

3D HISTECH

**TMA Grand Master  
2.8  
User's Guide**

June 5, 2018

Rev. 1

GM28-UG-EN Rev1

For research and education uses only, not for use in diagnostic procedures.

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**Modifications not expressly approved by the manufacturer could void the user's authority to operated the equipment under FCC rules.**

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## Declaration Of Conformity

3DHISTECH Ltd. declares that the product TMA Grand Master is designed and produced with consideration of specified requirements according to the IEC 61326-2-6:2005 standard, and conforms to the directives and other standards listed below:

IEC 61010-1:2001 (ed. 2), "Safety requirements for electrical equipment for measurement, control, and laboratory use – Part 1: General requirements"

IEC 61010-2-101:2002 (ed. 1), "Safety requirements for electrical equipment for measurement, control and laboratory use.

DIN EN 550 11:2009, Class B, "Limits and methods of measurement of radio disturbance characteristics of industrial, scientific, and medical (ISM) radio-frequency equipment"



This product has been tested to the requirements of CAN/CSA-C22.2 No. 61010-1 and ANSI/UL 61010-1 by TÜV Rheinland.

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## Character Formats and Symbols

<i>Example</i>	Abbreviation or term that is explained in the section <a href="#">Terms and Abbreviations</a> .
<b>Example</b>	Words or characters that appear on the screen. These include field names, screen titles, pushbuttons and menu names, paths or options.  Keys on the keyboard. For example, function keys (such as <b>F11</b> ) or the <b>Ctrl+O</b> key combination.
<i>Example</i>	Cross-references to other documents or sections within this document.
 <b>Warning!</b>	Indicates that you need an additional module to use the feature, there are prerequisites for the task or that special care should be taken when using certain feature of the device.
 <b>Important!</b>	An important piece of information or a recommendation. The application will work if you choose not to follow the recommendation but its performance might be less than optimal.
 <b>Tip!</b>	A suggestion to use the application in some other way or to some interesting purpose.

## Terms and abbreviations

<b>Digital slide / Slide</b>	Slide digitized with a scanner microscope, for example Panoramic SCAN. Consists of an MRXS file and a folder with the same name as the MRXS file.
<b>Donor block</b>	The donor block is a standard tissue block that may be from surgical pathology, autopsy, or research material.
<b>Recipient block</b>	The tissue cores are removed from the donor and inserted into a “recipient” paraffin block.
<b>Clone Block</b>	A duplicate (triplicate, quadruplicate, etc.) of a recipient block with identical layout and core order.
<b>TMA</b>	Tissue microarrays – The tissue microarray consists of an array of cylindrical cores of paraffin-embedded tissue that are removed from preexisting “donor” paraffin blocks.
<b>PCR</b>	Polymerase Chain Reaction, a biochemical technology used for a variety of applications, but the primary aim of the method is to exponentially amplify particular DNA sequences.



# 1 Intended Use

**TMA Grand Master** is a software-controlled electronic laboratory device that automates the creation of tissue microarrays (TMAs) and also the process of PCR sampling.

The creation of TMA blocks (by taking tissue core samples from donor blocks and inserting them into recipient blocks) and the insertion of extracted tissue cores into PCR tubes is controlled by using a graphical user interface. The built-in digital camera units of **TMA Grand Master** give you a clear image of each donor block, so you can aim the puncher more accurately; an additional camera takes pictures of the block labels. You can also save an image of each donor block with markers showing the positions from where the tissue cores have been extracted.

You can export block-related data to different types of files (.xls, .xlsx, .ods, and .csv) through the **TMA Grand Master** software application to track associations between recipient block positions and the ID of the donor block from which the core tissue was inserted into the recipient block.

## 1.1 Main Features of TMA Grand Master

- It has a robust and stable mechanical main unit.
- It has an intuitive operation control via the keyboard and the mouse of a PC connected to the main unit.
- The device measures the height of donor blocks (the value is displayed next to the donor block thumbnail image) based on which the software calculates the depth of punch, drill, and insertion. Thus, embedded cores are placed correctly into the recipient block resulting in an even surface level.
- It makes image creation possible when a TMA block is created either for reference or for archiving during a research project.
  - For donor block: locations where core tissue was extracted from.
  - For recipient block: various stages of filling it with core tissue.
- Block identifiers are stored in a database from which each block data within a Project is automatically loaded after the ID is entered, furthermore the whole project assembly data can be restored after exiting and restarting the software without saving any project data.
- Maximum TMA handling capacity:
  - Up to twelve recipient blocks and 60 donor blocks at same time.
- It is capable of receiving 6 PCR cassettes with a holding capacity of 10 PCR tubes. The software allows you to transfer four cores into each tubes, so a maximum number of 240 up to 480 tissue samples can be collected in 6 PCR cassettes during a project if not interrupted.

## 2 TMA Grand Master Hardware

### Hardware:

- **TMA Grand Master** main unit
- Control computer with a monitor, a mouse and a keyboard
- USB cables between the main unit and the control computer
- Accessories box

### Blocks:

- Base molds for paraffin blocks

### 2.1 TMA Grand Master Main Unit

#### Front View

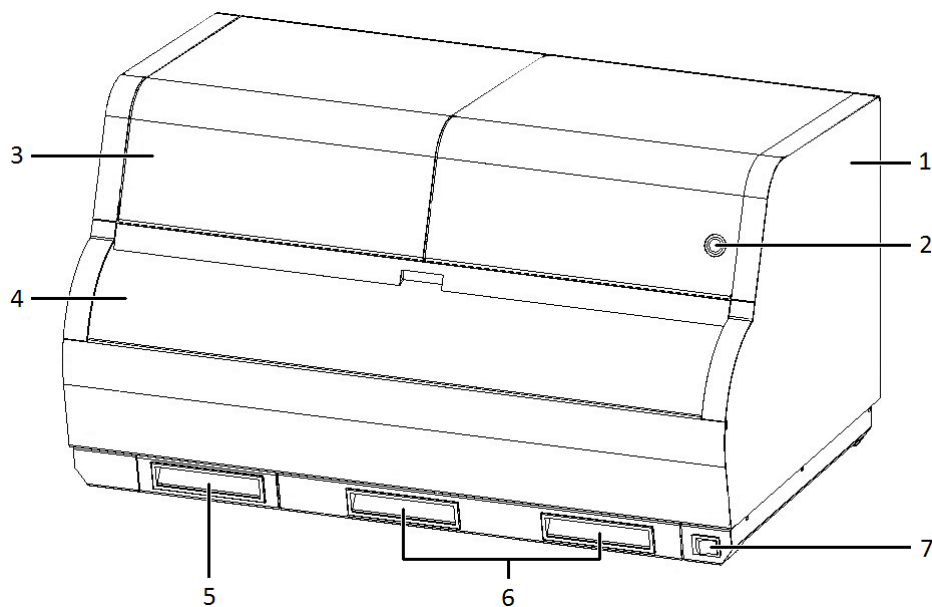
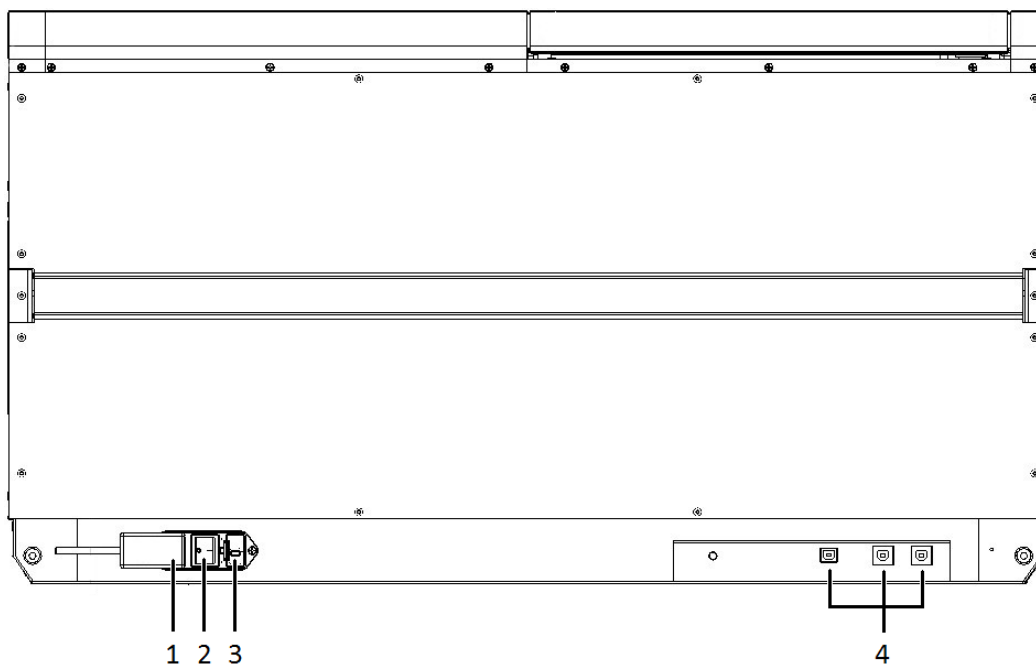


Figure 1 – TMA Grand Master front view

1. Protective housing
2. Door opener button
3. Tool change compartment door
4. Protective window
5. Trash container for paraffin flakes and discarded core material
6. Grips for service compartment door
7. Front power supply switch

**Back View****Figure 2 – TMA Grand Master back view**

1. Terminal point for the power supply cord
2. Main power supply switch
3. Fuse compartment
4. USB ports to connect with the computer.

## 2.2 Cabling

For required cable connections, the supplied cables must be plugged in as shown in the figure above. To connect the main unit with the computer any of the three USB ports can be used.

**Warning!**

All cable connections must be checked for firm seating. Defective cables must not be connected to any part and must be replaced with cables in proper operating condition. Contact Thermo Fisher Scientific support in such cases.

**Important!**

The use of an uninterruptible power supply (UPS) is recommended but optional.

**Warning!**

Only connect external devices that are safety extra low voltage rated to the TMA Grand Master instrument to avoid the risk of electrical shock.

## 2.3 Delivery

### Package 1

- **TMA Grand Master** main unit (packed in a mandatory polyethylene container in a cardboard box)
- Accessories in a plastic box (drill bits, punchers, and pistons), paraffin block base molds, accessories and tools for the assembly. The size and the content of the box can vary according to your purchase order. For further information on the basic accessories, see section **10.2 Accessories**.

**Important!**

Accessories are classified as consumable goods, therefore warranty cannot be applied to these items. The life-span of tools highly depends on the types of extracted tissue, the method of fixation and embedding, and the mode of use.



Figure 3 – Tool box

## Package 2

- Control computer (with mouse and keyboard)
- Monitor for the control computer
- Cables



### Important!

Microsoft Office package or license is **NOT** delivered with **TMA Grand Master**.

If you want to use an Excel worksheet to store the donor block information to be used during the creation of a TMA block and if you want to export the TMA block information to an Excel worksheet, you need to install Microsoft Excel or OpenOffice on the control computer.

## 2.4 Installing and Configuring TMA Grand Master Hardware



### Warning!

Only qualified personnel may install **TMA Grand Master** and perform the initial start-up procedure. Thermo Fisher Scientific **Service** technicians install and configure **TMA Grand Master** and hand it over to you in operating condition.

## 2.5 Transporting the TMA Grand Master Main Unit

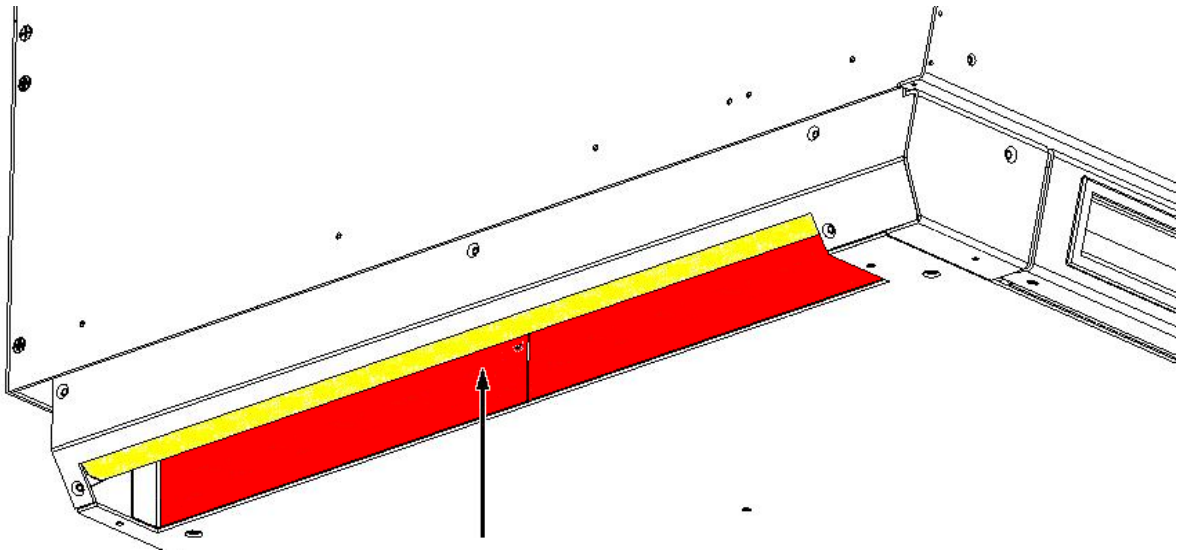


### Warning!

If you need to move **TMA Grand Master** to another location, transport it in its original packaging only.

1. Switch off the **TMA Grand Master**, the control computer and the monitor, and unplug all cables.
2. Close the door of the main unit.

3. Lift the main unit by its recessed transporting handles that can be found both sides of the bottom plate, underneath the side-plates of the main unit.



**Figure 4 – Transporting handle**

4. Place the device into the designated cardboard box onto the bottom protective foam.
5. Arrange protective padding on the four top corners.
6. Pack the accessories into their box.
7. Put the main unit and the accessory box to their designated places in the road box.
8. Close the box and tape it.

## 3 Installation of TMA Control Software

### 3.1 Prerequisites for the TMA Control Software Installation

Prerequisites	Description
Hardware	<b>Recommended:</b> Intel® Core™ i5-4570 Quad-Core, 3.2 GHz, 4GB RAM
Monitor Screen resolution	<b>Recommended:</b> UXGA (1680×1050 or 1920×1080 True Color) or better at 96 Dpi
Operating system	Microsoft Windows 7 Professional 64-bit SP1 EN or Microsoft Windows 10 Professional 64-bit EN
Disk space	<b>Recommended:</b> 3GB – for application software, drivers, prerequisite and temporary files 500 GB – for saving the TMA database, and for storing digital slides

### 3.2 TMA Control Software Installation



#### Important!

Thermo Fisher Scientific service technicians perform the installation and configuration of the **TMA Control** software.

The following installation procedure is for information purposes only – follow the below steps only if you need to re-install the software, or upgrade to a newer software version.



#### Warning!

The control PC on which the SW application of TMA system runs, shall not be considered as general purpose personal computer.

In order to achieve error-free operation, 3DHISTECH Ltd. prohibit the modification of the PC configuration as well as the installation of any additional software.

Any action that is prohibited by this manual can cause malfunction of the system.

1. Launch the **TMAControl\_2.8\_RTM\_x64.exe** file that you received on a 3DHISTECH Installation Disc or downloaded in a compressed file.
2. Follow the instructions in the installation wizard.

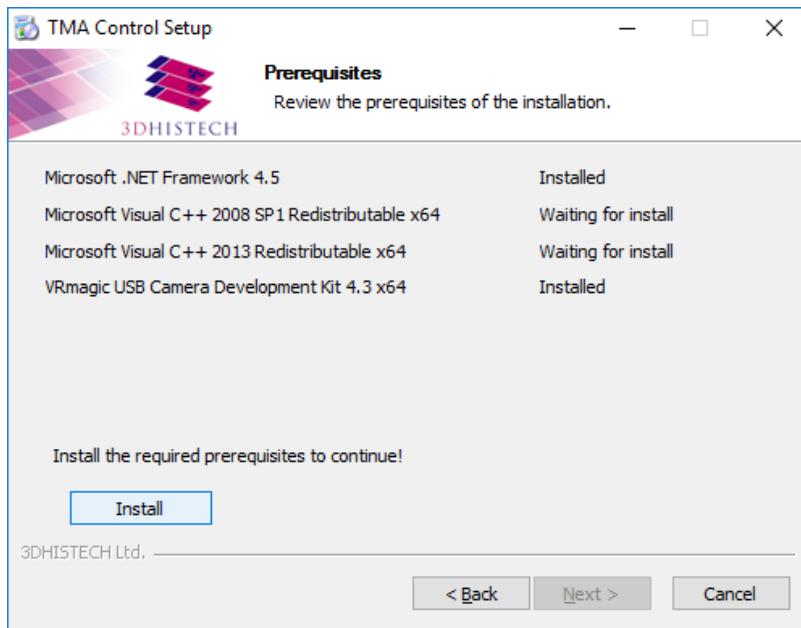


3. Accept the End-User License Agreement, and click **Next**.

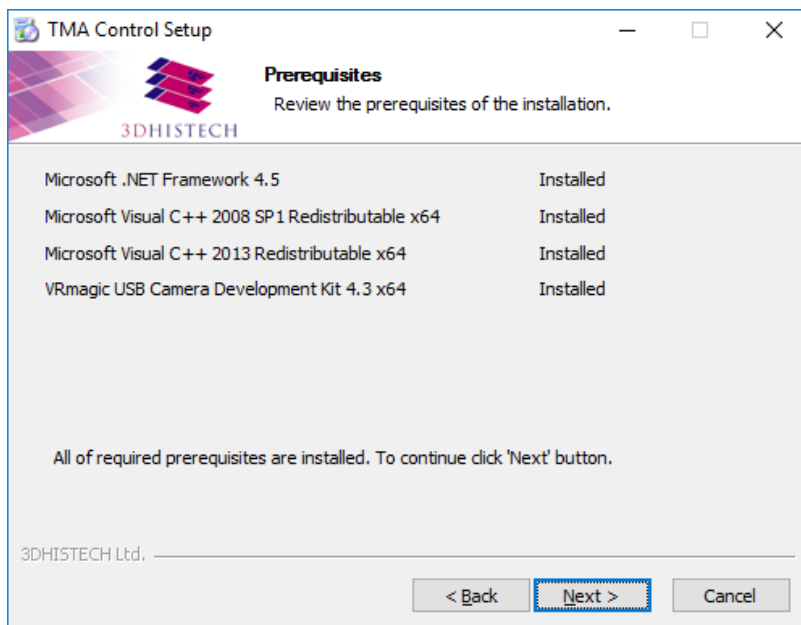




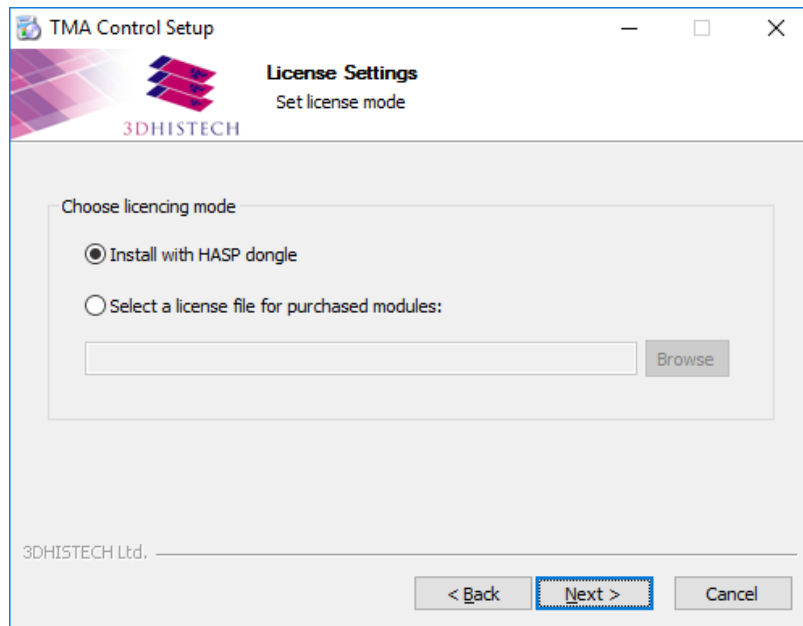
- The installer notifies you if it cannot find the prerequisites. Click **Install** to start the installation of missing prerequisites.



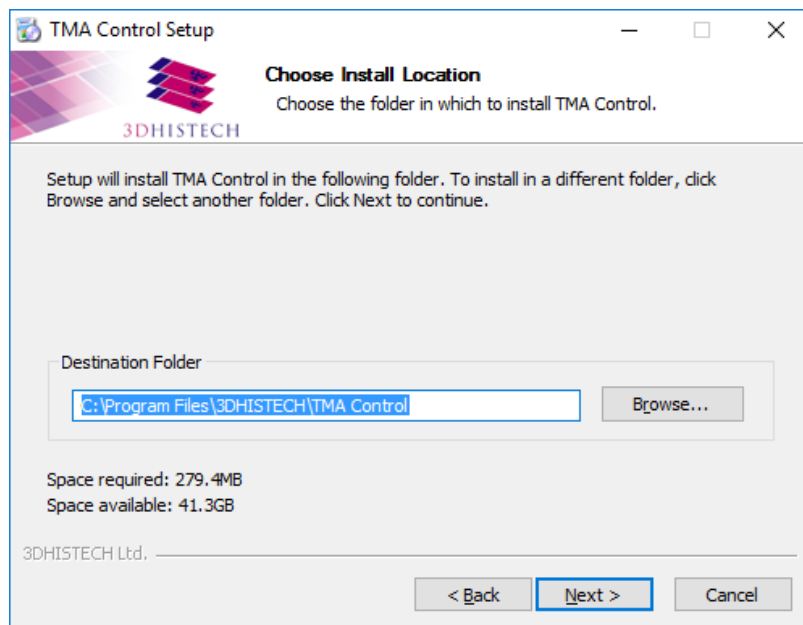
- Click **Next** to continue with the installation of the TMA Control software application.



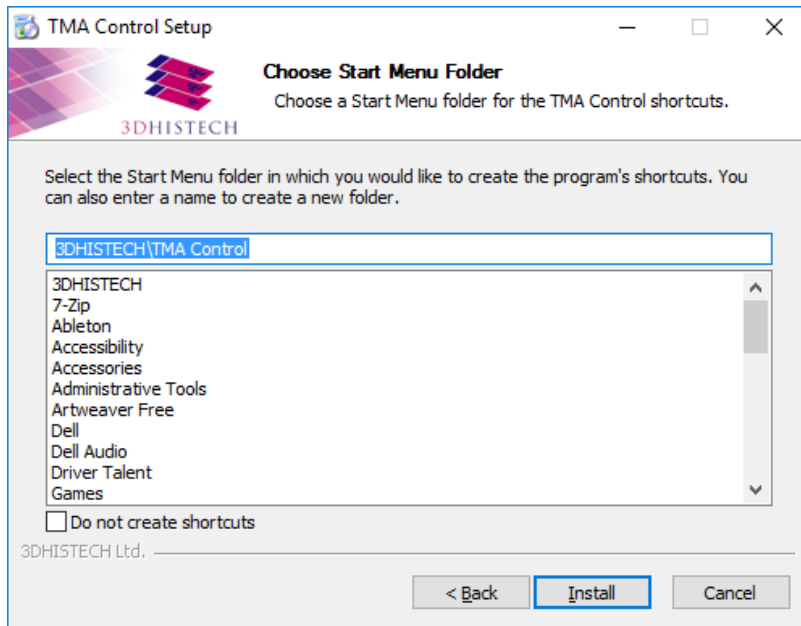
6. Select the type of license – browse for the license file or select HASP dongle.



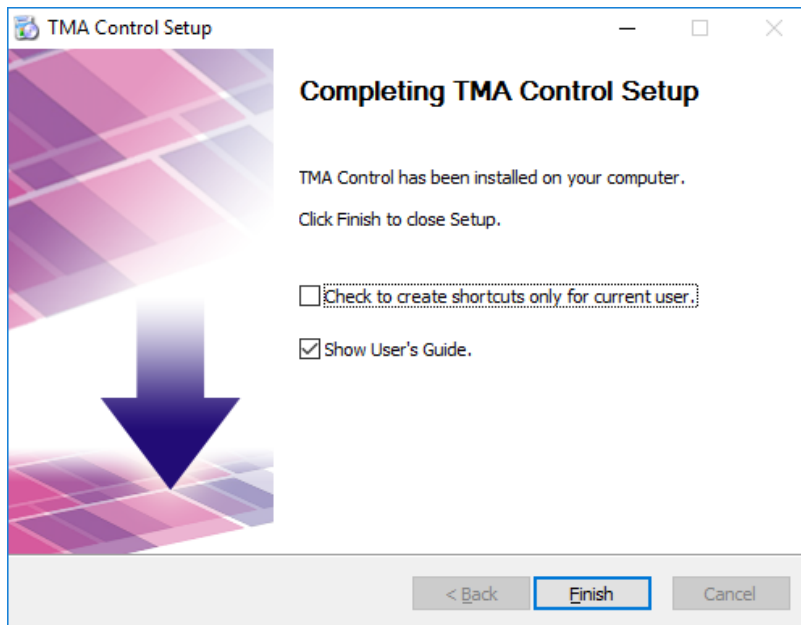
7. Choose the installation folder for the TMA Control software application. Click **Browse** for locating a different folder than the default one, then click **Next** to continue.



8. Choose the Start menu folder.



9. After completing the installation of TMA Control, click **Finish** to close the wizard.



**Important!**

After the installation, RW access right to database and configuration file must be granted for Admin and Standard users.



## 4 Operating the Main Unit

### 4.1 Switching the Main Unit On or Off

#### Turning the Power On

1. Switch on the TMA Grand Master (first, the main switch on the back panel – see **Figure 2 (2)**, then the one in the front – see **Figure 1 (7)**).
2. Turn the control computer and the monitor on.

#### Turning the Power Off

Each time you finished working with TMA Grand Master, do the following:

1. Close the software application on the control computer.
2. Switch off the TMA Grand Master.
3. Turn the control computer and the monitor off.

### 4.2 Starting the TMA Control Application

You can start the program by double-clicking onto the program icon of the desktop.



#### Warning!

If you start the software, but the hardware is turned off, a warning message appears. Switch on the main unit then click **Retry** in the message box.

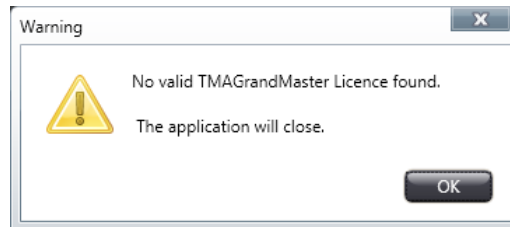


#### Warning!

If you receive a warning message after starting the software, that informs you about having insufficient disk space on your designated drive, free up a necessary amount of disk space, then restart application.

**Warning!**

You receive a warning message after starting the software, if not having a valid license for running the application.

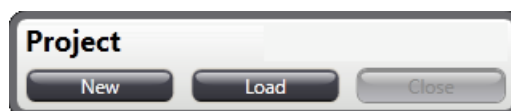


A separate license is necessary to activate the PCR function of the TMA Control software.

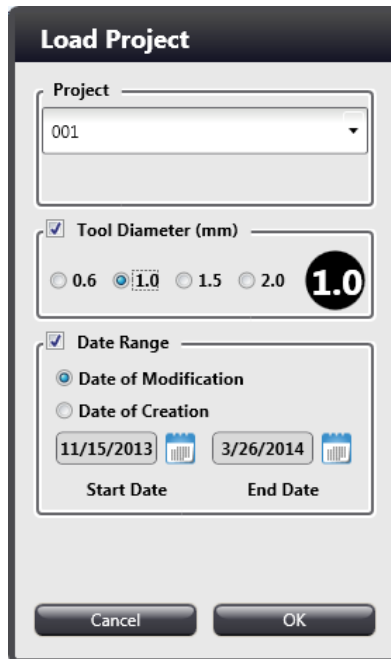
If you start the application for the first time, a **New Project** window is displayed in which you must enter a name for the project.



If you already have worked on projects previously and you want to create a new project, click **New**; and if you want to load a project that has been saved previously, click **Load** in the **Project** panel that is located at the top right corner of the application window.



To load an existing project, the following window is displayed after clicking **Load**, in which you can select the desired project to be loaded, and narrow project list by activating **Date Range** and/or **Diameter** filters. When writing the name of the project to be loaded, suggested projects appear on the list according to the entered text string.





The screenshot shows a dialog box titled "Load Project". It features a "Project" dropdown menu with "001" selected. Below this is a "Tool Diameter (mm)" section with a checked checkbox and radio buttons for 0.6, 1.0 (selected), 1.5, and 2.0, accompanied by a large "1.0" button. The "Date Range" section is also checked, with "Date of Modification" selected over "Date of Creation". It displays a "Start Date" of 11/15/2013 and an "End Date" of 3/26/2014, each with a calendar icon. At the bottom are "Cancel" and "OK" buttons.

According to the database driven project handling, each time you restart the software (even without saving the current process of the actual project before exiting) all the data is loaded automatically to restore the previous state.

### 4.3 Main User Interface

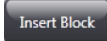
This version of TMA Control offers two different views of recipient and donor block panels. Based on the loading and processing method of blocks the normal view includes thumbnails of all recipient tray positions, and as for donor blocks the selected tray is displayed in its full capacity.




The other view mode helps users to identify blocks and their statuses more easily. Click  at the top of recipient blocks panel, and  at the right end of donor blocks panel to switch to this view.



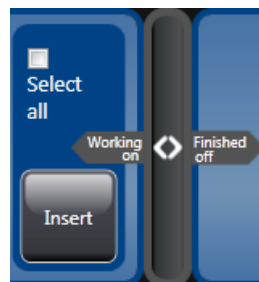


If you want to load a recipient block into the unit, click  at the **Unused Block(s)** panel header.

As for donor blocks, first click the  button, then if there is a free slot on the actual tray, the door can be opened (otherwise wait until the closest tray with a free slot on it is rotated to loading position) and the block can be inserted.

After inserting blocks, a thumbnail image will be displayed on the **Unused Block(s)** panel if a block has been loaded into a recipient block tray, and if a donor block was loaded into a slot on a donor block tray, its image will appear on the left section of the donor blocks panel at the bottom of the main application window.

At the donor panel a separator can be dragged sideways and is used for dividing donor block panel to display TMA block thumbnails that are being processed and that are finished.





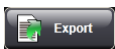


### 4.3.1 Main Toolbar

The main toolbar of the TMA Control software is located at the top of the application window.



Figure 5 – Main toolbar

The following functions are available for you to select from the main toolbar:

-  - **Log in** to a dedicated CaseCenter server
-  - **Tool change**
-  - **Export** project data
-  - **Import** Donor Block IDs, clinical/patient data, or medical information
-  - **Stop** process

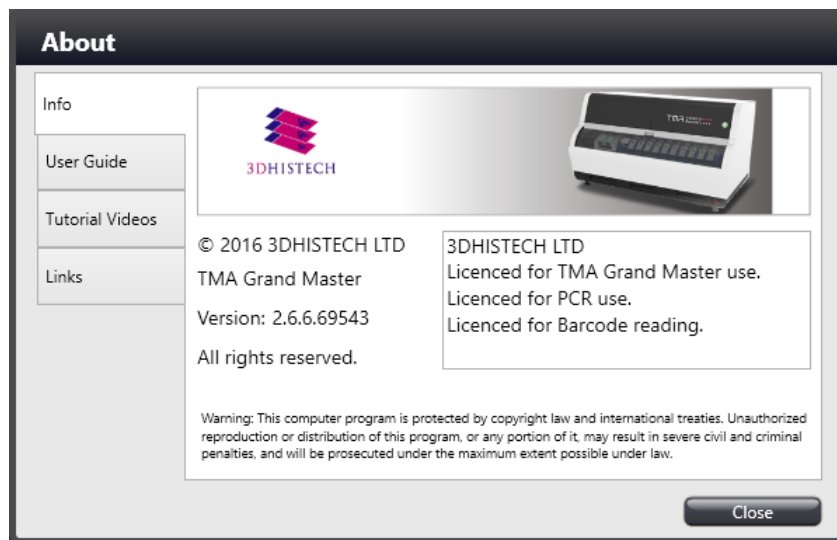


- **Settings** window contains the settings for some important features in TMA Control, including Overlay, Annotation, Restore Medical Information Database, Depths, Images, Layout, Barcode, Language, and Theme. See section **6 Settings** for more information.

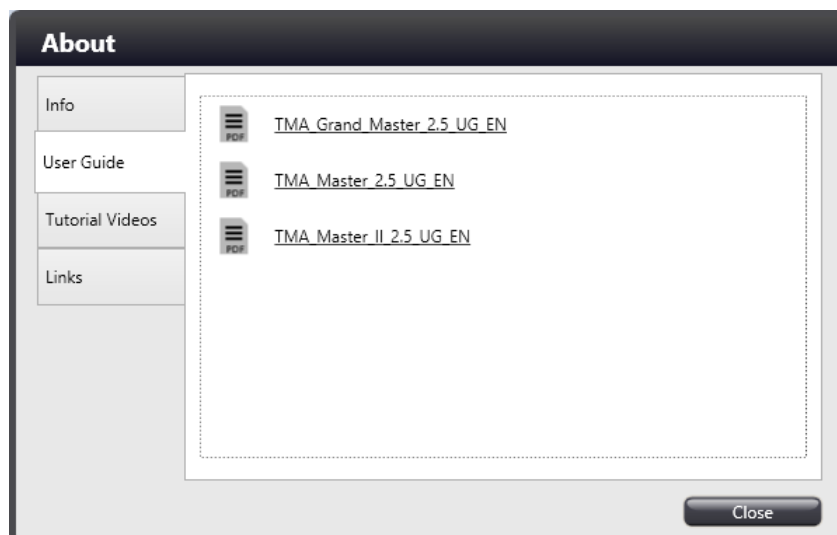


- **About** window contains details of TMA Control software, and includes the following panels:

- **Info** – displays software version information and licensed features.

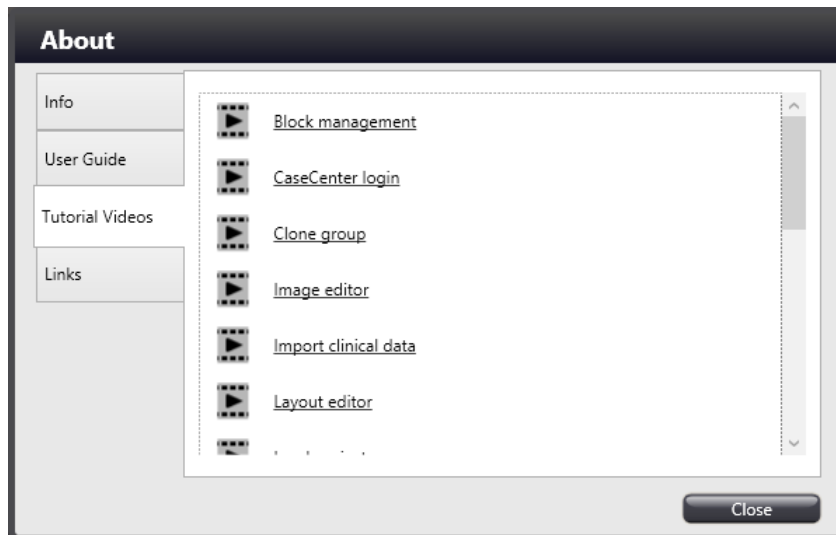


- **User Guide** – Manuals of TMA Grand Master, TMA Master, and TMA Master II can be accessed and opened directly by clicking the links.

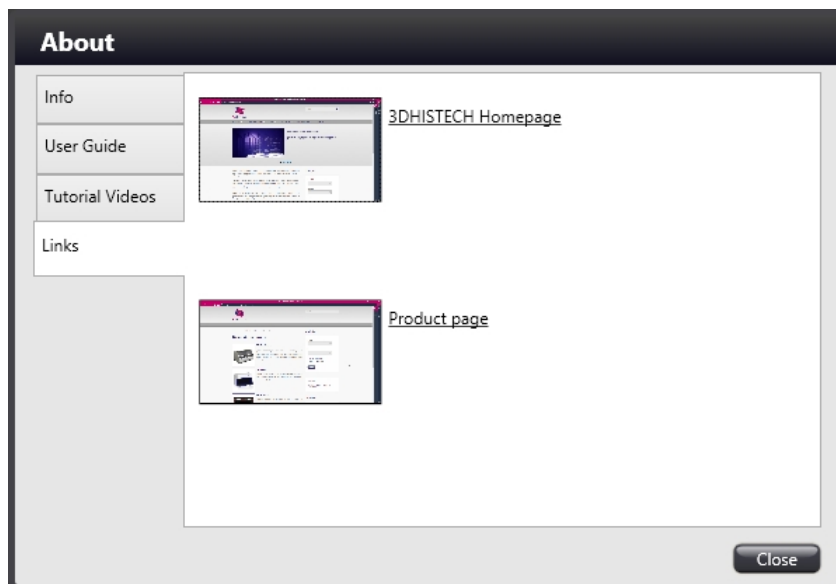


- **Tutorial Videos** – Selected tutorial videos are listed and can be opened by clicking the links.

**NOTE:** Before opening the videos, make sure to copy video files to <C:\Program Files\3DHISTECH\TMA Control\Videos\TMA Grand Master> folder from the installation disk. This folder may be hidden, and thus requires authentication.



- **Links** – Company and product web page links are displayed here.



- **Exit application**

## 4.4 Inserting and Removing Blocks

### 4.4.1 Block preparation

**Warning!**

If the paraffin swells through the bottom or the sides of the plastic cassette, cut off the excess paraffin before inserting the block into the main unit.

**Warning!**

Working on extra hard tissues (for example, not decalcified) may end up breaking the puncher needle.

**Important!**

To ensure the good quality of recipient blocks, make sure that the top surfaces of both, recipient and donor blocks are parallel to the plastic bottom of the cassettes, and there are no dents or cavities in the paraffin layer.

If any defect is visible, cut the top layer of the block to make it even, otherwise embedded cores may be damaged after creation (for example, the top section of the core is sticks out of the paraffin block, that can be easily broken down).

#### 4.4.2 Cleaning block and PCR cassette preparation



##### Important!

Before inserting a PCR cassette into its slot, ensure that the cover plate and tubes are uncontaminated. One PCR cassette can be inserted into its slot before the first position on each donor tray. The correct orientation of the cassette and its cover plate is shown on **Figure 6**.

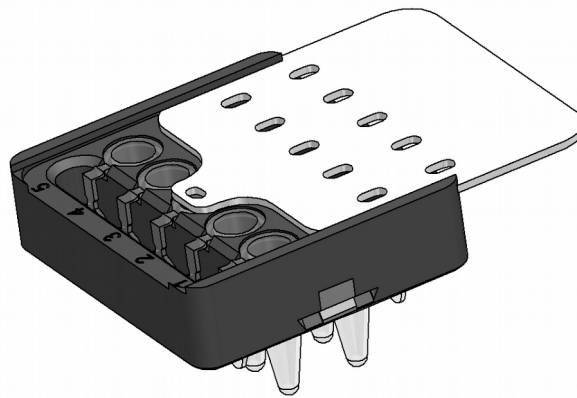


Figure 6 – PCR cassette




##### Important!

If TMA Control cannot successfully identify the loaded PCR cassette, clean the slot area and the cassette, then insert the cassette again. For cleaning blocks use regular (37mm size) blocks only.

To avoid contamination, cleaning blocks are used before each PCR sampling. A cleaning block is a virgin recipient block from which paraffin core is extracted and placed back with the puncher, hence cleaning its surface.

Upon selecting the cleaning block on the user interface, an automatic layout is generated based on the size of the puncher in use.

If not every cleaning position had been used up during a previous project session, you can use that block further on but make sure to manually mark the first free position.



**Important!**

Before starting a larger project it is advised to calculate the number of cores that will be inserted to PCR tubes, so placing a sufficient number of cleaning blocks accordingly.


The number of cleaning spots depending on the puncher diameter are the following:

Puncher diameter	Number of cleaning spots
0.6mm	252
1mm	144
1.5mm	72
2mm	50



### 4.4.3 Inserting a block into the main unit





1. Recipient block positions are displayed in a double-column on the left side of the screen. Tray positions of donor blocks are identified by six buttons (A-F), tray capacity is 10 blocks each.

- For the recipient blocks (1) click the  button next to the image of the specific block pairs. Depending on the donor block tray that you want to rotate to inserting position, click the tray ID: A – F (2). Alternatively, if the new view is activated, click **Insert Block** (3) on the Unused Block(s) panel if you want to insert a new recipient block, and click **Insert** (4) at the donor panel to insert new donor block into the donor block tray selected automatically by the software.



- The donor/recipient block holder cylinder turns to the loading position with its appropriate side. The ID of the corresponding tray is marked with green, also the slot is lit for easier identification.
- The door opener button turns green (button status is shown at the right side of the main toolbar). The light pulsates for about 10 seconds and it is possible to open the door within this time frame (countdown is displayed in place of the  button).
- Push the door opener button to open the door.
- Press down the flap in front of the block slot.
- Slide the block into position with the slanted side towards the back of the machine.
- Release the flap when the block is in position.
- Close the door.
- The column turns into the next position, the height of the inserted block is measured (also, the presence of the block is checked). These data are saved for later use (for drilling, punching operations, and depth of insertion) and based on the measurements, the software calculates the distance of the objective from the surface of the recipient block in order to take an accurate photo of it.
- Follow the steps 1-9 if you want to insert additional blocks into other trays. If the cylinder is at the proper position, it is not necessary to click the tray ID then the  button.

#### 4.4.4 Removing a block from the main unit

1. Recipient block positions are displayed in a double-column on the left side of the screen. Donor block tray positions are identified by six buttons (A-F). The **Change Blocks** buttons are responsible for rotation of the donor block holder cylinder.
2. Depending on which donor block tray is needed to be rotated to the block removal position, click the tray ID (A-F). For the recipient blocks click the  button next to the image of the specific block pairs.
3. A donor/recipient block holder column turns to the loading position with its appropriate side.
4. The door opener button turns green. The light pulsates for about 10 seconds and it is possible to open the door within this time frame (countdown is displayed by a  icon at button area).
5. Push the door opener button to open the door.
6. Press down the flap in front of the block slot.
7. Remove the block from its position and release the flap.
8. Close the door.

#### 4.4.5 Removing a PCR cassette from the main unit




##### Warning!

After removing PCR cassettes, make sure that cores are not clung to the port edges of the cover plates. Before carefully removing the cover plate of a PCR cassette, gently tap on it a couple of times to let all the samples fall entirely down to the bottom of the PCR tubes.

### 4.5 Changing the Drill Bit and the Puncher

**TMA Grand Master** is delivered with drill bits and punchers of different sizes. The following instructions demonstrate how to change drill bits, punchers and pistons to match the hole diameter of a defined layout.

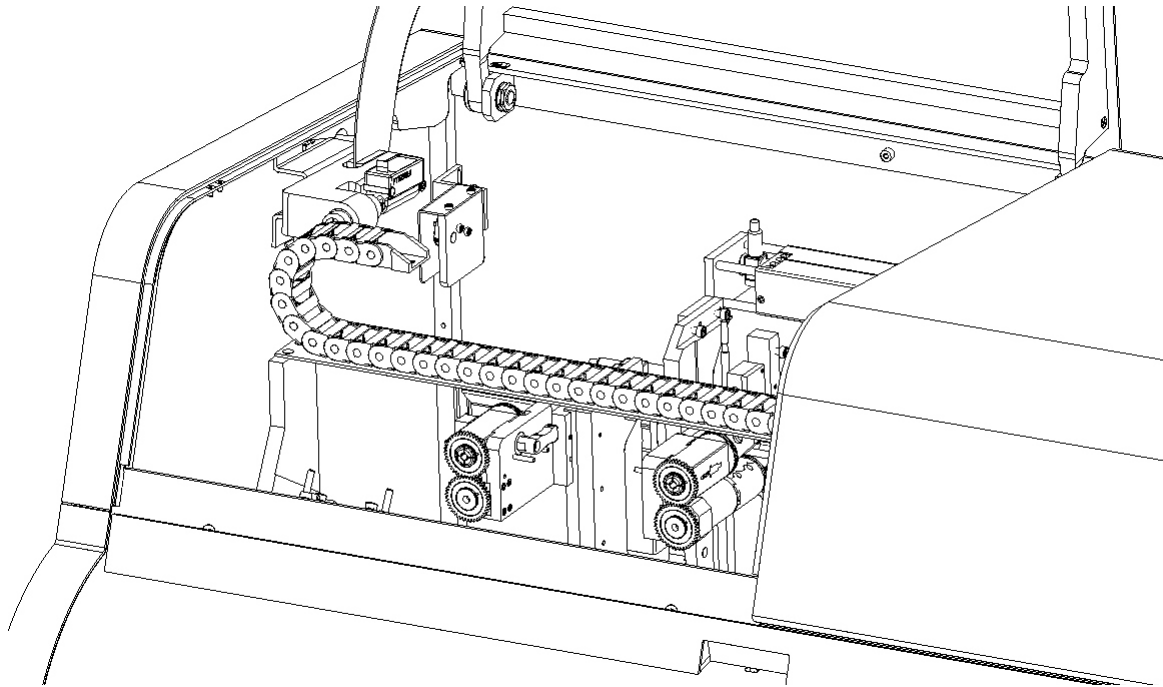
1. Start the TMA Control application, then click the  button at the main toolbar.
2. According to the appearing message on your screen, follow the steps to change the tools of the same size both for the puncher and the drill bit.

##### You are requested to:

1. Open the block feeder door, then open the tool change compartment door
2. Change the drill bit and the puncher
3. Close the door back

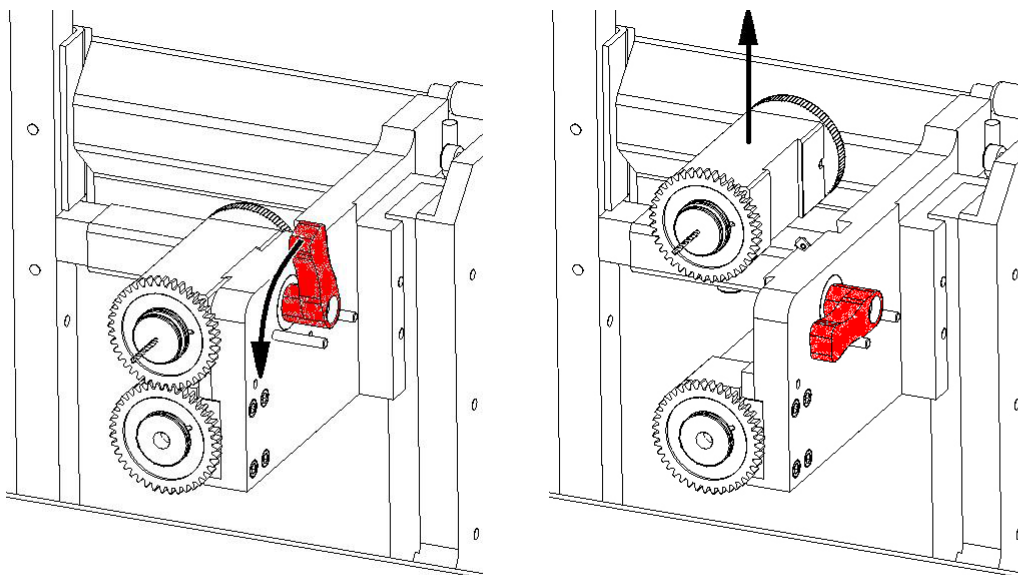


3. Open the tool exchanger compartment door.



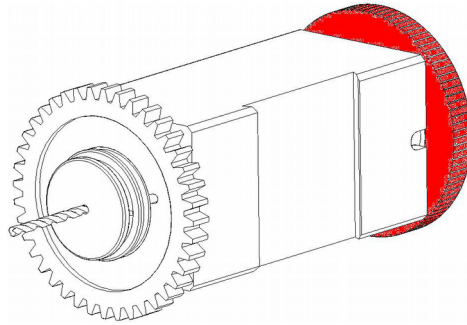
**Figure 7 – Tool compartment**

4. Loosen the drill chuck locking lever (marked with red) that fixes the drill chuck in position and remove the drill chuck by lifting it upwards.



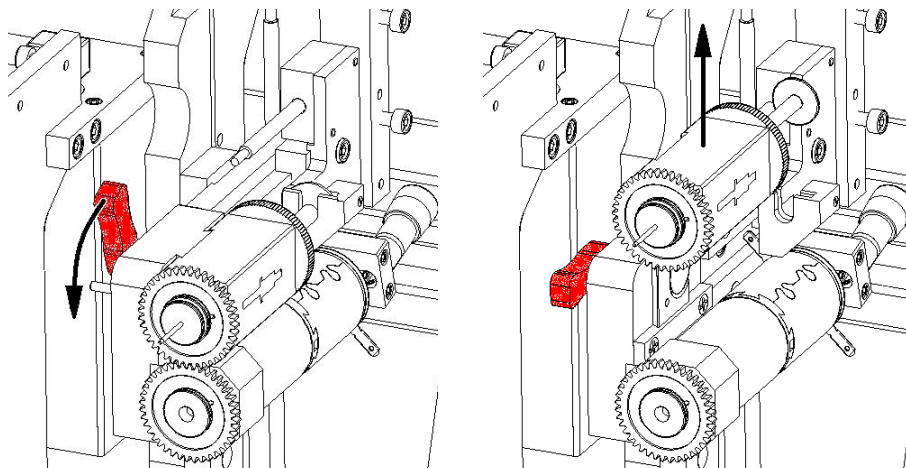
**Figure 8 – Removing the drill chuck**

5. Hold the front cog wheel firmly and loosen the rear cog wheel (marked with red) and turn it anticlockwise about two turns (360-720 degrees), then remove the drill bit from the drill chuck.



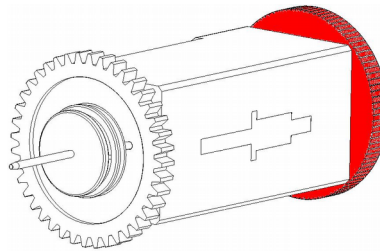
**Figure 9 – Drill chuck**

6. Insert the drill bit you want to use into the drill chuck, and push it inwards as much as you can.
7. Hold the front cog wheel firmly and tighten the rear cog wheel (clockwise). Make sure with the help of the tool that the upper cog wheel is secured firmly.
8. Insert the drill chuck into its position and fix it with the locking lever. Ensure that the two cog wheels (motor and drill chuck) are aligned exactly.
9. Loosen the puncher chuck locking lever that keeps the puncher chuck in position and remove the puncher chuck assembled with the piston.



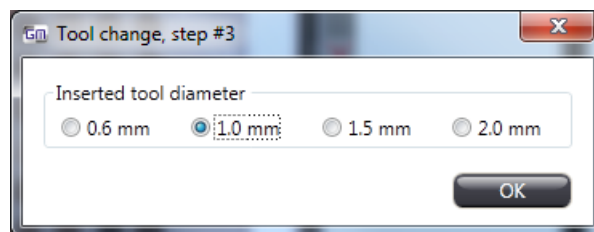
**Figure 10 – Removing the puncher chuck**

10. Pull out the piston, then hold the front cog wheel firmly and unscrew the rear cog wheel (marked with red) by turning it anticlockwise about two turns (360-720 degrees), and now you are able to remove the puncher.



**Figure 11 – Puncher chuck**

11. First, insert the new piston in the puncher chuck, then insert the puncher into the puncher chuck matching the size of the piston. Tighten the rear cog wheel, holding the front cog wheel firmly.
12. Insert the puncher chuck into its position and fix it with the puncher chuck locking lever. Ensure that the two cog wheels (motor and puncher chuck) are aligned exactly, and move the piston into position making attention to place the piston collar to the groove on the console.
13. Close the door of the tool change compartment.
14. In the pop-up window, select the diameter of tools you have placed in and click **OK**.



## 5 Using TMA Grand Master

This TMA Grand Master device is designed to create TMA blocks and make it available for you to place extracted cores into PCR tubes at the same time, within the same process. With the operating software you may set processes for creating TMA blocks or PCR sampling exclusively or both.

### 5.1 Creating TMA Blocks with TMA Grand Master

You can place up to sixty donor blocks and up to twelve recipient blocks in the tray (you can design a separate layout for each of them). However, the drill bit size must be the same for the batch drilling. You can prepare TMA blocks in batch mode:

- insert all the 60 donor blocks, mark the punching positions, then leave the device running
- OR**
- insert donor blocks into trays continuously (10 blocks per tray) and mark punching positions. Thus, meanwhile the unit works on the selected blocks, you can place additional blocks and mark drilling positions on them, so you can work simultaneously with the TMA Grand Master.

You can create up to twelve identical TMA blocks by taking out one tissue core sample, and inserting it into each recipient block.

Then, you can either create several slides from the TMA blocks, or you can just keep one of the TMA blocks as a backup.

When you are filling the recipient block from up to sixty donor blocks (maximum number of donor blocks), the digital camera of **TMA Grand Master** gives you an image of each donor block so you can aim the puncher accurately.

Additional recipient blocks can be inserted into empty slots during a running process, but their removal is not yet available.

Recipient block-related data can be exported into a spreadsheet file tracking the associations between the recipient block positions and the ID of the donor block from which the core tissue was inserted into the recipient block.

For more information on data export to spreadsheet files, see section **5.7 Exporting donor block data**.

### 5.1.1 Before You Start



#### Warning!


Do not use paraffin blocks which dimension values are higher than specified (**24mm (W) x 37mm (H) x 10mm (D)**), otherwise the drilling and punching heads may be damaged. If the paraffin blocks are larger, mold them again with the base molds delivered with **TMA Grand Master**.

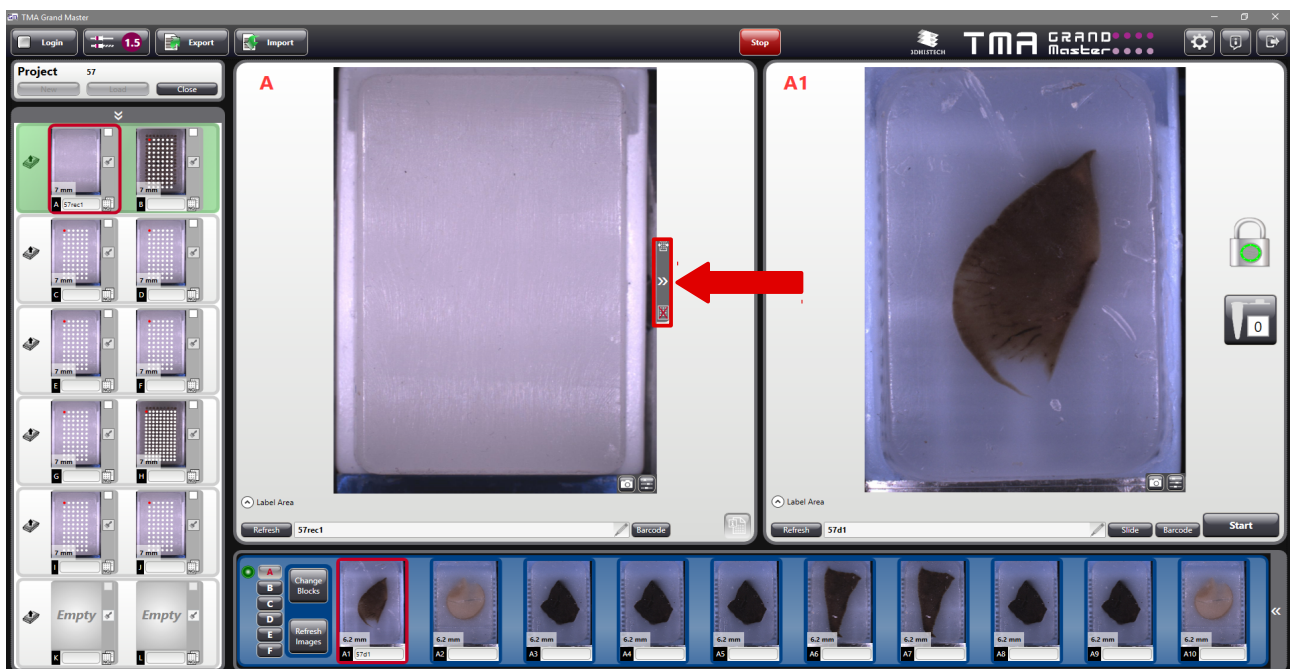
- Make sure that the cassettes with the paraffin blocks are properly inserted into the slots.
- Make sure that the drill bit is of appropriate size and that it is fixed in its position.

For more information see section **11. Cassette and Block Dimensions**.

## 5.2 Working with Recipient Block Layouts

### 5.2.1 Creating a recipient block layout

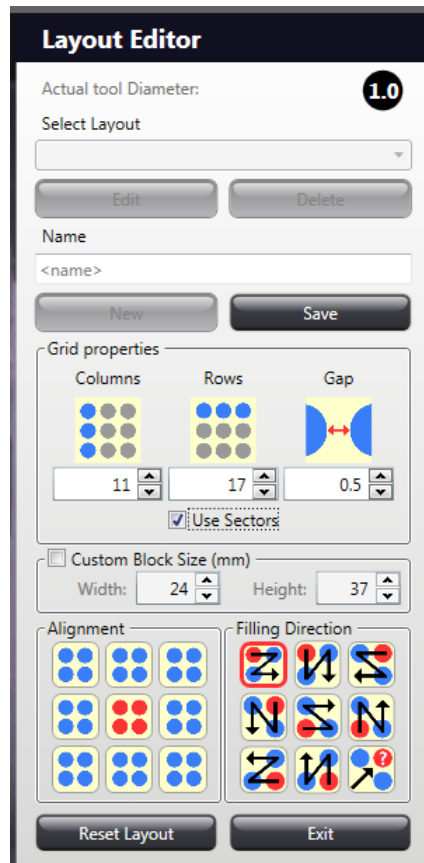
To create a layout, click the arrow or  at the upper section of the **Layout** button next to the recipient block image.



**NOTE:** There is a  icon at the bottom of this button, and if you click it the layout will be deleted.

New layout (TMA block array) can be created or edited in the Layout Editor window. Already existing layout can be selected from the **Select Layout** drop-down list.

When you create a new pattern, you define the block layout. Type the name of your new layout into the **Name** textbox (maximum length is 20 characters).



- The **Actual tool Diameter** field at the top of the Layout Editor panel informs you about the tool diameter of the puncher and the drill bit inserted into the device. This value cannot be modified, and will be applied for the layout to be created.
- Set the number of **Columns**, **Rows**, and **Gap** value in the Grid properties section.

**NOTE:** After insertion the puncher moves sideways to break the core. As this movement is not possible in some cases (without contacting with an already inserted core), please raise the **Gap** value to prevent contamination and the core from being damaged. If setting a lower value than advised, the software informs you to raise the value, but it does not prohibit the usage of a lower **Gap** value.

- If you want to create a pattern in which some of the grid positions (column/row intersection) are not marked as a hole to drill, disable those positions you want **TMA Grand Master** to skip during drilling.
  - Single hole: in the layout, click a core position that you want to leave out.
  - Columns, rows, or field selection: while keeping the mouse button pressed, select the unwanted area on the layout.

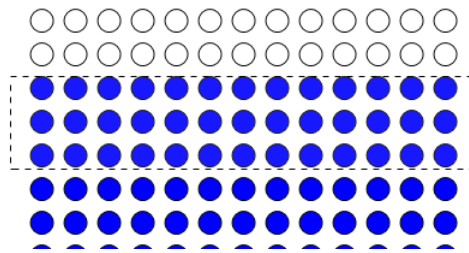

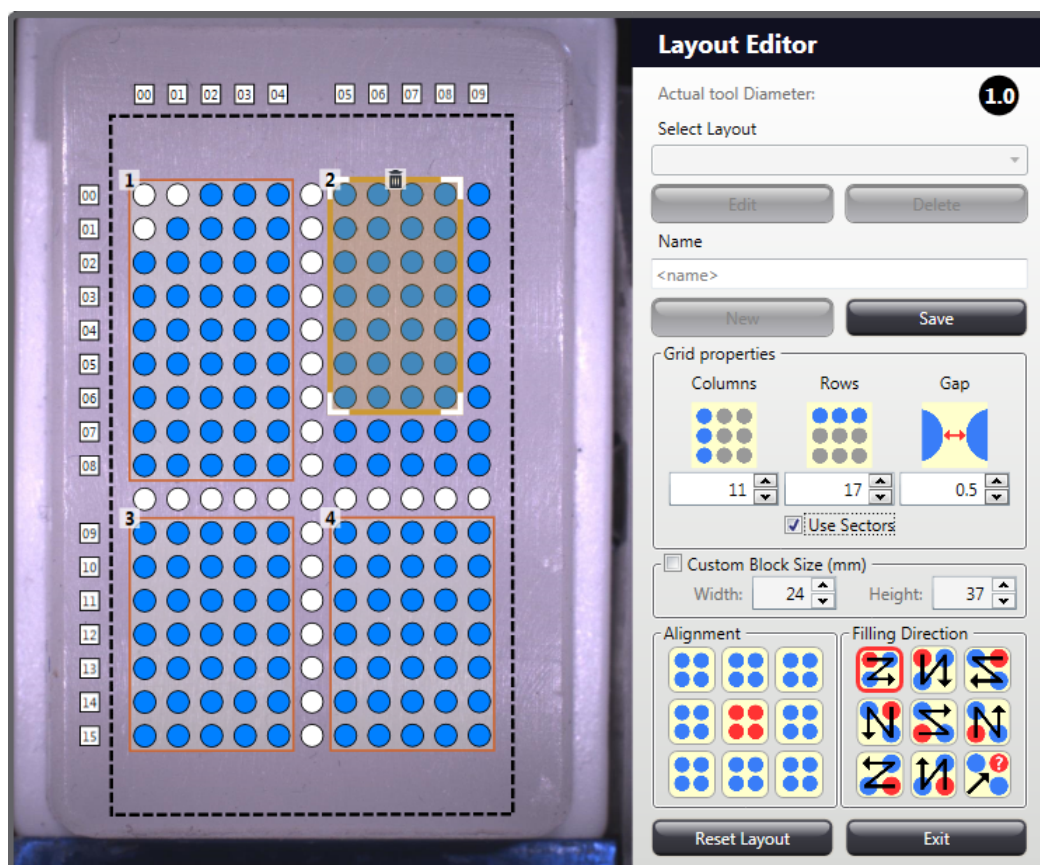


Figure 12 – Layout pattern

- If you activate the **Use Sectors** function, the layout can be divided into several sectors. Mark an area within the array with the mouse by drawing a border around the group of insertion positions.

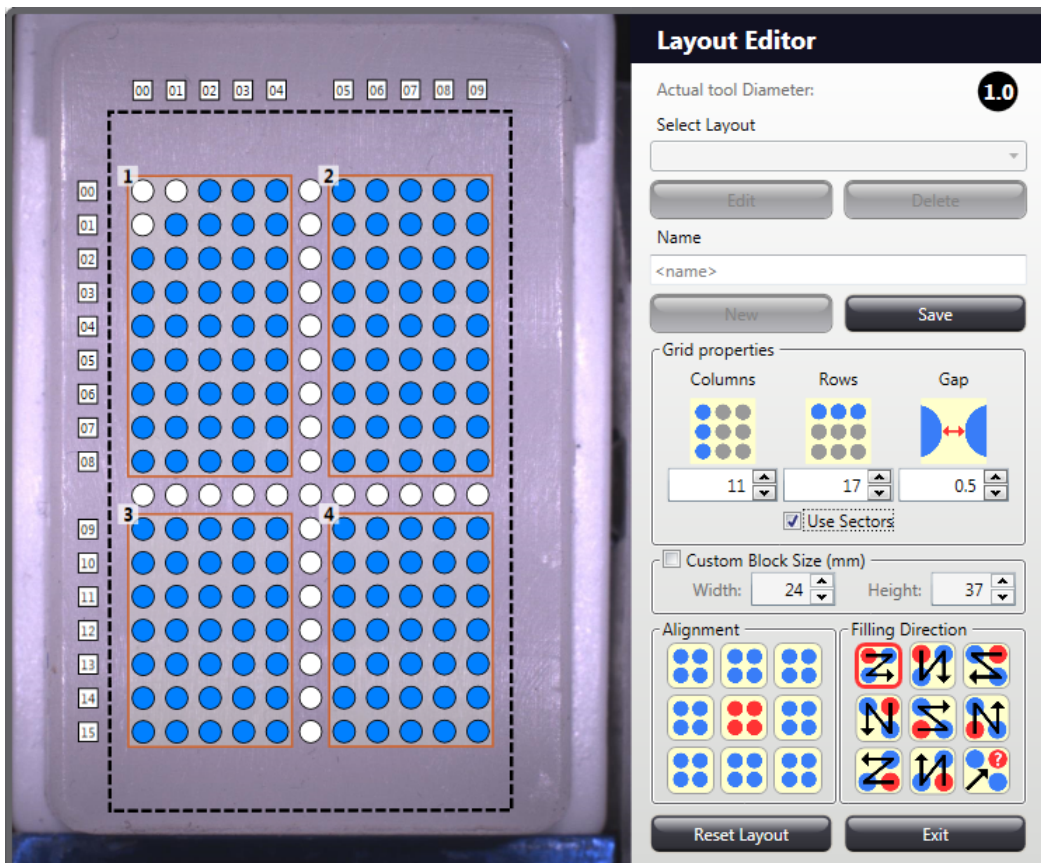
Sector area can be modified by dragging the marking border to the desired direction, and the entire selection area can be moved to a desired direction by dragging. The selected sector can be deleted by clicking the  button at the top of the border.



- The filling of sectors will be processed uniquely during TMA block creation, one sector is completed at a time, then the device processes the upcoming sector you have created.

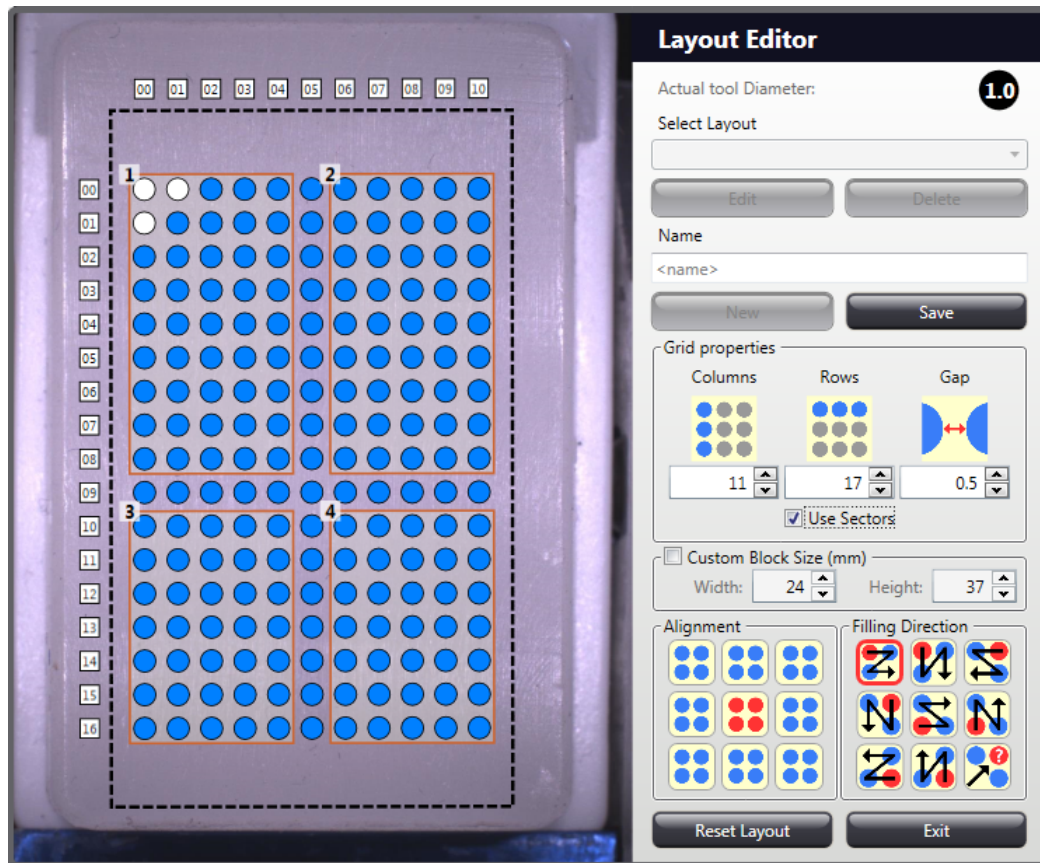
It is available for you to create a TMA block on which the sectors are separated by leaving out rows and columns between the sectors by selection.


The dividing areas can be selected by drawing with the right mouse button thus turning those spots inactive.





- It is also available to use dividing rows and columns in the block by leaving active spots between the sectors that can be filled up with Agarose or other tissue (for example, liver) that differs in color from the core tissue. The separator matrix is created after all the sectors have been processed.



- When working with special blocks that have different sizes than displayed by default, activate the **Custom Block Size** function and set the correct measurements.
- Pattern alignment can be set at the **Alignment** pane of the window.
- Select the desired method of filling for the specific layout under **Filling Direction**. The  icon represents random filling as a filling method for blind studies.

**NOTE:** When using the **Sequential Scoring** function of the TMA Module, the horizontal (default) filling method can be applied only, others will not work. Therefore we recommend TMA module users to select the option **Numbering from Database** instead.

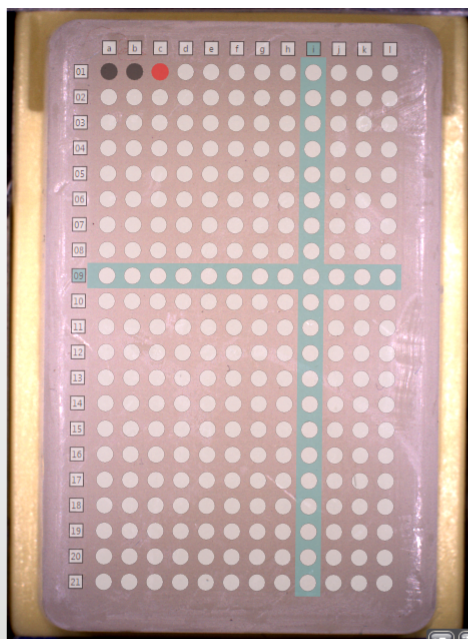
- When finished creating a layout, click **Save**. To create an additional layout, click **New**. If you do not wish to create further layouts, click **Exit**.

**Important!**


The table below shows the maximum number of holes can be drilled into a paraffin block depending on hole sizes:

Paraffin Block Size (mm)	Hole Sizes (mm)	Max. No. of Holes	Color of Drill Bit
<b>37×24</b>	∅ 0.6	16×31 = <b>558</b>	N/A
	∅ 1.0	13×22 = <b>286</b>	black
	∅ 1.5	9×15 = <b>135</b>	magenta
	∅ 2.0	7×12 = <b>84</b>	blue

The selected layout scheme with layout labeling (if selected) is applied on the recipient block image. The icon of the filling direction is presented at the top left corner of the recipient block panel. For more information on layout labeling, see section **6 Settings – Layout**.



## 5.2.2 Modifying a recipient block layout

1. Open **Layout Editor** window by clicking the  button next to the recipient block image.
2. To modify a block layout, select the name of the desired layout from the drop-down list, then click **Edit**.
3. Follow steps 3-8 in section **5.2.1 Creating a recipient block layout**.
4. Click **Save**.
5. If you do not wish to modify further layouts, close window and apply the actual layout for the recipient block by clicking the arrow at the right side of the panel.

### 5.2.3 Deleting a recipient block layout

If you wish to delete the layout for the selected block, click  next to the block image

OR

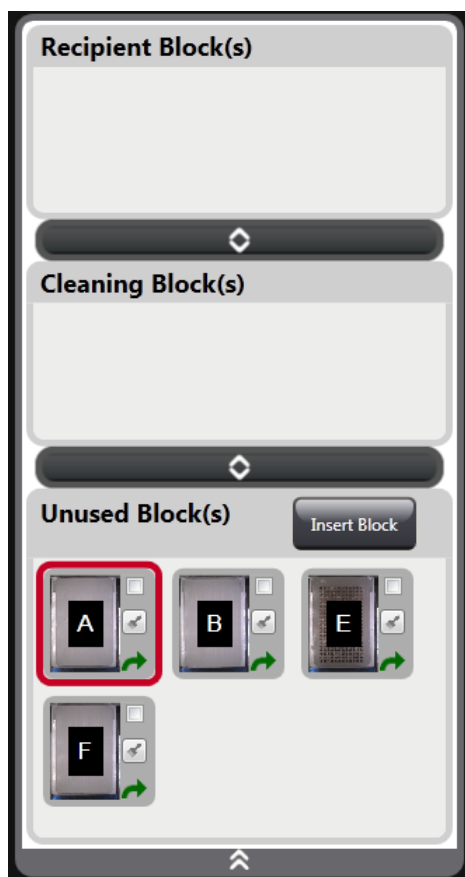
- Open either the Layout Editor window.
- Select the layout you want to delete from the drop-down menu and click **Delete**.



**NOTE:** You cannot delete a layout if it has already been used in a TMA project.

- If you do not wish to delete further layouts, click **Exit** to close the window.

## 5.3 Inserting Recipient Blocks

1. Switch on the TMA Grand Master main unit, the control computer and the monitor, and start the TMA Control application on the control computer.
2. Insert recipient blocks into the main unit as explained in section **4.4.3 Inserting a block into the main unit**.
3. In the classic view of the recipient block panel, block thumbnail images are refreshed each time after you have inserted a block into a slot.




- First, click the block thumbnail, then type in a block ID, or add a layout.
- In the new view for recipient blocks, the following options are available for you to choose from after the block thumbnail image is displayed in the **Unused Block(s)** panel:
- Click the block image then type in the ID, add a layout.
- The block will be moved to the **Recipient Block(s)** panel if you tick the selection box at the top right corner of the thumbnail image, or if you mark a core on a donor block to be transferred to this recipient block.
- Click  to mark block as cleaning block, then it is moved to the **Cleaning Block(s)** panel.
- Click  then the tray into which the block has been loaded will be rotated to the unloading position.

4. Select a layout for the recipient block:
  - a) Click the image of the recipient block for which you want to add a layout:
  - b) Select a pre-defined layout from the **Select Layout** drop-down list in the Layout Editor window, then click **Use this layout**. Note, that only those layouts appear on the list which include spots of same diameter as set for tools.
  - c) If the necessary layout is not yet created, design one (see section **5.2.1 Creating a Recipient Block Layout** – step 3 and on).



### Important!

A layout assigned to a recipient block can be removed by clicking  only if no core is selected to be transferred, otherwise this button turns inactive. A recipient block that has an assigned layout with no selected cores can be removed from its slot, and after recording its image, the representative image of the slot on the interface is displayed as **Empty**.




### Warning!

Make sure that:

- you have selected a correct layout for the inserted block, so that corresponding dimension values, both of the layout and the block, are identical. For example, if **Custom block size** option is selected, do not choose a layout dimension 24x37 for a block with a size of 20x18.
- the tool inserted is of the same diameter as in the selected layout.

- d) You can create *clone blocks* which means that a recipient block can be multiplied in terms of layout and core order, therefore the software makes it available for you to group identical blocks.

To create groups, click the  tab below the preview of the recipient blocks, then select the desired group number that is also marked by a specific color for the easier identification.

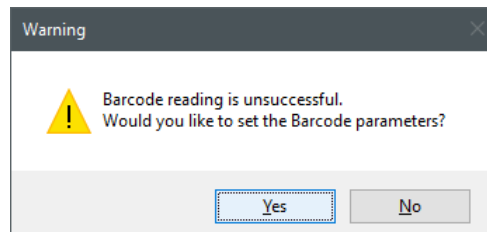


- e) To create several blocks with different layouts, repeat steps a)-c).

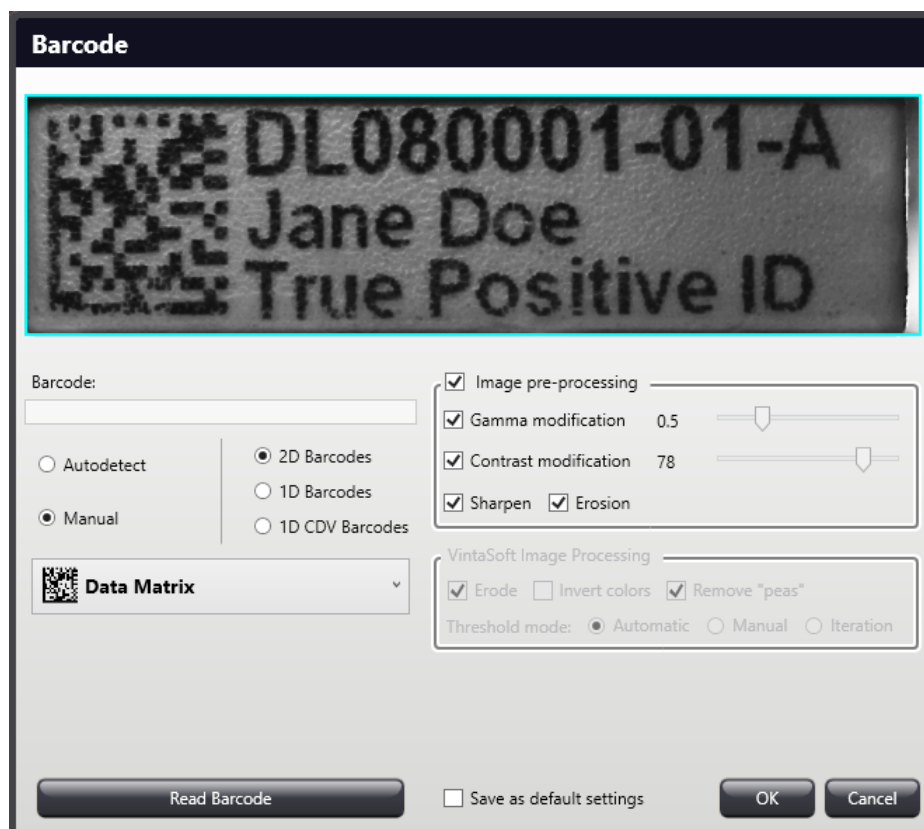
**Important!**

If loading a PCR cassette in the tray, make sure to insert the necessary amount of cleaning blocks into recipient block positions.

- The recipient block barcode is automatically identified, but if not recognized properly, the following message appears:



- Click **Yes**, and the Barcode window is opened in which you can modify settings.



- If the recipient block does not have any barcode, type in the recipient block ID below the preview image of the recipient block.
- Repeat steps 2. and 5. until you have typed in all the block IDs you want to use.
- Click the schematic picture of the first recipient block you want to use in the project.




## 5.4 Inserting Donor Blocks

1. Insert donor blocks into the first tray, positions A1-10. For more information see section **4.4.3 *Inserting a block into the main unit.***

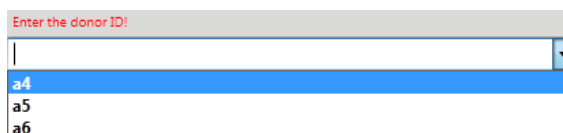


### Warning!

Make sure not to insert paraffin blocks that do not contain tissue samples in the slots of the donor tray, because the puncher piston may stuck and break into the block causing severe malfunction.

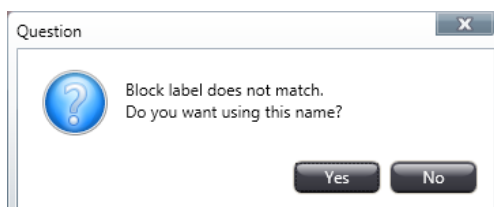
2. On each tray, donor block positions are numbered from left to right, starting with **1**. Click the schematic picture of the first donor block you want to use. The camera also records the label area of the donor block. The label area below the preview image is displayed by default. If the label is upside-down, click .
3. The Donor block ID must be entered into the text field below the donor block image. After entering the donor block ID and hitting enter (or clicking the  button), the label area disappears automatically. Click  to make the label area reappear.

**NOTE:** If you have already imported donor block data from a file (the last imported data is used, and also merge is recommended), the list of Donor IDs relevant to the string appear while entering the ID. Search for the ID from the list and click it to accept.



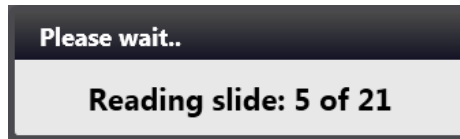
See section **5.7 Import Data** for more information on how to import block data.

**NOTE:** When reloading a project, blocks must be loaded to the same positions with the previously set IDs entered into the label field. Otherwise you can accept the new position by clicking **Yes** in the window displayed as below.

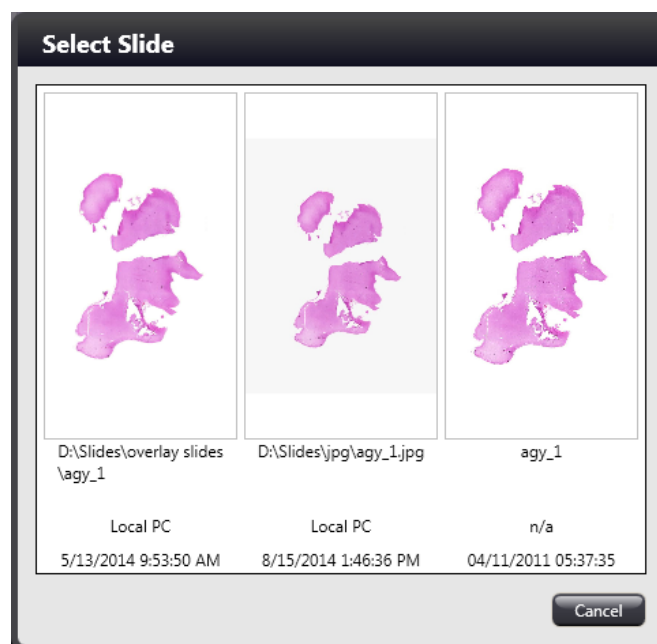


If you have already logged in to CaseCenter, after accepting the donor ID, click **Slide** and the software automatically searches for the corresponding slide stored on the server. Furthermore, if other locations have been defined in the Settings window for overlay images, more images can be found with an identical ID.

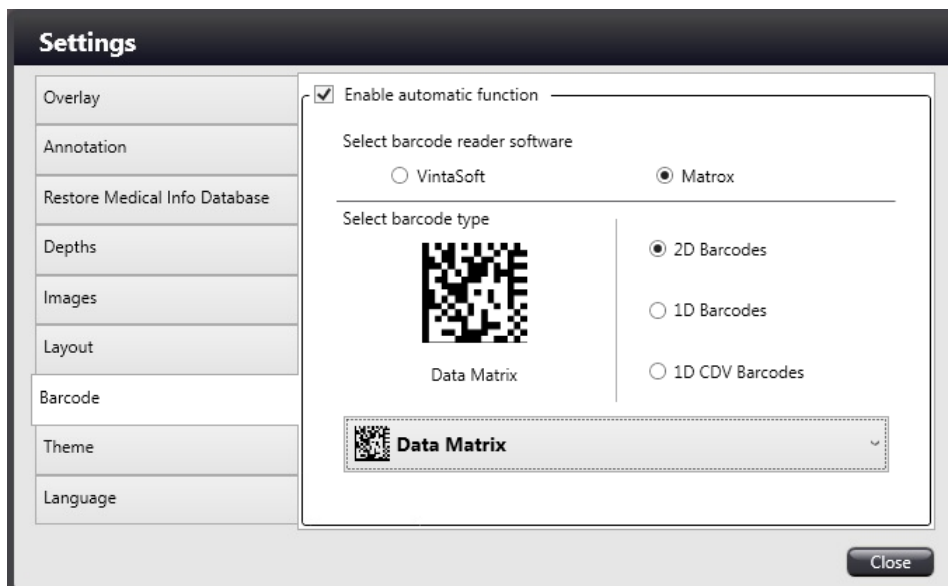
See section **6 Settings** for more information.




4. If a case, slide, or digital image (jpg) is found with matching IDs, their thumbnails are displayed in a window from which you can select one to use it as an overlay.



- After the barcodes of donor or recipient blocks are identified, they are automatically displayed both in the **Recipient Block ID** and **Donor Block ID** fields. If barcode reading had not been previously set, the Barcode panel of Settings window appears in which you can specify the barcode type and set it as default for the entire project.



**NOTE:** Barcode reader recognizes ASCII 32-166 characters only, extraneous characters will be deleted from the string.

- If you want to remove a donor block from the device, click  at the bottom right corner of the donor block thumbnail displayed at the donor panel.



## 5.5 Launching the transfer process

The TMA Grand Master is capable of creating TMA blocks and core sampling into PCR tubes at the same project, or you may as well use any of the two options exclusively. If you want to use the PCR sampling function of TMA Grand Master, simply insert the necessary amount of PCR cassettes into the designated slots. The software automatically scans their presence and positions during loading block and/or cassettes to donor trays.

The PCR button on the right of the donor block image is automatically displayed if a PCR cassette is properly inserted to its slot on the donor tray you have selected to work on.




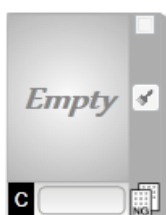


**NOTE:** The first tube position must always be on the left bottom of the cassette, and the cover plate tab faces to the left side of the device. After you have activated the PCR function by clicking the PCR button, make sure to insert cleaning blocks (or mark a sufficient amount of recipient block as cleaning blocks).



You can use TMA Grand Master also in mixed mode (TMA and PCR) and the software makes it available for you to select some of the blocks on recipient trays as cleaning blocks. Only if the PCR mode is activated you can select a recipient block as a cleaning block.


To mark a recipient block as a cleaning block click the  icon at the right side of the block thumbnail image.



When recipient (or cleaning) blocks, donor blocks, and PCR cassettes are inserted, the transfer process can be started.

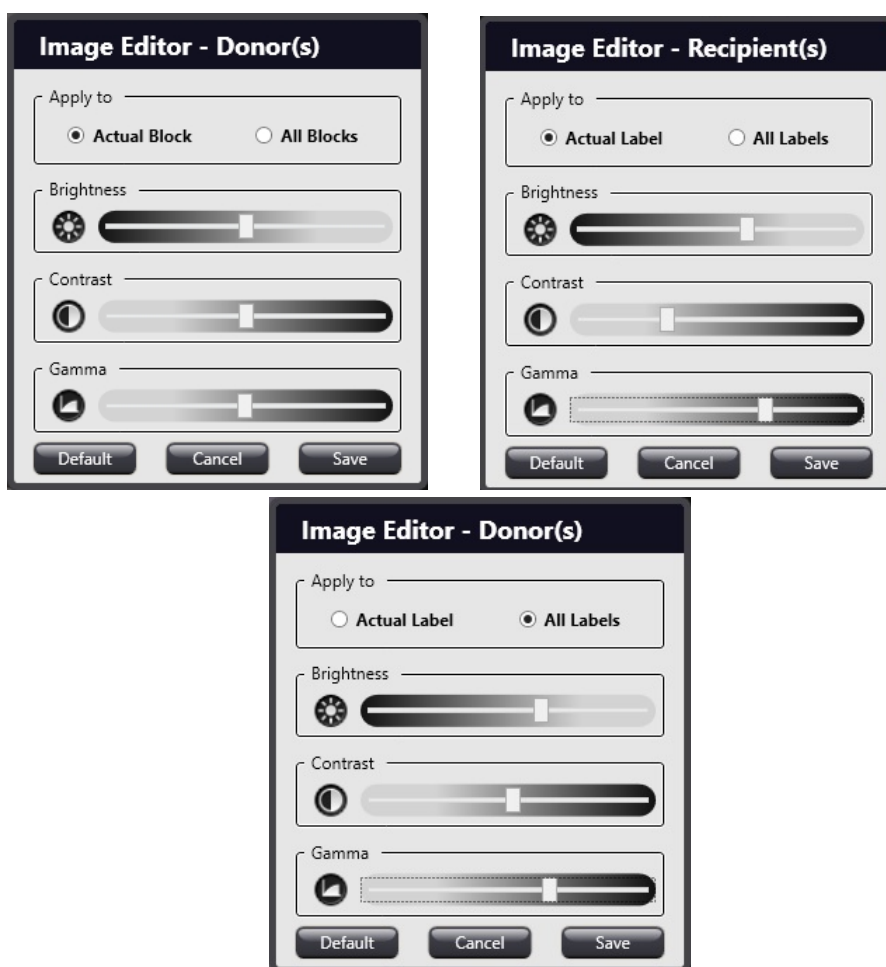
**NOTE:** If using TMA Grand Master in PCR mode only, and if necessary, it is available for you to insert cleaning blocks into empty slots during the process without interrupting it.

Sometimes it is required to alter image settings such as brightness, contrast, or gamma to make label images more identifiable or donor and/or recipient block images appear visually better for identifying relevant areas (for example, if the donor block holds adipose tissue) before placing markers at the right spots, and also to validate correct insertion of cores, mainly when extracted from a faint donor tissue.

Click  at the bottom right corner of the block image or its label, then the **Image Editor** window opens.

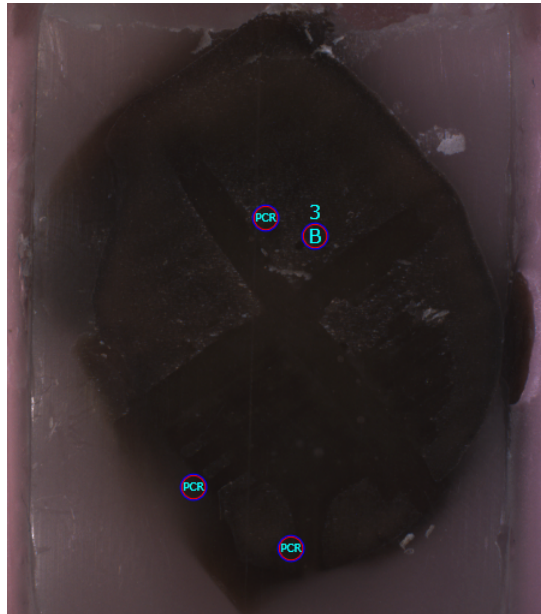
**NOTE:** **Image Editor** function is inactive if a block is marked as cleaning block. If there is no such button visible on the block image, go to **Settings/Images** panel, then activate **Image Editor** function. For more information, see section **6 Settings**.

Modify settings by dragging sliders to the required direction to create an image that is acceptable for you. Select the scope of applicable settings at the **Apply to** section – **Actual Block** or **All Donors**, and **Actual Label** or **All Labels**. Click **Close** to save settings and exit Image Editor, or click **Default** to restore default values.



Before starting the transfer process follow the sequence of steps below to place markers on donor blocks from which locations cores will be extracted to the selected recipient positions or PCR tubes.

1. To place a PCR marker on a donor block, first click the PCR button on the left side of the donor image. The number of PCR markers placed on the donor block appears in the PCR button. Place TMA markers on desired areas of the donor block where tissue core should be extracted from, then click the position of the recipient block layout that you want to fill with the core sample.



### Important!

Each donor position has its adherent PCR position (for example, A6–PCR6) and because of the maximum number of PCR markers allowed to place on a donor block is four (1.5/2.0mm) or eight (0.6/1.0mm), each PCR tube can contain up to four or eight cores of the corresponding donor block. A PCR cassette (when loaded with 10 PCR tubes) is capable of receiving 40 or 80 cores total.



### Important!

It is available for you to import markers already placed on the virtual slide.

**Important!**

PCR process is not supported in case the software was restarted after exiting without closing it properly or loading the project that has been saved previously.

2. If you want to remove an existing marker, click it with the right mouse button. The corresponding layout position of the deleted marker will therefore be free for the next defined marker.
3. Core transfer from the donor block(s) to the recipient block or PCR tubes starts after clicking the **Start** button below the image of the donor block.

If you have not entered Recipient block ID, nor Donor block ID for the selected transfer, a window opens in which you must enter the IDs.

**TMA Grand Master** inserts each core into the next available spot, and proceeds from left-to-right and from top-to-down order in the layout grid of the TMA block.

If you have activated the new view for donor blocks, the block on which you have selected a core to be transferred and clicked **Start**, the thumbnail of that specific block will be moved to the back end of the block queue.

**NOTE:** You can interrupt the punching process anytime by clicking the **Stop** button. The stop function (represented by the **Stop** button in the application window) can be called by pressing a relevant hotkey that is the **Pause** key by default. Use this key if it is more difficult to interrupt the process by clicking the **Stop** button.

The Stop window is displayed after either clicking the **Stop** button, or pressing the **Pause** hotkey. TMA Grand Master finishes the actual process before stalling. Select an option then click **OK**.

4. During the process, the colors of the cores on the layout varies according to their statuses.

Color markings of cores and their statuses are as follows:

- – transferred;
- – processing;
- – in queue;
- – first available position

Additional markers placed on the donor block preview image after the process is started, will be displayed as ● on the recipient preview image.



Upon clicking **Start** they will turn to ● and processed accordingly. You can refresh the image of the label and block by pressing the **Refresh** button next to the block. Accordingly, the process state is also displayed on the blocks represented by gear icons of the same color as on the recipient layout image:

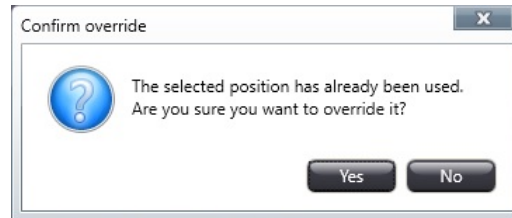
- Blue – marked, but processing has not started yet
- Green – process is started and scheduled
- Yellow – process is running

When you place the cursor over the location of an extracted core, the spot on the recipient block is marked by the center point of the blue crosshair.



On the other hand, upon moving the mouse cursor over a core on the recipient block layout the information (thumbnail image, label and donor block data) of the processed core can be viewed, the marker position of the actual core is displayed in purple on the donor block image.

Repunching of cores is available for you (can be initiated both at the donor and the recipient image) in case you need to remove another tissue segment from the donor block or the core could not be removed for some reason from the donor block. Right-click the marker or the spot on the layout then select **Repunch**. Confirm operation by clicking Yes in the pop-up message window.



5. If punching is completed to all the selected donor blocks, remove the completed donor blocks from the tray (as described in section **4.4.4 Removing a block from the main unit**) and insert new donor blocks in the tray.

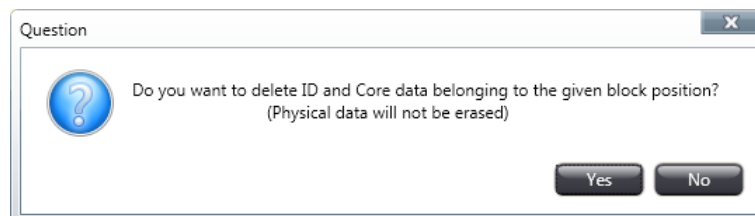


### Important!

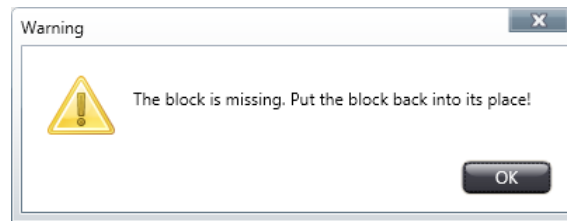
Because the compartment door can be opened during the process, make sure not to remove a recipient block to which a core will be transferred from a donor block, since only donor block operations are monitored by the application.

If you remove a donor block that is finalized (each selected core is transferred), and you are replacing it with a donor block having a similar text on its label area and label matching identifies it as the donor block you have removed, click the red cross icon next to the Donor ID field.

Click **Yes** in the pop-up window to delete ID and the markers of the previously used donor block.



If you remove a donor block to which cores are selected to be transferred, the software displays a message to warn you to place the block back to its position.



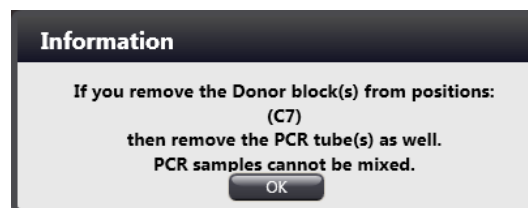
The lock on the right side of the donor block represents the status of the door of the device. If this icon pulsates in red and green, it means that there is a donor block from which all of the selected cores are extracted. If this happens, you must click the lock button first on the GUI, then the button on the door to open it.

The lock automatically turns green after a process is finished. Each time after you remove or replace a block, the camera records the block position, so the software displays an updated image almost instantly.



### Important!

Make sure when removing finished donor block (if every core selected for PCR transfer has been extracted and loaded into the PCR tube) together with the relating PCR tube. The following message is displayed to inform you about position number of the donor and the relating PCR tubes.

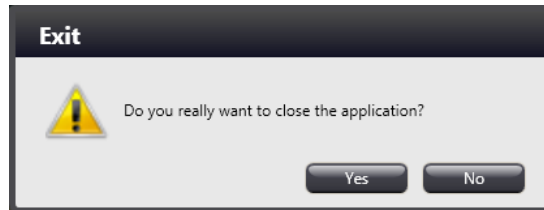


### Important!

If you replace the donor block but the PCR tube for the given position remains in the cassette and additional cores will be selected for PCR extraction, the PCR tube will contain cores from different blocks.

6. To export donor block-related data into a spreadsheet file after finishing the blocks, click the **Export** button in the toolbar. For more information, see section **5.9 Exporting donor block data**.

7. If TMA Grand Master has finished the creation of TMA blocks and samples have been transferred into PCR tubes, do the following:
  - Exit the TMA Control application by clicking **Exit**.
  - If you have exported data, and you want to exit the application, click **Yes** in the displayed window.



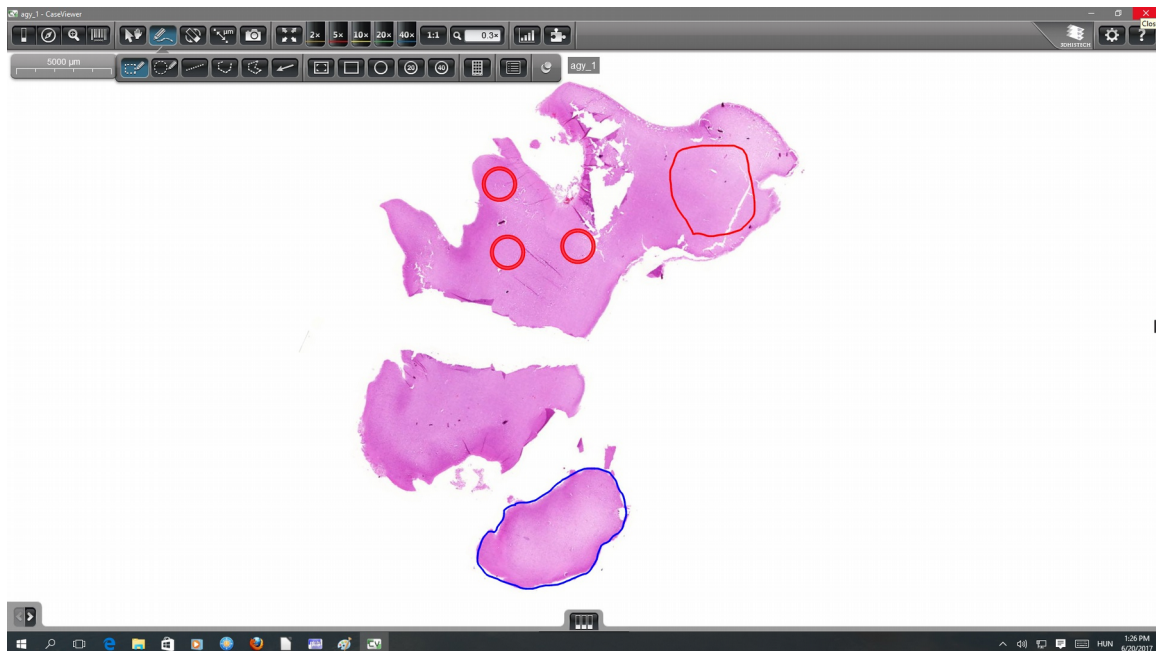
- Turn the main unit and the power supply off.
- Clean the main unit. For more information, see section **7.2 Cleaning Tasks**.

## 5.6 Slide overlay

With the **Slide overlay** function it is available for you to select a slide image (from various sources and of different formats) to overlay the donor image with it. The digitized slide image (located either manually or automatically) can be refined and aligned to match the position of the block image.

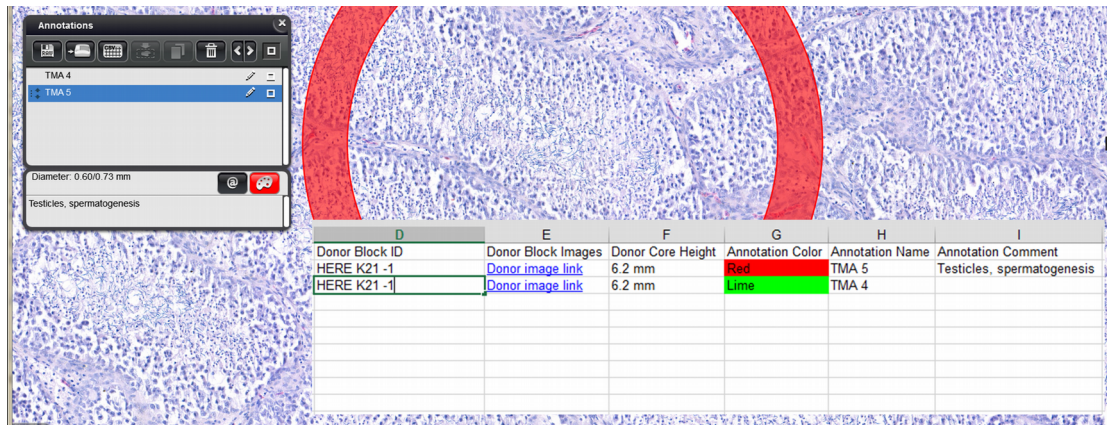
Slide overlay settings can be modified on the **Overlay** panel of the Settings window. For more information on settings, see section **6 Settings**.

Prior to overlaying a slide on the donor image, TMA Markers can be placed on the slide in CaseViewer with the TMA Marker function (refer to section **3.2 Functions – 6. Annotation mode in CaseViewer User's Guide**).







If a note has been added to a marker in CaseViewer, the note and the color of the marker will be displayed in the Excel sheet in a separate column when exporting block data.



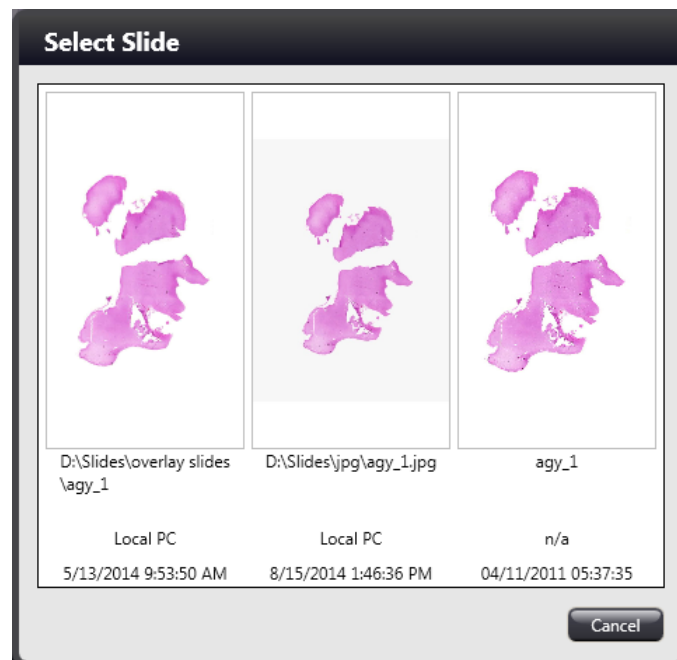
**NOTE:** TMA Control software is compatible also with Panoramic Viewer, but adding notes to TMA Markers is not supported.

To initiate the overlay procedure follow these steps:

1. Enter donor block ID, and hit Enter key or click .
2. Click .

**NOTE:** When hitting **Enter** the search for the appropriate slide image will not be started.

3. If connected to a CaseCenter server, the images of the related case will be displayed. If more than one images are found in the set locations (slide, JPG, CC) then select one image from the images displayed in the **Select Slide** window.



If the software cannot find a slide or image at the defined locations, the **Browse Overlay Slide** window is opened in which paths of slide and/or jpg images can be set in the text boxes for automatic overlay. To manually locate and import the image click **Browse slide**, **Browse jpg** or **CC Connect**.



**NOTE:** For the best matching results, Automatic Overlay function performs better when MRXS files are searched for by defining location with the **Browse slide** option. At other images types make sure that the image of the entire block is captured and saved.

**NOTE:** CaseCenter server connection can be established only if the URL of the dedicated CaseCenter server is displayed. CaseCenter address cannot be modified if displayed. For setting server connection details, click **Login** at the main menu bar of the TMA Control window.

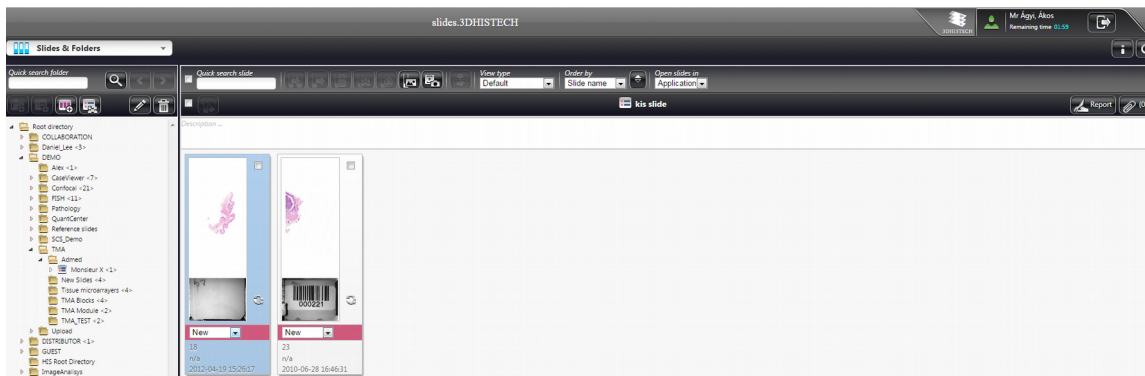
To connect to a dedicated CaseCenter server click **CC connect**. First, select server address, then enter your user name and password before clicking **OK** in the **CaseCenter Login** window.



4. Label view image helps you to select the proper slide; rotate label image by 180° degrees if necessary. To continue, click **Next**.


- In CaseCenter, browse for the slide in the folder tree, then left click on the slide to import it.

**NOTE:** Make sure that **Open slides in Application** option is selected in CaseCenter.



- If automatic search has succeeded and one image is found according to the specified ID (in one of the set folders) the image will be applied on the donor image.

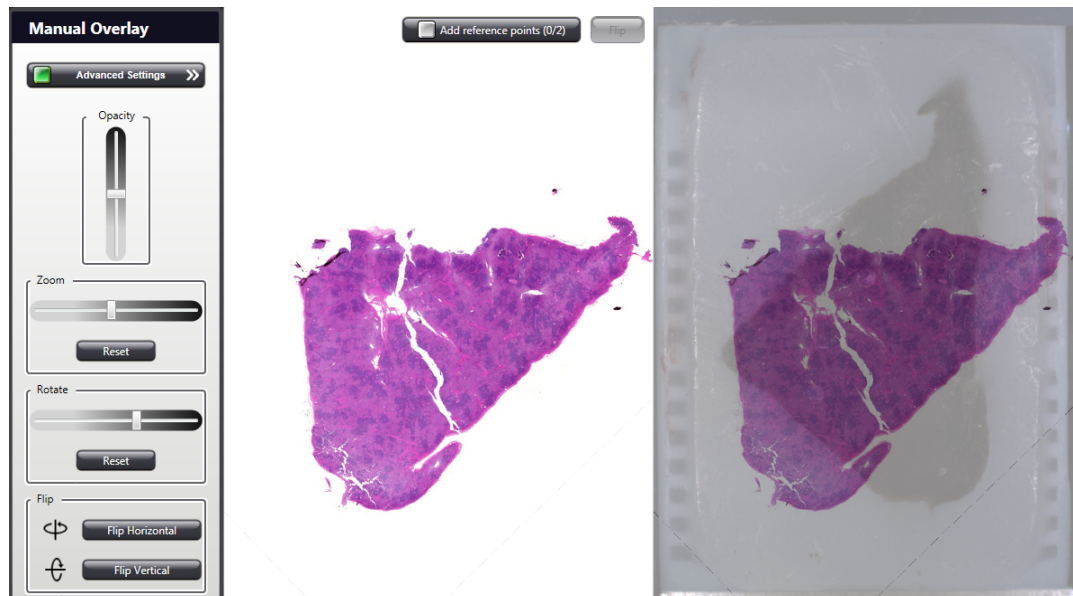
**NOTE:** If you modify the donor ID, and you have not yet placed any marker on the image, the applied overlay slide image will be deleted.

- Slide image is rotated to the appropriate orientation automatically, but if you would like to select the matching slide image with a different automatic orientation, click  at the top of the overlay editor button.

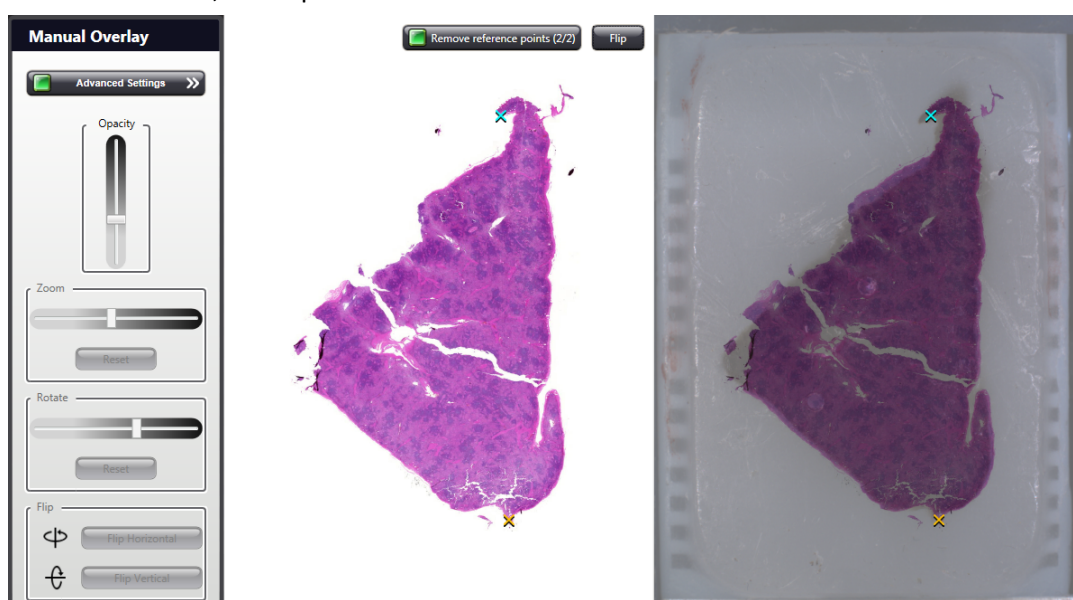


- Furthermore, if automatic slide overlay function did not provide acceptable result, click  at the left side of the donor image to open **Manual Overlay** window.

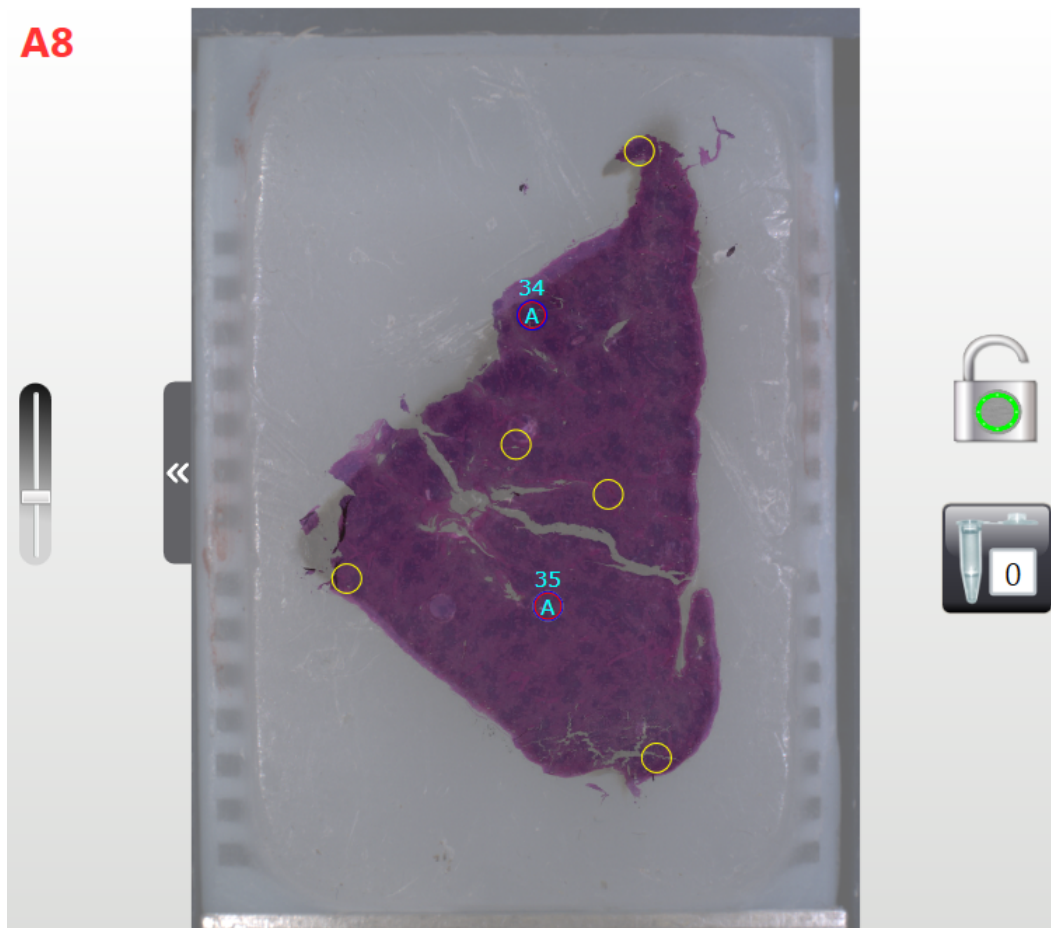
9. In the appearing **Manual Overlay** window, imported slide image is displayed at the left and as overlaid on the donor image at the right, accordingly, additional functions such as **Opacity**, **Zoom**, **Rotate**, and **Flip** are available for you in the extended panel to set the proper orientation.



- Flip slide image if needed by selecting one of the options **Flip horizontal** or **Flip vertical**. Position slide image (drag, rotate, zoom) to correspond with the block image.
- If manual positioning does not result in an acceptable overlay, enable the function **Add Reference Points** by clicking the button so that it turns green.
- Place two reference points on the block image, and refine their positions on the slide image. When moving the reference points the donor slide image is automatically aligned. If reference points are misplaced, you can delete all of them by clicking the **Remove reference points** button. After marking reference points the functions zoom, rotate, and flip become inactive.



- You can also modify the transparency level of the JPG image layer by moving the **Opacity** slider, allowing you to set how much the slide image should obscure the donor block image. Opacity slider (the set value is saved for the specific donor) is designed to adjust the amount of overlay so that the donor and slide images can be aligned more accurately.
- If you click the >> icon and close the overlay window, the TMA markers will be displayed on the donor block image in the main window.



- Confirm marker positions by clicking on them. Close spots will be automatically dragged to the marker positions by the software.

**NOTE:** By holding the **Ctrl** key while placing the marker it will not be dragged to close spots automatically.

- By setting the sufficient amount of transparency of the image layer, marker positioning becomes easier. To modify the opacity level of the applied image, use the slider on the left of the donor block image.
- The diameter of the marker is set identical with the size of the loaded tool. Markers become displayed with the same color as previously defined with the TMA Marker feature of the CaseViewer.

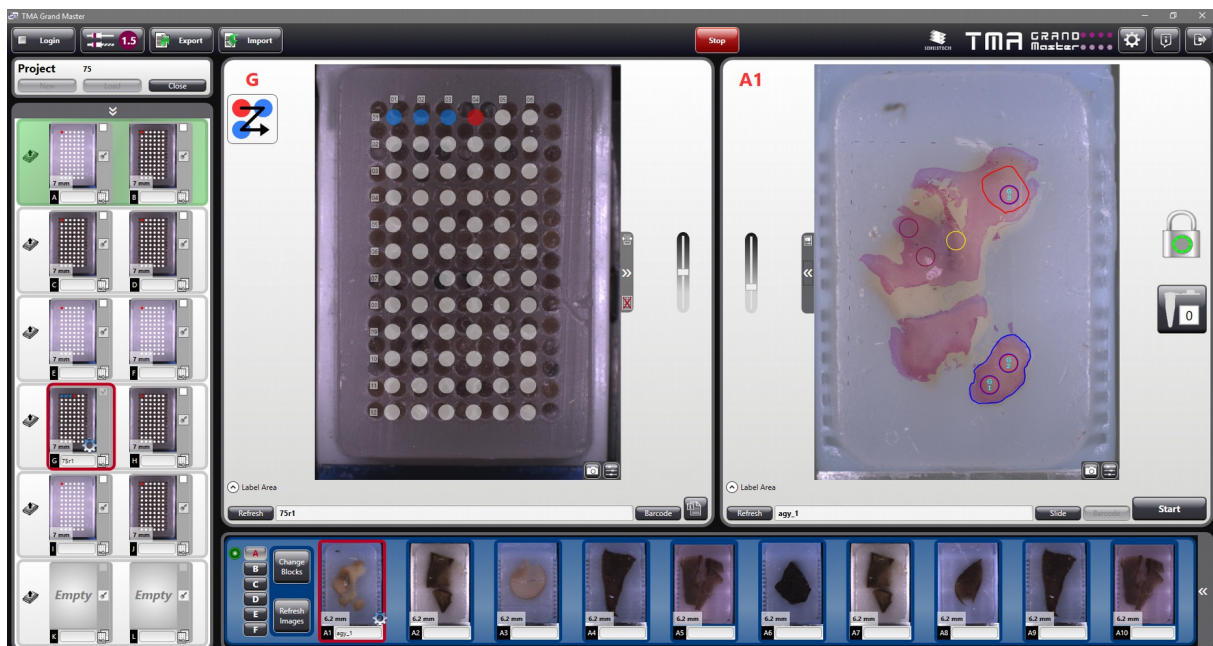
**NOTE:** As marker colors and their names will be displayed in the relating cells of the *Annotation color* column on the export sheet, to omit the usage of those colors that can be represented by their hexadecimal codes only, the following colors are suggested to be used for easier identification of tissue types based on the color chart of TMA Markers in CaseViewer (see below image):



Color	RGB values
Red	255, 0, 0
Yellow	255, 255, 0
Green	0, 128, 0
Blue	0, 0, 255

For other colors and their RGB values, please follow this link:  
[http://www.rapidtables.com/web/color/RGB\\_Color.htm](http://www.rapidtables.com/web/color/RGB_Color.htm)

- On the final overlaid donor image also the closed annotations created in CaseViewer and saved to the slide appear. These annotations may be of help when selecting appropriate regions for extraction.



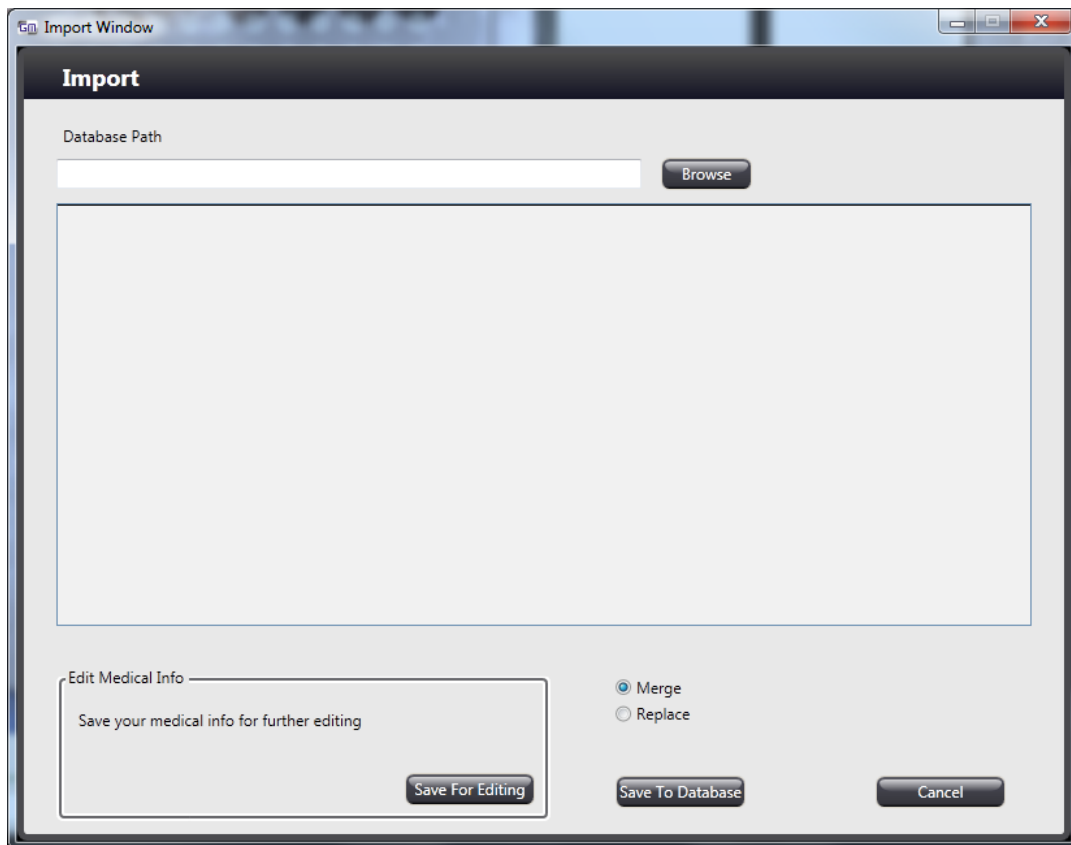
**NOTE:** The annotation visualization can be turned off in the **Settings**, and also the size of markers to display can be selected on the **Annotation** panel. By default those TMA markers appear on the donor image that match the size of the actual tool inserted. For more information, see section **6 Settings**.

8. If you have finished, press the **Start** button to launch the transfer process.
9. You can refresh the image of the label or block by pressing the **Refresh** button below the donor block image.

## 5.7 Import data

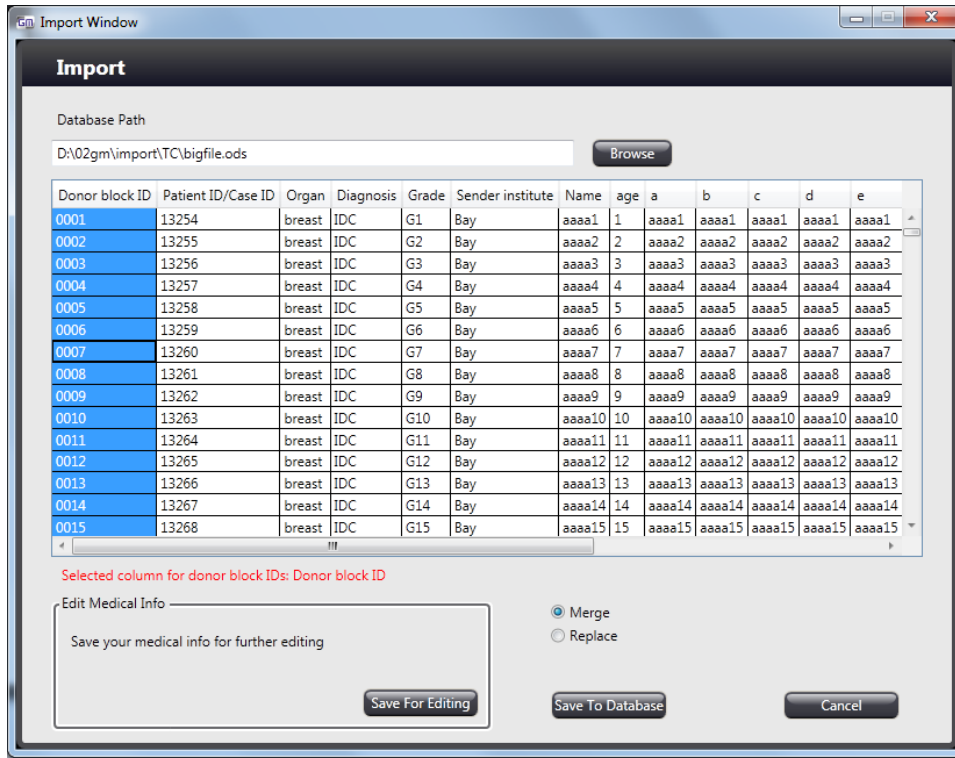
To import donor block-related data, do the following:

1. Click **Import** at the main menu bar of the application window.

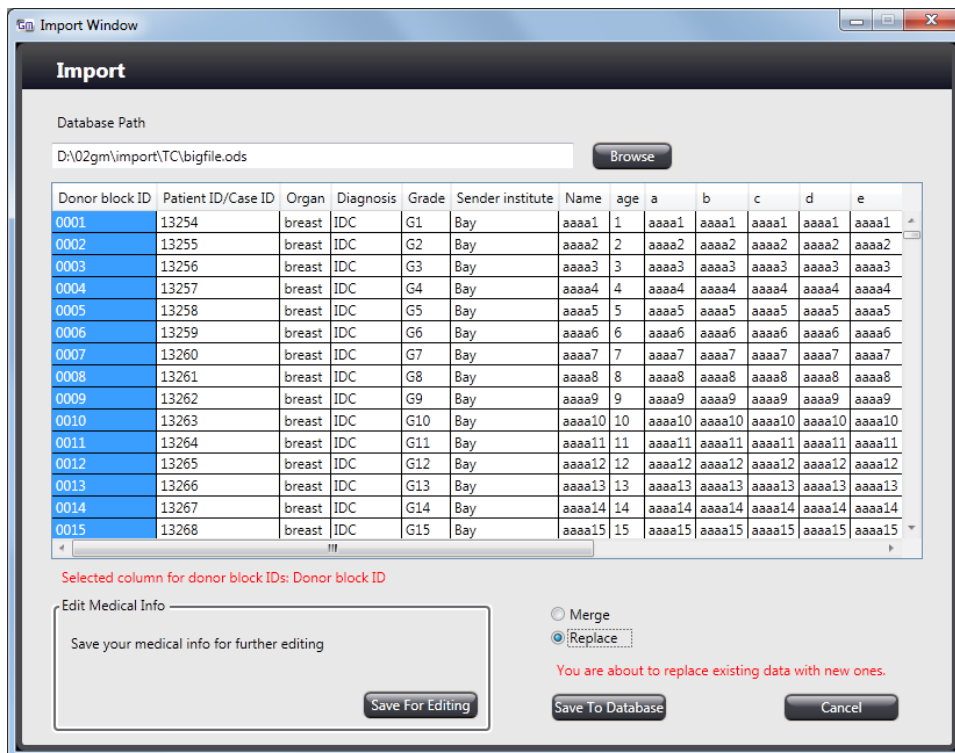


2. Click **Browse** in the Import window to search for the data file to be imported. If the ID of the donor block loaded into the device exists in the imported database, the data set of the specific donor block can be appended to the database.

- The content of the **MedicalInfos** data sheet can be modified with the **Merge** or the **Replace** function. The imported data are stored in the **MedicalInfos** data sheet that can be selected as a record when exporting.



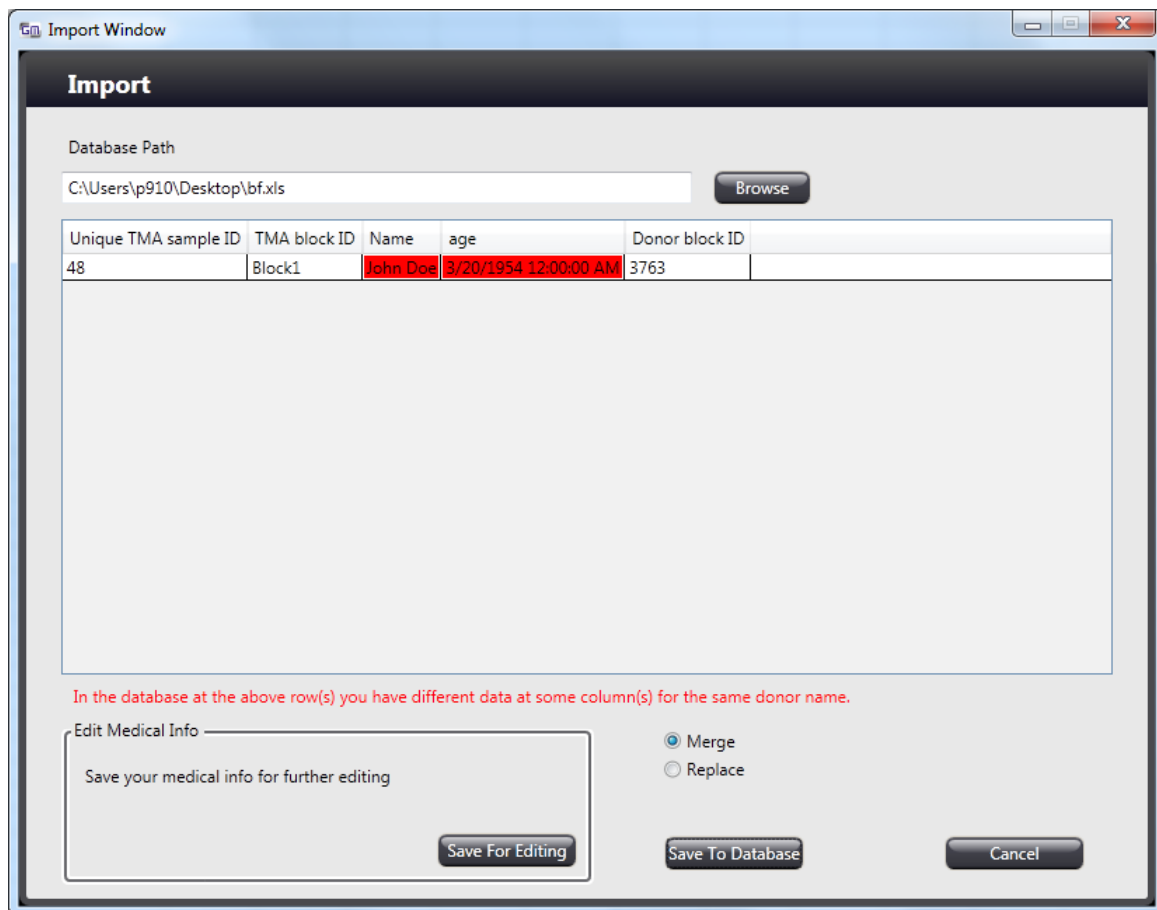
- Select **Replace** to overwrite existing data with the new ones.





In this case, the already existing data is archived and can be accessed after clicking **Settings**. Click **Restore** in the Settings window to restore the original data set (see **6 Settings** for more information).

5. To append new information to the existing data set, select **Merge**, so additional columns will be inserted into the sheet, **Donor Block ID** will become **Donor Name**, no other data will be overwritten.
6. Differences in the data (for example, if donor data of a specific block do not match – name, age, etc.) are highlighted with red in the window.



The database cannot be modified manually, but can be saved with the **Save for Editing** option. Click **Save to Database** to save imported data.

## 5.8 Restore medical information database

The program makes it available for you to restore a medical information database, therefore, all the data during handling the project before exporting can be omitted. For more information on how to restore a database, see section **6 Settings**.

## 5.9 Exporting donor block data with TMA Register

### 5.9.1 Export

If you have finished the transfer process from donor to recipient block(s), you can export block-data to a spreadsheet file (separate worksheets will be created within the file for each block).

If you want to fill other sample cores into the blocks at another time, these files can be used and to which donor block data can be appended.

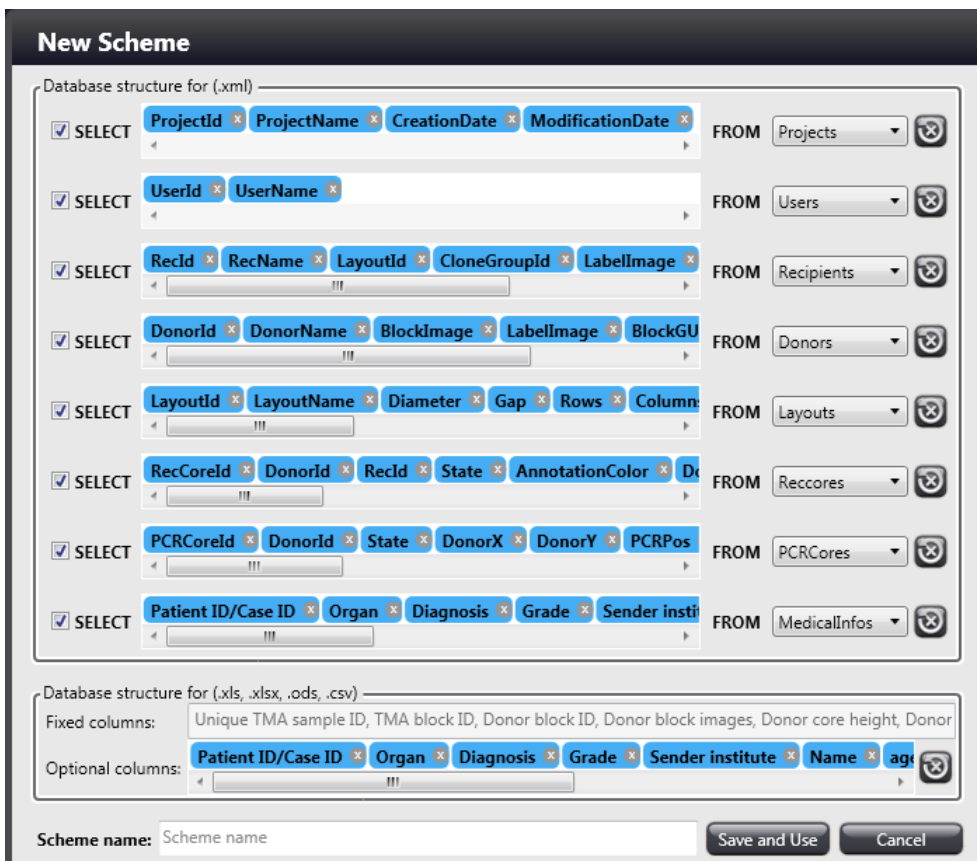
Depending on the mode you operate TMA Grand Master in (either mixed mode or TMA only, or PCR mode only) the Export Window contains different fields and options for export settings.

1. In mixed or TMA mode, after the TMA blocks are created and you want to save block-related data, click the **Export** button in the main toolbar and the Custom Export window appears.

Select a project from the **Project** drop-down list. You can filter the list by activating and specifying the tool diameter used in the project after activating **Tool Diameter (mm)** filter option. Once activated, in the **Date Range** section select **Date of Modification** or **Date of Creation** then set **Start Date** and **End Date** for more filtering option. Click to set date in a pop-up calendar window.

Schemes can be defined based on database-driven project handling by creating a scheme or selecting one from the **Scheme** drop-down list.

If you want to create a new scheme, first click **New** then you can custom-define a record set from the SQL database of the related project.





**NOTE:** Make sure to select appropriate fields when creating a new scheme.



Database records are freely selectable and erasable from the set.

The **MedicalInfos** record is empty by default, if there is no data imported yet.

**NOTE:** previously imported clinical data can be exported together with TMA datasets.

Save scheme by entering a name to the **Scheme name:** field, and clicking **Save and Use**.

- Moving blocks from the **Recipient Blocks:** field to the **Coherent Blocks:** field one-by-one by clicking  creates separate databases for each block. Click the  button to move all recipient blocks to the **Coherent Blocks:** field.

To create a single database summing up data for multiple blocks, you can group them by left clicking while holding the **Ctrl** key on the **Group items**, and finally click the  button, but if you choose to create separate for each of the selected groups, click .

- Set database name, path, and type.

To export data to a new file (will be generated by the application), browse for the folder by clicking **Browse** at the Database Name, Path, and Type section, type in a file name, and finally, select the desired file format (ODS/XLS/XLSX/CSV).

**NOTE:** Open file with the appropriate software, for example, use Excel to open file in XLS or XLSX, or OpenOffice Calc to open file in ODS format.

- Click **Save** to create the output file, or **Cancel** to exit the window without saving.

The generated spreadsheet contains four worksheets:

- Lookup** sheet is on which there are six columns. **Unique TMA Sample ID**, which is the position of the tissue core in the recipient block, the **TMA Block ID** if you are using several blocks in the same project, and the **Donor Block ID**. As the TMA Module cannot handle special characters of **TMA Block ID**, fields of **TMA Block ID** column contains automatically generated names that can be recognized and used by the TMA Module.

**TMA Block Name** as an extra column on the sheet contains Recipient names (may include special characters). The depth values related to the specific donor blocks are listed under the **Donor Core Height** column.

	A	B	C	D	E	F
1	Unique TMA sample ID	TMA Block ID	TMA Block Name	Donor Block ID	Donor Block Images	Donor Core Height
2		1 RB_1	75r1_cl1	75d1	<a href="#">Donor image link</a>	6.2 mm
3		2 RB_1	75r1_cl1	75d1	<a href="#">Donor image link</a>	6.2 mm
4		3 RB_1	75r1_cl1	75d1	<a href="#">Donor image link</a>	6.2 mm
5		4 RB_1	75r1_cl1	75d2	<a href="#">Donor image link</a>	6.2 mm
6		5 RB_1	75r1_cl1	75d2	<a href="#">Donor image link</a>	6.2 mm
7		6 RB_1	75r1_cl1	75d2	<a href="#">Donor image link</a>	6.2 mm
8		7 RB_1	75r1_cl1	75d3	<a href="#">Donor image link</a>	6.2 mm
9		8 RB_1	75r1_cl1	75d3	<a href="#">Donor image link</a>	6.2 mm

The **Donor Block Images** column lists image links (images stored in separate folders at the same location as the spreadsheet file, and donor image file names receive the block ID). Upon clicking a link on the Donor Block Images column the image of the block is displayed in a separate window.



- II. **RB\_1** sheet contains recipient block-related data table where the core IDs are shown according to their positions in the layout.

	A	B	C	D
1	75r1_cl1	X1	X2	X3
2	Y1	1	2	3
3	Y2	4	5	6
4	Y3	7	8	9
5	Y4	10	11	12
6				

- III. **RB\_1\_Donor** sheet contains recipient block-related data table where the Donor Block IDs are shown according to their positions in the layout.

	A	B	C	D
1	75r1_cl1	X1	X2	X3
2	Y1	75d1	75d1	75d1
3	Y2	75d2	75d2	75d2
4	Y3	75d3	75d3	75d3
5	Y4	75d4	75d4	75d4
6				

IV. An **Information** sheet includes all the following data:

- TMA block name
- Height (recipient actual height)
- Project name
- Creation date
- Modification date
- Diameter
- Layout name
- Layout size (row x column)
- Donor count
- Core count

	A	B	C	D
1		RB_1	RB_1_Clone	RB_2
2	<b>TMA block name</b>	75r1_cl1	75r1_cl2	75r2
3	<b>Height</b>	7	7	7
4	<b>Project name</b>	75	75	75
5	<b>Creation Date</b>	6/20/2017 1:32:50 PM	6/20/2017 1:32:50 PM	6/20/2017 1:32:50 PM
6	<b>Modification Date</b>	6/20/2017 1:39:03 PM	6/20/2017 1:39:03 PM	6/20/2017 1:39:03 PM
7	<b>Diameter</b>	1.5	1.5	1.5
8	<b>Layout name</b>	15k	15k	15full
9	<b>Layout size (row x column)</b>	4x3	4x3	15x9
10	<b>Number of Donor</b>	4	4	26
11	<b>Number of Core</b>	12	12	135
12	<b>Clone Group</b>	Clone 1	Clone 1	



**Tip!**

If you want to import the exported data to **TMA Module**, you need to create a worksheet named to Slides including stain types, recipient block IDs, and slide names.

In mixed mode, the application creates a separate file for PCR-related data. The file name is extended with the PCR suffix. The worksheet includes Donor ID and image with the relevant number of PCR sample.

	A	B	C
1	Donor Block ID	Donor Block Images	SampleCount
2	75d1	<a href="#">Donor image link</a>	1
3			
4			

If cores have been transferred to PCR tubes only, activate **Save PCR data** option, enter database-related parameters (Name, Path, Type) and browse for the location of the database file you are about to create.

1. Type a database name at the relevant field if you want create a new file.
2. Click **Browse** to set the destination folder of the file, and select the file type.  
**NOTE:** When opening XLS files in OpenOffice, links to external images cannot be opened.
3. Click **Save** to create the output file, or **Cancel** to exit the window without saving.
4. The created database includes three columns on one sheet, including donor-related data and image, and the number of transferred cores.

## 5.9.2 Search

The TMA Register window includes a **Search** panel through which TMA data stored in the database can be filtered, and you can search for **Date**, **Project name**, **Recipient Block Name**, **Donor Block Name**, **Diameter** and **Medical Information data**.

The screenshot shows the TMA Register Search panel. It is divided into three main sections: Date, Search, and Medical Information. The Date section has a dropdown menu showing '7/8/2016 - 11/25/2016'. The Search section has three input fields: 'Project name', 'Recipient name', and 'Donor name'. Below the 'Recipient name' field is a list of recipient names with checkboxes: '37rec' (checked), '38rec' (checked), '39rec' (unchecked), and '40rec1' (checked). Below the 'Donor name' field is a list of donor names with checkboxes: '37rec' (checked), '38rec' (checked), '39rec' (unchecked), and '40rec1' (checked). The Search section also has 'Add New Search' and 'Reset' buttons. The Medical Information section has a dropdown menu and a list of medical information items with checkboxes. Below the Medical Information section are 'Add New Search' and 'Reset' buttons. At the bottom of the panel are two buttons: 'Block Info' (with a green square icon) and 'Core Info' (with a grey square icon). Below these buttons are two checkboxes: 'Recipient' and 'PCR'.

In the **Date** section the date of the first created project is applied as starting date.

In the **Search** section **Project name**, **Recipient name**, **Donor name**, and **Diameter** preferences can be defined. During entering a text string in any of the fields, corresponding values are listed below the field.

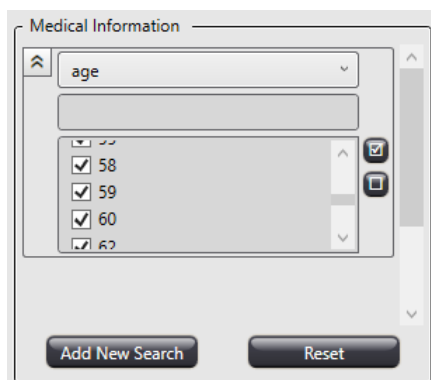
**NOTE:** When selecting the **Donor name**, PCR donor heights are not listed if the data are created with a previous software version (older than v2.7)



If **Block info** button is active, and **Diameter** filter option is added, results are listed according to **Recipient name** in the first column.

If **Core info** button is active, results are listed based on the information of all the selected core. It is also available to display Recipient and PCR core data in the table.


In the **Medical information** section, the number of search criterion is defined by the number of medical information field.

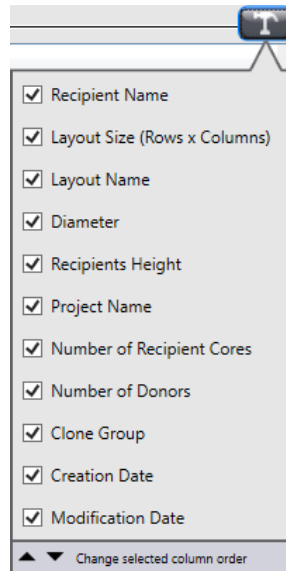


Results related to the set filter parameters automatically appear on the list at the right side of the window.

No	Recipient Name	Layout Size (Rows x Columns)	Layout Name	Diameter	Recipients Height	Project Name	Number of Recipient Cores	Number of Donors	Clone Group
34	26rec	21x11	1	1	7	26	71	6	
35	27rec	4x3	1kl	1	7	27	12	4	
36	27rec2	3x2	1kis	1	7	27	5	1	
37	28rec	21x11	1	1	6.205	28	1	1	
38	gj	16x12	1k	1	7	3	165	11	
39	30r	21x11	1	1	6.143	30	6	2	
40	31rec1	18x11	2. tesyt	1	7	31	74	3	
41	32rec	16x12	1k	1	7	32	77	4	
42	32rec2	4x3	1kl	1	7	32	12	3	
43	33rec	4x3	1kl	1	7	33	3	1	
44	35rec1	9x12	1_20eles	1	6.312	35	3	1	
45	36rec	21x11	1	1	7	36	67	4	
46	36rec2	16x12	1k	1	7	36	17	2	
47	37rec	10x7	1kk	1	7	37	70	3	

Table columns can be reordered by dragging, and their order is reversible by clicking the header.

**Search Result** table is expandable with other columns after clicking  and selecting the desired preferences. Here, the order of columns displayed in the table can be set as well by dragging header names to the desired position.

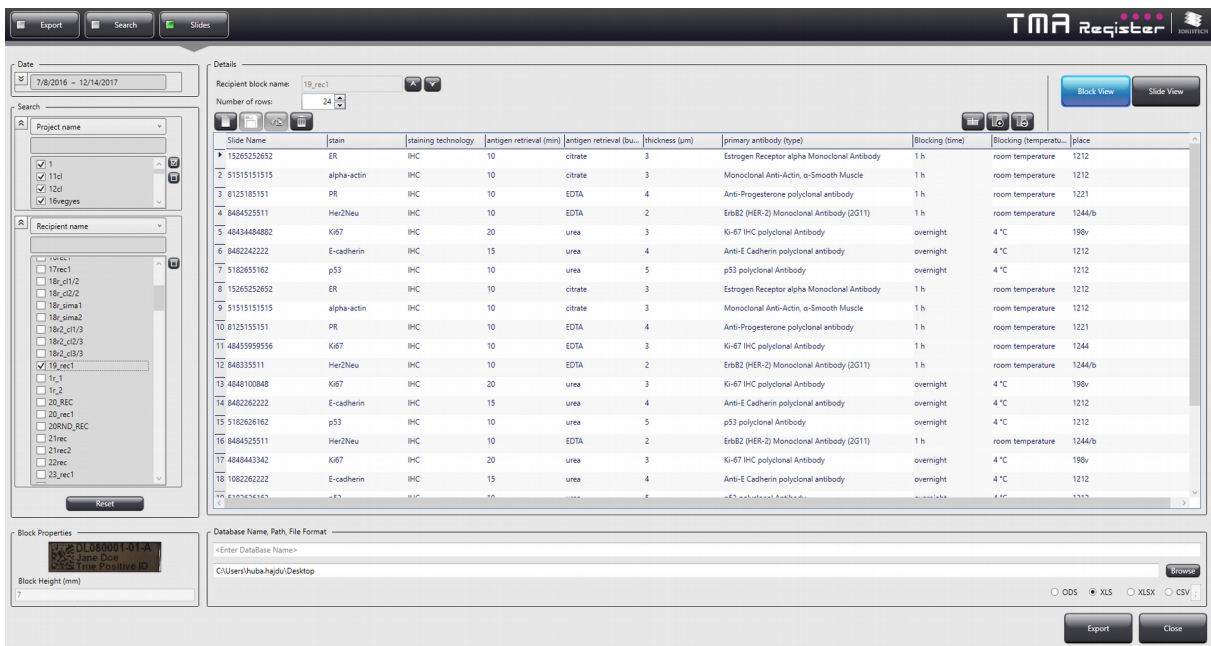




**NOTE:** If an additional filter is added, the previously set filter setting will be inactive and cannot be modified.

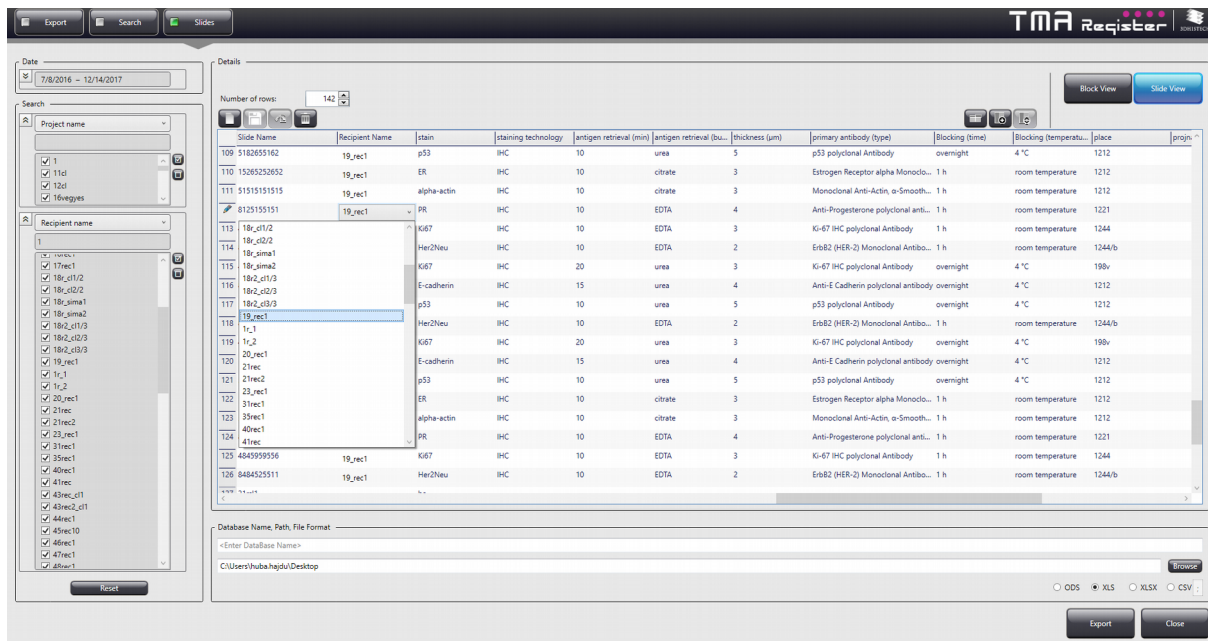
### 5.9.3 Slides


The TMA Register feature enables you to append various TMA Slide data, such as slide name, stain, organ, etc. to the already existing Recipient blocks on the **Slides** panel. It is available for you to filter Recipient blocks based on date, project name, and/or Recipient block name. There are two separate methods for uploading TMA Slide data: **Block view** and **Slide view**.

In **Block view**, only one selected Recipient block can be linked with the corresponding TMA Slides.







In **Slide view**, first enter TMA Slide data, then select multiple Recipient blocks to be linked with based on filter settings. In both views, use  to select all filter list items, and click  to select none.

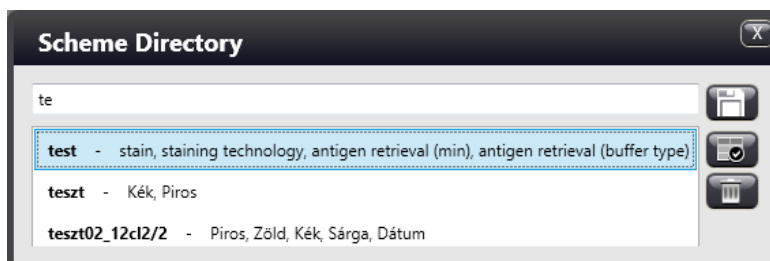


Data entry is performed in a table, in which columns and containing data can be ordered, and are freely variable and editable. A new, empty table can be created by clicking .

The following functions are available for you to select from to modify table composition:

-  – Save column scheme
-  – Add new column
-  – Reorder column entries

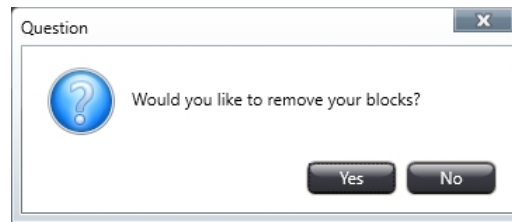
Column headers can be saved as a scheme, and this scheme can be reused another time. Click  to save table as a scheme. In the Scheme Directory window when typing the name for the scheme to be saved, the list of already existing schemes are displayed automatically, so you will not overwrite a scheme by mistake. Scheme can be loaded only if there is no data in the table.



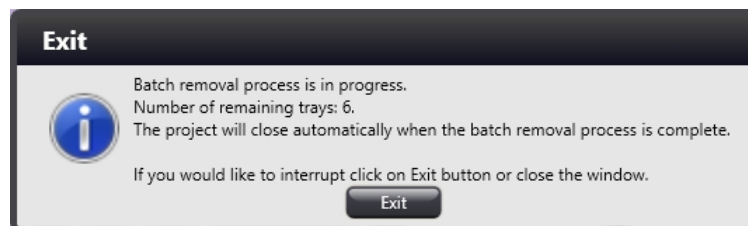
As an option, you can export TMA Slide data to the following file formats: ODS, XLS, XLSX, and CSV at the bottom of the window. First enter database name into the top field, then path to the bottom field, finally select file format, and click **Export**.

## 5.10 Batch removal of blocks

When you close a project, the software offers you to remove all the blocks (donor and recipient) from the device in one session.



After clicking **Yes**, first open the door, remove blocks, then close the door. Once the door is closed, and the drum turns to the next tray position, repeat procedure until all the blocks have been taken out from the device. If all the blocks have been removed, the software closes the project. If you want to interrupt the removal of blocks, click **Exit**.

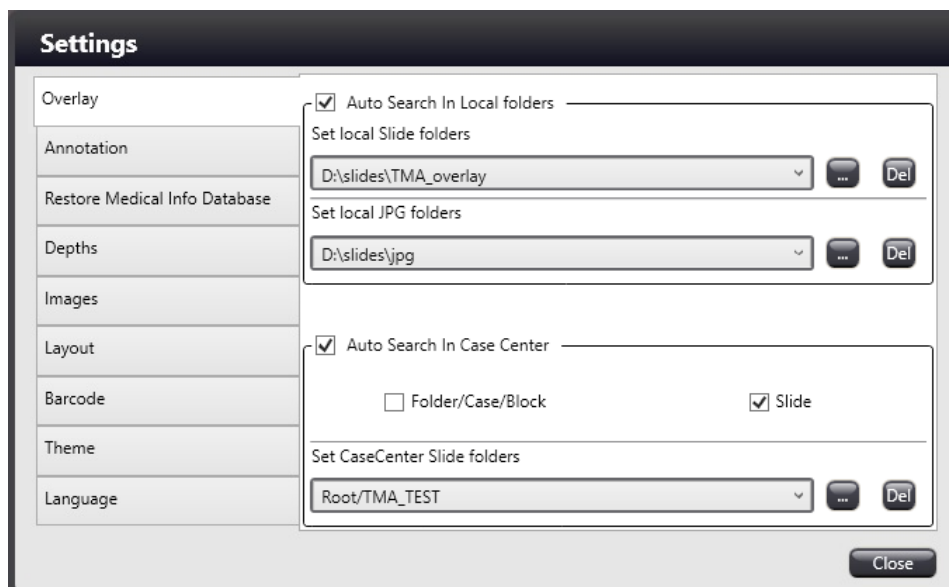


## 6 Settings

The Settings window contains nine panels on which function-related options can be activated and further settings can be modified.

### Overlay

Slide image locations can be set for the Overlay function, both in local and CaseCenter folders.



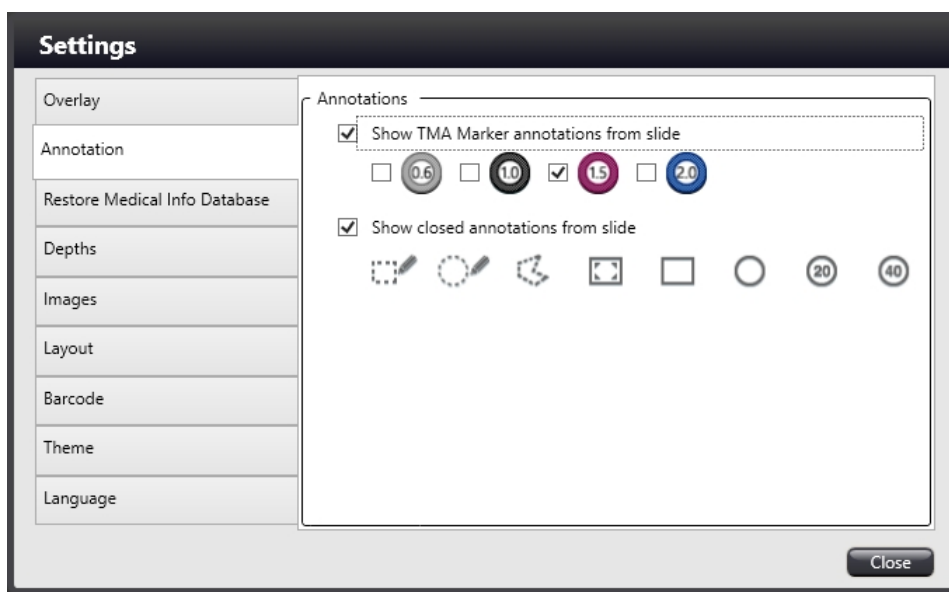
Select **Auto Search In Local Folders** to search for slide and JPG images directly in local folders you have set under the sections **Set local Slide folders** or **Set local JPG folders**. Activate **Auto Search In CaseCenter** to add results for Overlay function based on **Folder/Case/Block** and/or **Slide** criteria.

Type in or browse for folder paths for automatic search (either for Slides or JPG images). Folders that have been set can be displayed after clicking the down arrow, and after you have selected an item from the list, it can be deleted by clicking **Del**.

**Annotation**

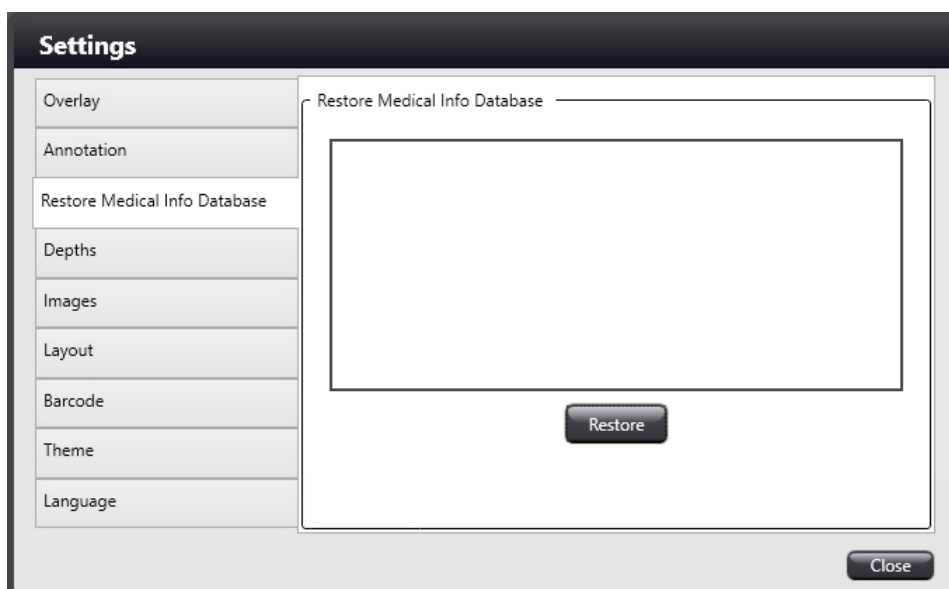
Annotated areas (such as TMA markers and closed annotations) of the slide can be displayed on the donor image. Activate **Show TMA Marker annotations from slide** option and select the size of marker to be displayed (the marker size identical with the size of the actual tool inserted is selected by default). Activate **Show closed annotations from slide** option to allow the visualization of annotations of the slide.

**NOTE:** The export file includes marker/annotation data such as name, color, and comment.



**Restore Medical Info Database**

On the Restore Medical Info Database panel select the database that you want to restore, then click **Restore**. The database then will be used as the basis for your project data.



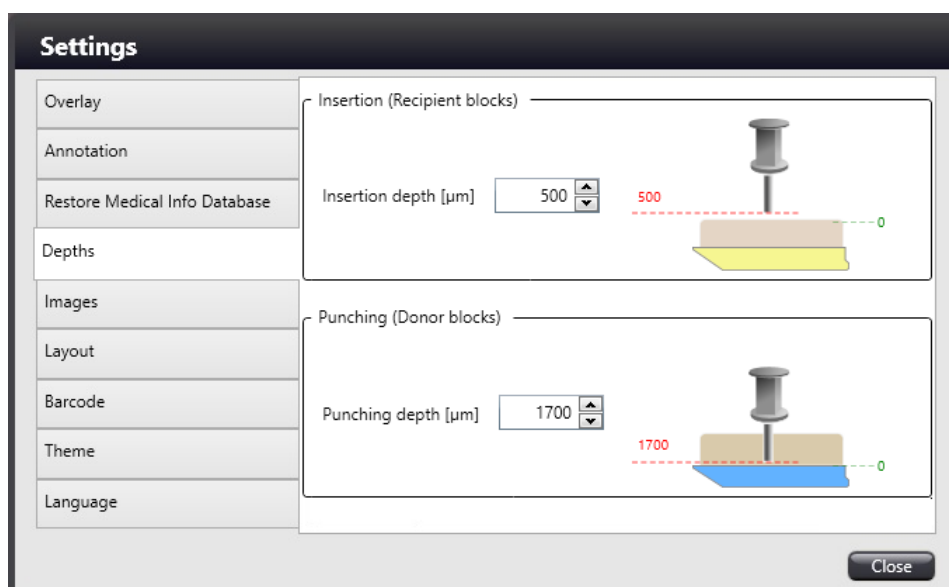
## Depths

- **Insertion depth ( $\mu\text{m}$ )**

Depth of insertion into the recipient block can be set either by setting a negative or a positive value, so that the tip of the puncher is positioned below or above the surface of the block inserting the core at a required height. Value ranges from  $-500\mu\text{m}$  to  $+500\mu\text{m}$ .

- **Punching depth ( $\mu\text{m}$ )**


Punching depth adjustment might be necessary to perform an accurate core removal (depending on the location of the tissue within the block). Value ranges from  $-500\mu\text{m}$  to  $+13000\mu\text{m}$ .

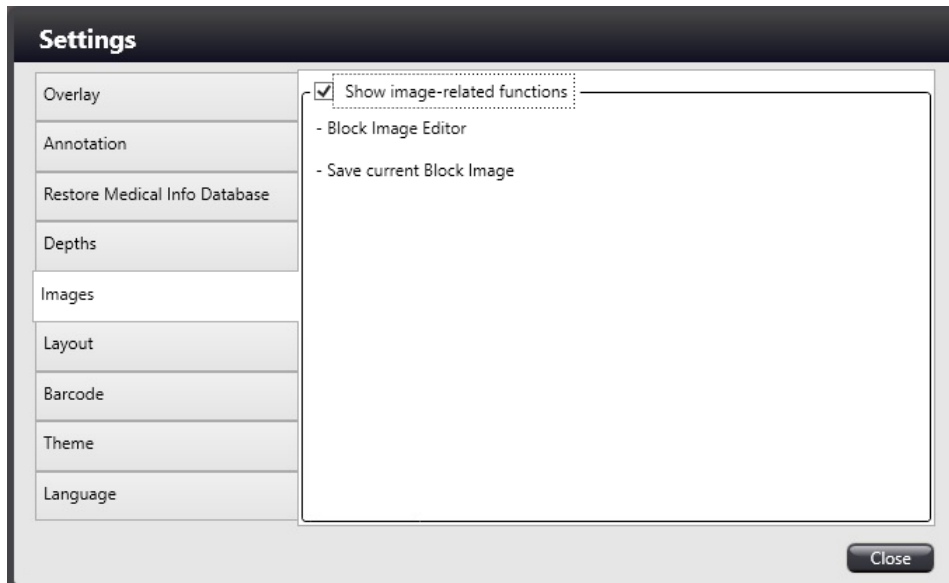


### Warning!

If the tissue specimen sticks to the base plate of the cassette so that the puncher cannot take out the core entirely or properly, you may specify a negative value at the **Punching depth ( $\mu\text{m}$ )** field. Bear in mind that the puncher needle should be moved with care deeper than the level of the base plate of the cassette, since the needle can be damaged during core removal.

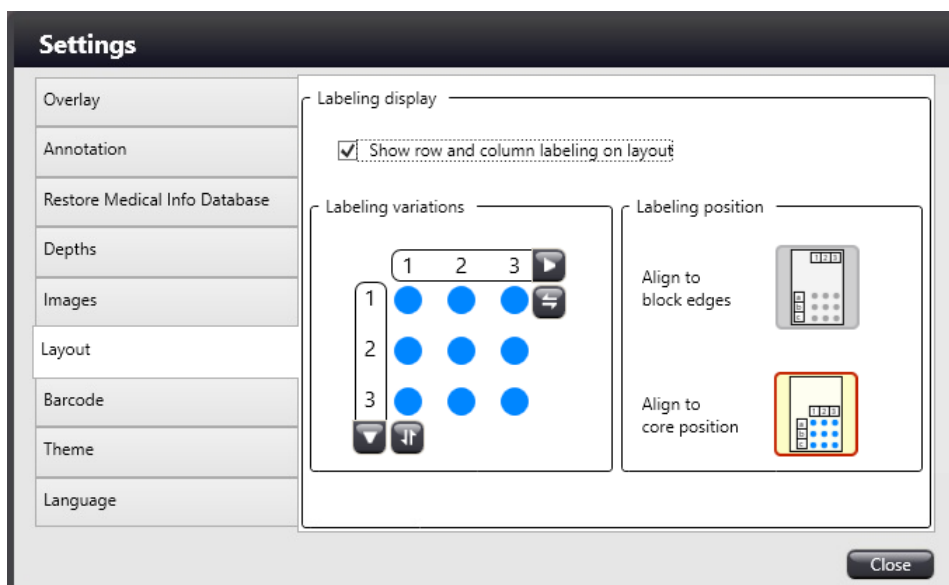
### Images

Upon activating the **Show image-related functions** option, a  button will be displayed below the bottom right corner of the block images. By clicking this button the Image Editor window can be opened. With the **Save current Block Image** option, block images can be saved.

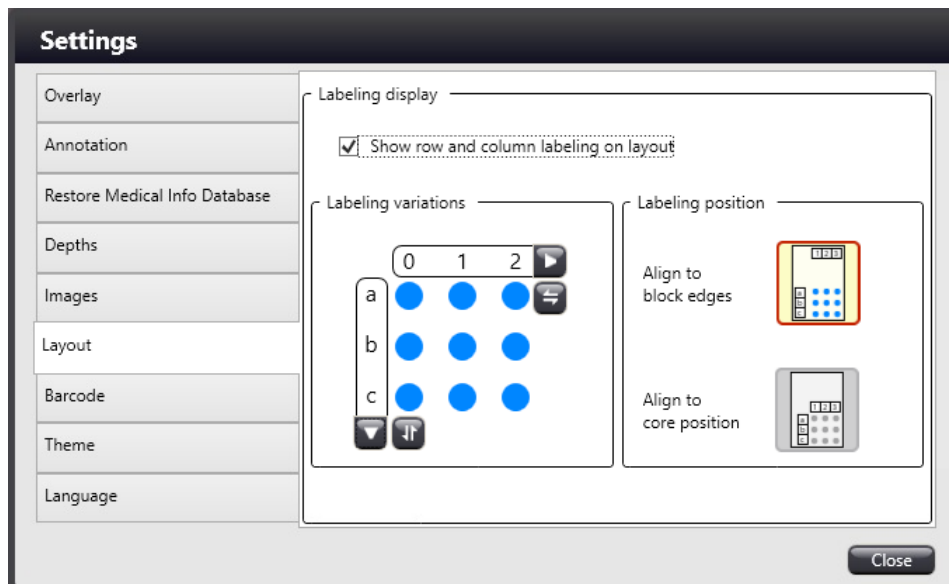


### Layout

Layout numbering direction and row/column labeling settings are presented in this panel.








- **Labeling display**

Activate the **Show row and column labeling on layout** option to display labels in layout editor and on the recipient block image.

- **Labeling variations**

Click  to switch between the following predefined labeling variations for rows/columns:

- 0,1,2,3...
- 1,2,3...
- a,b,c...

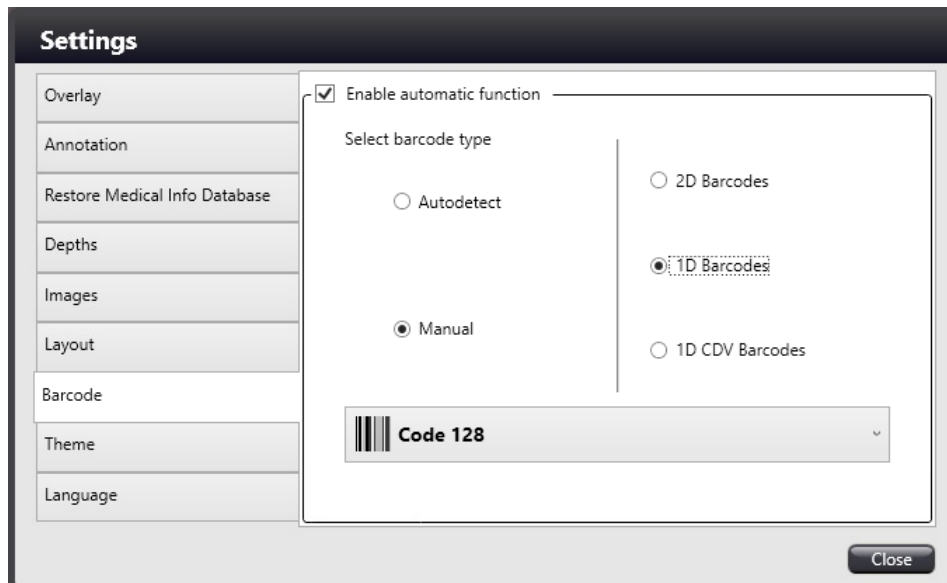
Labeling direction (increasing/decreasing) can be set for rows and columns separately by clicking .

- **Labeling position**

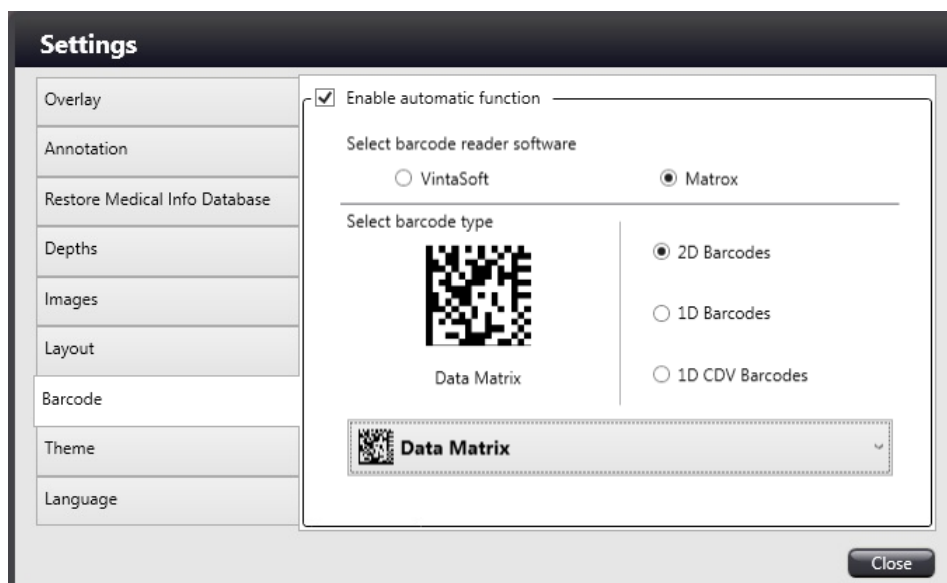
Select one of the positioning modes **Align to block edges** or **Align to core position**.

## Barcode

Tick **Enable automatic function** to set the identifiable type of barcode that is specified manually (select **Manual**) or activate **Autodetect** to allow the program the automatic identification without specifying the barcode type, thus blocks with any kind of barcode will be identified during creating a project.



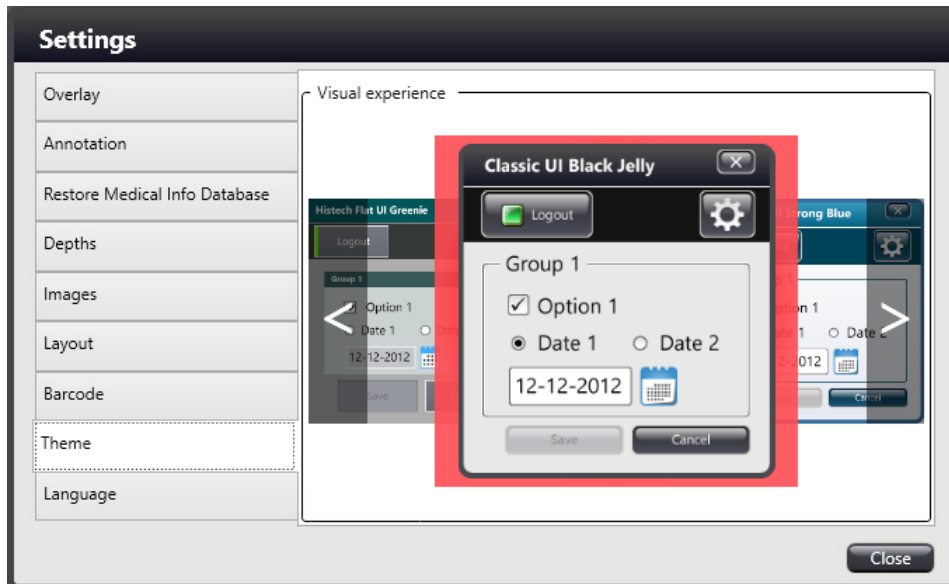
For software versions older than 2.7 the default barcode reader is selectable after the upgrade. Select **VintaSoft** to process barcodes with the embedded reader or **Matrox** to work with MIL dongle.



**NOTE:** VintaSoft occasionally cannot read Data Matrix barcodes. Once the **Matrox** option is selected, set the type (2D, 1D, 1D CDV) and the subtype of the specific group from the drop-down list.

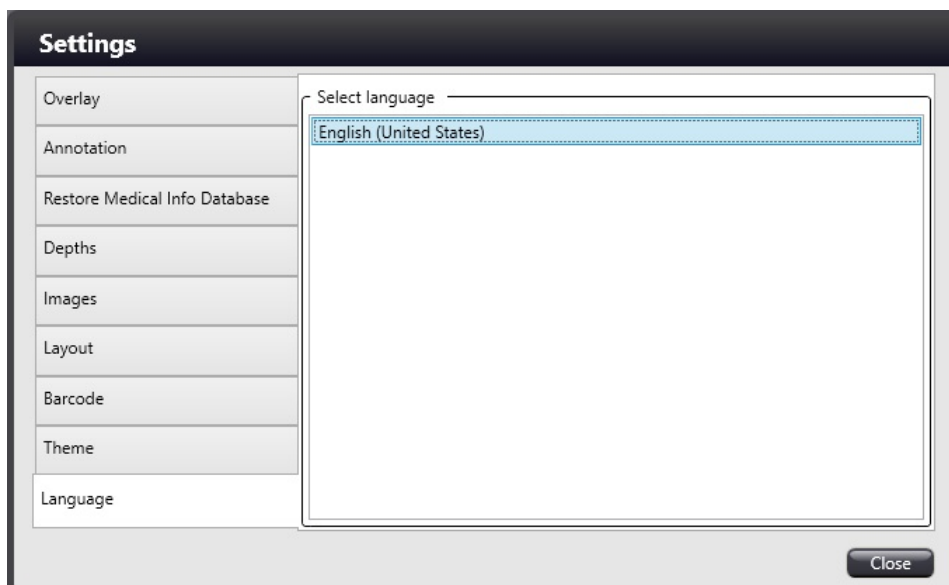
### Theme

The graphic user interface now has different types of visualization skins, select a preferred skin type by clicking the arrows (left of right). The elements according to the selected skin type are displayed in the Visual experience section of the window.



### Language

The language of the software can be selected from the list.



## 7 Maintenance of TMA Grand Master

Follow the maintenance and cleaning tasks discussed in this section to ensure the fail-safe operation of the TMA Grand Master device.



### Important!

It is the user's responsibility to perform all the maintenance and cleaning tasks.

### 7.1 Preventive Maintenance of the Main Unit

- Keep the **TMA Grand Master** main unit away from dust.
- Do not keep and operate the main unit in a humid room. Air humidity in the operation room must be under 75%. In a humid climate, make sure that **TMA Grand Master** is installed in a bright, dry, and properly ventilated room with less than 75% air humidity.
- After each use, switch off the power supply and close the transparent door.
- Wipe off water-soluble contamination with a microfiber tissue or with a slightly moistened piece of cloth. You may also use detergent.
- Wipe off oil or grease contamination / traces from the surface of the main unit with a cotton swab dipped into acetone but keep away acetone / ethanol from mirrors and lenses. It is forbidden to clean mirrors and lenses with ethanol / acetone.

The user should prevent any kind of fungal contamination on the opto-mechanical parts of the **TMA Grand Master** main unit:

- If the relative air humidity is continuously greater than 75% for three days and the temperature is between +15 and +35 °C.
- If the room is dark and does not have proper ventilation.
- If dust settles and fingerprints are left on the optical surfaces.

### 7.2 Cleaning Tasks

Empty the container when you finished drilling the recipient block or at the latest when you finished the session.

1. Make sure that the TMA Grand Master is switched off.
2. Pull out the trash container.
3. Empty contents into the dedicated waste disposal container.
4. Insert the container back into the main unit.

### 7.2.1 Opening the Service Compartment Door

Service compartment might be cleaned in order to remove dust or objects dropped in. To remove the door of the service compartment do the following:

1. Switch off the TMA Grand Master device.
2. Pull out the trash container (1).

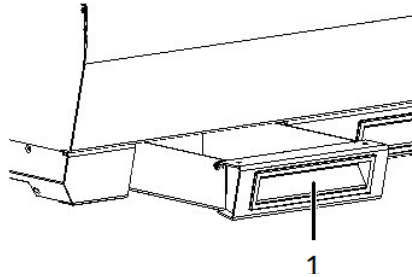


Figure 13 – Trash container

3. Release lock by pulling out the lever (1) at the inner panel, and move it to the marked position (2).

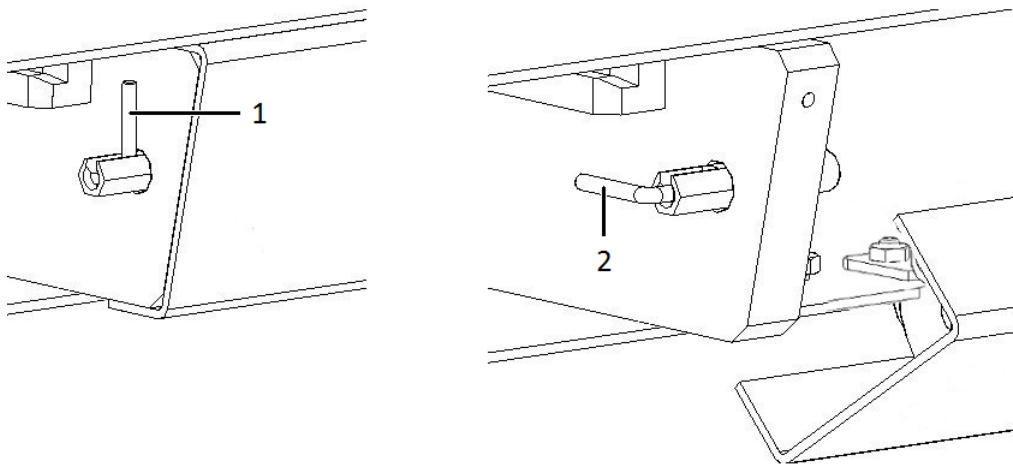
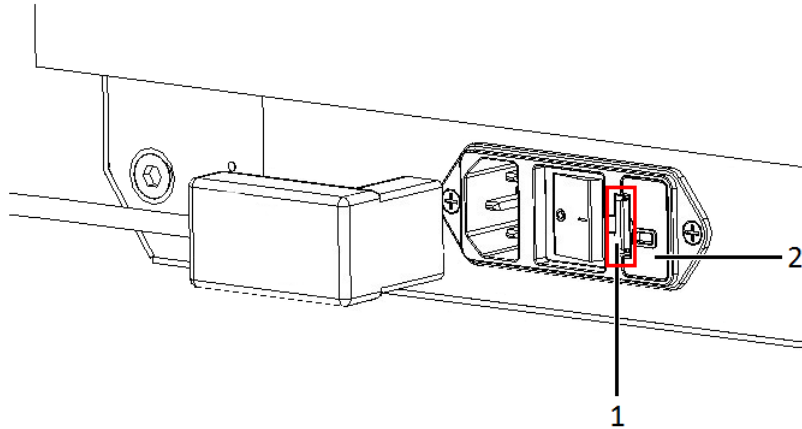


Figure 14 – Opening the service compartment door

4. Grab the handles, and open the compartment door.
5. Clean the compartment area.
6. Close the door, then lock the lever.

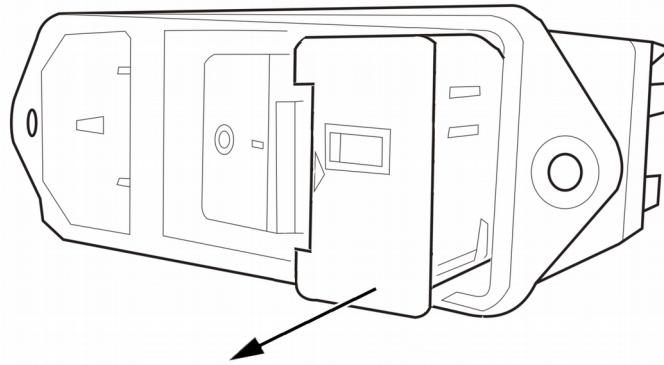
## 7.3 Replacing fuses of the main power switch

1. Switch off the main power supply and disconnect the power cable.
2. The fuse compartment is located next to the main power supply switch at the back side of the TMA Grand Master.
3. Release lock (1) by pushing the lever to the right, so the insert (2) can be pulled out.



**Figure 15 – Releasing the lock of the fuse compartment**

4. Remove insert from the compartment.



**Figure 16 – Removing the fuse compartment**

5. Replace fuses, put the insert back into its mounting, and push it inwards until you hear a snap, so the lever locks.

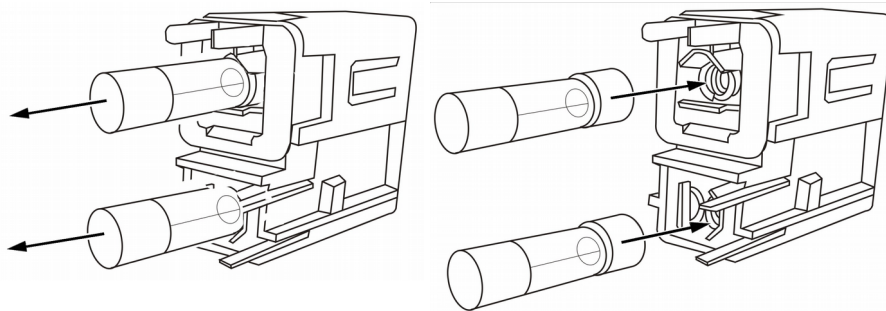


Figure 17 – Replacing the fuses

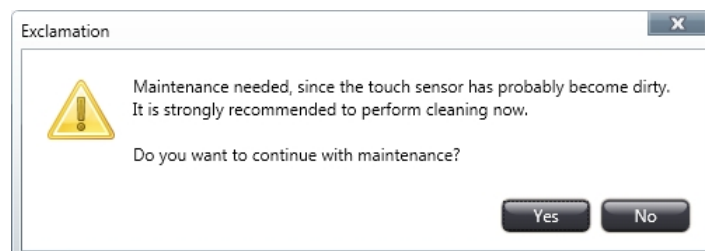


**Important!**

Use T3.15A/250V fuses only.

## 7.4 Contaminated Tray or Touch Sensor Surface

If during initialization (after switching on the TMA Grand Master device) the program detects possible contamination at the surface of the **F** donor block tray between the positions **F9** and **F10**, or of the touch sensor, the following message appears on the screen:



- Click **Yes**, then follow the instructions regarding cleaning the tray surface.

**First, you are requested to:**

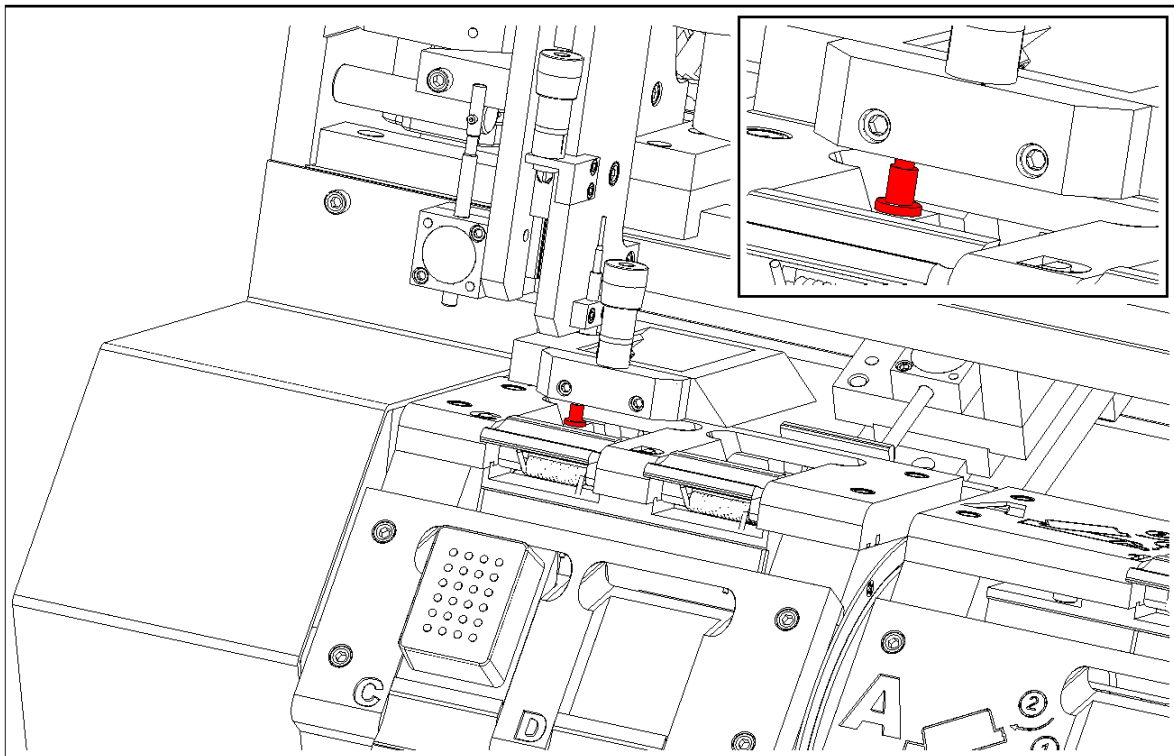
1. open the door,
2. remove any dirt from the space between donor positions F9 and F10,
3. close the door back.

- After performing the above actions, and you have closed the door, the touch sensor must be cleansed as well.

According to the instructions in the following message, by using a dry and clean cloth, gently rub the bottom surface of the touch sensor (sensor is marked with red in **Figure 18**).

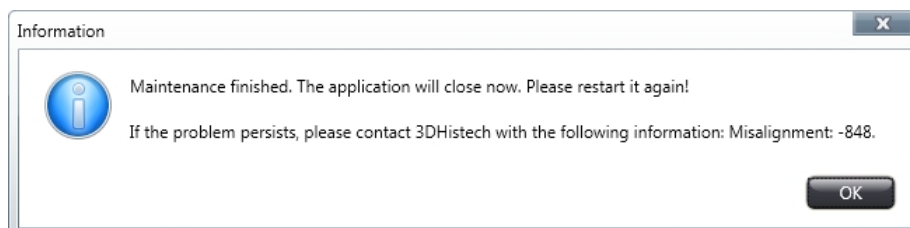
**Further, you are requested to:**

1. open the door of the tool exchanger compartment,
2. carefully clean the bottom surface of the touch sensor,
3. close the door back.



**Figure 18 – Touch sensor**

- After you finished with the cleaning tasks, you receive the following message:





## 8 Troubleshooting TMA Grand Master

### 8.1 Hardware-related issues

#### TMA Grand Master Does Not Work at All

**What to do:** Contact Thermo Fisher Scientific support.

#### Error During Initialization (Maintenance issue)

**Cause:** The surface of the tray between the positions F9 and F10 or the touch sensor is contaminated.

**What to do:** Clean the surface of the tray then the touch sensor at the specified areas.

For more information, see section **7.4 Contaminated Tray or Touch Sensor Surface**.

#### Block Image in the Application is of Poor Quality

**Cause:** Imaging errors.

**What to do:** Contact Thermo Fisher Sci support.

#### Puncher Falls Out During Punching

**Cause:** The puncher needle is detached from the collar.

**What to do:** Use another puncher.

#### The Puncher Does Not Pick Up the Core

**Cause:**

- a) The extracted tissue sample is placed too deep into the paraffin: it touches the head of the block holder (it goes too deep).
- b) The hole in the end of puncher became too narrow.

**What to do:**

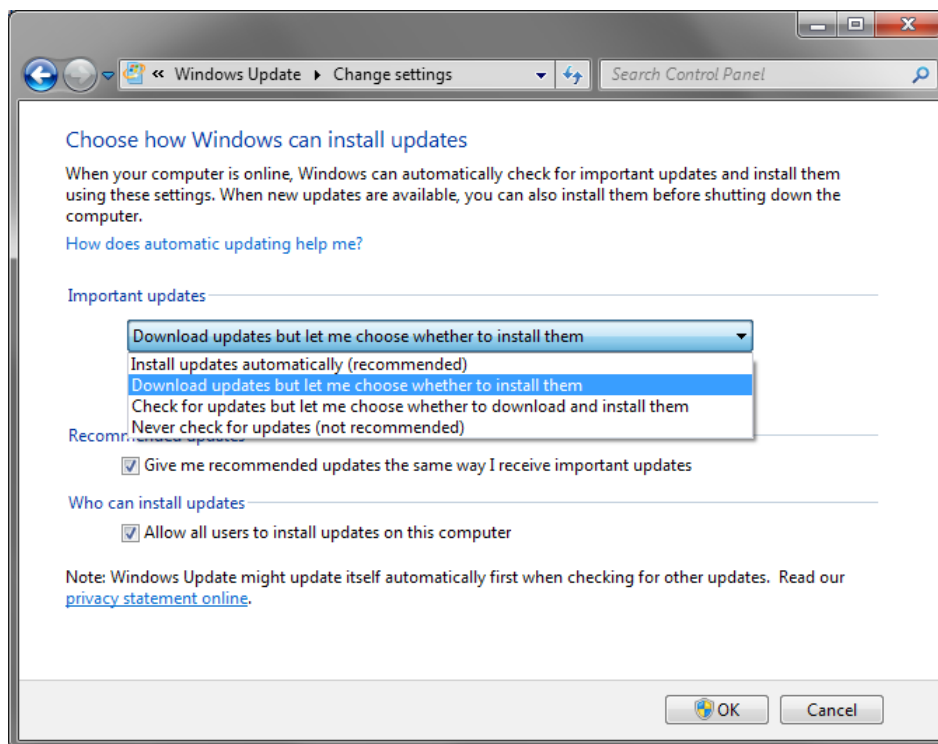
- a) Either you must take the core from another place or you must prepare a new donor block from the same tissue sample.
- b) Use a new puncher.

## 8.2 Software-related issues

### Windows 7 Update

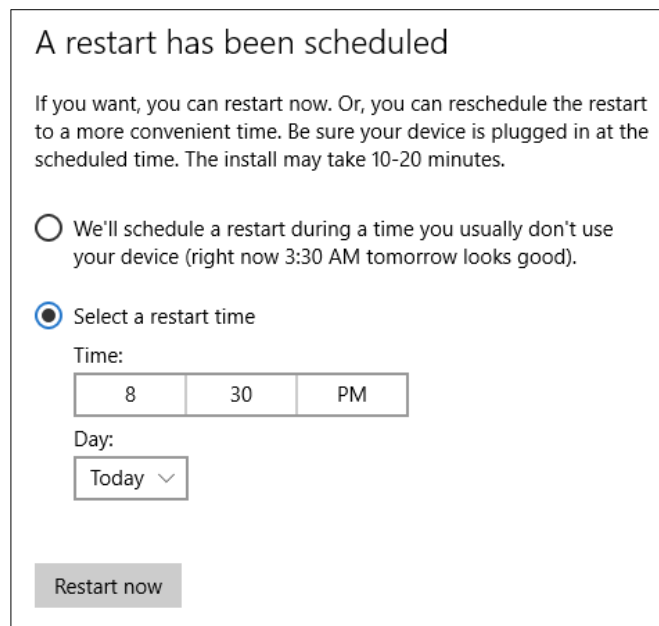
If Windows 7 Update is launched during working with TMA Grand Master, make sure not to restart Windows 7 after the update process is finished. Follow the below steps to avoid the automatic reboot of your PC after a major update via Windows Update:

- Go to **Start menu / Control panel / Windows Update / Change settings**
- Select **Download updates but let me choose whether to install them** item from the **Important updates** drop-down list.
- Click **OK** to accept changes and close the window.

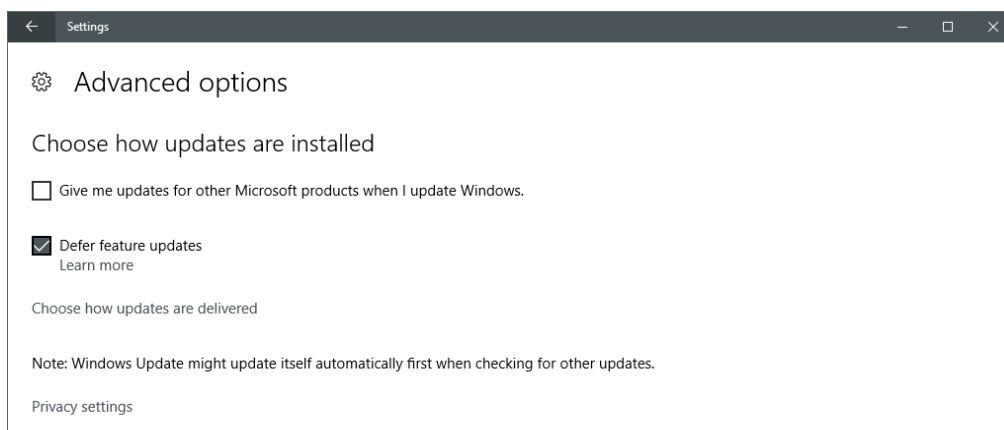


## Windows 10 Update

If running TMA Control in Windows 10, make sure to select the restart time with care if the pop-up window comes up – select a time when the TMA Control program is not running.



It is also recommended to use **Defer feature upgrade** option that can delay feature updates, and security updates will be available only.



## HDD is inaccessible/not writable

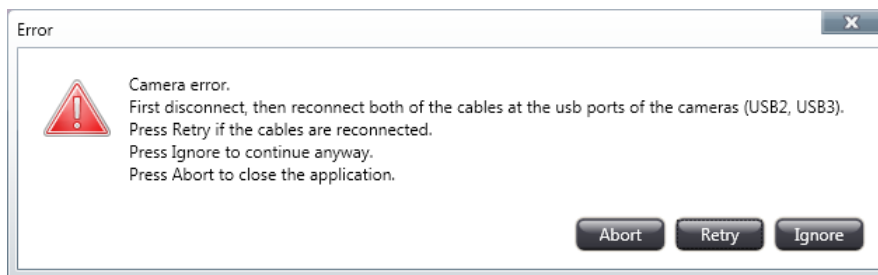
The System Administrator must ensure accessibility by the control software to some folders on the computer. For instance, write access must be granted to: *C:\ProgramData\3DHISTECH\TMAControl* folder, its sub-folders/files, and in addition, enable the software to modify registry logs.

## Block image and label area not visible

**Cause:** Problem with preview camera – COM driver registry entry is missing

**Solution:** Restart GTMA software application. If the problem still persists, try to reinstall it.

## “Camera Error” message is received



**Cause:** Camera cables are not connected properly.

**Solution:** Follow instructions in the message box.



### Important!

The folder in which log files are contained is “*C:\ProgramData\3DHISTECH\TMAControl\_LOG*”

Log files can be updated by running the “*log\_refresh.bat*” file.

## 9 Cassette and Block Dimensions

The dimensions of the **plastic cassettes** suitable for **TMA Grand Master** are as follows:

- 29 mm (H) x 41 mm (W) x 6 mm (D)

The **paraffin blocks** can have the following dimensions:

- 24 mm (H) x 37 mm (W) x 7.5 mm (D)

**NOTE:** If using the 3DHISTECH block moulder, the thickness (depth) of the block is 13.5 mm.

- The smaller size (7.5 mm in depth) means the paraffin thickness from the upper edge of the plastic cassette.
- The height of paraffin blocks in parentheses means their total depth together with the plastic cassette.



### Warning!

Do not use paraffin blocks which dimension values are higher than **24mm (W) x 37mm (H) x 10mm (D)**, otherwise the drilling and punching heads may be damaged. If the paraffin blocks are larger than they should be, mold them again with the base molds delivered with **TMA Grand Master**.

## 10 Technical Description of the Hardware

### 10.1 Physical Dimensions and Weight

Name of the Unit	Dimensions in mm* (Width x Depth x Height)	Weight in kg*
TMA Grand Master main unit	807×505×444	48
Control Computer	206×560×440	Max. 10
Monitor (22")	512×44×352	Max. 3.3

\* approximate values

### 10.2 Accessories

Accessory	Dimensions in mm	Number of items
Base mold for paraffin blocks	37×24×7,5	3
Drill bit*	∅ 0.6 / ∅ 1.0 / ∅ 1.5 / ∅ 2.0	2 / 2 / 2 / 2
Puncher*	∅ 0.6 / ∅ 1.0 / ∅ 1.5 / ∅ 2.0	3 / 3 / 3 / 3
Puncher chuck and Drill bit chuck	N/A	2
Piston*	∅ 0.6 / ∅ 1.0 / ∅ 1.5 / ∅ 2.0	1 / 1 / 1 / 1

\* For Drill bits, Punchers, and Pistons there are four distinctive color markings for each different sizes as follows:

- colorless – ∅ 0.6mm
- black – ∅ 1mm
- magenta – ∅ 1.5mm
- blue – ∅ 2mm

## 10.3 Objective and Cameras

Component	Description
Objective	16 mm focal length
Camera type	VR Magic
Camera resolution	3,14 Million Pixel

## 10.4 Ambient Conditions

Condition	Suitable Range
<b>Shipment (packed)</b>	
Ambient temperature	-40°C to +70°C
<b>Storage</b>	
Ambient temperature	+10°C to +40°C
Maximum relative air humidity	75% at 35°C
<b>Operation</b>	
Ambient temperature	+10°C to +40°C
Maximum relative air humidity	75% at 35°C
Maximum altitude	2000 m
Air pressure range	500 hPa to 1060 hPa
Degree of pollution	2

## 10.5 Operating Data

<b>Category of operating environment</b>	closed room facilities
<b>Electrical protection class</b>	I
<b>Internal protection degree</b>	IP 20
<b>Electrical safety</b>	in compliance with EN 61010-1 (IEC 61010-1) and taking CSA & UL regulations into account
<b>Over-voltage category</b>	II
<b>Radio interference suppression</b>	in accordance with EN 55011 class B
<b>Noise immunity</b>	in accordance with EN 61326-2-6:2005
<b>Main unit line input voltage</b>	24 V DC $\pm$ 1 V
<b>Mains supply voltage</b>	90-240V
<b>Mains frequency</b>	50-60 Hz
<b>Power rating</b>	300W



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