible from this tab.

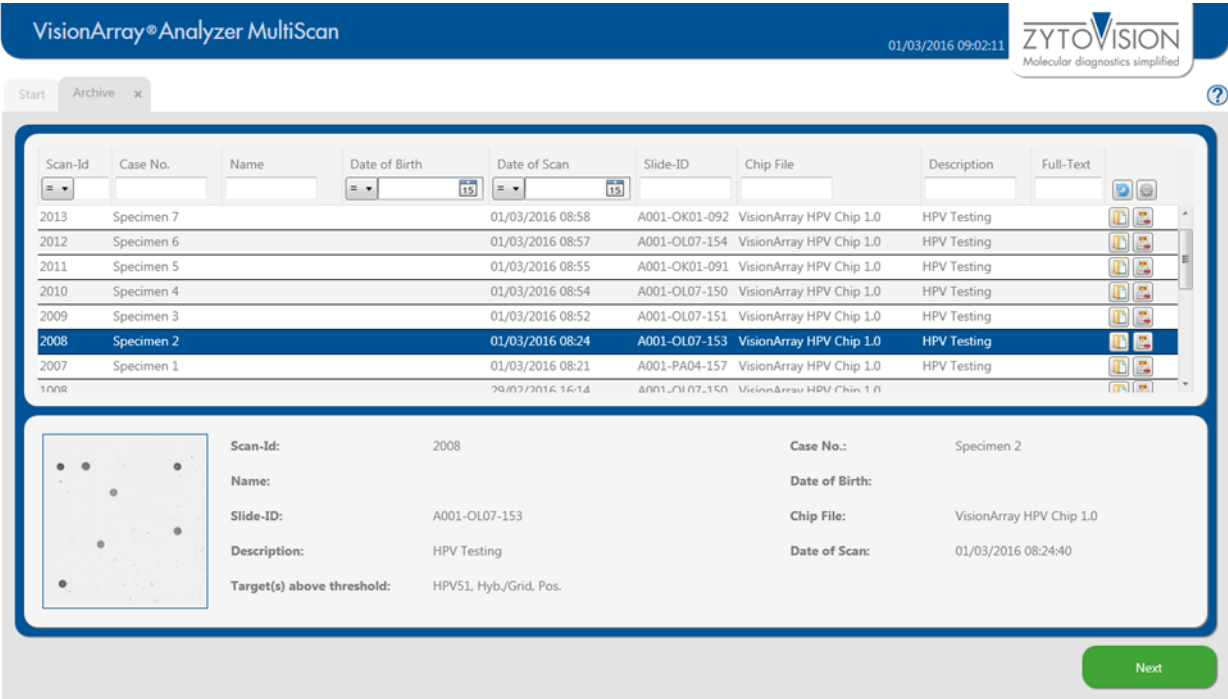


Figure 19: Archive tab

The database entries are displayed in table format (Figure 19). The information corresponds to the entered data in the Scan tab. The columns can be individually adjusted. Columns can be inserted or hidden via the setup icon , or moved into different positions by clicking and holding the column with the mouse and dragging them to the desired position. The database display is set to the default settings by selecting *reset* under  or after restarting the program.

It is possible to search the single columns or with the *Full-Text Search* the whole database for specific datasets. The button  deletes all entries in the search masks.

By selecting a single dataset, a preview of the scan is shown. The dataset of interest can be opened with a double click or by selecting it and clicking the open-icon  or **Next**. The selected dataset opens in the Analysis view and can be edited or the report can be opened as described above (see chapter 12).

A dataset can be deleted irretrievably by clicking the delete button .

17. Data Storage and Security

All scans or analyses that were produced by the VisionArray Analyzer Software are stored in an internal database located on the enclosed external hard drive in order to guarantee the protection of personalized data and data loss due to technical issues with the computer.

We recommend making regular backups of the data on a secondary external device in order to avoid data loss (see chapter 9).

18. Help Function

The Help Function can be activated via the question mark  in the upper right corner in order to open a comprehensive guide for every tab of the VisionArray Analyzer Software.

Our experts are available to answer your questions. Please contact helptech@zytovision.com



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