TMA Master II
2.8
User's Guide

June 5, 2018
Rev. 1

Contents

Disclaimer

Intellectual property related to the 3DHISTECH products are as follows:

EP 1,789,831; US 7,663,078; EP 2,024,772; JP 2009-512685; US 12/301,781; EP 1,644,767; JP 2007-516451; US7,327,515; EP 1,994,398; JP 2008-557835; US 12/281,566; U0700210; US 6,246,785; HU0900142; HU0700404; PCT/HU2007/000065; EP 08762668.5; US 12/663,537; PCT/AT2006/000492; JP 2008-542552; EP 06817469; US 12/095,545; PCT/AT2006/000493; EP 06817470.5; US 12/095,596; HU0900741; US 61/264,732; US 11/826,752; P0401870; PCT/IB2005/050344; US 11/662,976; HU0700409; US 12/042,050; US 77/636,144 and 007502032.

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For performance evaluation only, the performance characteristics of this product have not been established.

Declaration Of Conformity

3DHISTECH Ltd. declares that the product TMA MASTER Tissue Microarrays Creator (Hardware version 02) CE marked laboratory equipment is designed and produced in keeping with the company quality management system certified according to ISO 9001 and EN ISO 13485 standards and conforms to the directives and other standards listed below:

- IEC 61010-1:2010
- EN 61326-1: 2013
- EN 55011:2009
- CAN/CSA-C22.2 No. 61010-1
- ANSI/UL 61010-1

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

3DHISTECH Ltd. performed broad risk assessment and risk control activities for the safe use of this product. Under normal and proper conditions of use, the operation of the device is not harmful to the operator's or other personnel's health or safety. There is no operator (user) action required in case of residual risks.

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For the latest information on 3DHISTECH products and services, please visit our website at: http://www.3dhistech.com.

Character Formats and Symbols

Example	Abbreviation or term that is explained in the section Terms and Abbreviations.
Example	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 **F11**) or the **Ctrl+O** key combination.
Example	Cross-references to other documents.
 **Warning!**	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.
 **Important!**	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.
 **Tip!**	A suggestion to use the application in some other way or to some interesting purpose.

Terms and abbreviations

Digital slide / Slide	Slide digitized with a scanner microscope, for example Pannoramic SCAN 150. Consists of an MRXS file and a folder with the same name as the MRXS file.
Donor block	The donor block is a standard tissue block that may be from surgical pathology, autopsy, or research material.
Recipient block	The tissue cores are removed from the donor and inserted into a "recipient" paraffin block.
TMA	Tissue microarrays – The tissue microarray consists of an array of cylindrical cores of paraffin-embedded tissue that are removed from preexisting "donor" paraffin blocks.

Safety Warnings

Warning!

Danger of pinching!

If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.

Maximum force: 25 Newton

Warning!

Operate the **TMA Master II** main unit only when the protective window is closed and it is secured with the latches. Do not reach into the device during operation.

The protective window can only be removed when changing the puncher or drill bit.

Warning!

Danger of pinching!

Be careful when closing the protective window as your fingers may get pinched.

Warning!

The **TMA Master II** may not be operated by other than properly instructed persons. Operating personnel must be fully aware of the potential dangers which a particular field of application involves. The **TMA Master II** is a precision instrument which may suffer a significant reduction in operational functions or even physical destruction following intervention performed in any nonconforming manner.

Warning!

If the equipment is used in a manner not specified by the manufacturer, the protection provided by the equipment may be impaired.

1 About TMA Master

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

You can define on a graphical user interface where exactly **TMA Master** should drill holes in up to four paraffin blocks to create recipient blocks.

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 a PCR cassette is controlled by using a graphical user interface. The built-in digital camera of **TMA Master** gives you an image of each donor block, so you can aim the puncher more accurately. You can also save an image of each donor block with markers telling where the tissue cores were extracted from.

Furthermore, you can import donor block data from an Excel worksheet. You can export another Excel file from **TMA Master** that tracks the association between the 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 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.
- It offers an adjustable punch depth to ensure accurate positioning of the core tissue in the recipient block and to prevent damages to the recipient block hole that will exclude its accidental overfilling.
- 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.
- It offers a maximum simultaneous drilling capacity of 5 recipient blocks.
- Maximum TMA handling capacity:
  - Either 4 donor blocks and 1 recipient block

    or
  - 1 donor blocks and 4 recipient blocks.

1.2 New Features

- Language localization enabling a multi-language interface – textual elements of the GUI are editable on the fly
- Slide annotations and markers of different sizes can be displayed on donor image
- Repunching of cores can be initiated both from the donor and the recipient side
- The total number of PCR cores of 0.6mm and 1.0mm transferred to a tube is increased from 4 to 8
- Image Editor for donor label images
- Faster processing of slide overlay

2 TMA Master II Hardware

Hardware:

- **TMA Master II** main unit with a 24 V power supply
- Control computer with a monitor, a mouse and a keyboard

  (Optional, configuration is order-specific)
- USB cables between the main unit and the control computer
- Accessories box

Blocks:

- Base molds for paraffin blocks

2.1 TMA Master II Main Unit

Front View

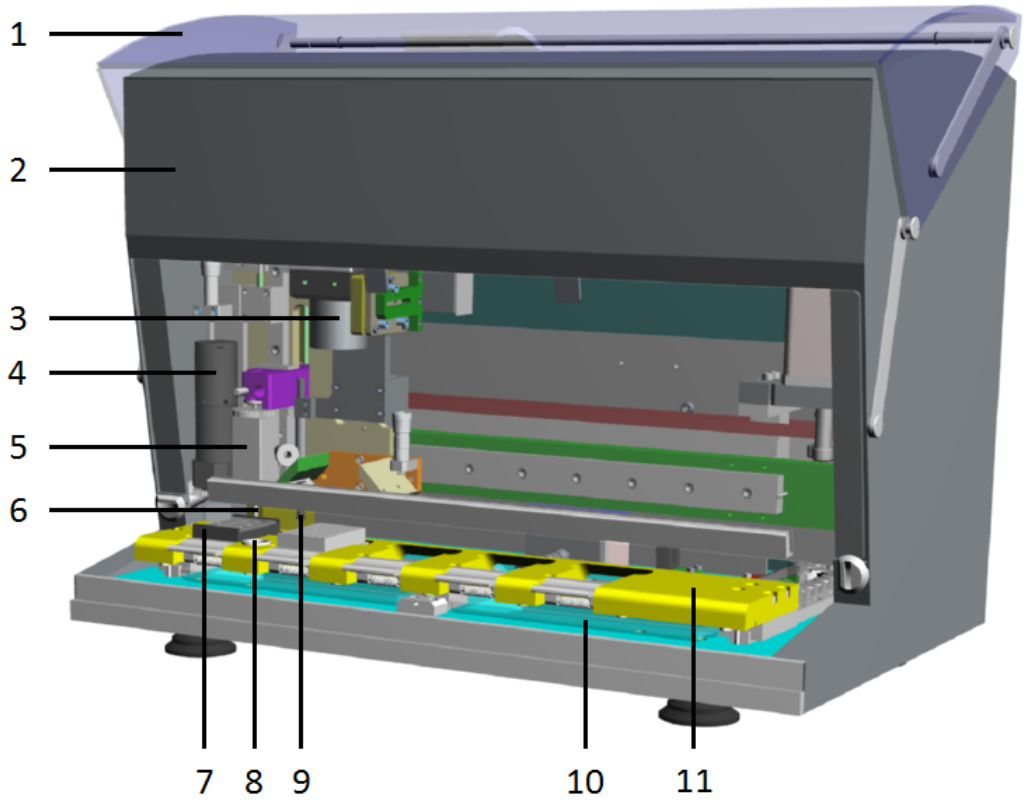


Figure 1 – Parts of the TMA Master II unit

1. Protective door
2. Device housing

3. VRMagic camera
4. DC motor
5. Drill or puncher chuck
6. Puncher or drill bit
7. PCR cassette
8. Tray for discarded core material
9. Touch sensor
10. Trash container for paraffin flakes
11. Block tray

Back View

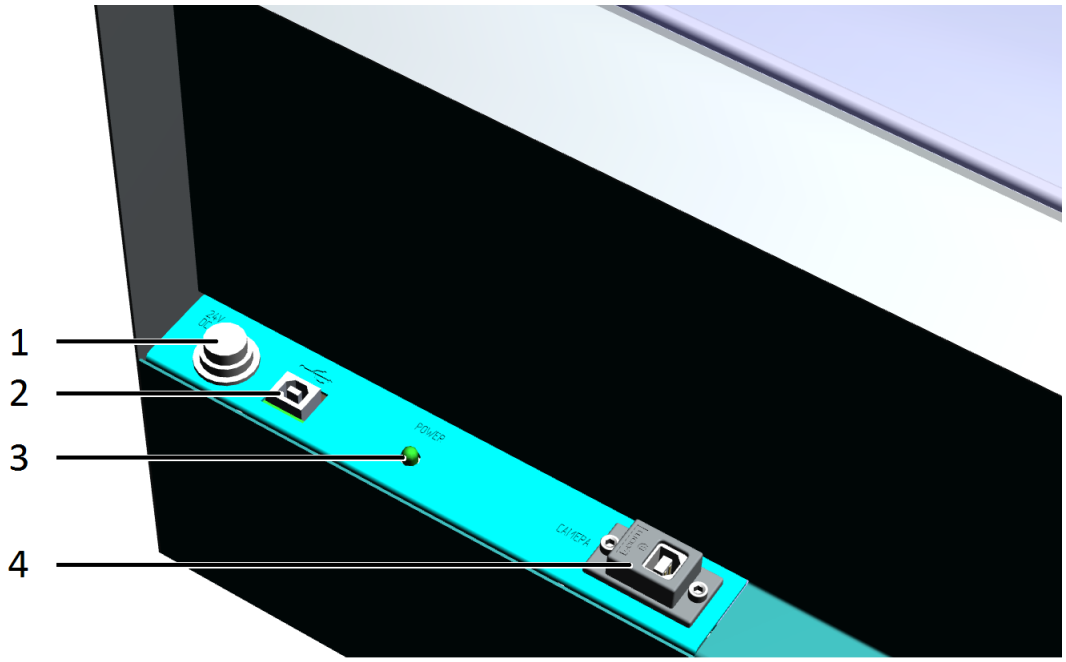


Figure 2 – Back view of the TMA Master II unit

1. Terminal points for the power supply cord (+24 V DC) to link the **TMA Master II** main unit with the dedicated external power supply.

> **Warning!**
>
> Always use the dedicated external power supply (*SINPRO – MPU101-108*) for the TMA Master II device! See ***section 2.2*** for more information.

2. USB port (to connect the main unit to the control computer)

3. Ready-for-operation LED indicator
4. USB port (output for the camera)

Warning!

Only connect external devices to the instrument which are approved to avoid the risk of electrical shock.

2.2 Power Supply for the Main Unit

For the proper operation of the TMA Master II device a *SINPRO – MPU101-108* external power supply unit must be connected between the mains power and the device.

Front panel:

1. main power switch
2. power supply connector

Back panel:

3. detachable power cord to connect the external power supply unit with the main unit

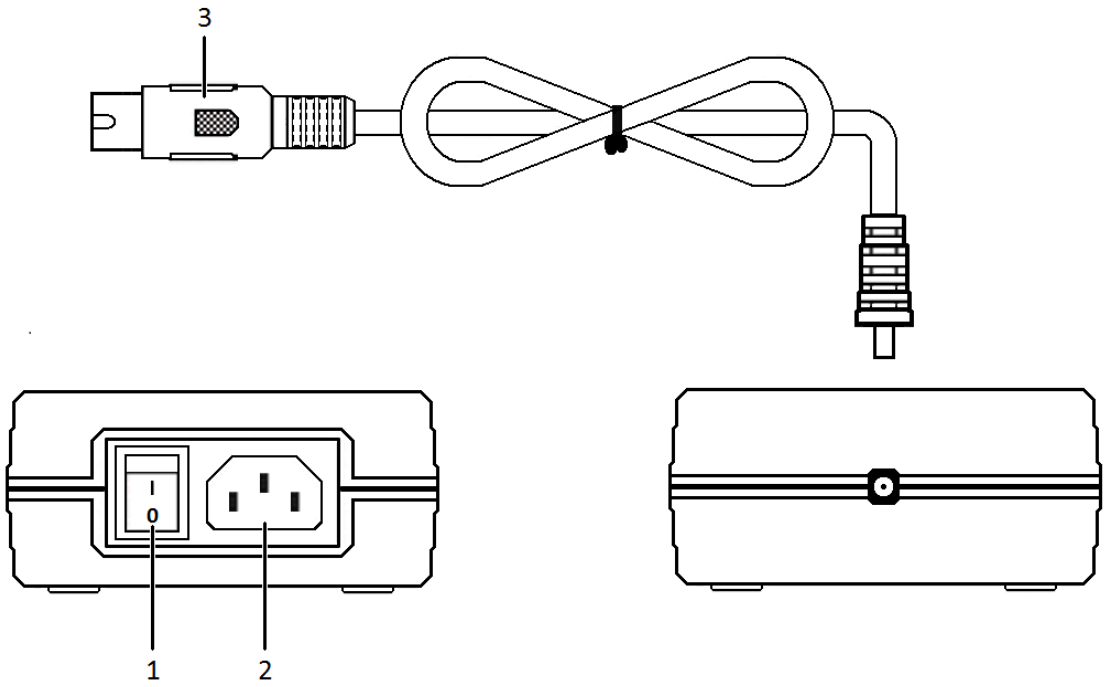


Figure 3 – External power supply unit

2.3 Cabling

For the required cable connections, the supplied cables must be connected as shown in *Figure 2* and *Figure 3*.

> **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 the Thermo Fisher Scientific **Service** for support in such cases.

2.4 Delivery

You can order the following packages separately or combined:

Package 1

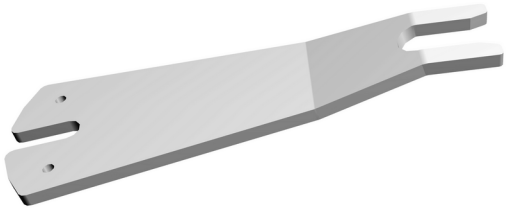
- **TMA Master II** main unit (packed in a mandatory polyethylene container in a cardboard box)
- Accessories in a plastic box (drill bits, punchers, pistons, tool, and drill bit and puncher chuck), paraffin block base molds, accessories and tools for the assembly. The size and the content of the box can vary according to your purchase order. For further information on the basic accessories, see ***section 8.3***.

Accessories box

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.

Tool



- External power supply unit

Package 2

- Control computer (with mouse and keyboard)
- Cables

Package 3 (optional)

- Monitor for the control computer

Important!

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

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 either Microsoft Office or Kingsoft WPS Office package on the control computer.

2.5 Installing and Configuring TMA Master II Hardware

Warning!

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

Important!

Do not position the equipment so that the power switch of the external power supply unit or its electrical connector is inaccessible.

2.6 Transporting the TMA Master II Main Unit

Warning!

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

1. Switch off the external power supply unit of the **TMA Master II**, the control computer and the monitor, and unplug all cables.
2. Fix X-axis actuator belt of the main unit with zip-ties.
3. Close the door of the main unit, tape the door to the machine and put on the supporting foam frames on the side.
4. Pack the accessories into their box.
5. Put the main unit into the smaller box and put the accessory box on top of it; the foam shows the place for the accessory box.
6. Tape the smaller box and put it into the larger box.
7. Place the external power supply unit back to its box and put it into the larger box, next to the **TMA Master II** main unit.
8. Close the larger box and tape it.

3 TMA Control Software Application

3.1 Prerequisites for the Installation of TMA Control Software

Operation system	Microsoft Windows 7 Professional 64-bit SP1 EN or Microsoft Windows 10 Professional 64-bit EN
Hardware	**Minimum:** Intel® Pentium™ P4, 3GHz, 1GB RAM **Recommended**: Intel® Core™ i5-4570 Quad-Core, 3.2 GHz, 2GB RAM
Screen resolution	**Minimum**: 1680×1050 **Recommended**: FullHD (1920×1080)
Disk space	**Recommended**: 150 – 500GB

NOTE: You receive a product-specific license when purchasing any of the 3DHISTECH applications.

3.2 Installing TMA Control Software Application

Important!

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

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.

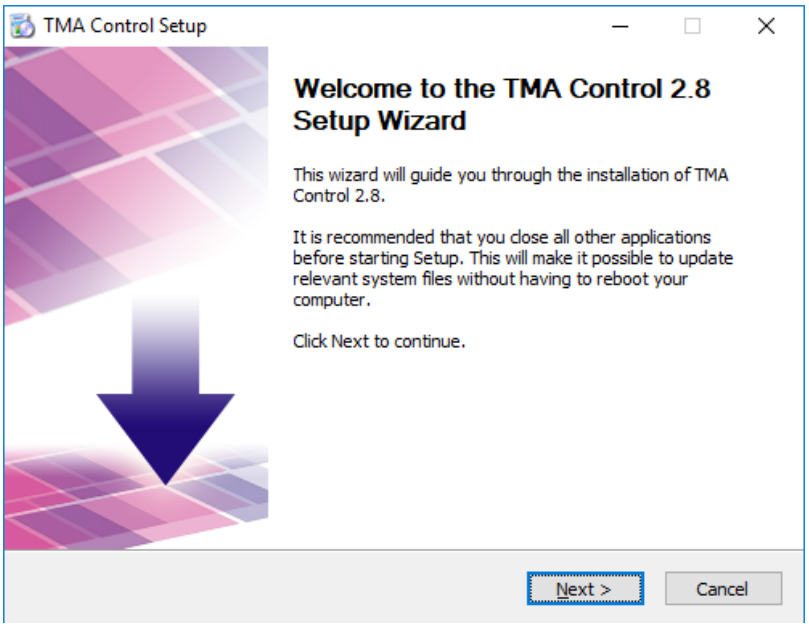
In case the control computer is not part of the order, only the **TMA Control** software and the configuration application are delivered on an installation disc.

Warning!

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

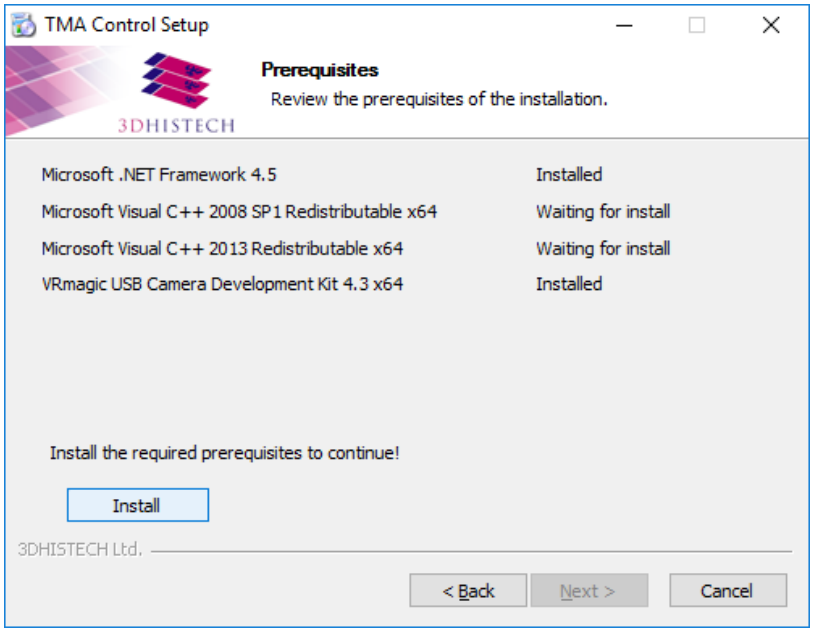
In order to achieve error-free operation, Thermo Fisher Scientificprohibit the modification of the PC configuration as well as the installation of any additional software.

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.

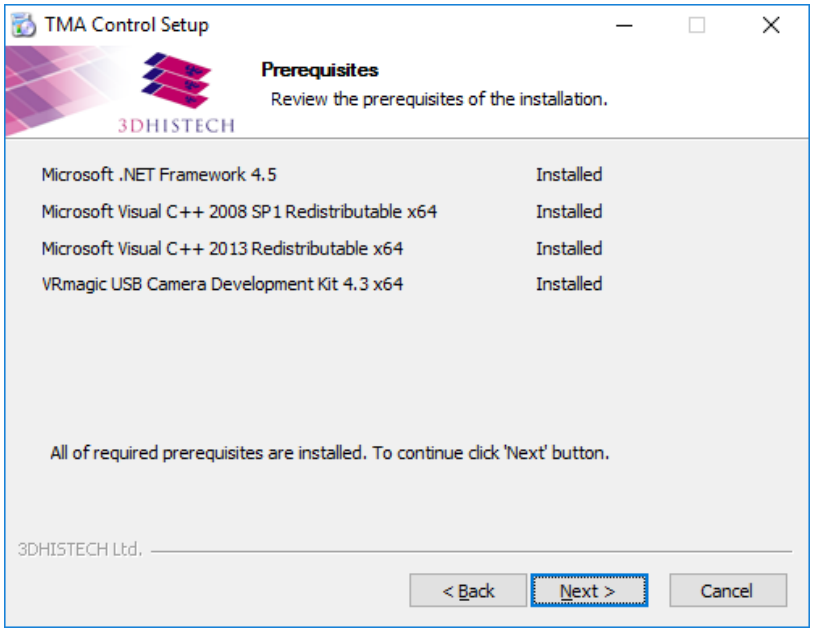


3. Accept the End-User License Agreement, and click **Next**.

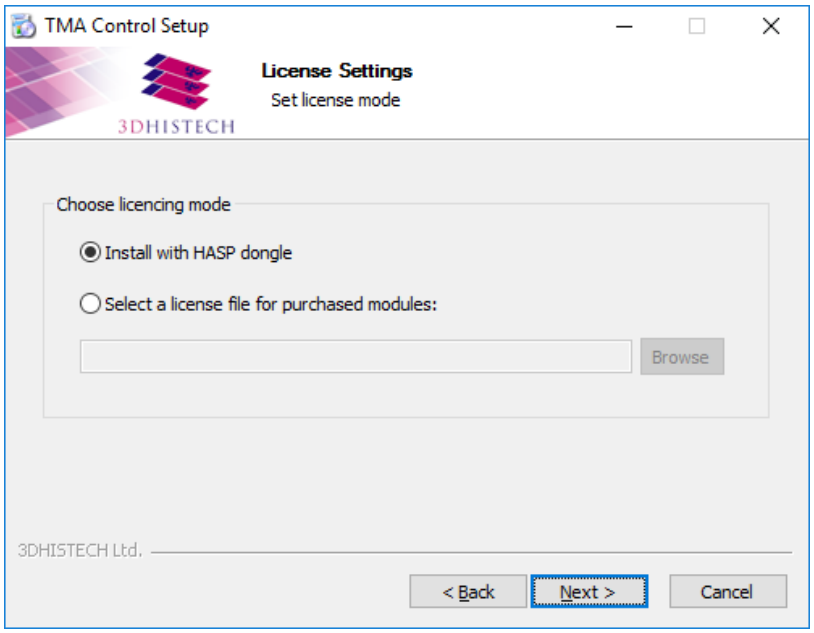
4. The installer notifies you if it cannot find the prerequisites. Click **Install** to start the installation of missing prerequisites.



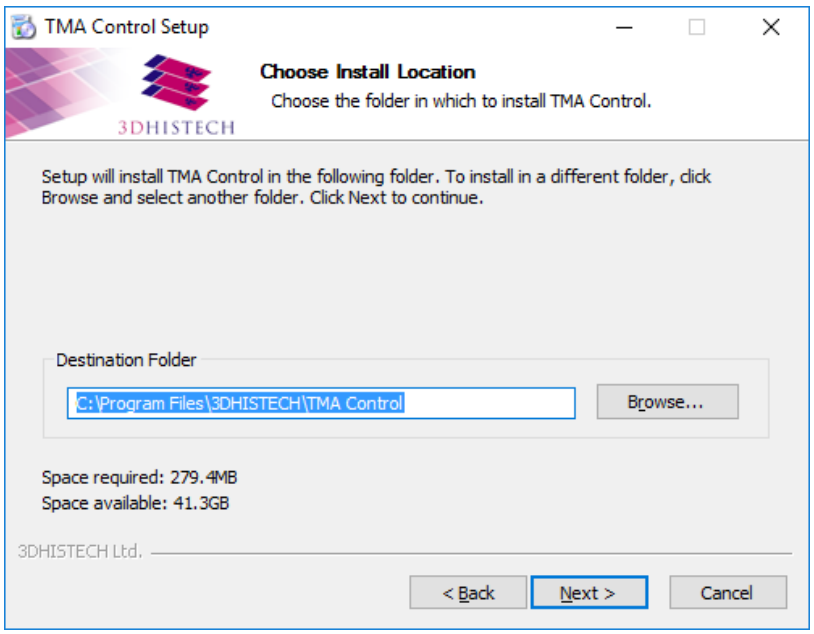
5. Click **Next** to continue with the installation of the TMA Control software application.



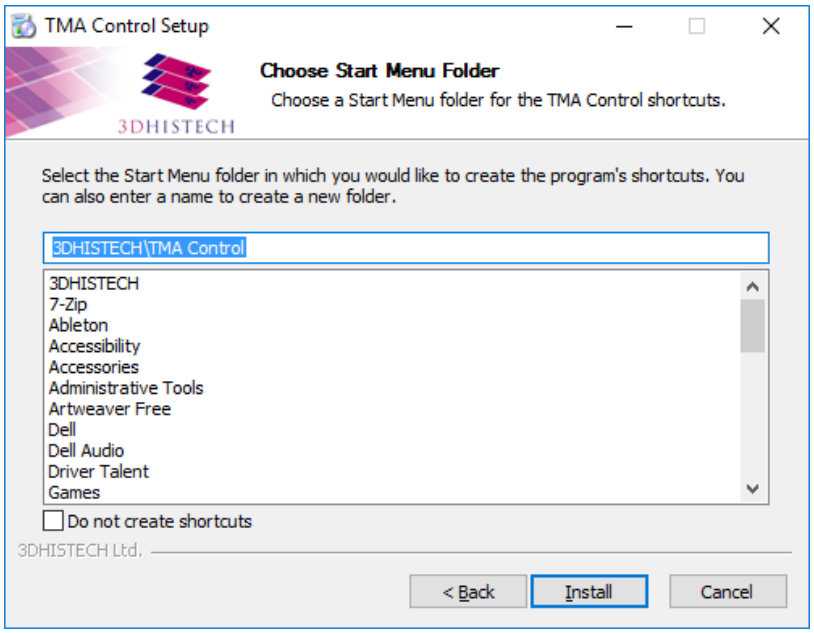
6. Select the type of license – browse for the license file or select HASP dongle.



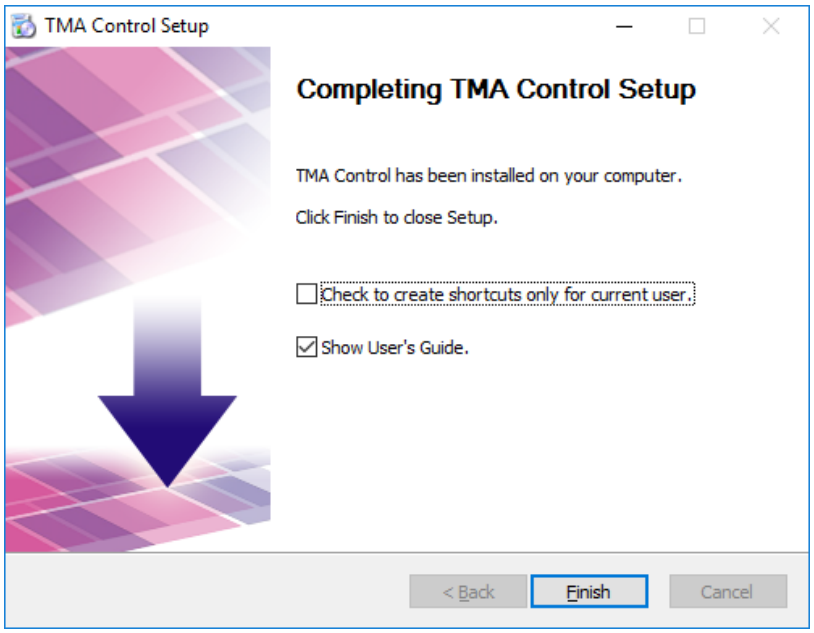
7. Choose the installation folder for the TMA Control software application. Click **Browse** for locating a different folder than the default one, then click **Next** to continue.



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 power supply.
2. Turn the control computer on.
3. Switch the monitor on.

Turning the Power Off

1. Close the software application on the control computer.
2. Switch off the power supply with the main power switch.
3. Turn the control computer off.
4. Switch the monitor off.

4.2 Starting the TMA Control Application

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

Warning!

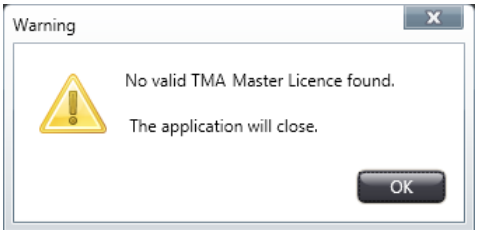
If you start the software, but the hardware is turned off, a warning message appears. Switch on the main unit then restart the software.

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.

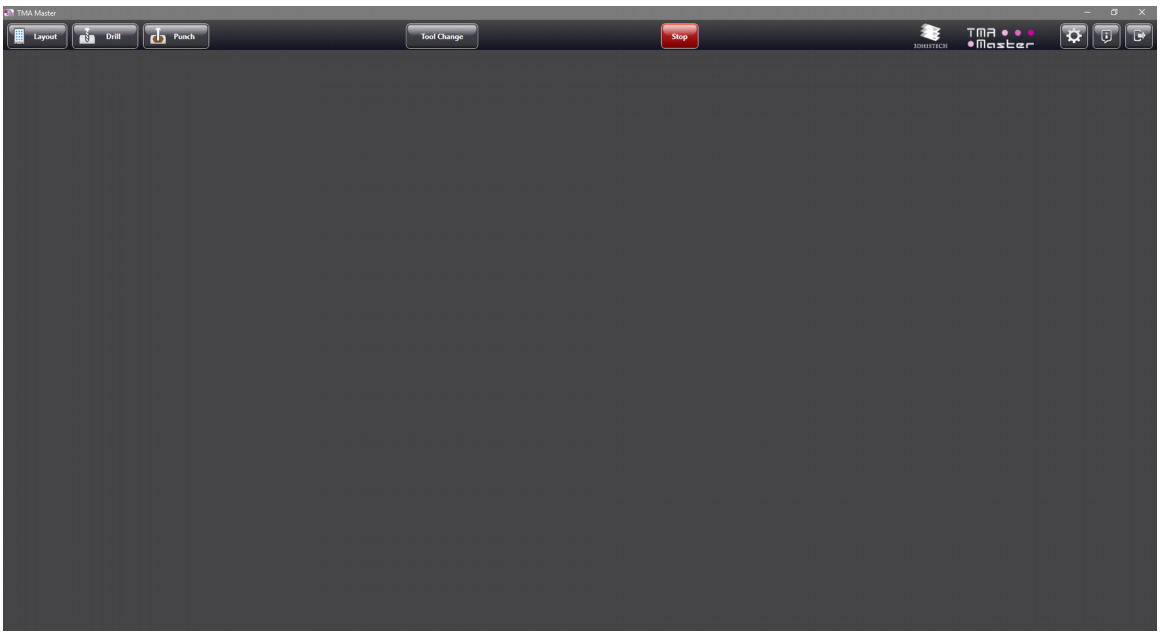
Important!

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

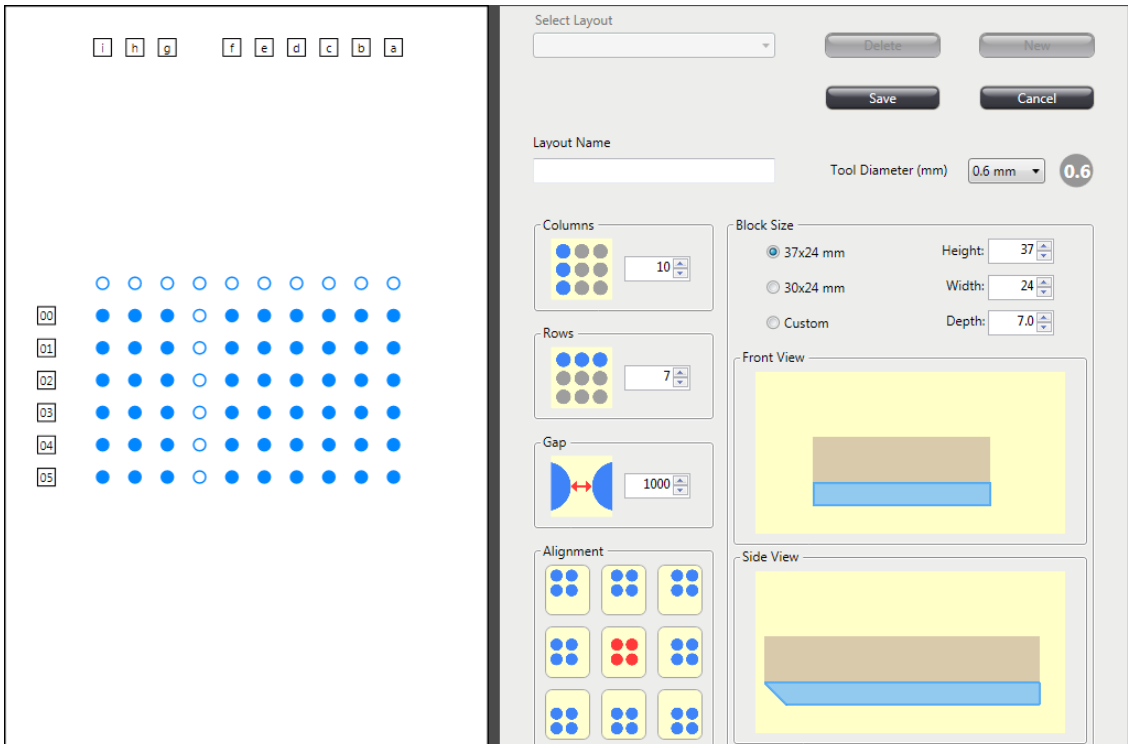


A separate license is necessary to activate both the PCR and the barcode reading functions of the TMA Master software.

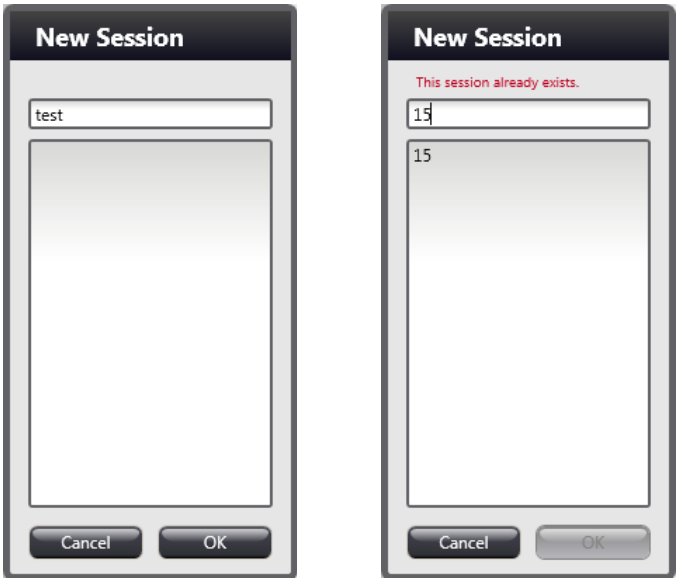
- If you launch **TMA Control** for the first time, a layout must be created first. **Drill** and **Punch** buttons are inactive.



- Create a layout as described in ***section 5.2***.

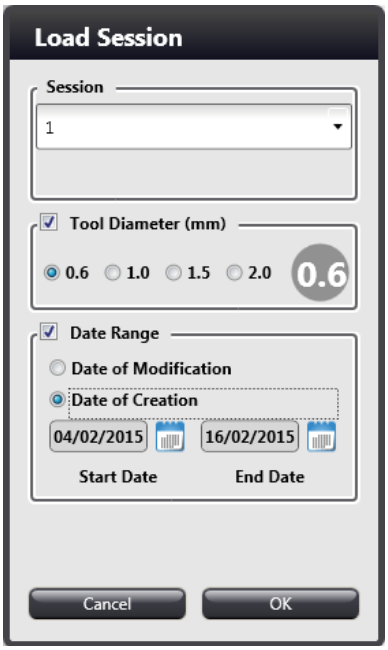


- If at least one layout has been created, the first TMA session can be created on the **Punch** form. The **New Session** window is displayed in which you must enter a name for the session. If you enter a name that already exists on the session list, the message *"This session already exists"* appears above the text field to warn you to enter a different session name.



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

After clicking **Load**, the Load Session window is displayed.



Select the desired session to be loaded, and also you can narrow down session list by activating **Date Range** and/or **Diameter** filters. When writing the name of the session to be loaded, suggested names appear on the list according to the entered text string.

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

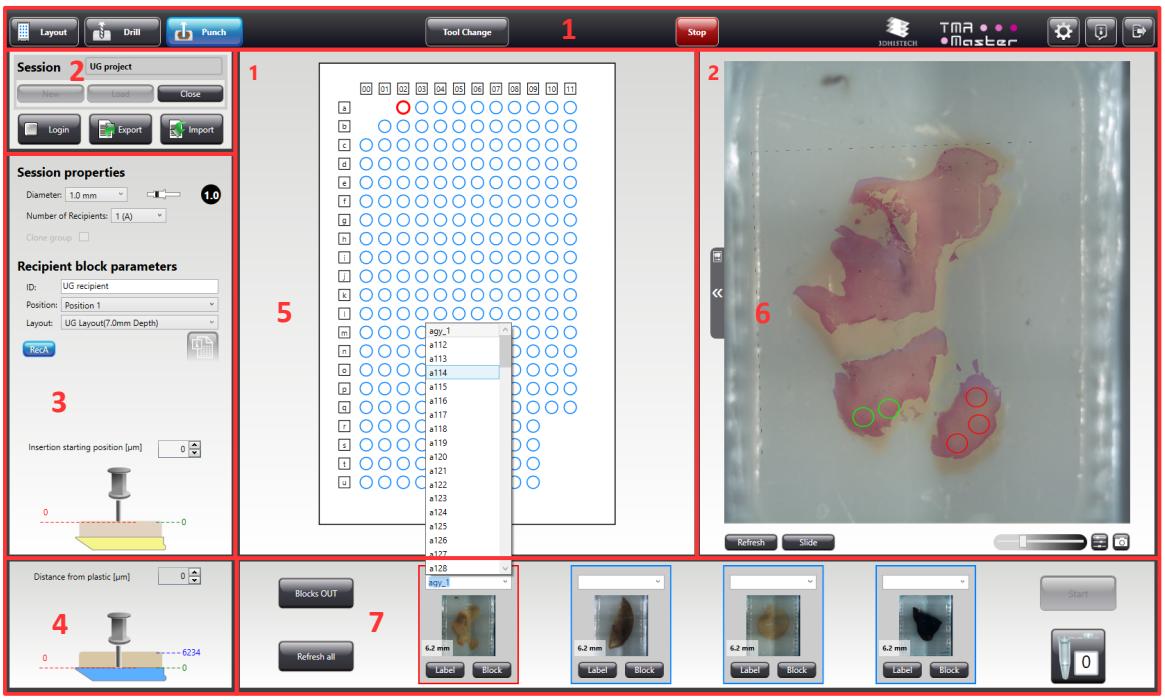
Important!

Only an existing session with the relevant layout can be loaded.

If you want to use layouts that were created by using **TMA Master** software installed on **Windows XP**, copy the *layouts.xml* file located in the folder *"C:\Documents and Settings\<user name>\Application Data\TMA Master"* and paste it into the following folder when running **Win7**: *"C:\ProgramData\3DHISTECH\TMA Master".*

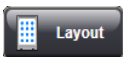
When launching the program, the presence of the *layouts.xml* file and its data will be added to the database, then the XML file will be deleted.

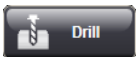
4.3 Main User Interface

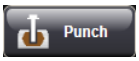


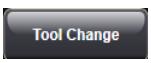
This version of TMA Master offers a simple but detailed view of recipient and donor blocks. Based on the loading and processing method of blocks the main window includes a layout view of recipient blocks, also a preview image and thumbnails of donor blocks.

The main window consists of the following parts:

1. **Toolbar**
   - 

– Opens the **Layout Editor** window
   - 

– Switch to **Drill** panel
   - 

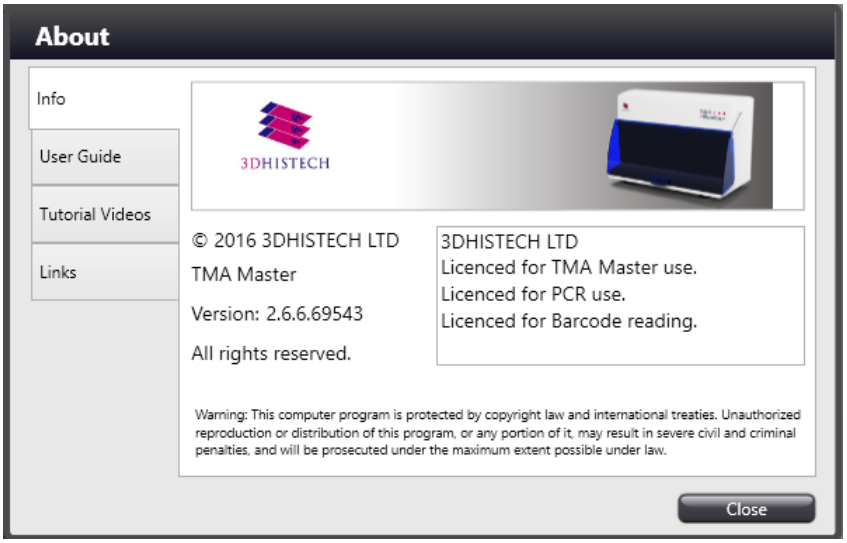
– Switch to **Punch** panel
   - 

– Initiate **Tool Change** operation
   - 

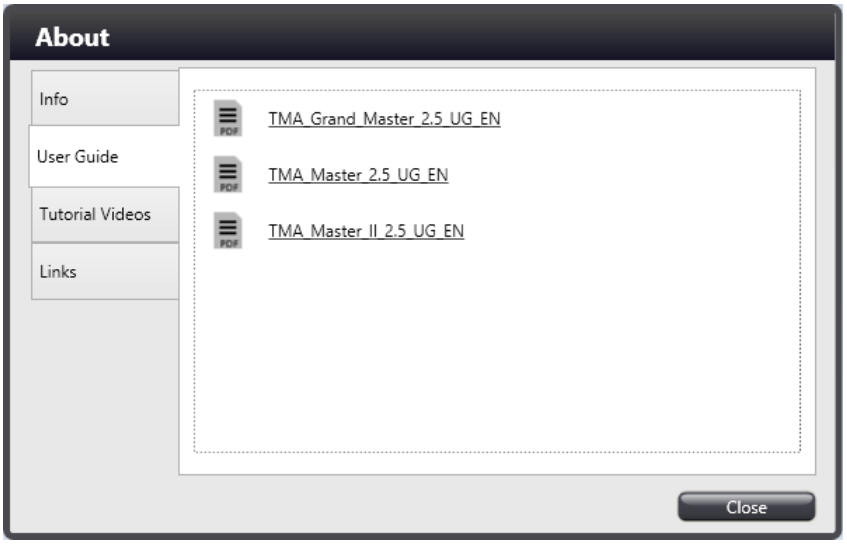
– **Stop** the running process
   -  – Opens **Settings** window containing the settings for some important features in TMA Control, including Overlay, Annotation, Images, Session, PCR, Layout, Barcode, Theme, and Language. See section ***9. Settings*** for more information.

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

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

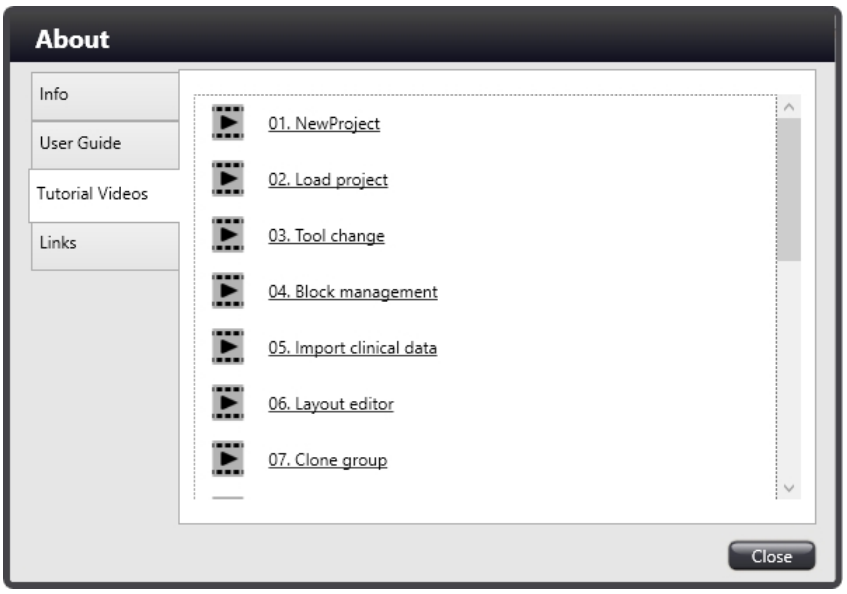


  - **User Guide** – Manuals of TMA Grand Master, TMA Master, and TMA Master II can be accessed and opened directly by clicking the links.

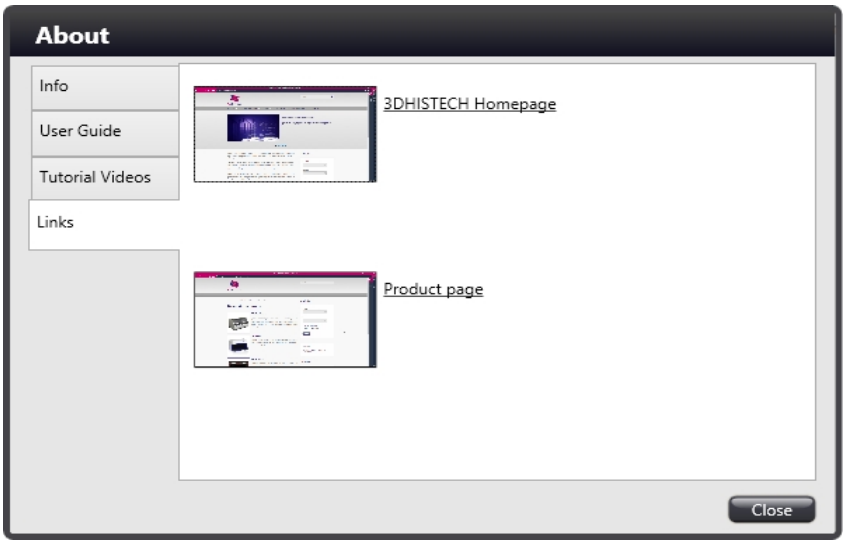


- **Tutorial Videos** – Selected tutorial videos are listed and can be opened by clicking the links.

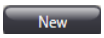
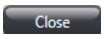
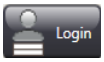
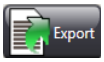
  NOTE: Before opening the videos, make sure to copy video files to *<C:\Program Files\3DHISTECH\TMA Control\Videos\TMA Master>* folder from the installation disk. This folder may be hidden, and thus requires authentication.



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



-  – **Exit** the program

2. **Session panel**
   -  – Create a new session
   -  – Load session
   -  – Close session
   -  – Login to a dedicated CaseCenter server
   -  – Export session data
   -  – Import clinical/patient data or medical information
3. **Recipient data panel**
4. **Distance from plastic – Punch depth**
5. **Recipient layout**
6. **Donor preview**
7. **Donor thumbnail bar**

4.4 Block and PCR cassette preparation

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 PCR cassette preparation

Important!

Before inserting a PCR cassette into the dedicated 1st position of the tray (rec1), ensure that the cassette and the tubes are sterile and free from contamination.

TMA Master II is capable of receiving one PCR cassette only. The cassette is designed to include a maximum of four tubes.

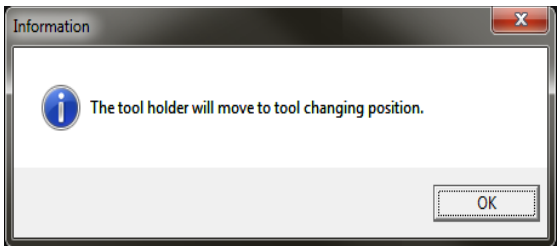
Figure 4 – PCR cassette for TMA Master II

4.5 Changing the Drill Bit

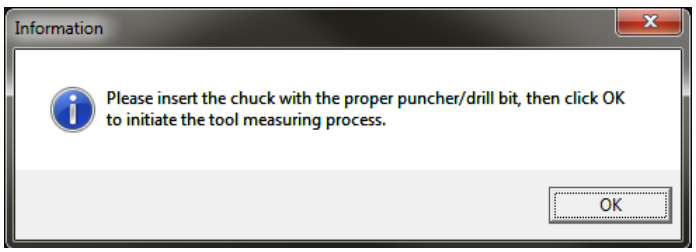
TMA Master is delivered with drill bits of different size. The following instructions help you change the drill bit to match the size of the holes in the recipient blocks.

> **Warning!**
>
> **Danger of pinching!**
>
> If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.
>
> Maximum force: 25 Newton

1. If blocks are inserted in the main unit, click Tool Change in the **Drill** window, and remove all blocks. For more information on how to remove blocks, see ***section 4.7***.
2. An information is displayed regarding positioning the tool holder. Click **OK** to continue.

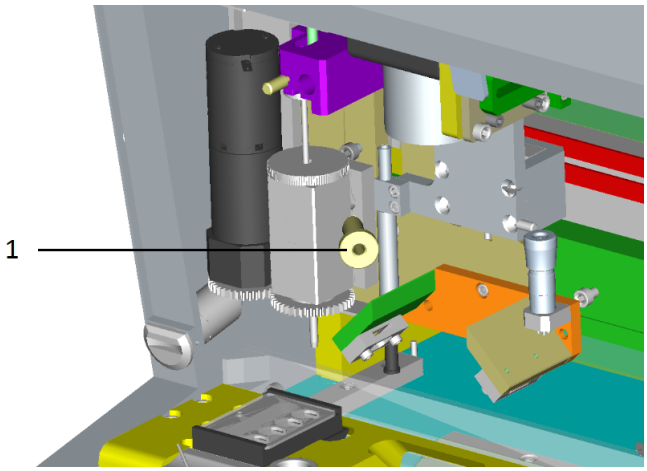


3. Remove the window by unscrewing the two latches at the bottom left and right side of the window with the tool provided in the accessories box.
4. Follow instructions displayed in the following message box:



> **Warning!**
>
> At this step, before initiating the operation, the device must be switched off, and unplugged from the external power supply unit.

- Loosen the screw (anticlockwise) that keeps the drill chuck (**1**) in position and take out the drill chuck.



- Remove the drill bit by holding the bottom cog wheel (black) firmly and unscrewing the upper cog wheel (anticlockwise).
- Remove the drill bit from the drill chuck.
- Insert the drill bit you want to use into the drill chuck. Push the drill bit in as much as you can.
- Hold the bottom cog wheel (black) firmly and tighten the upper cog wheel (clockwise). Make sure with the help of the tool that the upper cog wheel is secured firmly.
- Insert the drill chuck part into its position (drill sign inward and drill bit down) and tighten the screw (**2**) that keeps it in position.
- Ensure that the two cog wheels (motor and drill chuck) are aligned exactly. You can check with your fingers if they are exactly at the same height.

5. Put the window back to its closed position and secure it with the latches.

4.6 Changing the Puncher

TMA Master II is delivered with punchers in four sizes. The following instructions help you change the puncher to match the size of the holes in the recipient blocks.

Warning!

Danger of pinching!

If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.

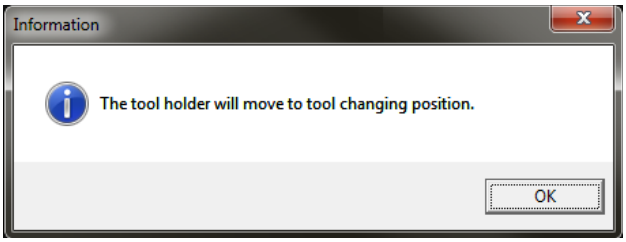
Maximum force: 25 Newton

Important!

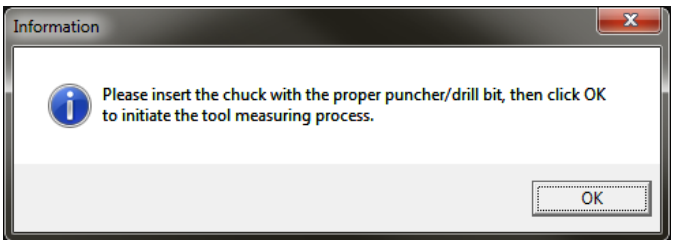
Three values are measured during tool change – diameter, needle length, piston length. It is advised to take measurements of these values manually as well. After detection the diameter value displayed is refreshed.

It is **NOT** recommended to modify parameter values manually.

1. If blocks are inserted in the main unit, click Tool Change in the **Punch** window, and remove all blocks. For more information on ow to remove blocks, see ***section 4.7***.
2. An information is displayed regarding positioning the tool holder. Click **OK** to continue.



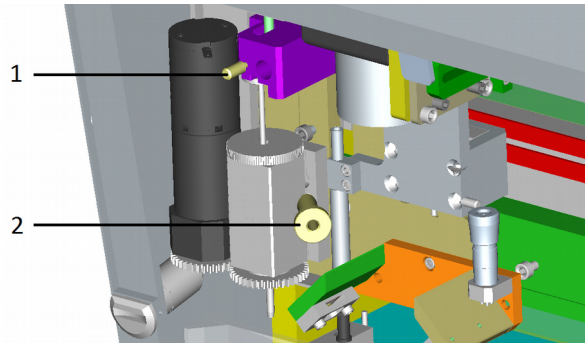
3. Remove the window by unscrewing the two latches at the bottom left and right side of the window with the tool provided in the accessories box.
4. Follow instructions displayed in the following message box:



Warning!

At this step, before initiating the operation, the device must be switched off, and unplugged from the external power supply unit.

- Remove the window of the TMA Master by unscrewing the two latches at the bottom left and right side of the window with the tool provided in the accessories box.
- Loosen the screw (anticlockwise) that keeps the piston in position (**1**) and push down the rim of the piston.
- Loosen the screw (**2**) that keeps the puncher chuck in position (anticlockwise) and take out the puncher chuck.



- Remove the piston from the puncher chuck.
- Remove the puncher by holding the bottom cog wheel (black) firmly and unscrewing the upper cog wheel (anticlockwise).
- Insert the new piston first.
- Insert the puncher into the puncher chuck matching the size of the piston. Tighten the upper cog wheel, holding the bottom cog wheel firmly.
- Insert the puncher chuck into its position and tighten the screw (**2**) that keeps it in position. Ensure that the two cog wheels (motor and puncher chuck) are aligned exactly. You can check with your fingers if they are exactly at the same height.
- Push the piston into position. The rim of the piston should touch the metal holder. Tighten the screw that keeps the piston in position.

5. Put the window back to its position and secure it with the latch.

4.7 Inserting and Removing Blocks

Warning!

Danger of pinching!

If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.

Maximum force: 25 Newton

4.7.1 Positioning of blocks in the main unit

The positions for the paraffin blocks in the tray are numbered 1 to 5 from left to right. The following table summarizes what action **TMA Master** can perform in which position.

Positions	Imaging	Punching /Drilling	Recommended Use
Position **1** (leftmost position)	No	Yes	For **recipient block** or **PCR cassette** only
Positions **2-5**	Yes	Yes	For **recipient** and/or **donor blocks**

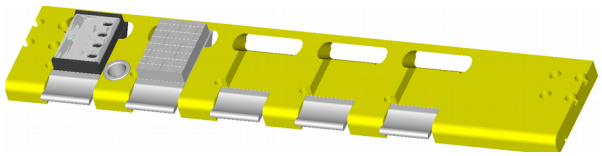
Warning!

In mixed mode (i.e. cores are being inserted both into recipient block and PCR cassette) recipient position must be set to **pos2** on the **Session Properties** panel.

4.7.2 Inserting a block into the main unit

Warning!

- Do not place blocks in the tray when the tray is under the puncher.
- If the paraffin swells through the bottom or the sides of the plastic cassette, cut off the excess paraffin before you insert the block into the main unit.



1. Click Blocks Out in the **Drill** or in the **Punch** window. The block tray will come forward.
2. Press down the flap in front of the block slot.
3. Slide the block into position with the slanted side towards the back of the machine.

Important!

PCR cassette can be inserted into the 1st slot only! Maker sure that the cover plate of the cassette is properly attached, and the orientation is correct.

4. Release flap when the block is in position.
5. Click Blocks IN in the **Drill** or in the **Punch** window and the block tray will slide to its place.

4.7.3 Removing a block from the main unit

Warning!

Do not remove blocks from the block tray when the tray is under the puncher.

1. Click Blocks Out in the **Drill** or in the **Punch** window. The block tray will come forward.
2. Press down the flap in front of the slot.
3. Remove the block from its position.
4. Release flap.
5. Click Blocks IN in the **Drill** or in the **Punch** window and the block tray will slide to its place.

5 Using TMA Master II

TMA Master II is designed to create TMA blocks and make it available for you to place extracted cores into a PCR cassette 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 Before You Start

Warning!

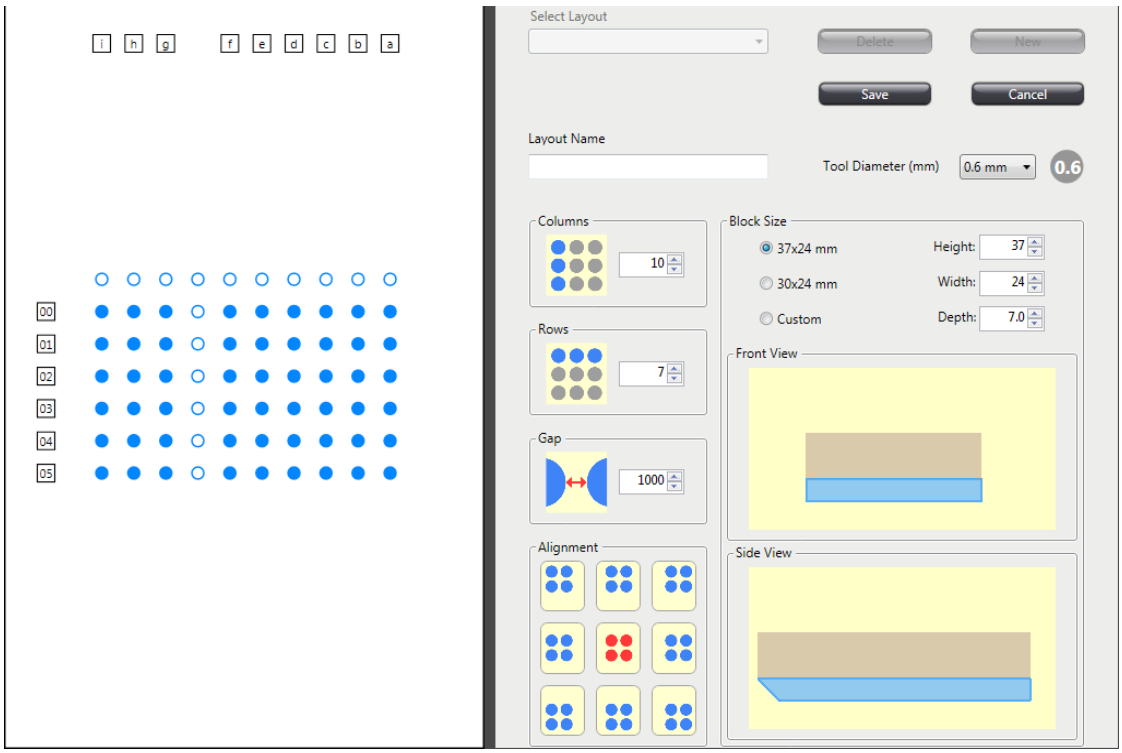
Do not use paraffin blocks which dimension values are higher than the specified (**24mm (W) x 37mm (H) x 8mm (D)**), otherwise drilling and punching heads may be damaged. If the paraffin blocks are larger, mold them again with the base molds delivered with **TMA Master**.

- 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.

5.2 Working with Recipient Block Layouts

5.2.1 Creating a Recipient Block Layout

Click Layout on the toolbar of the main window, and the **Layout Editor** window is opened.



When you create a new pattern, you define the block layout. Layouts that have been already created can be used – select the required layout from the **Select Layout** drop-down menu.

To define a block layout, follow these steps:

1. Type the name of your new layout into the **Layout Name** textbox (maximum length is 20 characters). The use of special characters (for example, '"', '*****', '**?**', '**!**', '**+**', '**,**' and '**.**') are not allowed.

2. In the **Block Size** panel the front and the side view of the block appears to help you with determining the recipient block measurements. Block width and height measurement values can be set at the right bottom corner of the window. Depth value is not necessary to be set as it is measured automatically.

   When working with special blocks that have different sizes than displayed by default, activate the **Custom** function and set the correct measurements.

3. Select a value at the **Tool Diameter** section for the puncher and the drill bit sizes.

4. Select the size of the **Gap** between the holes.

5. Select the number of **Columns** and **Rows**.

6. Pattern alignment can be set at the **Alignment** pane of the window.

7. 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 Master** to skip during drilling.

   - Single hole: click the hole that you want to leave out.
   - Columns and rows: click with the right mouse button, then select Row/Column to enable or disable them on the layout.

8. When finished creating a layout, click Save. When saving a layout, the program automatically adds the block depth value to the file name (for example, *7×12(84)2mm(7,5 mm depth*)).

9. To create an additional layout, click New.

The selected layout scheme 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.

The following table shows the maximum number of holes you can drill into a paraffin block:

Paraffin Block Size (mm)	Hole Sizes (mm)	Max. No. of Holes	Color of Drill Bit
30 x 24	Ø 0.6	16 x 22 = **352**	N/A
	Ø 1.0	12 x 16 = **192**	black
	Ø 1.5	9 x 12 = **108**	magenta
	Ø 2.0	7 x 9 = **63**	blue
37 x 24	Ø 0.6	18 x 31 = **558**	N/A
	Ø 1.0	13 x 22 = **286**	black
	Ø 1.5	9 x 15 = **135**	magenta
	Ø 2.0	7 x 12 = **84**	blue

5.2.2 Modifying a Recipient Block Layout

1. In the **Layout Editor** window select the layout you want to modify from the **Select Layout** drop-down list.

   NOTE: You cannot modify a layout that has already been used in previous sessions.

2. Modify layout parameters.
3. Click Save.

5.2.3 Deleting a Recipient Block Layout

1. Click Layout.
2. In the **Layout Editor** window select the layout you want to modify from the **Select Layout** drop-down list.
3. Click Delete.

   NOTE: You cannot delete a layout that has already been used in previous sessions.

5.3 Creating a Recipient Block

Warning!

Danger of pinching!

If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.

Maximum force: 25 Newton

Warning!

- Only operate the **TMA Master II** unit when the protective window is in its place.
- If you see excess paraffin on the side of the block, cut it off.

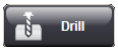
Tip!

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

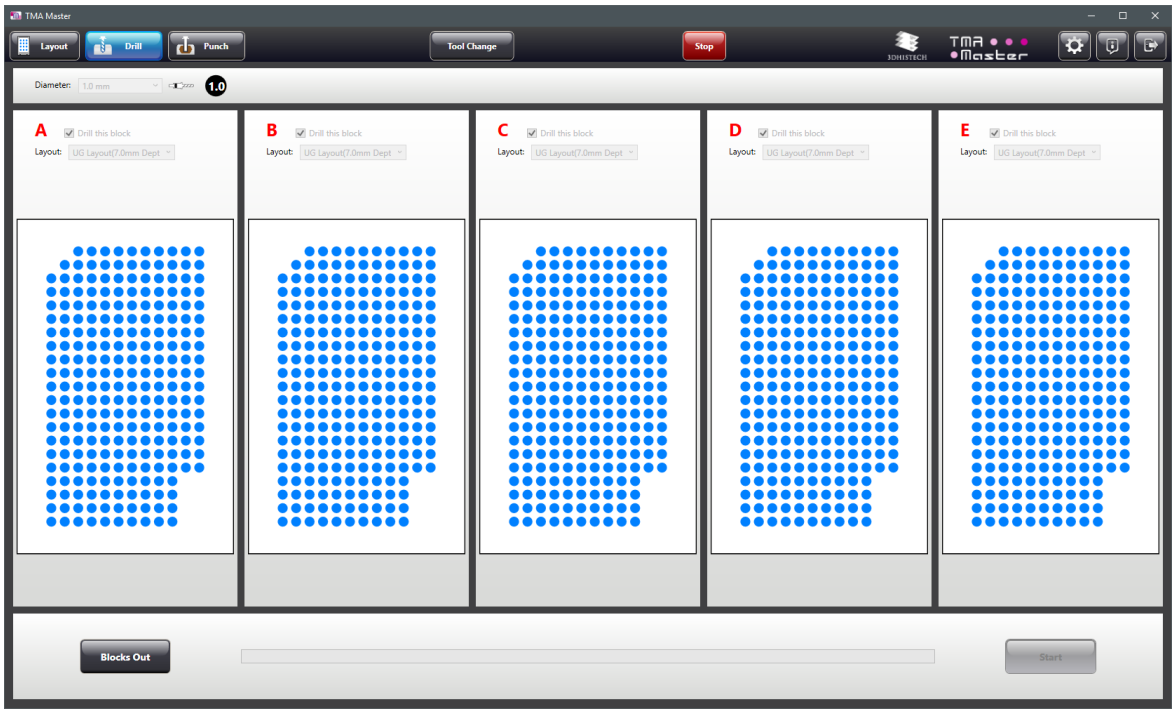
5.3.1 Before You Start

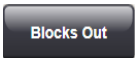
- Make sure that the cassettes with the paraffin blocks are in the tray.
- Make sure that the drill bit is of the appropriate size and that it is fixed in its position.

5.3.2 Creating a Recipient Block

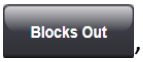
1. Switch on the **TMA Master II** main unit, the control computer and the monitor, and start the **TMA Control** application on the control computer.
2. Click 

on the toolbar and the **Drill** view is displayed.



3. Insert the paraffin flake containers.
4. If the appropriate drill bit / 0.6, 1, 1.5 or 2 mm/ is not in the main unit yet, insert it as explained in ***section 4.2***.
5. When finished, carry out steps 2 and 4 and then continue from here.
6. Select a layout from the drop-down list for each block.
7. Click 

in the application on the computer.
8. Insert the virgin blocks into the main unit as explained in ***section 4.4.2.*** Insert the virgin blocks in accordance with the checkboxes you selected in the drill menu.
9. Make sure that the window of the main unit is in its place with the wisp downwards.
10. Click **Start** to launch drilling process. The process can be followed on the monitor.
    - To stop drilling immediately, click **Stop**.
      If you restart later, **TMA Master II** starts drilling from the very beginning.
    - To interrupt drilling, click **Pause**.
      TMA Master II finishes drilling the hole and then stops.
    - To restart after the interruption, click **Continue**.
      TMA Master II continues drilling from the next hole in the layout.

12. Take the finished recipient blocks out of the tray and clean the core and paraffin flake containers. For more information, see ***section 10.2***.
13. If you want to create more recipient blocks, click 

, replace blocks with new ones and repeat the necessary steps.
14. If you have created a recipient block that you are going to fill from donor blocks right away, it is recommended that you do not remove the recipient block from the **TMA Master II** main unit. The block is already positioned in such a way that **TMA Master II** can insert the tissue cores as precisely as possible.
15. When you are done with drilling and you do not wish to create TMA blocks right away, exit the **TMA Control** application, then switch off the main unit and the power supply.
16. Clean the main unit. Refer to ***section 10.2***.

5.4 Before Creating a TMA Block

Warning!

Danger of pinching!

If the block tray is moved while the machine is in operation, objects or fingers put close to the block tray may get pinched.

Maximum force: 25 Newton

Warning!

- Operate the **TMA Master II** unit only when the protective window is in its place.
- To avoid any damage to the punchers, make sure that the donor blocks and recipient blocks are not higher than 10.0 mm. If the blocks are larger or taller than the cassette specifications for **TMA Master II**, cut off the excess paraffin.

Important!

The recipient block layout that you want to use must have already been created.

Tips

- You can interrupt TMA creation at any time: click Close on the **Session** panel, close the **TMA Control** software, then switch the control computer and the main unit off.
- When you restart your work, you can continue where you stopped by clicking Load on the **Session** panel.
- TMA can automatically export a series of images of the donor blocks to keep track of the positions from where specimen was extracted: click Settings then select the **Save Donor Images** checkbox. See ***section 9*** for more information.
- You can create snapshots of a donor block at any time by clicking .

5.5 Creating a TMA block

You can create up to four TMA blocks at the same time which offers you the following benefits:

- You can create four nearly identical TMA blocks by taking out neighboring tissue core samples from one representative region of a donor block, and inserting them one-by-one into each of the recipient blocks within a clone group.

  Then, you can either create several slides from the TMA blocks, or you can just keep one of the TMA blocks as a backup.
- You can use the extra recipient blocks for creating separate/different TMA blocks at the same time.

When you are filling the recipient block from up to four donor blocks, the digital camera of **TMA Master II** gives you an image of each donor block so you can aim the puncher accurately.

You can save an image of each donor block with markers telling where the tissue cores were extracted from.

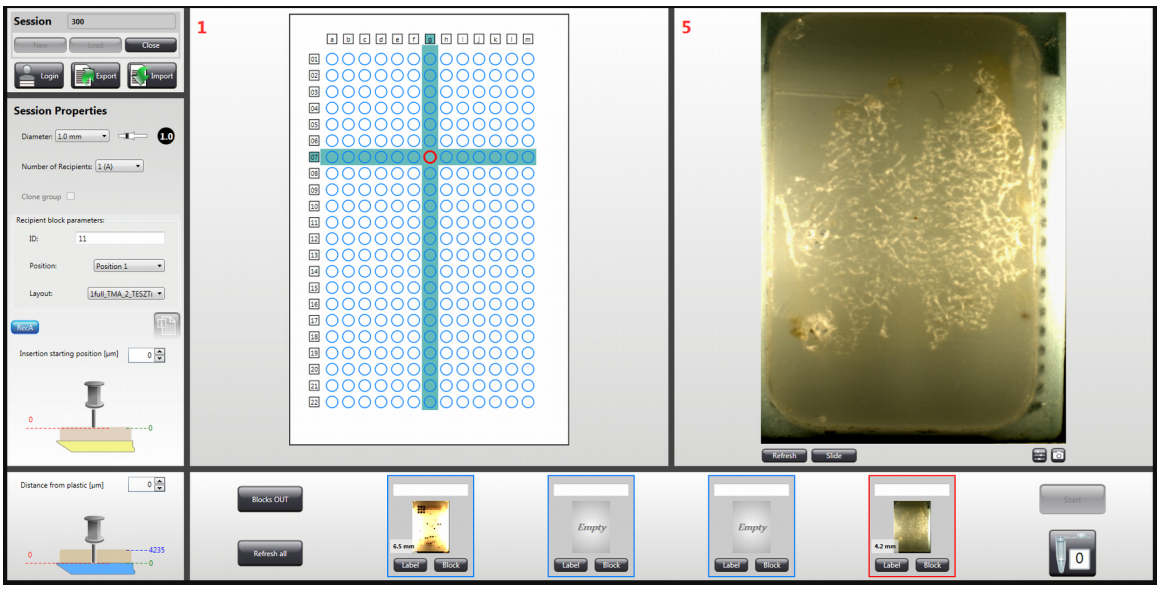
Furthermore, you can import donor block data from an Excel worksheet. You can export another Excel file from **TMA Control** that tracks the associations between the recipient block positions and the ID of the donor block from which the core tissue was inserted into the recipient block. See ***section 7*** for more information on importing, and ***section 8*** on exporting data.

1. Switch on the **TMA Master II** main unit, the control computer, and the monitor, then launch the **TMA Control** application on the control computer.
2. Click Punch on the toolbar, and **Punch** view is then displayed.
3. Pull up the protective window, and secure it in position with the latch.
4. If the puncher in the chuck is not of the appropriate size, then replace it. For more information on how to change a puncher, see ***section 4.6***.

5. Load an existing or start a new session.
6. Insert the necessary amount of recipient blocks and donor blocks (the first batch of the donor blocks) into the block tray:
   a) Click Blocks Out
   b) Insert recipient block(s)
   c) Insert donor blocks into positions 2 – 5

> **Important!**
>
> You can use **position 1** on the tray for recipient block or PCR cassette only.

7. Click Blocks IN in the window. The tray will be loaded, then after clicking **Label** or **Block** buttons below the thumbnail images the camera takes images of the inserted blocks. The touch sensor measures the height of recipient block(s), which value is displayed with green at the **Insertion starting position** image on the **Session Properties** panel.

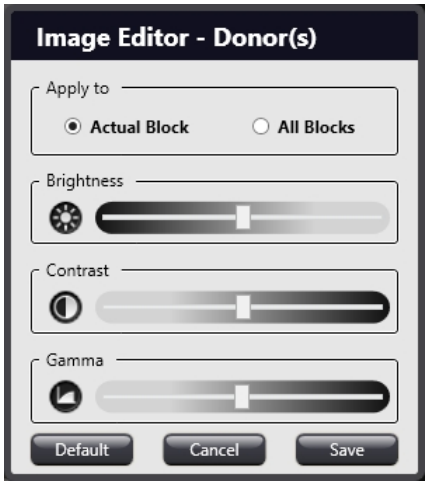


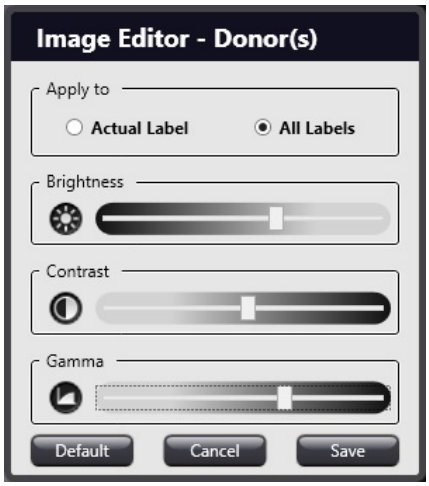
Sometimes it is required to alter image settings such as brightness, contrast, or gamma to make label images more identifiable or donor block images better for identifying relevant areas (for example, if the donor block holds adipose tissue) before placing markers at the right spots, and also to validate the correct extraction 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: 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 9***.

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.





8. Put the protective window back to its position (with the wisp downwards) and secure it with the latch.
9. If you want to continue filling a recipient block on which you have already worked, click **Load** first in the **Session** frame, then browse for the session. To fill a new recipient block, click **New** in the **Session** frame.
10. If you have started a new punching session, select the number of recipient blocks (maximum four blocks per session) and a suitable punching diameter in the **Session Properties** panel.

    If 2 or more recipient blocks are loaded into the block tray, the **Clone Group** option can be activated (only if there is no marker already placed on the block image). If this option is active, the software automatically switches between blocks during placing markers.
11. Select the desired block layout(s) from the **Select Layout** drop-down list. You can select different layouts if you are working with more than one recipient blocks.
12. Fill in the information about the recipient block.

a) Enter the identification number (**ID**) of the recipient block. If donor data are imported, the appropriate ID can be selected from the drop-down list above the donor preview image. See ***section 7*** for more information.

NOTE: When entering recipient or donor IDs the use of special characters (* ! . , ' ; ? ") are not supported.

b) Select which position the recipient block can be found in.

It is recommended that you use position 1 for the first recipient block because in this case the buttons for the donor blocks (RecA, RecB, and so on) correspond to the actual position of the donor blocks in the tray.

If you are working with more than one recipient block, the program swaps between them automatically, although you can change them as well.

TMA Master II can save donor block images of the marked tissue core locations. For more information see ***section 9***.

13. Enter or select **Donor Block ID**, or read the barcodes of the donor blocks. Barcode reading is a supplementary feature of the **TMA Control** software. This function is optional and available for you only if:

- **Matrox Imaging Library** (MIL) – a barcode detection software – is previously installed on the control computer
- Matrox dongle containing the barcode information database is plugged in
- You are using a licensed version of the **TMA Control** application and you have purchased the license for barcode reading function.

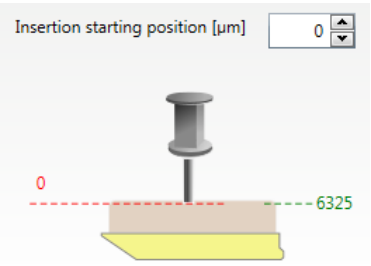
Important!

On how to enable barcode reading, and install Matrox dongle on your computer, see the appropriate version of the ***Matrox Imaging Library Installation Guide***.

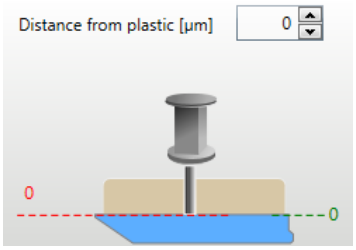
For more information on Matrox imaging solutions, follow the link below:
http://www.matrox.com/imaging/en/

See ***Appendix*** for more information on the barcode reading process and settings.

14. In the **Insertion starting position** field set the depth of insertion from the different from the default value if necessary. Value ranges from -500 to +500.



15. If your donor block is thicker than the recipient block, or if you want to specify how much above the plastic frame the punch head should stop, type or set the required value in micrometers in the **Distance from plastic** value field.



- If the donor block is thicker than the recipient block, measure the difference between them and type in the value to pick up and insert the core of the same height as the recipient block.
- Punching depth adjustment might be necessary to perform an accurate core removal (depending on the location of the tissue within the block).

  If the tissue sticks to the surface of the bottom plate of the cassette, the value can be decreased until the minimum of -500 to ensure successful core removal. Value ranges from -500µm to +13000µm.

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 **Distance from plastic (µm)** 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.

16. Select the positions of the cores to be extracted from the donor blocks.

    a) Click the preview image of the desired donor block. The image of the donor block appears on the monitor.

    b) Select the position(s) on the donor block where tissue core should be taken from; in the layout, click the position that you want to fill with core sample.

    Click  if you want to extract a sample into the PCR cassette.

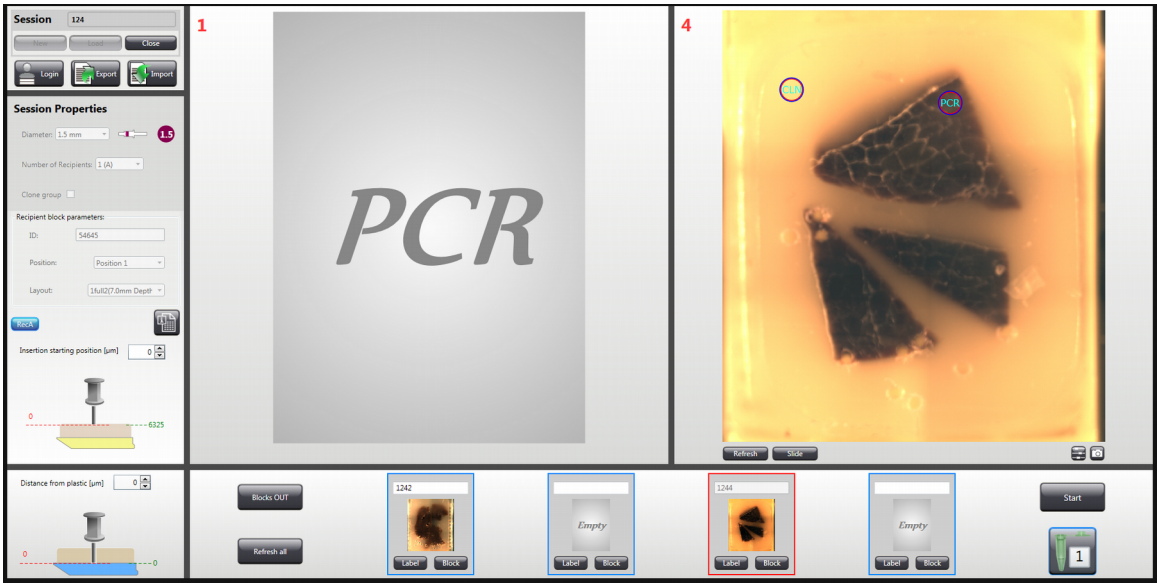
Important!

When PCR extraction mode is activated, and you have selected the first marker placed on the donor block as *'Cleaner Core'* (the cleaning function can be activated on the **PCR** panel of the **Settings** window), this first marker must be placed on an adiaphorous area of the donor block (that is not containing tissue section).

You can load 4 tubes into the PCR cassette and the maximum number of PCR cores that can be inserted into a PCR tube is four (1.5/2.0mm) or eight (0.6/1.0mm), so the full capacity of a cassette is from 16 to 32 cores. The tray will come forward after PCR core insertion process is finished, then the PCR cassette must be removed from the device.

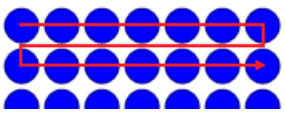
If you want to operate the device in mixed mode, reserve PCR extractions for the end of the session. It is your duty and responsibility to clean the puncher and the piston before the PCR sampling process in order to avoid cross-contamination.

When extracting cores into PCR tubes, the use of **2.0mm** puncher needle is advised for the best extraction result, but the use of **0.6mm** puncher is **NOT** recommended.



If you want to remove a marker, click it with the right mouse button.

TMA Master inserts each core into the next available hole, and proceeds from left-to-right and from top-to-down order in the grid.



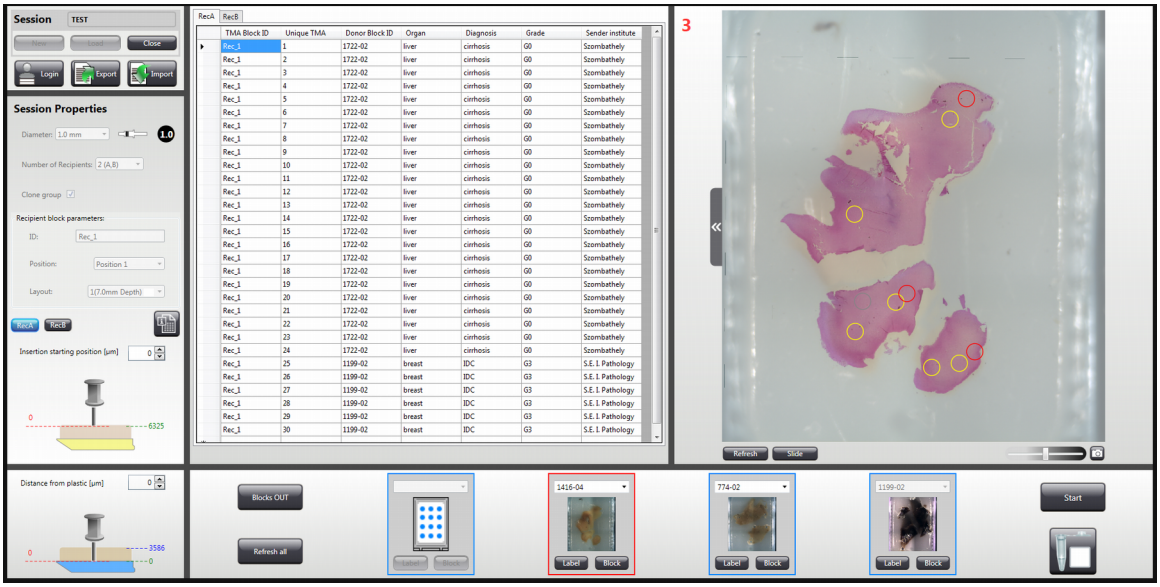
17. Cores are being transferred from donor block(s) to recipient block(s) or to the PCR cassette after clicking **Start**.

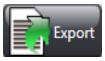
If the PCR function is activated, then a message appears instructing you to remove the PCR cassette from the device after the specified number of cores have been transferred. Remove the PCR cassette, then click **OK** to continue the process.

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.

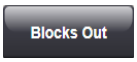
18. You can interrupt the punching process anytime by clicking **Stop**. In this case the **TMA Master** collects the core in the trash bin.
    a) Click Blocks Out.
    b) Remove the completed donor blocks and/or the PCR cassette from the tray and insert new donor blocks or a PCR cassette.
    c) Click Blocks IN.
19. Repeat steps 13 – 17 until you finish the recipient block.
20. Click Slide to refine the position of the digitized slide image to match the position of the block image. See ***section 6*** for more information on slide overlay.
21. You can refresh the image of the label or block by clicking the Refresh button below the donor block image.
22. Markers become displayed with the same color as previously defined with the TMA Master Marker feature of CaseViewer.
23. Finally, click Start to launch the process.
24. You can refresh the image of the label or block by clicking **Refresh** on the menu bar.

25. The **Information** button -  - is active only if at least one Donor Block ID is typed in, called from a preloaded Excel file, or its Barcode is read in, and placed a marker on the donor image. Upon clicking this button a preview image of an XLS sheet is displayed, listing markers placed on donor blocks in accordance with the related recipient blocks.



26. Click  when finished with creating recipient blocks to keep track of recipient block and donor block data. For more information see ***section 7*** and ***section 8***.

> **Important!**
>
> In the Punch window the **Recipient Block ID** cannot be identical with the already existing **TMA Block ID** in the Excel file.

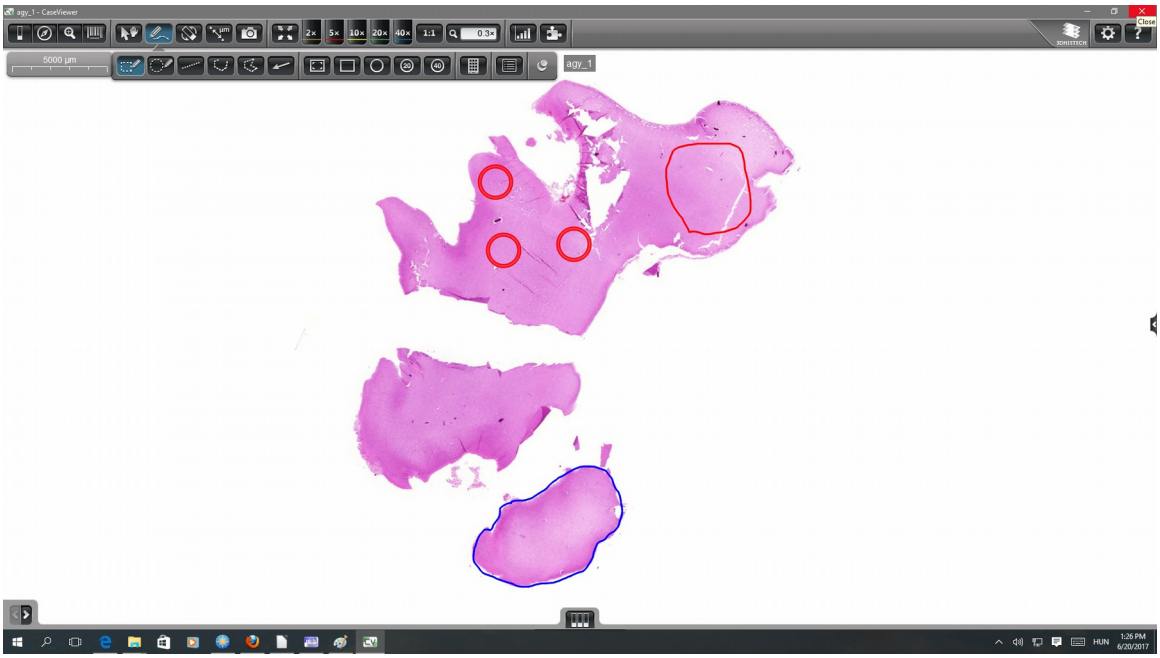
27. Click  and remove all the blocks from the tray.
28. Exit the **TMA Control** application on the control computer, switch the main unit and the power supply off.
29. Clean the main unit. For more information, see ***section 10.2***.

6 Slide overlay

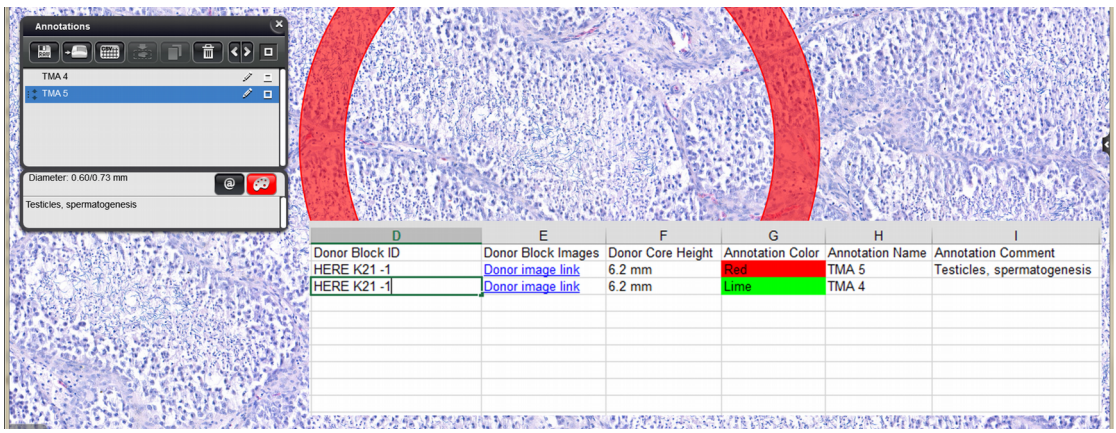
With the **Slide overlay** function it is available for you to select a slide image (from various sources and of different formats) to overlay the donor image with it. The digitized slide image (located either manually or automatically) can be refined and aligned to match the position of the block image.

Slide overlay settings can be modified on the **Overlay** panel of the Settings window. See ***section 9*** for more information on overlay 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**, this 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 Pannoramic Viewer, but adding notes to TMA Markers is not supported.

To initiate the overlay procedure follow these steps:

1. Enter **Donor block ID**
2. Click Slide
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.

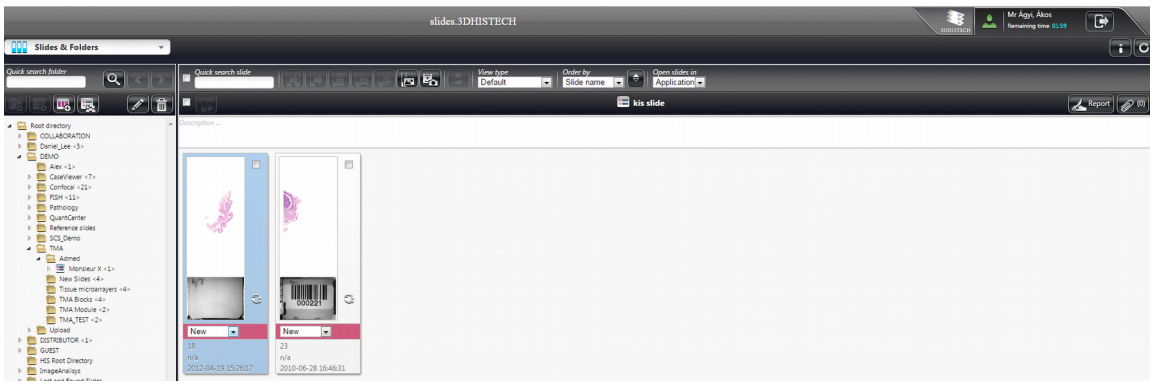
If the software cannot find a slide or image at the defined locations, the **Browse Overlay Slide** window is opened in which paths of slide and/or jpg images can be set in the text boxes for automatic overlay. To manually locate and import the image click **Browse slide**, **Browse jpg** or **CC Connect**.

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

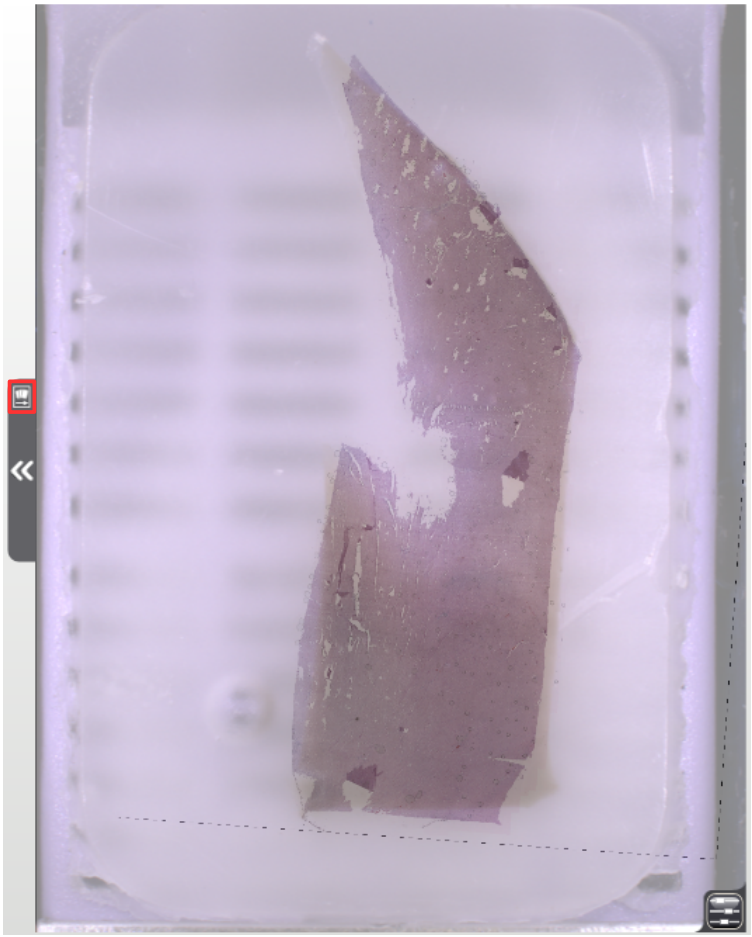


NOTE: Make sure that **Open slides in Application** option is selected in CaseCenter.

5. 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.

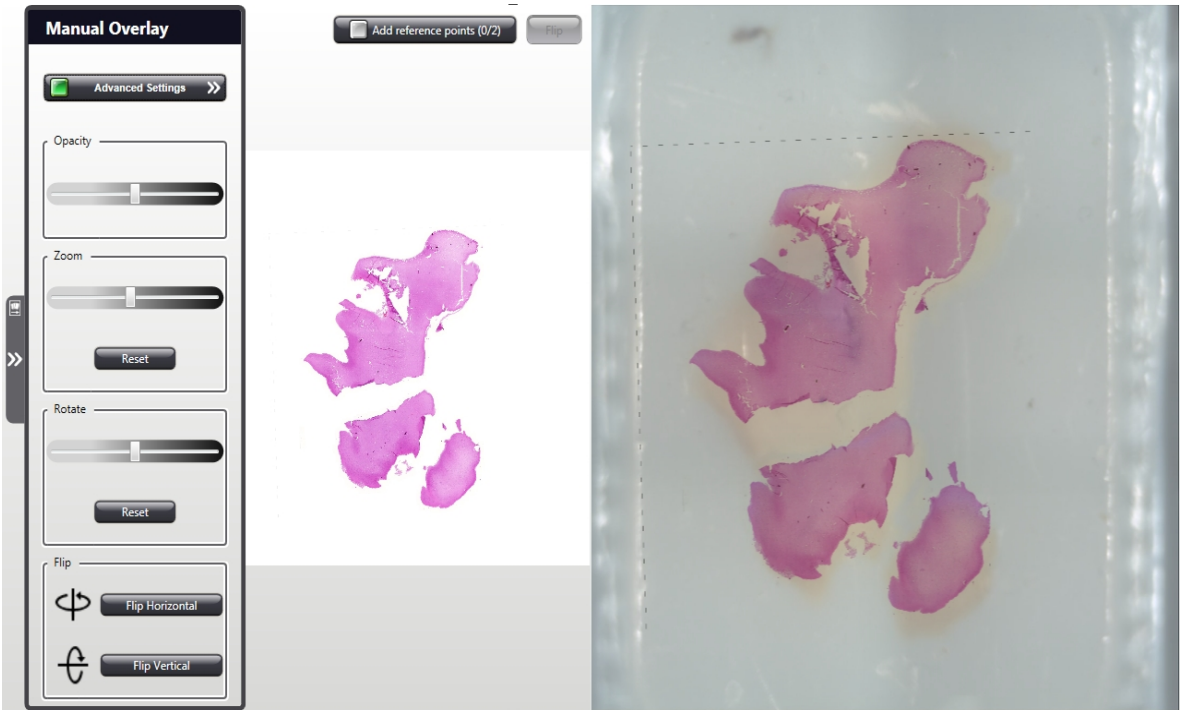
   NOTE: If you modify the donor ID, and you have not yet placed any marker on the image, the applied overlay slide image will be deleted.

6. 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.

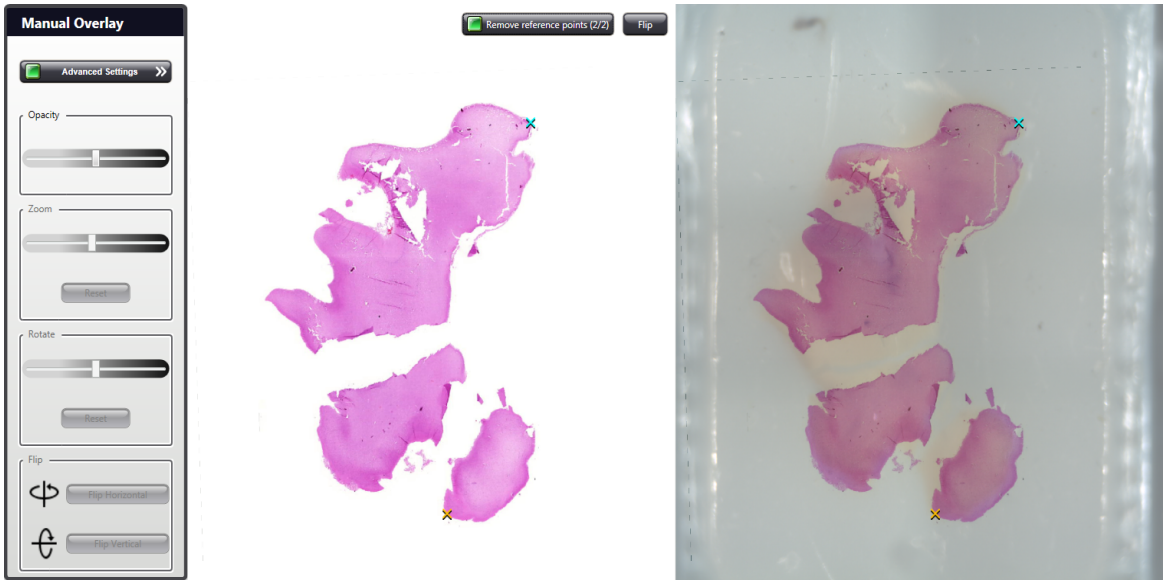


Furthermore, if automatic slide overlay function did not provide acceptable result, click at the left side of the donor image to open **Manual Overlay** window.

7. 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, after clicking Advanced Settings, additional functions such as **Opacity**, **Zoom**, **Rotate**, and **Flip** are available for you in the extended panel to set the proper orientation.



8. 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.
9. If manual positioning does not result in an acceptable overlay, click Add reference points (0/2) first, then 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.

10. 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 aligned more accurately.
11. If you close the overlay window, the TMA markers will be displayed on the donor block image in the main window.
12. 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.
13. 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.
14. 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.

Important!

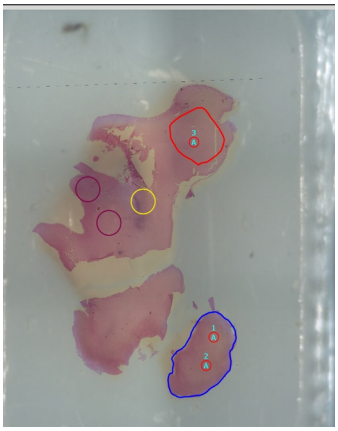
After the overlay image is set on the donor block, the puncher diameter can be modified if necessary, but the displayed size of TMA markers do not change accordingly. If you want to display markers of the modified size, reload slide for the donor block.

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

15. On the final overlayed donor image TMA Markers as well as 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 ***9 Settings***.

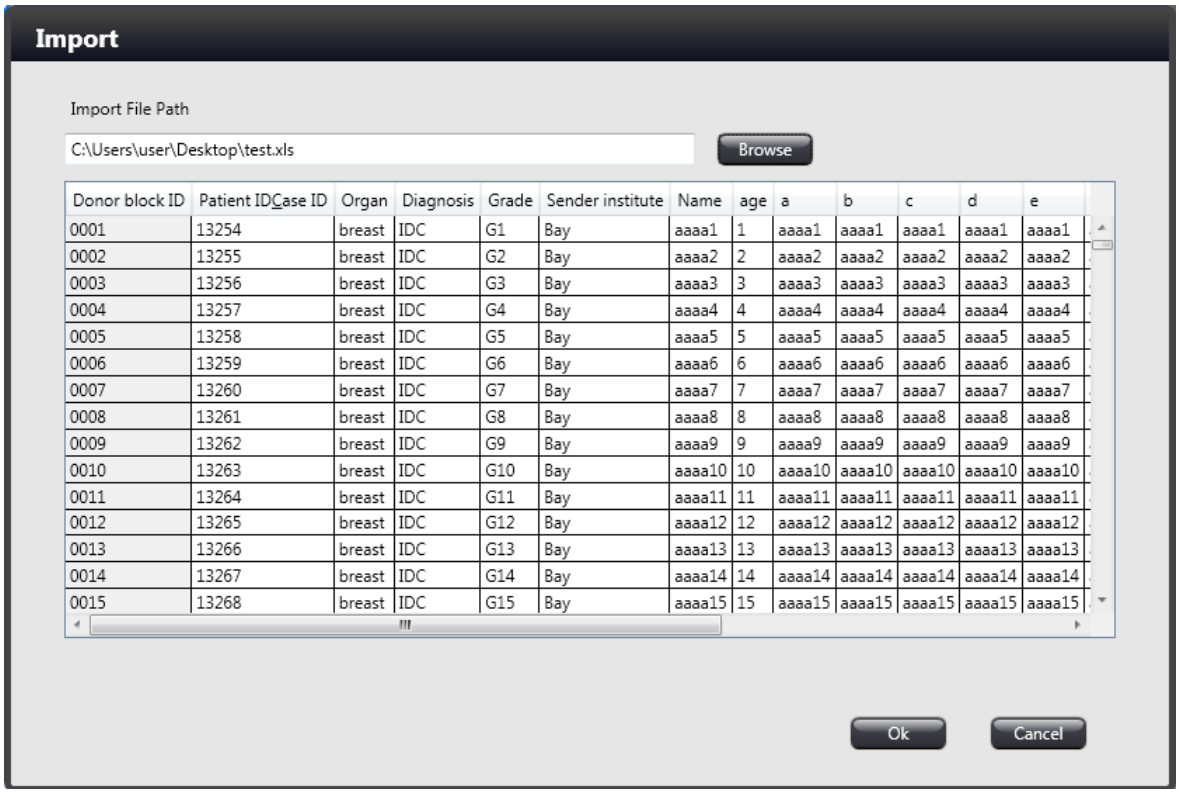
16. If you have finished, press the **Start** button to launch the transfer process.

7 Import data

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

1. Click 

at the toolbar of the application window, and the **Import** window appears.



Donor block ID	Patient IDCase ID	Organ	Diagnosis	Grade	Sender institute	Name	age	a	b	c	d	e
0001	13254	breast	IDC	G1	Bay	aaaa1	1	aaaa1	aaaa1	aaaa1	aaaa1	aaaa1
0002	13255	breast	IDC	G2	Bay	aaaa2	2	aaaa2	aaaa2	aaaa2	aaaa2	aaaa2
0003	13256	breast	IDC	G3	Bay	aaaa3	3	aaaa3	aaaa3	aaaa3	aaaa3	aaaa3
0004	13257	breast	IDC	G4	Bay	aaaa4	4	aaaa4	aaaa4	aaaa4	aaaa4	aaaa4
0005	13258	breast	IDC	G5	Bay	aaaa5	5	aaaa5	aaaa5	aaaa5	aaaa5	aaaa5
0006	13259	breast	IDC	G6	Bay	aaaa6	6	aaaa6	aaaa6	aaaa6	aaaa6	aaaa6
0007	13260	breast	IDC	G7	Bay	aaaa7	7	aaaa7	aaaa7	aaaa7	aaaa7	aaaa7
0008	13261	breast	IDC	G8	Bay	aaaa8	8	aaaa8	aaaa8	aaaa8	aaaa8	aaaa8
0009	13262	breast	IDC	G9	Bay	aaaa9	9	aaaa9	aaaa9	aaaa9	aaaa9	aaaa9
0010	13263	breast	IDC	G10	Bay	aaaa10	10	aaaa10	aaaa10	aaaa10	aaaa10	aaaa10
0011	13264	breast	IDC	G11	Bay	aaaa11	11	aaaa11	aaaa11	aaaa11	aaaa11	aaaa11
0012	13265	breast	IDC	G12	Bay	aaaa12	12	aaaa12	aaaa12	aaaa12	aaaa12	aaaa12
0013	13266	breast	IDC	G13	Bay	aaaa13	13	aaaa13	aaaa13	aaaa13	aaaa13	aaaa13
0014	13267	breast	IDC	G14	Bay	aaaa14	14	aaaa14	aaaa14	aaaa14	aaaa14	aaaa14
0015	13268	breast	IDC	G15	Bay	aaaa15	15	aaaa15	aaaa15	aaaa15	aaaa15	aaaa15

2. Click **Browse** to search for the data file (in XLS and ODS formats only) to be imported.

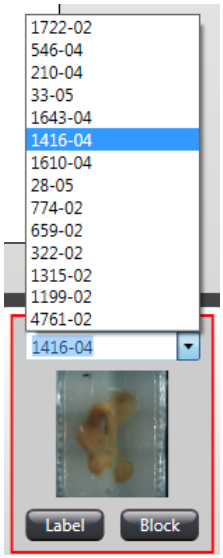
   If the ID of the donor block loaded into the device exists in the imported database, the data set of the specific donor block can be appended to the database.

   NOTE: The content of the selected data sheet cannot be modified.

> **Important!**
>
> When importing more than one data file during a session, only the data included in the last one will be presented in the export file.

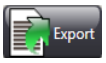
3. Click **OK** to accept data and close the **Import** window.

4. On the **Punch** view, at the block preview panel the **Donor block ID** can be selected from a drop-down list of imported IDs. During entering the block ID, the program automatically filters and displays the matching results.

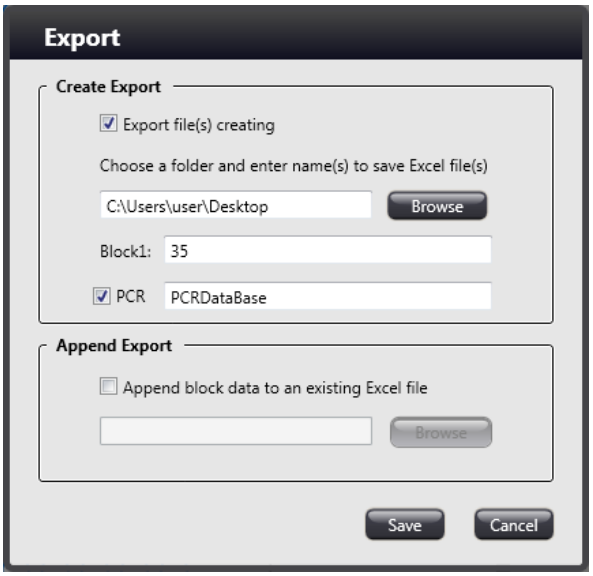


8 Exporting donor block data

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.

1. Click 

on the main toolbar once all the TMA blocks are created and/or cores have been transferred to PCR cassette and you want to save PCR / block-related data. The **Export** window appears.



If exporting data of multiple recipient blocks, the block number (as a string "_block1, _block2, etc.) can be added to the end of file names that you specify in **Block1**, **Block2**, etc.

2. Both of the options **Create Export** and **Append Export** can be activated.

   When both options are selected the data will be exported as a new file, and will also be appended to an existing one (file must be located before).

   - **Create Export** – Creates new XLS file. To export data to a new file (will be generated by the application), browse for the folder by clicking **Browse** and type in a file name.

     NOTE: Open file with the appropriate software, for example, use Microsoft Excel (Kingsoft or WPS Office Free, alternatively).

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

   - **Append Export** – Does not modify the Lookup table, only appends data to the bottom, and also creates new sheets for additional recipient blocks. Data related to Donor Block IDs included in the imported file will be appended to the final data file.

The generated spreadsheet contains three worksheets:

i. The first one is the **Lookup** table on which there are four columns.

	A	B	C	D
1	TMA Block ID	Unique TMA Sample ID	Donor Block ID	Donor Block Images
2	3DH-0.6	1	donor1	Donor image link
3	3DH-0.6	2	donor1	Donor image link
4	3DH-0.6	3	donor1	Donor image link
5	3DH-0.6	4	donor1	Donor image link
6	3DH-0.6	5	donor1	Donor image link
7	3DH-0.6	6	donor1	Donor image link
8	3DH-0.6	7	donor1	Donor image link
9	3DH-0.6	8	donor1	Donor image link
10	3DH-0.6	9	donor1	Donor image link
11	3DH-0.6	10	donor1	Donor image link

- **TMA Block ID:** individual identification number of the recipient block
- **Unique TMA Sample ID:** spot (core) number on the given TMA Block
- **Donor Block ID:** donor block's individual identification number

- **Donor Block Images:** hyperlinks to donor block images (images are 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, the image of the block is displayed in a separate window.

NOTE: When opening XLS files in OpenOffice, links to external images cannot be opened. It is advised that you open links in Microsoft Office instead (Kingsoft or WPS Office Free alternatively).

ii. The second sheet contains recipient block-related data table where the core IDs are shown according to their positions in the layout.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
1	3DH-0.6	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12	X13	X14	X15	X16
2	Y1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
3	Y2	17			18	19				20	21		22	23		24	25
4	Y3	26	27	28		29		30	31		32		33	34		35	36
5	Y4	37	38	39		40		41	42		43		44	45		46	47
6	Y5	48	49	50		51		52	53		54					55	56
7	Y6	57				58		59	60		61					62	63
8	Y7	64	65	66		67		68	69		70					71	72
9	Y8	73	74	75		76		77	78		79		80	81		82	83
10	Y9	84	85	86		87		88	89		90		91	92		93	94
11	Y10	95			96	97				98	99		100	101		102	103
12	Y11	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118	119
13	Y12	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135
14	Y13	136	137	138	139	140	141	142	143	144	145	146	147	148	149	150	151
15	Y14	152	153	154	155	156	157	158	159	160	161	162	163	164	165	166	167
16	Y15																

iii. The third sheet contains recipient block-related data table where the Donor Block IDs are shown according to their positions in the layout. The color of the marker is displayed as the background color of Donor Name fields and the Layout order fields.

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q
1	3DH-0.6_B	X1	X2	X3	X4	X5	X6	X7	X8	X9	X10	X11	X12	X13	X14	X15	X16
2	Y1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1	donor1
3	Y2	donor1			donor1	donor1				donor1	donor1		donor1	donor1		donor1	donor1
4	Y3	donor1	donor1	donor1		donor1		donor1	donor1		donor1		donor1	donor1		donor1	donor1
5	Y4	donor1	donor1	donor1		donor1		donor2	donor2		donor2		donor2	donor2		donor2	donor2
6	Y5	donor2	donor2	donor2		donor2		donor2	donor2		donor2					donor2	donor2
7	Y6	donor2				donor2		donor2	donor2		donor2					donor2	donor2
8	Y7	donor2	donor2	donor2		donor2		donor2	donor2		donor2					donor2	donor3
9	Y8	donor3	donor3	donor3		donor3		donor3	donor3		donor3		donor3	donor3		donor3	donor3
10	Y9	donor3	donor3	donor3		donor3		donor3	donor3		donor3		donor3	donor3		donor3	donor3
11	Y10	donor3			donor3	donor3				donor3	donor3		donor3	donor4		donor4	donor4
12	Y11	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4
13	Y12	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4
14	Y13	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4
15	Y14	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4	donor4
16	Y15																

Tip!

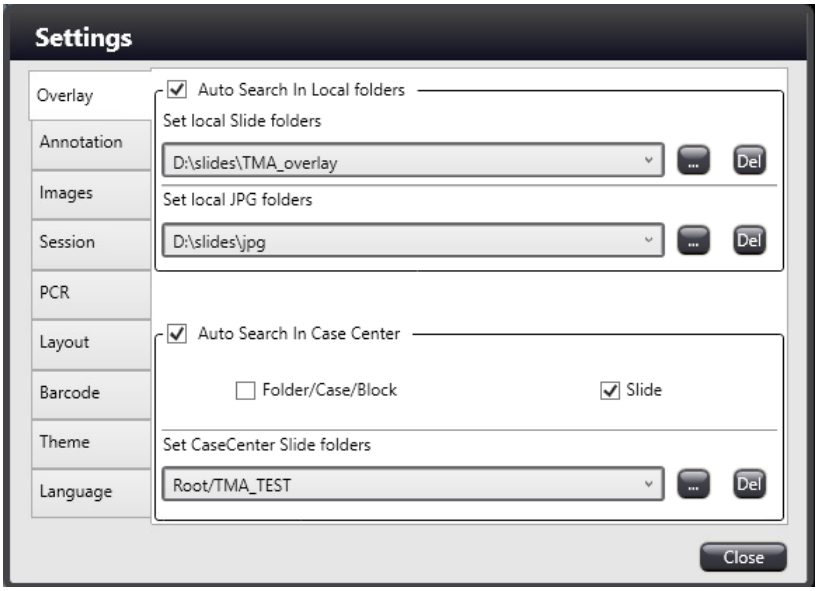
If you want to import the exported data to **TMA Module**, you need to create a worksheet called Slides including stain types, recipient block IDs, and slide names.

9 Settings

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

Overlay

Slide overlay settings can be modified on the **Overlay** panel of the Settings window.



- 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.

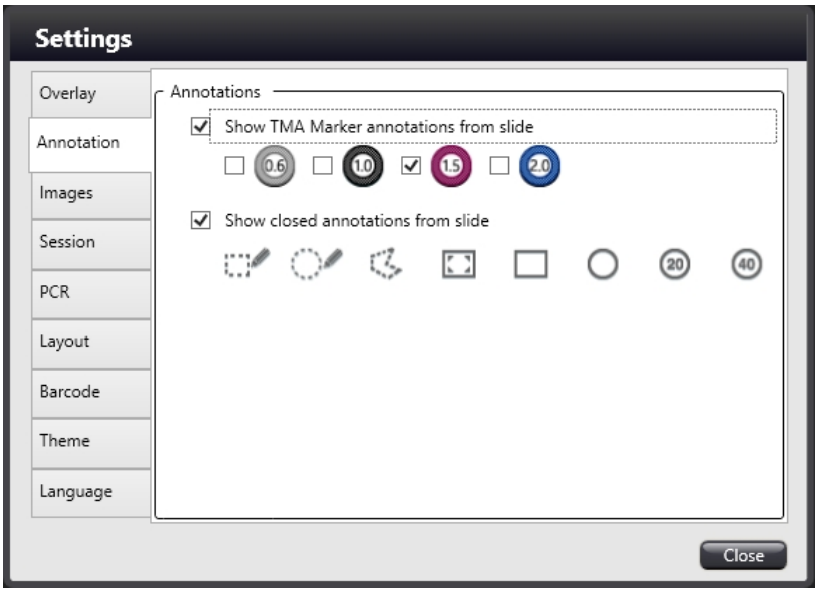
  Type in or browse for folder paths for automatic search (either for Slides or JPG images). Folders that have been set can be displayed after clicking the down arrow, and after you have selected an item from the list, it can be deleted by clicking Del.

  NOTE: If you set a path or paths of slide and/or jpg images, the software will automatically search for image when clicking Slide after you have entered the donor ID.

Annotation

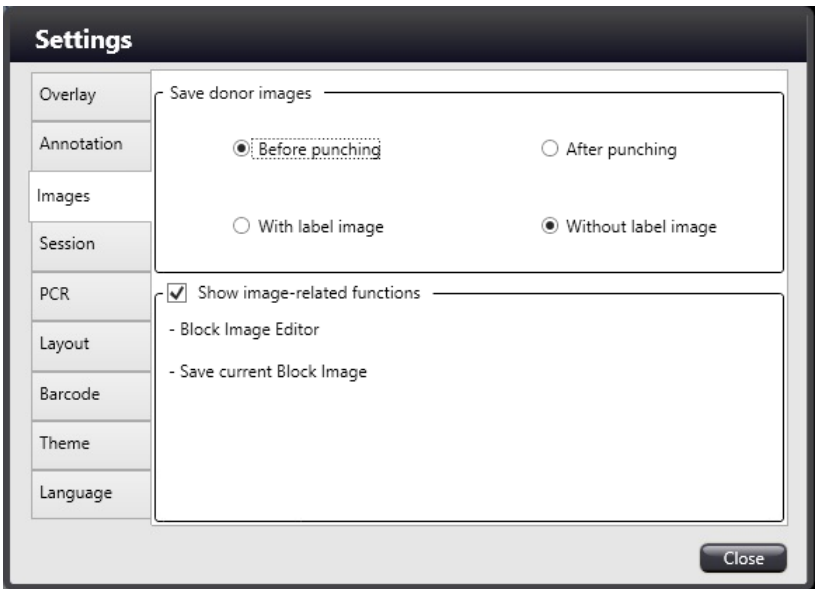
Annotated areas (such as TMA markers and closed annotations) of the slide can be displayed on the donor image. Activate **Show TMA Marker annotations from slide** option and select the size of marker to be displayed (the marker size identical with the size of the actual tool inserted is selected by default).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



Images

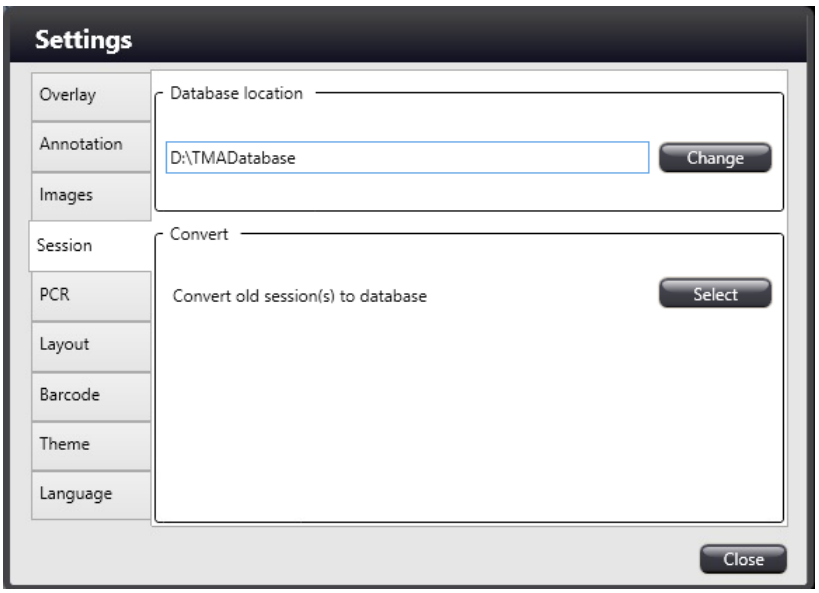
You have the following options to select from the **Images** panel:



- **Save donor images**
  - Tick **Before punching** checkbox to take an image of donor blocks before punching (right after loading them into their positions).
  - Select **After punching** to take an image of finalized donor blocks after punching.
  - **With label image** – Label area is recorded during creating preview images and not only when saving.
  - **Without label image –** Label area is recorded not during creating preview 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.

Session

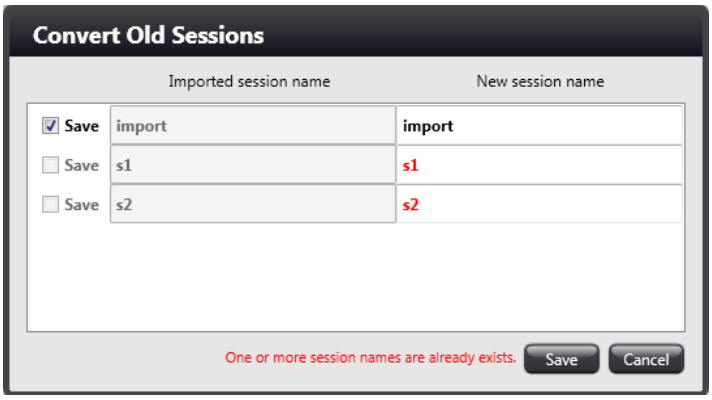


- The location of the session database can be modified by clicking Change.

  NOTE: It is advised to use the predefined location.

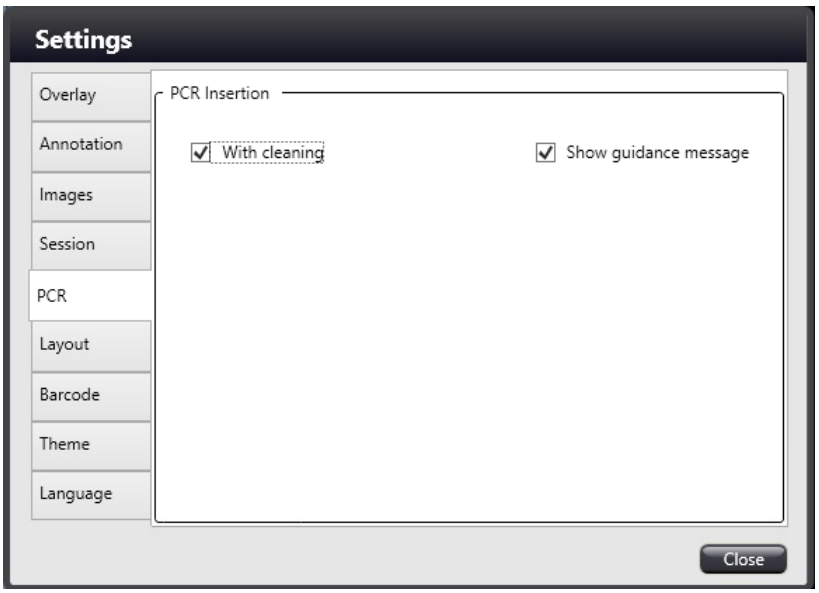
> **Important!**
>
> It is advised to archive database files that are included in the D:\TMADatabase hidden folder. Folder size can be huge, copying/moving may be time consuming. It is the Administrator's duty to make backup from database files.

- Old sessions can be converted thus enabling the program to access them.
    1. Click Select at the **Convert** frame of the panel.
    2. Open old session files.
    3. Select old sessions by ticking the selection boxes, then click **Save**. Existing files will not be overwritten, so you must define new file names before accept converting.



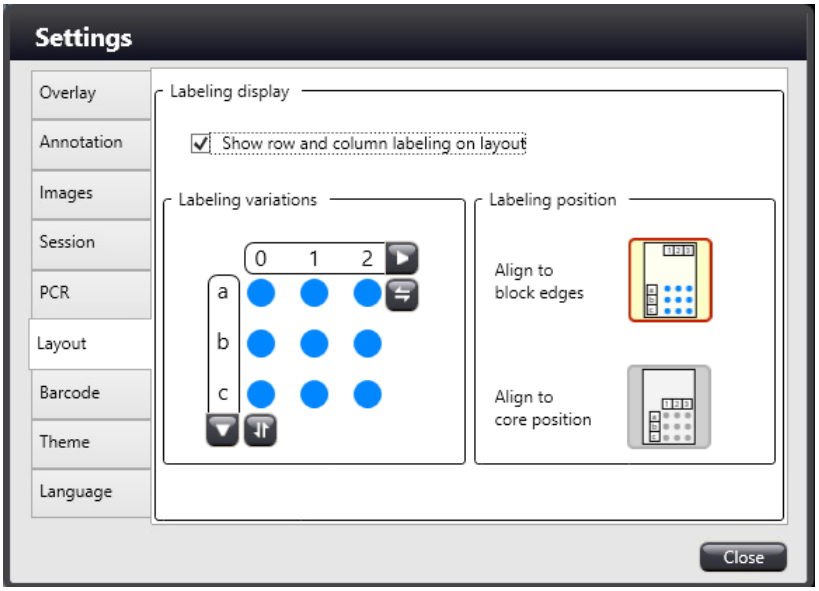
PCR

- Activate **With cleaning** option if you want to assign the first marker placed on the donor block as the cleaning core to prevent cross-contamination.
- Activate **Show guidance message** option if you need guidance during the procedure.



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**

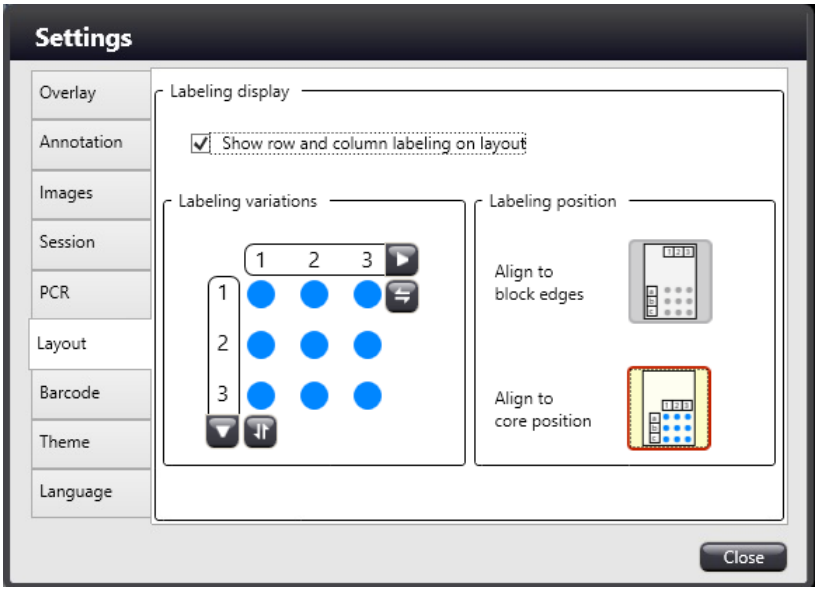
  Click to switch between the following pre-defined labeling variations for rows/columns:

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

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

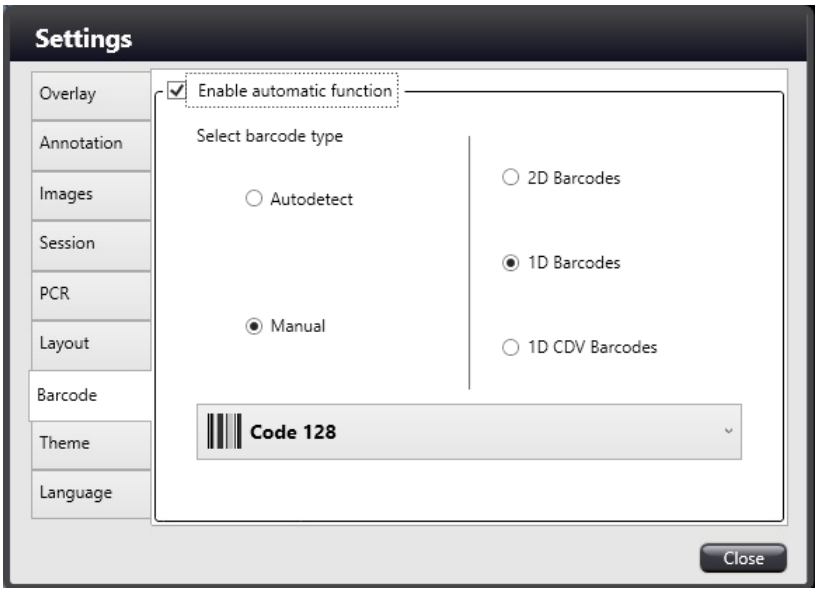
- **Labeling position**

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

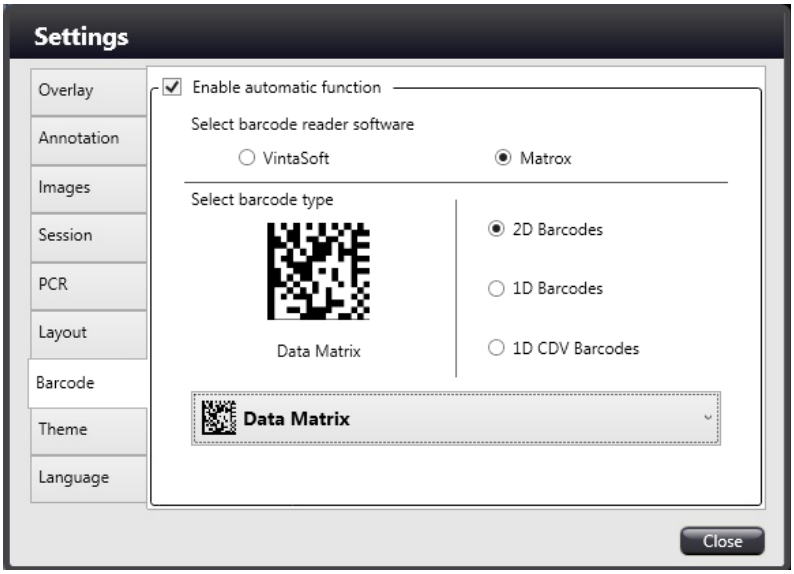


Barcode

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 2.6 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.

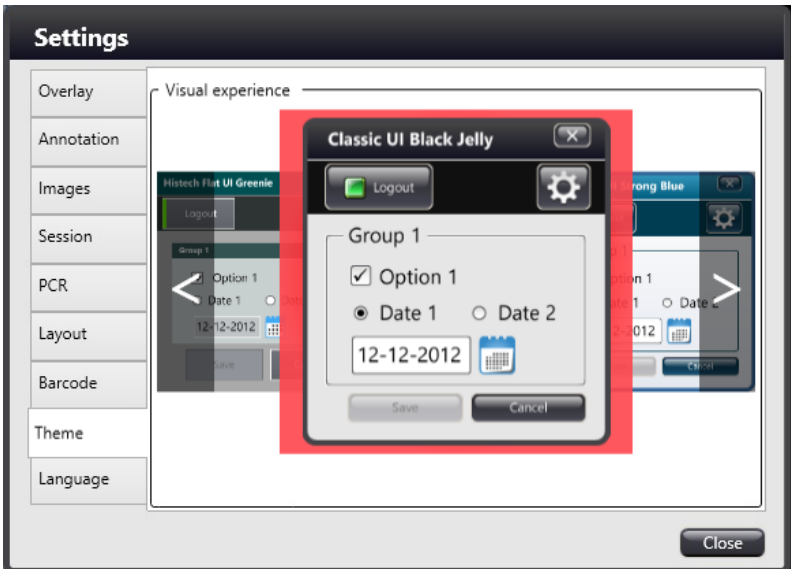


NOTE: VintaSoft occasionally cannot read Data Matrix barcodes.

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.

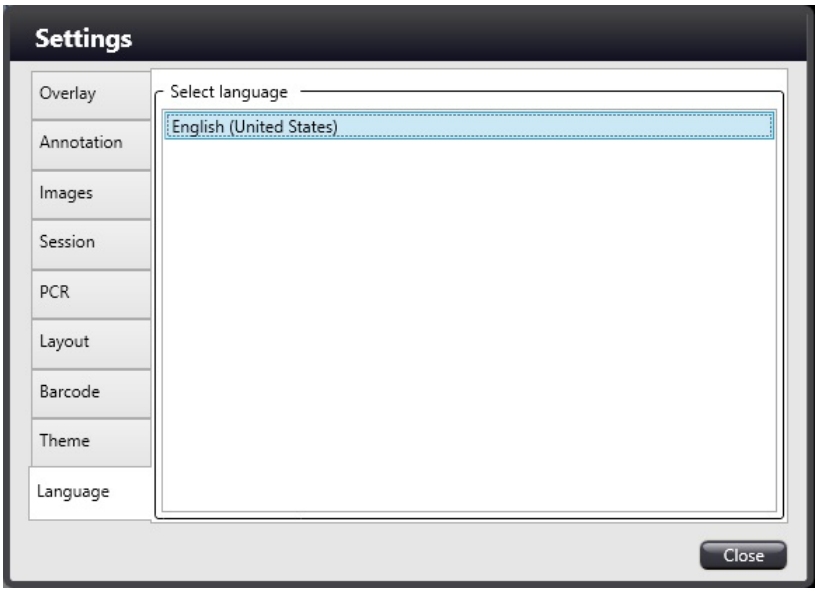
Theme

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.



10 Maintenance of TMA Master

Important!

The safety level of the equipment after servicing giving back to use is the same with the original equipment.

10.1 Preventive Maintenance of the Main Unit

- Keep the **TMA 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 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 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.

10.2 Cleaning Task at the End of Each Drilling or Punching Session

10.2.1 Emptying the trash container for core material

Core material that you discard during punching/insertion is collected in a trash container. You must empty the container when you finished drilling the recipient block or at the latest when you finished the session.

1. Make sure that the block tray is in the "IN" position inside the main unit.
2. Pull out the trash containers.
3. Empty their content into the dedicated waste disposal container.
4. Put the containers back into the main unit

10.2.2 Cleaning the TMA main unit

It is recommended that you clean the base plate of the machine (either with a vacuum cleaner or with a soft tassel) after have been used about 50 blocks.

11 Troubleshooting TMA Master

Important!

The safety level of the equipment after servicing giving back to use is the same with the original equipment.

TMA Master Does Not Work at All

Cause: The power supply is broken.

What to do: If the 24 V power supply is off, switch it on.
If the control computer is off, turn it on.
Check cable connections.

Block Image in the Application is of Poor Quality

Cause: Imaging errors.

What to do: Contact service.

Puncher Falls Out During Punching

Cause: The puncher chuck that should keep the punch in position has loosened.

What to do: Tighten the cog wheel with the tool.

Drill Bit Does Not Rotate

Cause: The drill chuck that should keep the drill bit in position has loosened.

What to do: Tighten the cog wheel with the tool.

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.

   Set the value in microns within the range of 0 and -500 in the **Distance from plastic** field.
b) You must use a new puncher.

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.

12 Technical Description of the Hardware

12.1 Physical Dimensions (Width x Depth x Height) and Weight

Name of the Unit	Dimensions in mm*	Weight in kg*
TMA Master main unit	380 x 240 x 290	8
Power Supply	170 x 300 x 110	2
Control Computer	206 x 560 x 440	max. 10
Monitor (19")	420 x 240 x 490	max. 3

* approximate values

12.2 Power Supply and Light Source

Accessory	Description
Power supply	24 V
LEDs	Luxeon LXHL MWGC

12.3 Accessories

Accessory	Dimensions in mm	Number of items
Base mold for paraffin blocks	30 x 24 x 7,5 / 37 x 24 x 7,5	3 / 3
Drill bit*	**Ø 0.6** / **Ø 1.0** / **Ø 1.5** / **Ø 2.0**	2 / 2 / 2 / 2
Puncher*	**Ø 0.6** / **Ø 1.0** / **Ø 1.5** / **Ø 2.0**	3 / 3 / 3 / 3
Puncher chuck or Drill bit chuck	N/A	2
Piston*	**Ø 0.6** / **Ø 1.0** / **Ø 1.5** / **Ø 2.0**	1 / 1 / 1 / 1
Trash trays for paraffin flakes	N/A	3
Trash trays for discarded tissue cores	N/A	2
PCR cassette	N/A	1

- For Drill bits, Punchers, and Pistons there are four distinctive color markings for each diameter:
    - colorless – Ø 0.6mm
    - black – Ø 1mm
    - magenta – Ø 1.5mm
    - blue – Ø 2mm

12.4 Objective and Cameras

Component	Description
Objective	16 mm focal length
Camera type	VRMagic (USB)
Camera resolution	3,14 Million Pixel

12.5 Ambient Conditions

Condition	Suitable Range
Shipment (packed)	
Ambient temperature	-40°C to +70°C
Storage	
Ambient temperature	+10°C to +40°C
Maximum relative air humidity	75% at 35°C
Operation	
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

13 Operating Environment

13.1 Operating Environment for the Main Unit

Parameter	Description
Category of operating environment	closed room facilities
Protection class	III
Internal protection degree	IP 20
Electrical safety	under DIN EN 61010-1 (IEC 61010-1) and taking CSA & UL regulations into account
Over-voltage category	II
Radio interference suppression	under EN 55011 class B
Noise immunity	under DIN EN 61326
Main unit line input voltage	24 V DC ±1 V
Main unit line input current	Max 2.5 A

13.2 Operating Environment for the External Power Supply – SINPRO - MPU101-108

Parameter	Value
Category of operating environment	closed room facilities
Protection class	I
Internal protection degree	IP 20
Line input voltage	100 V AC to 240 V AC
Line input frequency	50 / 60 Hz
Max. power consumption	100 VA
Secondary voltage	24 V DC
Max. secondary current	4.16 A

14 Control Computer and System Requirements

Unit-Name	Description
CPU	**Recommended**: Intel® Core™ i5-4570 Quad-Core, 3.2 GHz
RAM	**Minimum:** 2GB **Recommended:** 4GB
Hard drive	500 GB
Communication ports	2 x USB 2.0

15 Dimensions of the Plastic Cassettes and the Paraffin Blocks

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

Dimensions in mm	
Plastic Cassettes	**Paraffin Blocks**
29×41×6	24×30×7.5 (13.5)
29×41×6	24×37×7.5 (13.5)

Remarks:

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

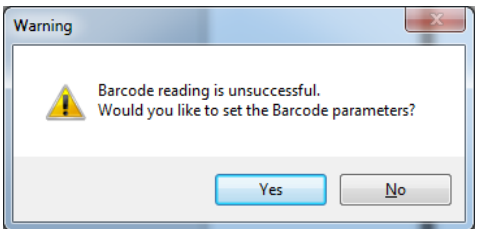
Warning!

Do not use paraffin blocks which dimension values are higher that specified in the table above, 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 Master**.

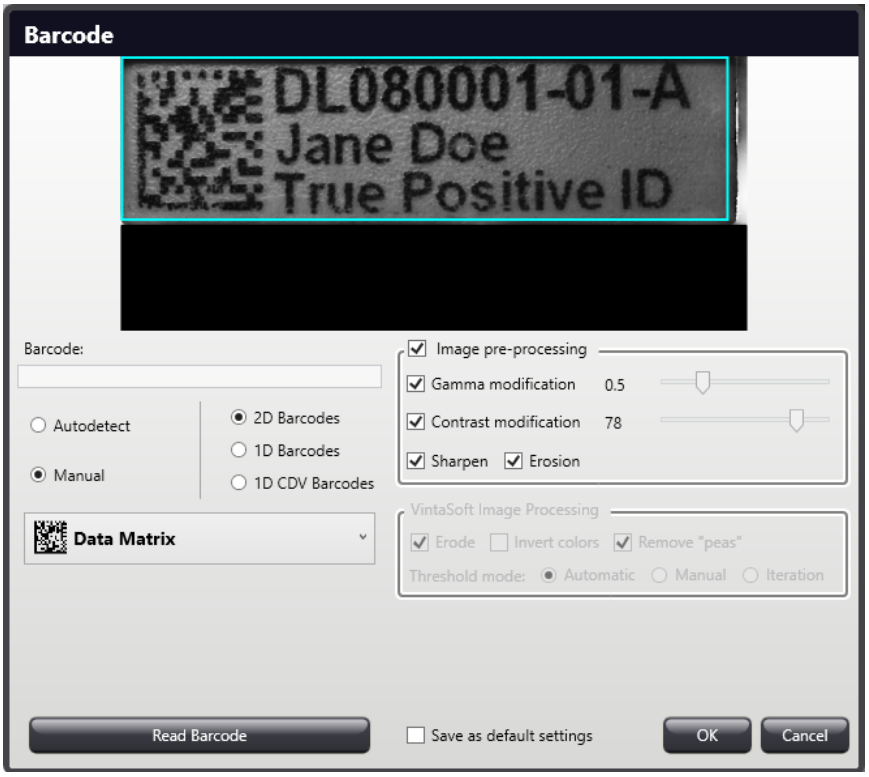
Appendix – Barcode Reading

1. Click the **Label** button of a donor block, then the image of the label is displayed.

2. Press the button, then the application reads the barcode on the block label. Rotate barcode image if necessary. If reading is successful, the barcode is displayed in the donor ID field, otherwise the program asks if you want to set the barcode parameters.



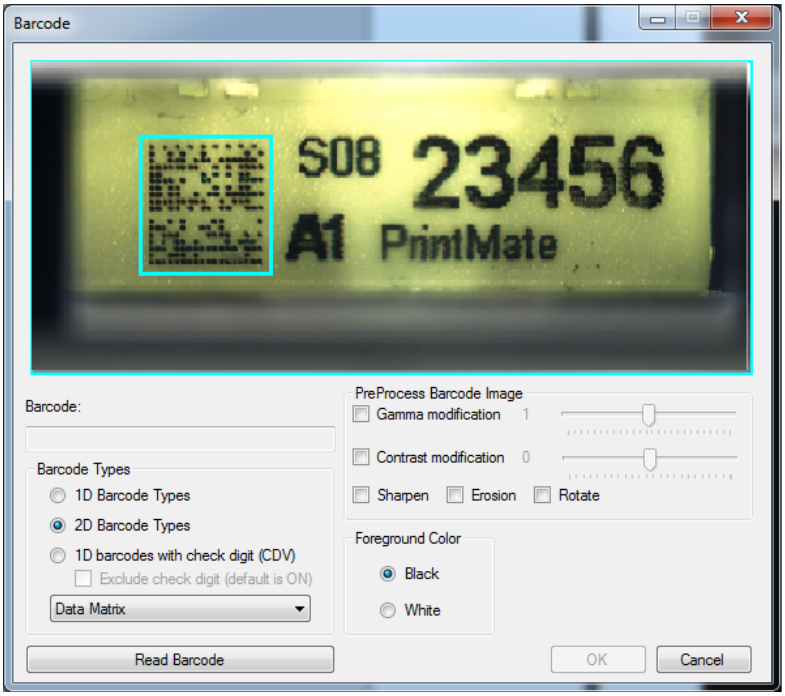
3. Click **Yes**, and the below **Barcode** window is displayed in which you can modify the parameters of barcode identification settings.



- In the **Image pre-processing** section you can modify **Gamma** and **Contrast** values. You can also select **Sharpen** and **Erosion** checkboxes to subserve the barcode identification process.

- Press the **Read Barcode** button when you are done with all the adjustments and settings, and the barcode is displayed in the window.

If you are using **Matrox** dongle for barcode reading, the following window is displayed:



- In the **Barcode Types** panel, set the appropriate type of the barcode.
- You can change the **Foreground Color** of the barcode.
- **Barcode string length** and **Maxicode Dot spacing** values can be set in the **Special Barcode settings** panel.
- In the **PreProcess Barcode Image** panel you can modify **Gamma** and **Contrast** values. You can also select **Sharpen** and **Erosion** checkboxes to subserve the barcode identification process.
- Press the **Read Barcode** button when you are done with all the adjustments and settings, and the barcode is displayed in the window.
- If the **OK** button is active, click it, so the window will close. The barcode is automatically displayed in the Donor Block ID field.

In case the reading has not succeeded this way, there is another solution for the problem:

- As you can see in the Barcode window, you can mark a specific barcode area by selecting it with the left mouse button. If you want to erase your selection (and would like the program to search for the barcode within the whole label area), click on it with the right mouse button.
- Finally, when everything is done, but Matrox is unable to detect the barcode, the message *"Barcode reading has not succeeded."* appears in the Barcode window.

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