H 007301 02.06

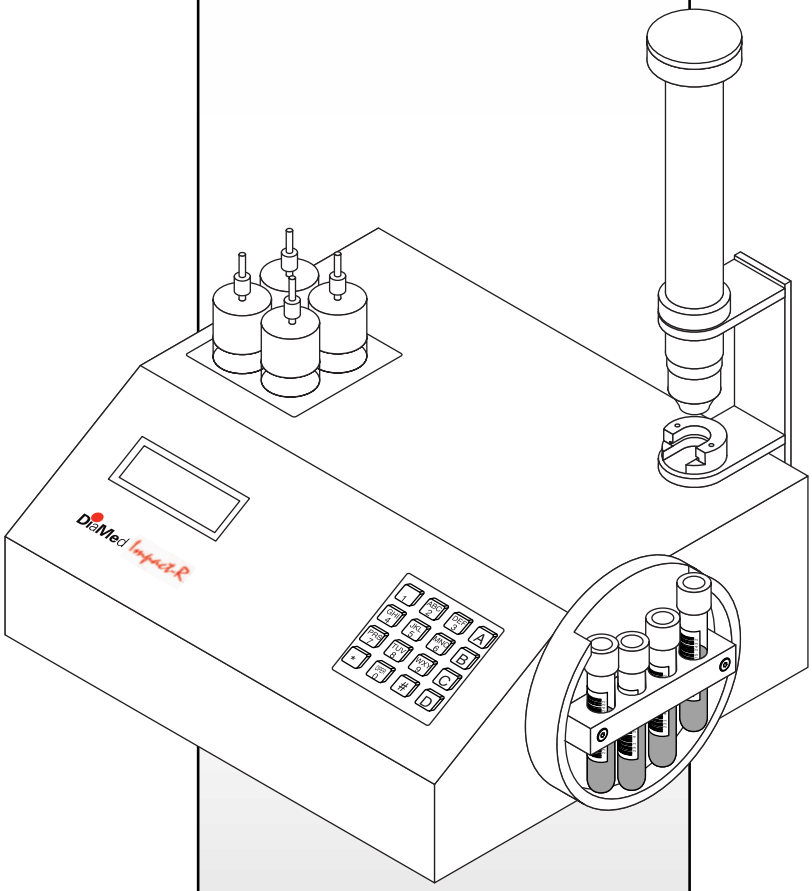
DiaMed
Haemostasis

User Manual

Impact-R

Cone and plate(let) (CPA) technology

A research device for platelet function analysis



Caution

Before operating the Impact-R, read this manual and take special note of all safety instructions.

Document

Impact-R User Manual

Version : 1.2

Nb. : H 007301

Version	Date	Comment
1.0	14.03.05	First issue, based on Impact-R Research V2.2
1.1	13.05.05	Editorial changes, adaptation to software V1.26
1.2	24.02.06	New blood processing procedure, software V1.28, minor changes

Printed in Switzerland

Table of Contents

Chapter overview

This chapter contains basic information on the structure of the document, its specifications and on the documentation.

1.1 Appropriate use

DiaMed AG's Impact-R tests the global function of patelet in whole blood samples under flow.

The DiaMed AG's Impact-R may only be used by trained and authorized personnel in a medical laboratory. It may not be used in the patient's direct environment.

Using the DiaMed AG's Impact-R is only permited in conjunction with the corresponding software or in a configuration which is authorized by DiaMed AG.

The use of any material other than the one specified in the User Manual (e.g. non-authorized substances) is forbidden.

The instructions contained in the present User Manual must be adherred to in order to avoid possible operational conflicts and / or personal danger.

1.2 Warranty limitations

Although the software has been tested, it is highly recommended to perform a backup of the computer before any installation and use of the software.

DiaMed AG denies any responsibility in case of:

- wrong use of the software;
- unauthorized modification (willingly or unwillingly);
- damages linked with the use of the software, in particular any data loss or any financial loss, which could possibly be attached to the use of the software.

When the device is connected to a host, the user takes the entire responsibility for an errorless transmission of the results (hardware, software, firmware, etc...) to this system.

In case of doubt, the English version of the present document is binding.

1.3 Conformity to directive and standards

The present product has been conceived in order to fully comply with the safety at work and function requirements. It is in conformance with the following European Union directives :

- 89/336/EEC (electromagnetic compatibility) and amended by the directives 92/31/EEC and 93/68/EEC;
- 73/23/EEC (low voltage equipment) amended by the directive 93/68/EEC;
- 98/79/EEC (directive on medical devices for in-vitro diagnostics);
- IEC61326-1 Class B;
- CRF 47 FCC Class B;
- Europe Directive Safety EN 61010-1.

1.4 Glossary

The following terms, among others, are used in the present User Manual.

1.4.1 Persons

Manufacturer

The manufacturer of the Impact-R is :

DiaMed SA, CH-1785 Cressier sur Morat.

Operator

The operator is the owner of a DiaMed AG's Impact-R both when using it as its owner and when transferring it to a third-party.

Personnel

The personnel gathers persons who have any kind of activity with the DiaMed AG's Impact-R and who are qualified in accordance with the manufacturer's requirements and who are consequently authorized.

Technical personnel

This terme designates the duly trained persons, who are allowed to perform specific tasks on the DiaMed AG's Impact-R.

For instance, an electrician is designated as technical personnel for the activities linked to wiring the DiaMed AG's Impact-R to the electrical network.

Personnel qualifications

Several kinds of personnel qualifications are required in order to perfom the activites related to the DiaMed AG's Impact-R. These qualifications are described in the corresponding sections of the present User Manual.

The personnel qualifications define the minimum requirements, which must be met by the authorized personnel.

Serious injury

A serious injury is an injury (ICAO definition) which is sustained by a person in an accident and which :

- requires hospitalization for more than 48 hours, commencing within seven days from the date the injury was received;
- results in a fracture of any bone (except simple fractures of fingers, toes, or nose);
- involves lacerations which cause severe hemorrhage, nerve, muscle or tendon damage;
- involves injury to any internal organ;
- involves second or third degree burns, or any burns affecting more than 5 per cent of the body surface;
- involves verified exposure to infectious substances or injurious radiation.

Light injury

Any injury not corresponding to the definition of a serious injury is considered as a light injury.

1.4.2 Product

This is the DiaMed AG's Impact-R distributed by the manufacturer.

1.5 Typographical conventions

The following styles are used in this manual.

1.5.1 Description

This style, use in conjunction with illustration numbers, is preceded with the corresponding numbers:

Example

(1) First element

(2) Second element

(3) Etc...

1.5.2 Command

Any software command, button, function key, window, icon, option, tab, checkbox, selection box, article, menu, tool bar, field and section used in this document is represented by a bold italic font.

Example:

The ***Exit*** command allows to quit the software.

1.5.3 Procedure

Each procedure step to be carried out step-by-step by the user is preceded by a letter.

Example

A. Open the drawer.

B. Put the microplate into position as shown.

C. Close the drawer.

1.5.3.1 Procedure result

A procedure result is shown by the following symbol ↳.

Example

A. Click on the ***Parameters*** button.

↳ The parameter window is displayed.

1.5.4 Cross reference

This style is used to help the user find complementary information linked to the current subject.

Example

See section “4.2.4 Sensor Board Positioning” on page 7.

1.5.5 List of items

This style is used in order to display a list of elements.

Example

- item 1;
- item 2;
- item 3.

1.5.6 Troubleshooting

The complete description along with the error message, the explanation and the remedy appears as follows :

Problem

- **Explanation, possible cause**

  ✔ Remedy

1.5.7 Warnings

In relation to the importance of the warning and its related risks, three warning styles are defined.

The safety aspects are used in accordance with the requirements contained in the following norms :

- ANSI Z535.4;
- ISO 3864 and ISO 3864-1:2002.

1.5.7.1 Danger

Used to designate an imminent and dangerous situation which, if not avoided, may lead to death or serious injury.

The primary risk is given in capital letter below the ⚠ DANGER symbol. However, mentioning a specific risk does not exclude the presence of subsidiary risks.

Example

⚠ DANGER

ELECTROCUTION

Never touch an exposed electrical wire. A contact with an electrical wire may cause an electrocution.

1.5.7.2 Warning

Used to designate a potentially dangerous situation which, if not avoided, may lead to death or serious injury.

Example

⚠ WARNING

Always disconnect the electrical cord before opening the device. A contact with an exposed electrical wire may cause an electrocution.

1.5.7.3 Caution

Used to designate a potentially dangerous situation which, if not avoided, may lead to light injury or cause equipment damage.

Example

⚠ CAUTION

Do not manipulate a broken mirror with bare hands as this operation may result in cuts.

The use of the CAUTION sign without the warning triangle means that the only risk consists in equipment damage.

Example

CAUTION

The use of other cleaning agents or hard objects may damage the device. Do not use other cleaning agents or products without obtaining first the authorisation of the manufacturer.

1.5.8 Recommendation and Note

When complementary information is required and if their non-compliance only leads to minor inconveniences, recommendations and notes are given.

1.5.8.1 Recommendation

Used to designate a prefered procedure or a recommended practice. DiaMed AG denies any responsibility in case of non-compliance with the recommendations.

Example

☞ ***Recommendation:*** *Check that the device is closed before switching it on.*

1.5.8.2 Note

Used to accompany a general remark or an purely informative comment.

Example

Note: *The reassembly of the device is performed in the opposite order of its disassembling.*

Chapter Overview

This chapter defines the safety instructions which guarantee a safe and troublefree operation of the DiaMed AG's Impact-R.

2.1 Introduction

2.1.1 Principle

The user must have read and understood this chapter before any intervention on the DiaMed AG's Impact-R device.

In case of unclear information, please contact the manufacturer or your local DiaMed dealer.

2.1.2 Importance of the safety instructions

Every safety and protection instruction which can be found in this manual must be adhered to in order to avoid personnel injury, property damage or environmental pollution.

In a similar manner, the legal bylaws, the measures in prevention of accidents and for the protection of the environment, as well as the recognized technical rules aiming at appropriate and safe working conditions which as applied in the country and at the place of use of the DiaMed AG's Impact-R device must be adherred to.

2.1.3 Disregarding the safety rules

Disregarding the safety rules, as well as existing legal and technical regulations, may lead to accidents, property damages or to environmental pollution.

2.2 Environmental conditions

⚠ WARNING

The DiaMed AG's Impact-R must not be located near a water tap or any other source of water.

This system may only be used in closed rooms and never in the immediate environment of patients.

The electrical safety of the DiaMed AG's Impact-R device is only guaranteed if the electrical installation is conform to the reglementation related to medical use buildings and laboratories and if this installation works properly.

The DiaMed AG's Impact-R device may not be used in buildings prone to explosion hazard.

CAUTION

The DiaMed AG's Impact-R must be kept away from any interference source.

The DiaMed AG's Impact-R device may not be stored under exposure to a direct sunlight, heat, dust or an excessive humidity (only use the device in a clean laboratory environment).

2.3 General safety instructions

⚠ DANGER

ELECTROCUTION

During maintenance operations, when the DiaMed AG's Impact-R is powered and its cover is removed, the device must not be left without proper watch.

⚠ WARNING

Maintenance and repairs may only be performed in conformance with the instructions and by the technical personnel authorized by the manufacturer.

The sole possession of the Service Manual does not allow the personnel to perform any kind of repair on the DiaMed AG's Impact-R.

Take into account all the warnings and follow all the instructions displayed on the DiaMed AG's Impact-R screen and which are printed in the documentation.

The DiaMed AG's Impact-R device may only be connected to an electrical power source given under «Operating Conditions», on page 6 of the Service Manual.

It is mandatory to use the products specified in the present User Manual to clean the DiaMed AG's Impact-R device. If you plan to use another product, only do so after obtaining the authorization from the manufacturer.

Using materials other than those defined in the User Manual (unauthorized dangerous goods for instance) is forbidden. Breaching this rule will be considered by the manufacturer as guilty negligence.

Never try to use replacement pieces other than those authorized by the manufacturer of the DiaMed AG's Impact-R device.

CAUTION

The DiaMed AG's Impact-R device must be used on an appropriate table.

Ensure that the ventilation around the DiaMed AG's Impact-R device is sufficient to avoid any excessive heating. A space of 100 mm behind the Impact-R device must be left clear of any obstacle.

The DiaMed AG's Impact-R device must only be used with software and with accessories supplied by the manufacturer.

The manufacturer's agreement must be obtained before using the DiaMed AG's Impact-R device in conjunction with other equipment.

Never let any liquid enter the device. In case of liquid spill inside the device, act immediately as follows:

A. Switch off the device using the main switch

B. Unplug the power cord

C. Dry up the device.

D. Clean and decontaminate the device.

E. Check electrical functions.

☞ ***Recommendation:*** *For further information, please contact your local DiaMed dealer or the manufacturer.*

2.3.1 Observations and informations

In case of defective operation or any other technical incident for which no remedy is described in this manual, please contact immediately the manufacturer or your local dealer.

Chapter contents

This chapter gives a basic description of the Impact-R system and its composition.

3.1 General description

3.1.1 General overview

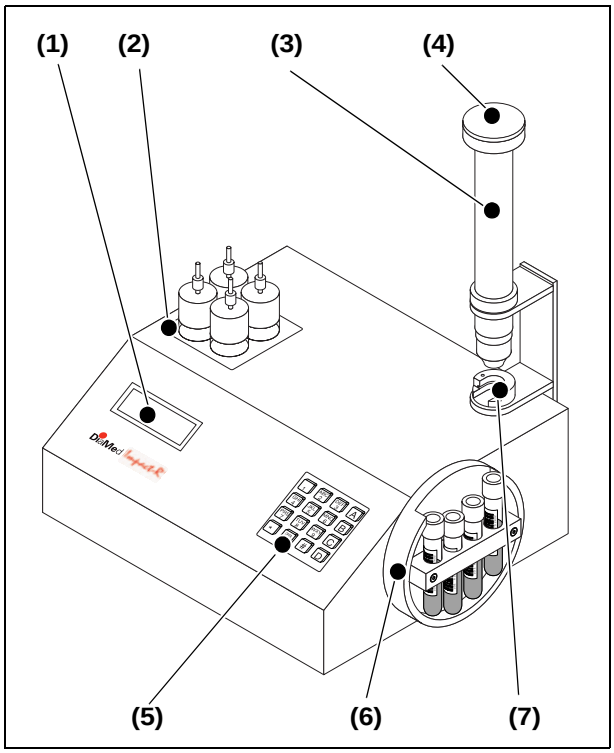


Fig. 3-1: General view

(1) LCD screen

(2) Well pad (motor 1)

(3) Microscope unit

(4) USB camera module

(5) Keypad

(6) Tube stir (motor 2)

(7) CMM sample tray

The Impact-R is a novel device for testing platelet function under close to physiological conditions. The device tests platelet adhesion and aggregation in an anti-coagulated whole blood (citrate buffer tubes) under arterial flow conditions (1800 s^{-1}; for 2 min). The laminar flow over the polystyrene surface of the well is achieved according to the cone and plate principal. The device can also give indication for patient response to drugs such as Aspirin or Plavix®.

Upon application of a blood sample (130 µl) into the polystyrene well, plasma proteins immediately adhere to the well surface and attract for platelets, resulting in platelet adhesion and aggregation on the well surface under flow conditions. Following removal by washing of the excess blood and staining of adhered platelets, a count of the results is performed by an image analyzer.

The results are expressed as the percentage of the well surface covered by platelets aggregates (percentage SC) representing platelet adhesion and the average size of the aggregates (AS in μm^2) representing platelet aggregation.

The Impact-R can also be used for the study of platelet function, screening of primary hemostasis abnormalities including thrombocytopenia and monitoring their therapies. It can be used for testing both hypo- and hyper-function of platelets. Furthermore, it provides a quick method for monitoring the response to various anti platelet drugs.

3.1.2 System requirements

3.1.2.1 Minimum PC requirements

PC ..... Pentium® III 500 MHz Processor
Operating System ..... Windows 2000 (With SP4)
Memory ..... 32 Mb RAM
Graphic card ..... 16 Mb 3D Graphic accelerator card
Hard disk ..... 20 Gb space
CD-ROM drive ..... 4 X Speed
USB port ..... Available USB 2.0 port

3.1.2.2 Preferred PC requirements

PC ..... Pentium® 4 1.8 Ghz Processor
Operating System ..... Windows XP Home/Pro
Memory ..... 128 Mb RAM
Graphic card ..... 64 Mb AGP card
Hard disk ..... 40 Gb space
CD-ROM drive ..... 48 X Speed
USB port ..... Available USB 2.0 port

3.1.3 Operating conditions

3.1.3.1 Environmental

Working temperature range ..... 10 - 35°C.
Humidity, non-condensing ..... 5 - 95%.

☞ ***Recommendation:*** *The device is not intended to work in a direct sun light.*

⚠ CAUTION
The biological ambiant temperature range for platelet testing is 18°C - 28°C.

3.1.3.2 Power

Voltage ..... 90 - 240 V
Frequency ..... 50 - 60 Hz
Current ..... 1 Amp.

3.1.3.3 Maintenance

⚠ WARNING
By an authorized technician only.

3.1.3.4 Rated engine speeds

Motor 1 ..... 400 ~ 1800 RPM in 10 RPM increments / 0 ~ 999 seconds
Motor 2 ..... 4 ~ 10 RPM / 0 ~ 999 seconds

Both engines repeat process ..... 1 ~ 999 times.

3.1.4 Testkits

CAUTION

The tests must be performed using the testkit developed for the Impact-R.

Impact-R Testkit (50 Tests), Id 47600

Reference	866050
Cones	1x 50 pces
Wells	5x10 pces
Pipette tips	1x 55 pces
«May-Grünwald» staining solution.....	1x 100 ml

Chapter contents

This chapter describes the windows, menus and commands of the ***Image Analysis*** software.

4.1 Software structure

After starting the software, the ***Enter Program Password*** screen appears.

Note: *The user will be required to enter his User Name and Password information every time the system starts.*

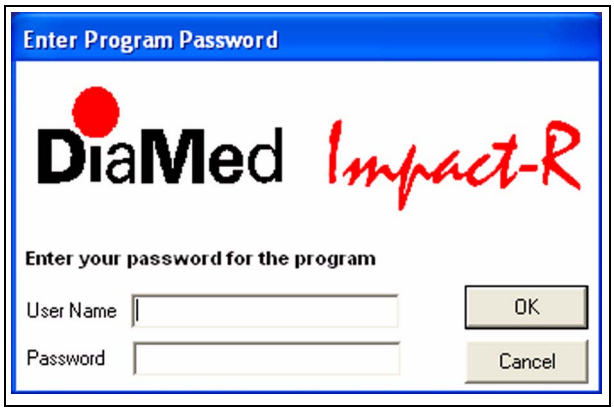


Fig. 4-1: Login screen

If the login is correct, the ***Image Analysis*** main screen appears.

This screen is made of the following elements :

(1) Image Analysis main menu

See section "4.2 Image Analysis main menu" on page 19.

(2) Image Analysis tool bar

See section "4.3 Image Analysis tool bar" on page 31.

(3) Image Analysis ***Start*** form

See section "4.4 Start form" on page 32.

Note: *This screen is only present if the* ***Begin With Start Form*** *option is selected.*

See section "4.2.1.7 Options" on page 25.

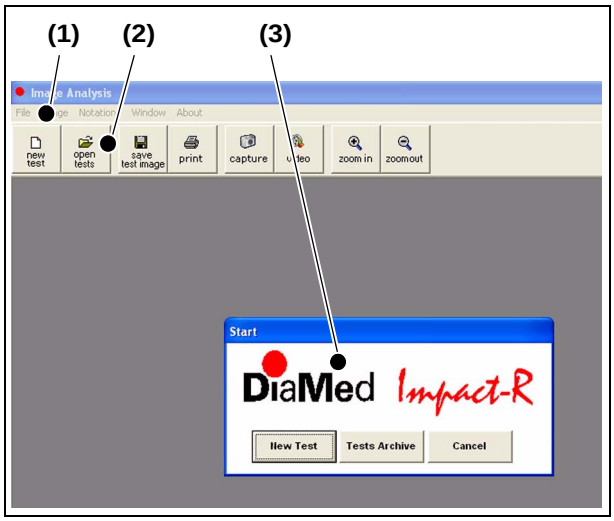


Fig. 4-2: Main screen

4.2 Image Analysis main menu

This menu is composed of 4 sub-menus and one command :

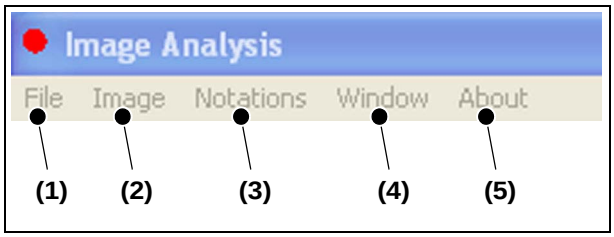


Fig. 4-3: Image Analysis main menu

(1) File menu

See section "4.2.1 File menu" on page 20.

(2) Image menu

See section "4.2.2 Image menu" on page 27.

(3) Notations menu

See section "4.2.3 Notations menu" on page 30.

(4) Window menu

See section "4.2.4 Window menu" on page 31.

(5) About command

This command permits to display the version of the ***Image Analysis*** software.

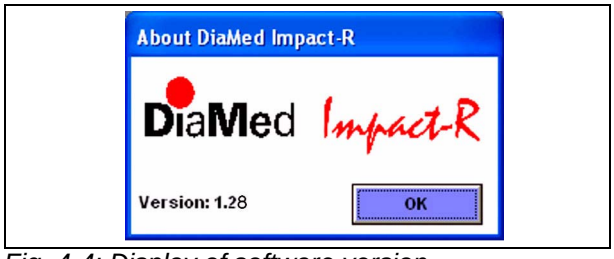


Fig. 4-4: Display of software version

4.2.1 File menu

This menu enables access to tests and images. It also permits to access to the options, to modify the user password and to launch the calibration procedure.

(1) New Test :
To launch a new test. The ***New Test*** window will be displayed to edit the test description.

See section "4.2.1.1 New test" on page 21.

(2) Open Tests :
To open previously saved tests (Tests archive).

See section "4.2.1.3 Tests archive (administrator mode)" on page 23.

(3) Open Image :
To open previously saved image.

(4) Delete Image :
To delete a selected image. A confirmation is required.

(5) Delete Test :
To delete a selected test. A confirmation is required.

Note: *The corresponding test images must have been previously deleted with the* ***Delete Image*** *command.*

(6) Options :
To define software settings. The ***Options*** window will be displayed.

See section "4.2.1.7 Options" on page 25.

(7) Users :
To modify the user's password.

See section "4.2.1.8 Users" on page 26.

(8) Save Image :
To save a selected unsaved image. The ***Save Pictures*** window will be displayed.

See section "4.2.1.9 Save image" on page 26.

(9) Print Image :
To print a selected image. A confirmation is required.

(10) Calibrate :
To auto calibrate the Impact-R device.

See section "5.1 Microscope validation and focus adjustment" on page 34.

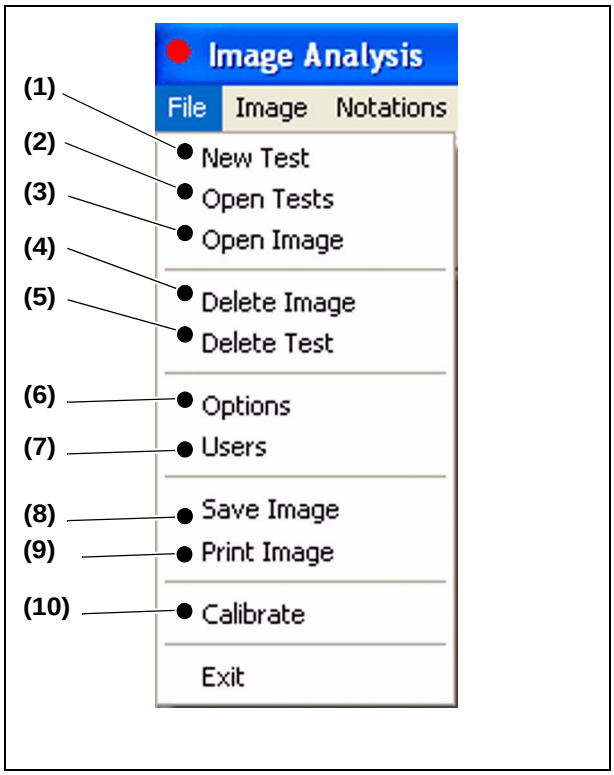


Fig. 4-5: File menu

4.2.1.1 New test

This screen is displayed when the operator creates a new test.

***Note:** The **Patient ID** and **Patient Name** fields are mandatory.*

(1) Patient ID (mandatory field) :
To enter an identification for the patient.

(2) Patient Name (mandatory field) :
To enter the name of the patient.

(3) Test Date (locked field) :
The date of the test is displayed. It is a read only field. This field is created from the oerating system date of the user's computer.

***Recommendation:** The user must check that the computer operating system is displaying the correct time and date to avoid false information entered into the database.*

(4) Test Type :
There are currently 5 test types available :

- Platelet function
- Aspirin test
- Plavix® test
- Validation
- user defined

To determine the test type, the user must choose the correct test out of 5 options from a pull-down menu. The initial 4 tests are locked. However, the 5th test is a "user-defined" test which has limited manipulation capability through the ***File-Options*** menu.

See section "4.2.1.7 Options" on page 25.

(5) Technician Name (locked field) :
The user name of the operator (used to log into the system) is displayed. It is a read only field.

(6) Remarks :
Free text field.

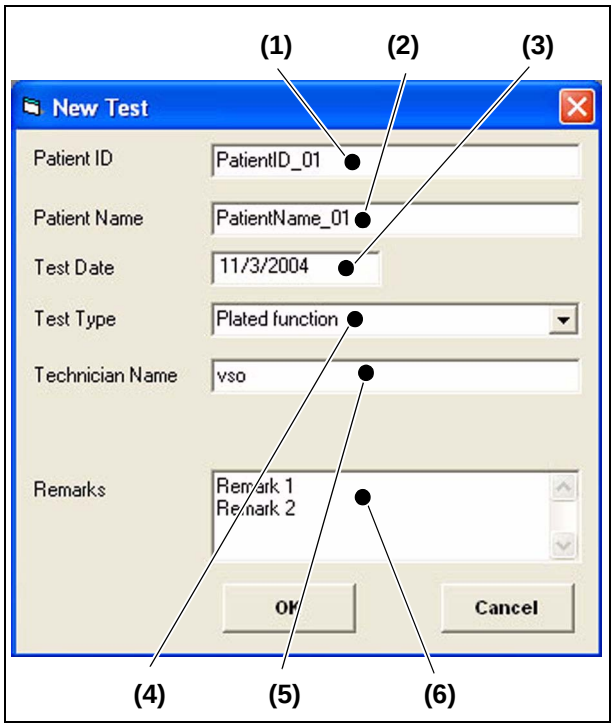


Fig. 4-6: New test window

4.2.1.2 Test data

This information window is displayed during a test. It displays the information entered when creating a new test.

See section "4.2.1.1 New test" on page 21.

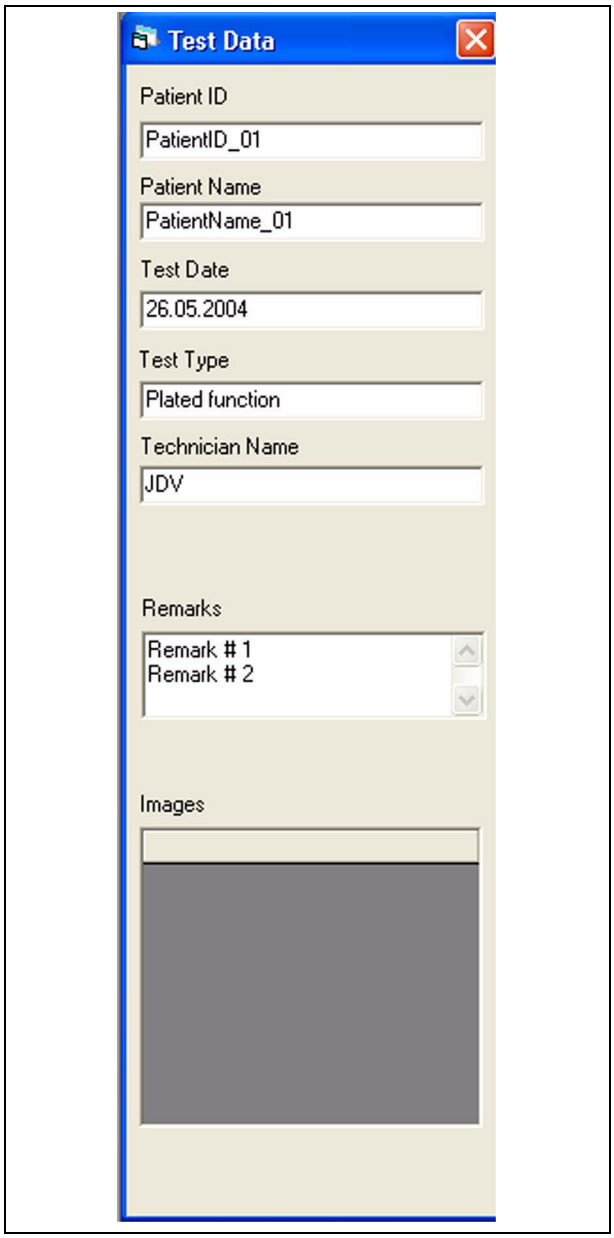


Fig. 4-7: Test data

4.2.1.3 Tests archive (administrator mode)

After highlighting one or more specific test(s) in the archive list (10) the administrator can perform several commands :

(1) Edit Test :
To edit a selected test (if it is still unlocked).

See section "4.2.1.5 Test archive edit" on page 24.

(2) Delete Tests :
To delete one or more test from the archive.

***Note:** This only delete the test registration in the archive (Logic erase).*

(3) Show Deleted Tests :
Shows a list of all deleted tests with a menu option to undelete them.

(4) Filter :
To filter the tests using a criteria. Choose a display filter for the archive. It can be a name, ID, test or a date. Part or whole.

See section "4.2.1.6 Test archive filter" on page 24.

(5) Show All Tests :
To reset the filter criteria and display all saved tests again.

(6) Export Table :
Exports the archive (Part or whole) to a Microsoft Excel® file format (List only).

(7) Export Selected Tests :
Exports a test or a number of tests to a compressed file format, which later can be used by another ***Impact-R*** system.

(8) Import Tests :
Used to import a compressed file (extension ".ipr") containing another system exported tests.

(9) Duplicate Test :
To duplicate an archived test. It can be used if further work is needed on a locked test.

***Note:** Although it is a duplicate, the test unique number (TestID) will change, marking it as a different test on the system.*

(10) List of saved tests (archive)

***Note:** The default display setting of the archive is by ascending order of the test number (Unique number). The Administrator/User can change the order of ascending / descending archive fields by pressing the relevant field description. This setting will return to default when exiting the archive.*

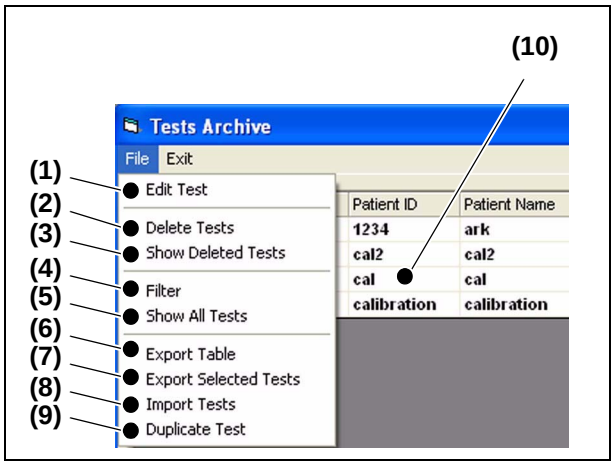


Fig. 4-8: File menu for administrator

4.2.1.4 Tests archive (user mode)

In a regular user mode, most functions were removed to restrict the ability to manipulate the system. As noted, all functions opted out except editing a test (before it was locked) and the archive filter.

See section "4.2.1.3 Tests archive (administrator mode)" on page 23 for more information about the commands.

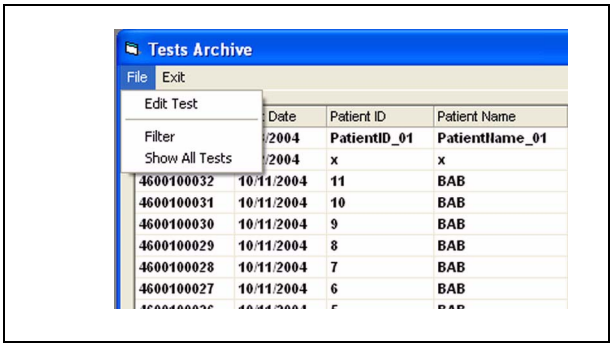


Fig. 4-9: File menu for user

4.2.1.5 Test archive edit

This window is displayed to edit and modify the fields for a saved test.

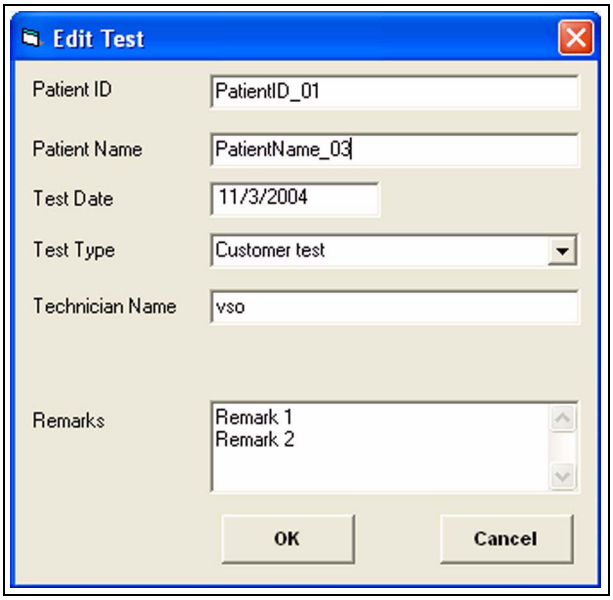


Fig. 4-10: Test archive edit

4.2.1.6 Test archive filter

This window is displayed to filter the saved tests using a criteria.

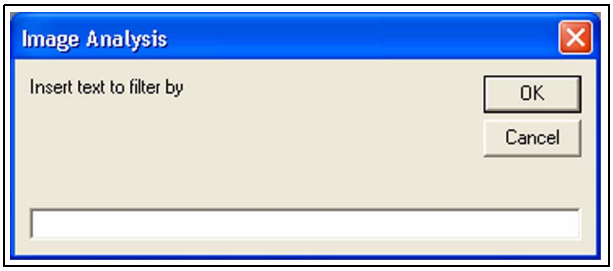


Fig. 4-11: Test archive filter

4.2.1.7 Options

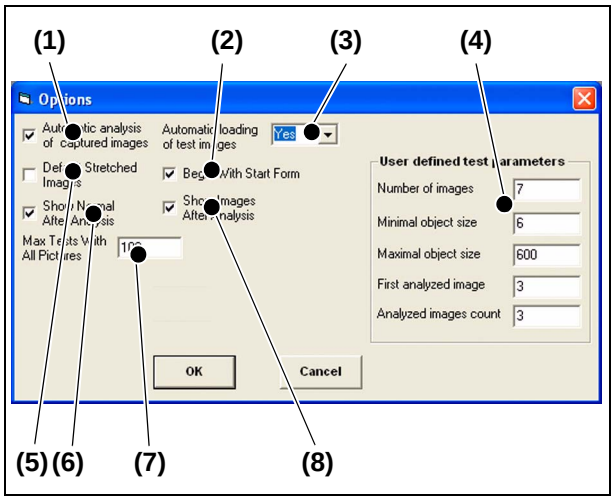


Fig. 4-12: Options window

(1) Automatic analysis of captured images :
If checked, the system analyses the captured image immediately. If not, the operator has to launch the command manually.

(2) Begin With Start Form :
If checked, the ***Start*** form window will be displayed when launching the Image Analysis software.

See section "4.4 Start form" on page 32.

(3) Automatic loading of test images :
3 items are available for this option :
- No : When the operator loads a saved test, the corresponding images are not loaded automatically.
- Yes : When the operator load a saved test, the corresponding images are loaded automatically.
- Ask : When the operator loads a saved test, he will be asked to load the corresponding images (see Fig. 4-13).

Fig. 4-13: Load images confirmation

(4) User defined test parameters :

⚠ WARNING

The user defined parameters may only be used in non-IVD User defined mode.

To define the test parameters such as:

- Number of images – Number of images to taken by the program.
- Minimal object size – objects smaller then the indicated size will be deleted (Unit size in pixels)
- Maximal object size - objects larger then the indicated size will be deleted (Unit size in pixels)
- First analyzed image – Images are numbered according to the SC ascending order - define the first image to be analyzed
- Analyzed images count – Define the number of Images to be analyzed.

(5) Default Stretched Images :
If checked, no side scroll bars are displayed for a picture. The image will be adusted to the window.

(6) Show Normal After Analysis :
Normal chart and normal image are only displayed in the ***Analyse results*** window if this option is selected.

(7) Maximum Test with all Pictures :
Maximum number of tests to be saved with all captured images. Default number is 100.

Note: *As default, the system saves 100 full tests. The following 900 tests are saved with data and best image (chosen by the program). The 19 000 tests thereafter with data only (Total of 20 000 tests). Changing the value of this field does not change the end value of 20 000 saved tests.*

CAUTION
Check that system resources are sufficient (e.g. disk space) before attempting to change this setting."

(8) Show Images After Analysis :
Best captured image of the test and normal image are only displayed in the ***Analyse results*** window if this option is selected.

See section "4.2.2.1 «Impact-R Test results» form" on page 28.

4.2.1.8 Users

This screen appears after the launching of the ***File - Users*** command. It permits to the current user to modify its password.

See section "6.4.2 Modify the password for the current operator" on page 52.

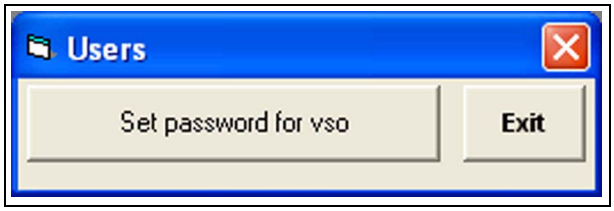


Fig. 4-14: Modify the password of the user

4.2.1.9 Save image

This screen appears after the launching of the ***File - Save Test Image*** command. It permits to save an unsaved image and enter a description for the picture in the ***Remarks*** field (1).

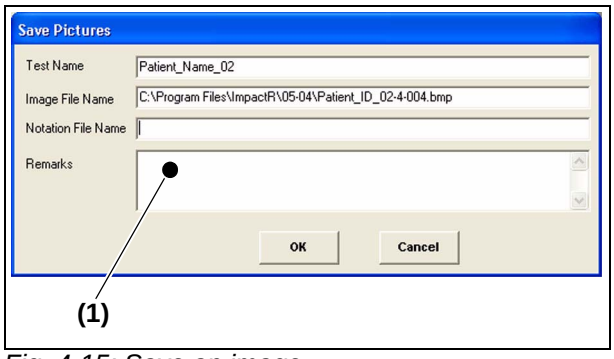


Fig. 4-15: Save an image

Note: *An unsaved image is displayed with an asterisk "*" (see figure beside).*

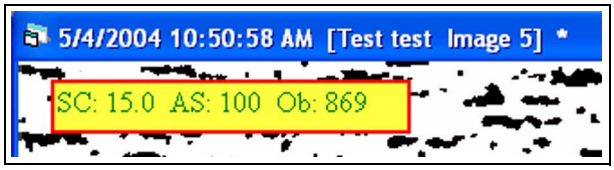


Fig. 4-16: Unsaved image

4.2.2 Image menu

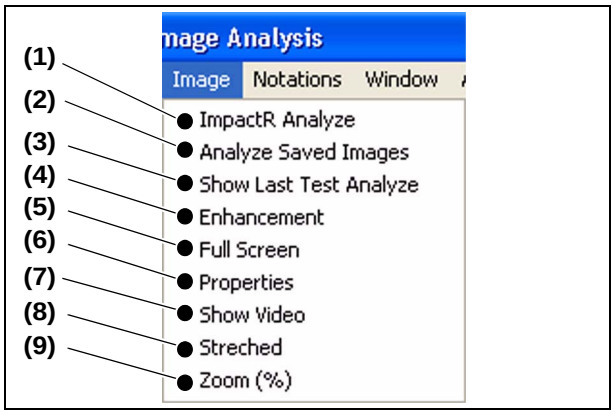


Fig. 4-17: Image menu

(1) ImpactR Analyze :
To analyze a specific image. Opens a small window on the image showing Surface Coverage (SC), Average Size (AS) and Object number (Ob). See figure 4-18 for details.

*Note: It is possible to select the **Automatic analysis of captured images** option to start this command automatically. Default setting for this option is **On**.*

See section "4.2.1.7 Options" on page 25.

(2) Analyze Saved Images :
To analyse the whole test file (for an IVD test setting: images 4, 5, and 6 of 7 images). Images are numbered in accordance with the SC ascending order.

See section "4.2.1.7 Options" on page 25.

The results are displayed in the ***Analyse Results*** window.

See section "4.2.2.1 «Impact-R Test results» form" on page 28.

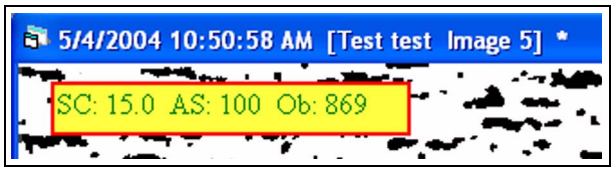


Fig. 4-18: Result of the analysis

(3) Show Last Test Analyze :
To display the ***Analyse Results*** window of the last test.

(4) Enhancement :
To open a popup window with basic image manipulation capabilities. It is a function for the technician.

See Service Manual for more details.

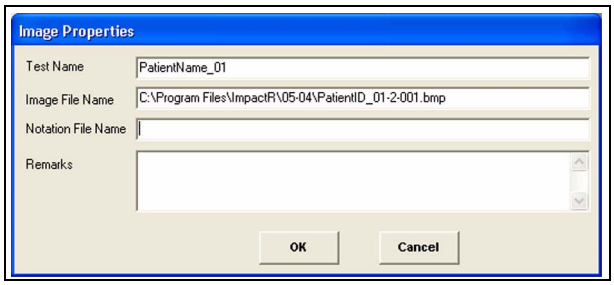


Fig. 4-19: Image properties

(5) Full Screen :
To spread the selected image on full screen mode.

(6) Properties (see Fig. 4-19) :
To display the properties of the selected image.

(7) Show Video:
To start the live video mode.

See section "6.5 Live Video" on page 54.

(8) Streched :
To stretch an image inside the window (no side scroll bars).

(9) Zoom (%) (see Fig. 4-20) :
Opens a popup window to define the zoom percentage for a selected image.

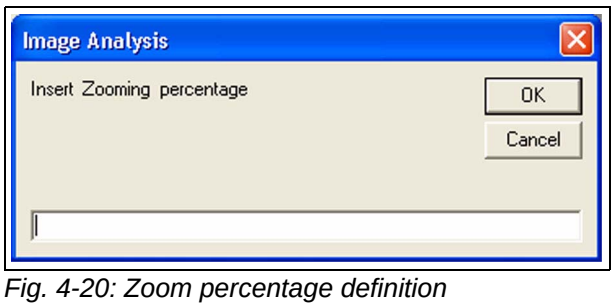


Fig. 4-20: Zoom percentage definition

4.2.2.1 «Impact-R Test results» form

This screen displays the ***Report page*** of an analysis.

After receiving the analysis the user can create a hard copy of the report by pressing the ***Report*** file menu on the upper left corner of the screen and mark the ***Create report*** command.

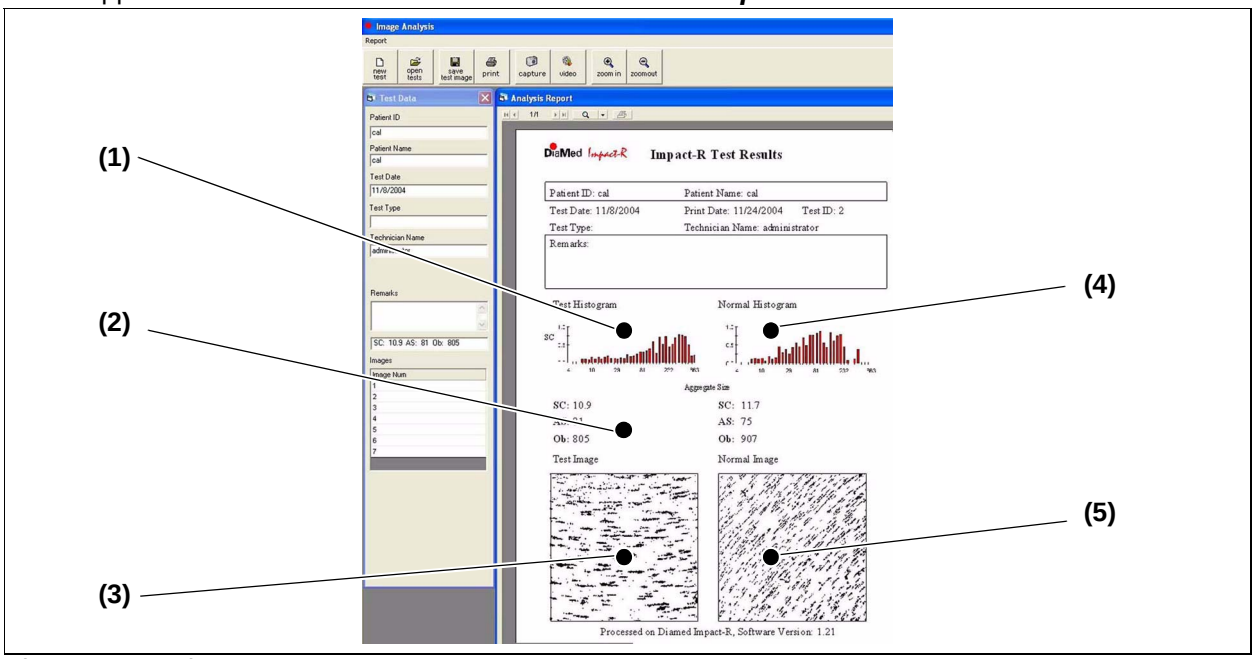


Fig. 4-21: Results

(1) Graphical representation of the test (test histogram)

(2) Values SC, AS and Ob for the test

(3) Best captured image of the test

(4) Graphical representation of a normal test (reference)

(5) Image of the normal test (C:\Program Files\Impact-01\ImpactR\normal_BW.bmp).

SC values in the Platelet/Aspirin/Plavix® tests are rounded to the decimal point above 8% and results with 0.1% increments below 8%. Validation/User defined tests will show values with 0.1% increments from 0.1% and upwards.

Note: *Normal chart (4) and normal image (5) are only displayed if the* ***Show Normal After Analysis*** *option is selected.*

⚠ WARNING

Platelet/Aspirin/Plavix® tests will show their own normal reference Histogramm/Image accordingly. Validation and User Defined tests will not display any reference for normal values. For the User-defined test, the program will indicate on the result page the following phrase: "USER DEFINED TEST. NOT FOR CLINICAL DIAGNOSTICS"

Note: *Best captured image of the test (3) and normal image (5) are only displayed if the* ***Show Images After Analysis*** *option is selected.*

See section "4.2.1.7 Options" on page 25.

After receiving the analysis report the user can create a hard copy of the report by launching the ***Report - Create report*** command on the upper left corner of the screen.

Note: *Choosing to create a hard copy of the report will lock the test for further analysis.*

Before creating the hard copy, the user will be prompted twice. First to confirm that the user understands that the test will be locked for further analysis, and second to allow the user to conceal the patient identifying information.

This is recommended if the hard copy is to be used for other purposes then those under patient-doctor relationships.

Note: *When creating a report, the user can choose between sending the report for printing on his defined printer or saving the report as a .PDF file.*

4.2.3 Notations menu

(1) Show / Hide :
To show or hide analysis results (see Fig. 4-23) for a selected image.

(2) Selection, Draw, Ellipse, Line, Rectangle and Text
To create your own marks - drawings on a selected image (see Fig. 4-24).

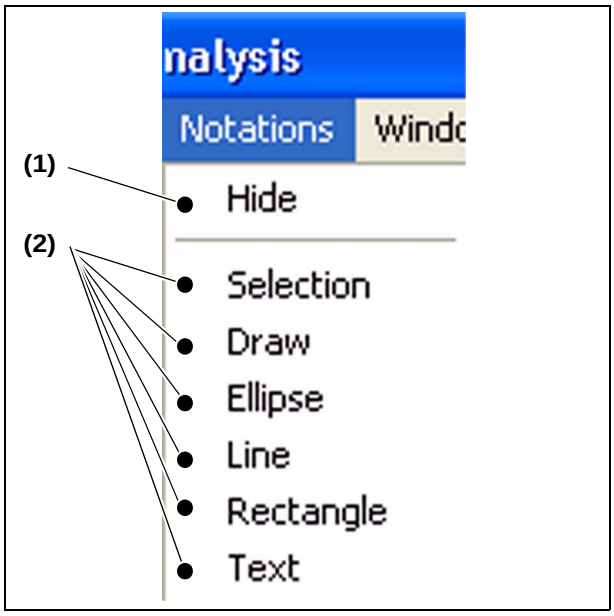


Fig. 4-22: Notations menu

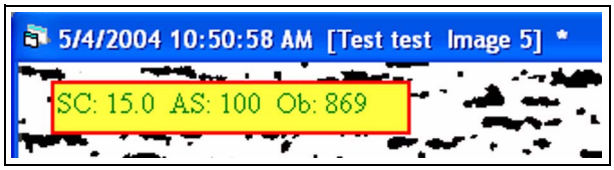


Fig. 4-23: Show analysis result

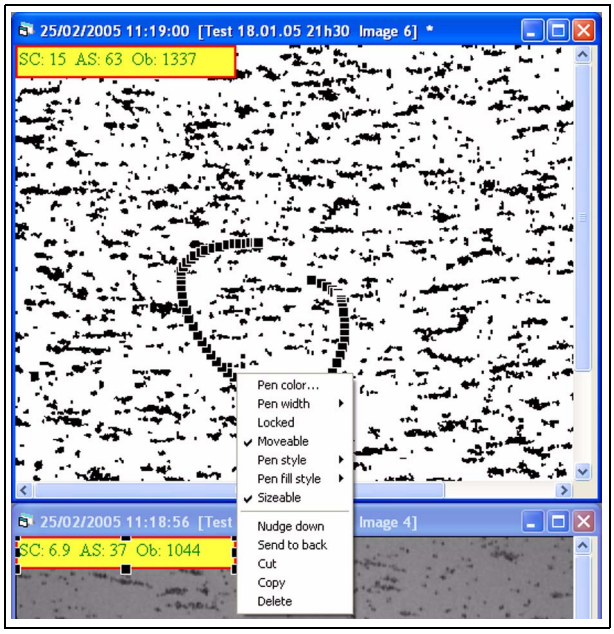


Fig. 4-24: Notations creation

4.2.4 Window menu

To define how many test images (1, 4, 9 or 16 pictures) will be displayed at once.

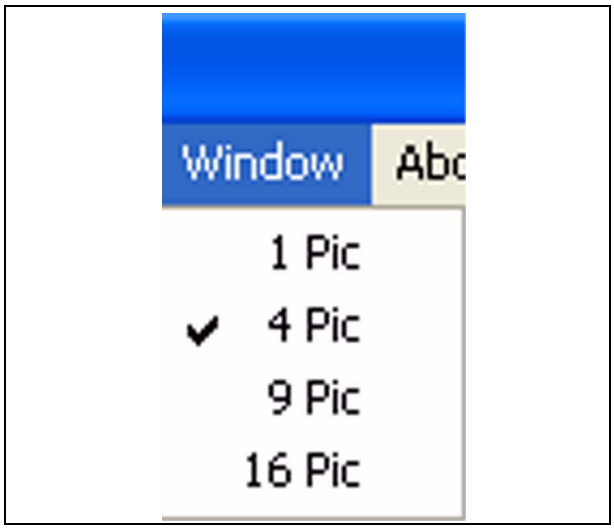


Fig. 4-25: Window menu

4.3 Image Analysis tool bar

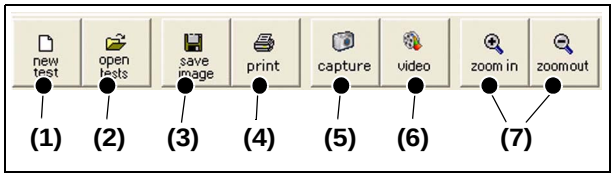


Fig. 4-26: Image Analysis tool bar

(1) New test :
To launch a new test. The ***New Test*** window will be displayed to edit the test description.

See section "4.2.1.1 New test" on page 21.

(2) Open tests :
To open previously saved tests (Tests archive).

See section "4.2.1.3 Tests archive (administrator mode)" on page 23.

(3) Save image :
To save a single captured image outside the regular full test mode. Image can be saved as .tif .jpg and .bmp formats.

***Note:** Only .bmp image can be used to receive image analysis results.*

See section "4.2.1.9 Save image" on page 26.

(4) Print :
To print a selected image. A confirmation is required.

(5) Capture :
To capture an image from the CMM.

(6) Video :
To start the live video mode.

See section "6.5 Live Video" on page 54.

(7) Zoom in / Zoom out :
To zoom in or out the selected image.

4.4 Start form

This screen is displayed when the ***Image Analysis*** software is started. It is only present if the ***Begin With Start Form*** option is selected.

See section "4.2.1.7 Options" on page 25.

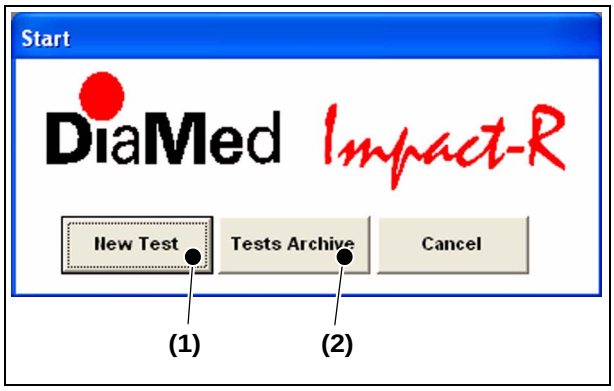


Fig. 4-27: Start form

(1) New Test :
To launch a new test. The ***New Test*** window will be displayed to edit the test description.

See section "4.2.1.1 New test" on page 21.

(2) Tests Archive :
To open previously saved tests (Tests archive).

See section "4.2.1.3 Tests archive (administrator mode)" on page 23.

See section "4.2.1.4 Tests archive (user mode)" on page 24.

See section "6.3 Using the archive" on page 47.

Chapter contents

This chapter describes the start-up and operating check of the Impact-R.

⚠ WARNING

The commissioning of the device must be performed by authorized personnel

CAUTION

Do not use the CMM to carry the device. Before installing the CMM make sure that the camera module is safely secured by gently turning it clockwise.

5.1 Microscope validation and focus adjustment

☞ ***Recommendation:*** *Each device is delivered with a validation well designed to allow the user to periodically (at least once a month) test the microscope focus and the analyzer performance.*

5.1.1 Validation

A. Insert the validation well into the microscope sample tray (1).

B. Switch the Impact-R on using the ***On/Off*** switch located on the back panel.

C. Analyze the validation well as noted in section “6.2.3 Image Analysis” on page 46. To validate a microscope using the device adjusted validation well (A stained blue-purple well) use the "Platelet function" test type.

⚠ **CAUTION**

Do not use the "Validation" test type from the new test window to validate your well." Validation" test type is reserved for validating the device with artificial validation well which will be introduced in the future.

D. Repeat the analysis three times, and calculate the mean SC and AS of the three tests.

Note: *If the mean SC and AS are in the range indicated on the validation well no further adjustment is needed.*

Note: *If the results are out of the range (in particular the AS) you have to check and correct the lens focus.*

See section “5.1.2 Focus adjustment” on page 35.

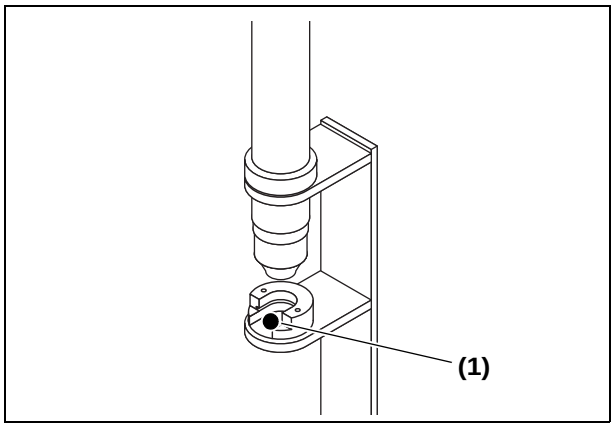


Fig. 5-1: CMM with well

5.1.2 Focus adjustment

A. Select the ***Live Video*** option using the ***Image - Show Video*** command.

See section “6.5 Live Video” on page 54.

B. Rotate the well in the slot clockwise and if the picture is not in focus slightly release the locking ring on the microscope, turn the lower part of the lens until you get a sharp and in-focus picture. Hold the lens in place and tight the locking ring.

Recommendation: *While in video mode, opening the video menu (mouse left click) and choosing the "Misc." tab will show the user an alternating numerical value representing the current focus value. Aiming for the highest possible value, the user can use this function to* ***assist*** *in better focusing the microscope*

C. Analyze the validation well again.

See section “5.1.1 Validation” on page 34.

Recommendation: *If the results are not in the specified range ask for technical service.*

5.2 Light calibration and Auto Correction

To minimize the chance for unreliable readings caused by changes in illumination or accumulation of dirt on the microscope parts, the program was incorporated with two modules.

The first one is the "Light Calibration". This process is triggered either once a day using the system clock or by the user by activating it through the "File" menu.

Light calibration is used to standardize the camera light exposure that can be affected by numerous sources including ambient light, illumination intensity and even variation in the device LED.

The second module is an "Auto-Correction" feature. Since dirt can accumulate either in the manufacturing process or during normal operation on the lenses of the microscope then this feature is used to correct, up to a certain level, the change in results created by the dirt. This module is engaged immediately after the light calibration.

If, for some reason, the camera parameters are not in the accepted range the user is prompted to clean the lens and try again. This procedure repeats 3 times. After the 4th unsuccessful attempt the program will prompt the user to contact technical support.

In any case, after 4 consecutive unsuccessful attempts the program will not allow the user to start a new test.

If the picture is "clean" enough then both modules will complete their operation and will let the user work without further notifications.

The user is highly encouraged to initiate these features every time a suspicion of unreliable readings takes place which can be linked to illumination or microscope contamination.

Both modules operation are almost "transparent" to the regular user and takes no more one Minute to complete.

Note : *first daily calibration sequence might last up to 3.5 minutes. Interrupting this sequence will lead to miscellaneous errors and program shutdown.*

⚠ CAUTION

Altering illumination setting or disregarding light calibration protocol will result in unreliable or abnormal readings.

5.3 ID-Pipetor EP- 3 standard settings for Impact-R (130µl and lowest speed)

In order to avoid platelet activation by aspiration or dispensing, it is important to pipette with these parameters!

A. Press the ***M*** button till the "P" appears on the screen.

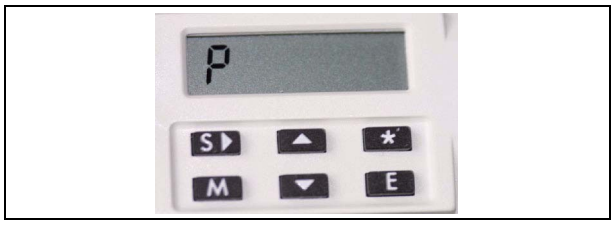


Fig. 5-2: Settings - 1

B. Press the ***E*** button and adjust with the arrow keys to 130µl.

C. Press the ***E*** button again.

Fig. 5-3: Settings - 2

D. Press the ***S*** button and adjust with the arrow keys to 1 (aspiration).

Fig. 5-4: Settings - 3

E. Press the ***E*** button again and adjust with the arrow keys to 1 (dispensing).

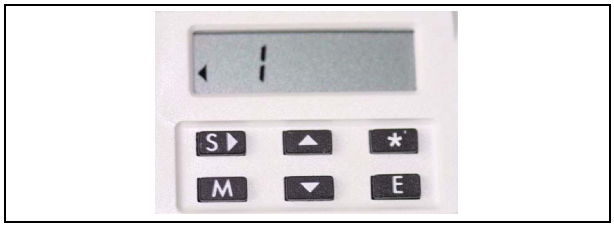


Fig. 5-5: Settings - 4

F. Press the ***E*** button.

G. Start pipetting.

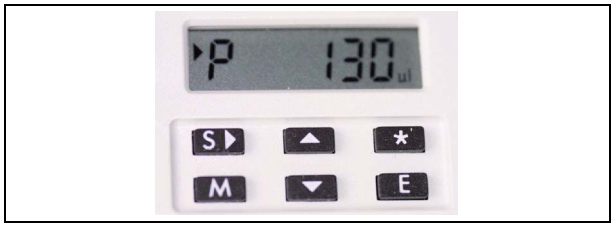


Fig. 5-6: Settings - 5

Chapter contents

This chapter describes all procedures and operations for a normal use of the Impact-R, in order to insure a proper handling and correct results.

⚠ DANGER

INFECTION

There is a risk of infection from skin contact with blood samples. Always wear protective gloves when working, in accordance with laboratory safety regulations.

6.1 Motors programming

6.1.1 Keypad functions

(1) Numkey ***1*** - Initiate Motor **1** (blood test)

(2) Numkey ***2*** - Initiate Motor **2** (blood mix)

(3) Alpha key ***A*** - Back field / Repeat last set motor 1

(4) Alpha key ***B*** - Next field / Repeat last set motor 2

(5) Alpha key ***C*** - End process / Skip stage entry

(6) Alpha key ***D*** - Delete / Clear all entries

(7) Key **#** - Clear all processes / Emergency stop

(8) NumKeys ***1*** to ***0*** - Data entry

(9) Key ***** - Backspace

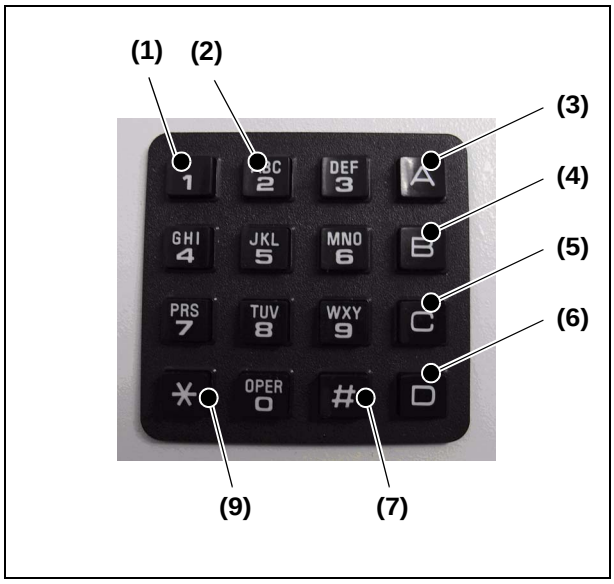


Fig. 6-1: Impact-R keypad

Note: *Each motor has up to 4 programmable cycles (sets).*

6.1.2 Motors initialization

A. Press ***1*** (1) to activate motor 1 (blood test).

B. Press ***2*** (2) to activate motor 2 (blood mix).

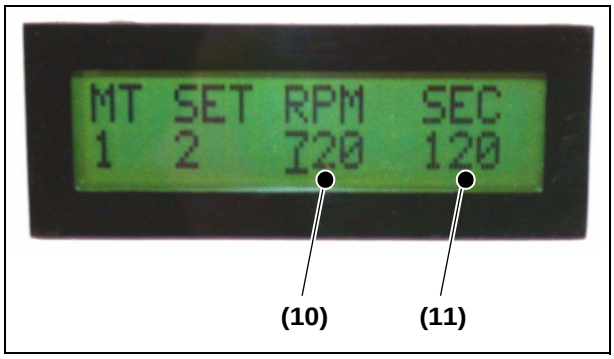


Fig. 6-2: Motors programmation

6.1.3 Motors programming

A. Enter RPM (10) and time (SEC) (11).

B. Press ***B*** (4) to jump to next field.

C. Move to the next set (total of 4 sets available), or press ***B*** (4) to skip.

D. To jump to the end, press ***C*** (5).

Note: *Pressing **C** (5) will not alter previously entered information. You need to clear that manualy.*

E. Enter value (12) for repeat cycles (up to 9).

You can now perform an analysis.

See section "6.2 Perform a test" on page 40.

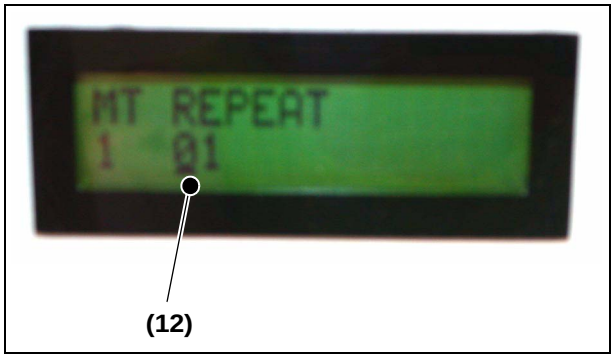


Fig. 6-3: Repeat cycles

6.2 Perform a test

6.2.1 Create a new test

A. From the toolbar, click on ***new test*** icon (1).

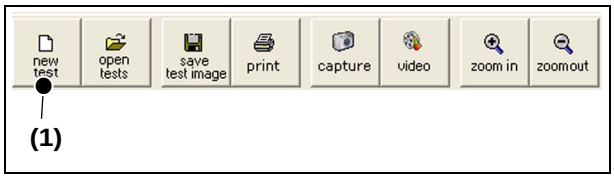


Fig. 6-4: Image Analysis tool bar

Note: *You also can launch the* ***File - New Test*** *command.*

Note: *If no other test type has been chosen, the default type will be «Platelet function».*

See section "4.2.1 File menu" on page 20.

See section "4.3 Image Analysis tool bar" on page 31.

The ***New Test*** window appears.

From this screen, you can now enter the patient information.

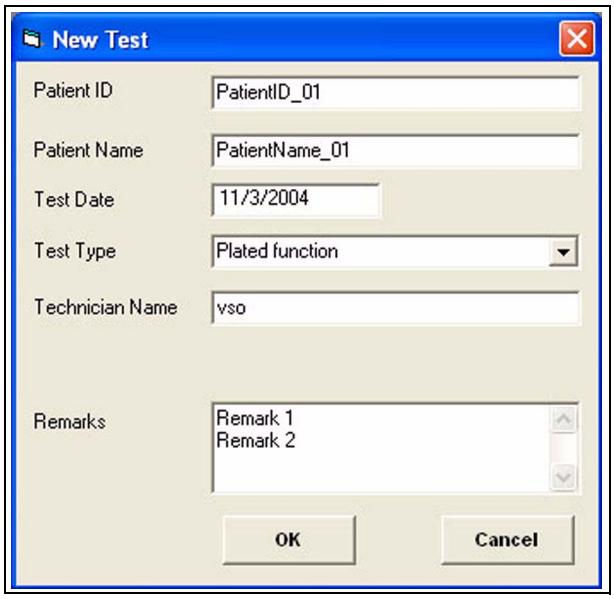


Fig. 6-5: New test window

Note: *The* ***Patient ID*** *and* ***Patient Name*** *fields are mandatory.*

See section "4.2.1.1 New test" on page 21 for more information about the fields.

B. Valid your entries with ***OK*** and process your sample.

See section "6.2.2 Process a blood sample" on page 41.

6.2.2 Process a blood sample

6.2.2.1 Preparation

A. Define the blood test parameters (motor 1). For a regular platelet test, define the following parameters: “set 1” - 0 rpm and 15 seconds (standard pre-incubation period); “set 2” - 720 rpm and 120 seconds; skip sets 3 and 4.

Note: *Your device has left the QC line with the above setting pre-selected into the memory*
SET 1: ***0*** *RPM for* ***15*** *seconds;*
SET 2: ***720*** *RPM for* ***120*** *seconds.*

⚠ CAUTION
Tested blood samples should be collected in BD 3.2% (0.105M) citrate tubes (Light blue cap).

⚠ CAUTION
Blood should be tested not earlier than 45 minutes and not later than 3 hours after collection.

B. Place up to 4 wells into their places.

CAUTION
It is highly recommended for novice users to use only two samples when using the device (preferably, one blood to be tested once with duplicate).

C. Check that the well is sitting flat on the pad.

D. If the well looks tilted, then turn the well slightly until it reaches the flat position.

E. Write the date and running number on each well using a permanent marker (“Bic®” Grip etc’).

Fig. 6-6: 4 Kits on motor 1 pad

F. Place a new cone on each well as shown.

Fig. 6-7: Cones on the wells

G. Assemble the bells over the cones and lift the bell by grabbing it on its sides to assure that the cone is attached to the bell as depicted.

Note: *Pulling the collet by the central pin releases the cone.*

Note: *The bell to the side shows how the cone is secured inside the bell.*

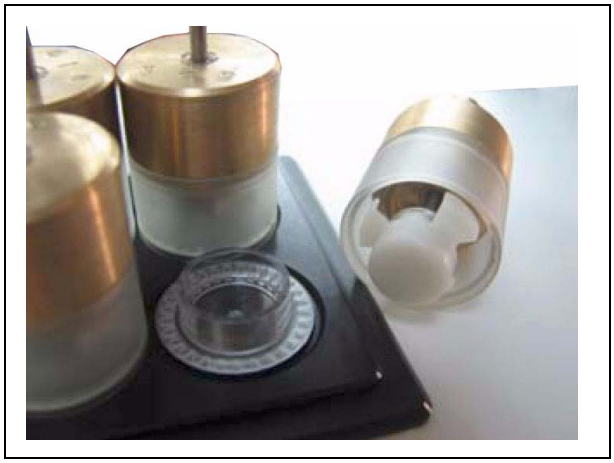


Fig. 6-8: Bells

H. Place the bells with the cones besides the motor 1 pad so you can reach it easily.

I. Attach a tip to your EP-3 Pipetor.

J. Make sure your EP-3 is calibrated to 130 µl and to speed setting 1.

K. Place the blood tubes on the tube rotator (Motor 2)

L. Press the ***B*** key to start a one-minute mix cycle

M. Verify that the tubes are rotating at 10 RPM for 1 minute.

N. When the cycle is complete immediately open the blood tubes.

⚠ CAUTION

If the tube is used for the first time after the blood was taken or if the tube was not touched for more than 10 minutes then place the blood tube in the tube rotator and let it rotate at 10 RPM for 1 minute (regular rotation)

Fig. 6-9: Tube rotator

O. Insert the tip into the first test tube, about half way into the blood, and press the button to collect the blood into the tip.

⚠ CAUTION

Picking the blood from a different level might cause unreliable results due to the tendency of the red blood cells to sediment to the bottom of the tube.

6.2.2.2 Pipeting

A. Insert the tip into the first well and drain it by pressing the Pipetor button again.

B. Release the blood over the center of the well when the tip edge is approximately at the height of the well wall.

⚠ CAUTION

Ensure that the tip does not touch the well bottom.

⚠ CAUTION

It is imperative that, at the end of the blood release phase, the blood drop formed in the middle of the well does not contain any air bubble. Such air bubbles can damage the formation of platelet aggregates on the well surface thus rendering the sample unreliable.

Fig. 6-10: Pipeting

C. After releasing the blood into the well, take the tip out.

D. Not more than 4-5 seconds thereafter, place the bell housing on the well to fully spread the blood over the well surface.

E. Dispose of the Pipetor used tip in a biological waste container.

F. **Without delay,** continue with the other tubes and repeat the sampling process as described above for the remaining blood test tubes.

⚠ CAUTION

You must complete the blood sampling process for the rest of the tubes in not more than 45 seconds.

Fig. 6-11: Placing the bell housing

6.2.2.3 Rotation and post-rotation actions

A. Push the “A” button to start the rotation procedure according to the pre-defined parameters.

B. After the rotation process is complete, take out the Bell housing with the cone still attached to the collet.

C. Pull up the collet central pin to release the cone from the collet above a biological waste container.

Fig. 6-12: Taking out the cone

D. Using a Pasture Pipette with a DiaMed tip attached to it, dispose off the excess blood remaining in the well by washing the well with regular tap water or saline solution.

☞ ***Recommendation:*** *Hold the well gently with your fingers.*

⚠ WARNING

In any case, do not touch the well’s inner surfaces.

Fig. 6-13: Disposing of the excess blood

E. Wash the well by directing a gentle water stream from the Pipette on the inner SIDE wall of the well.

☞ ***Recommendation:*** *The water should flow in a circular motion inside the well with the blood/water mixture flowing out into the biological waste container. When washing the well, make sure the water pressure that comes out from the Pasture Pipette is gentle enough. An aggressive stream might wash out the aggregates from the well surface.*

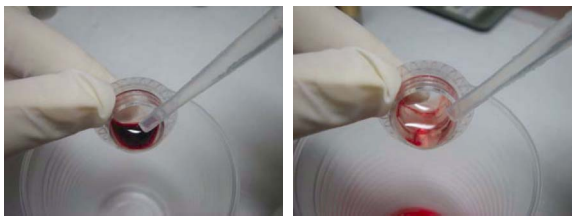


Fig. 6-14: Washing the well

F. Continue washing until the well looks clear and no blood residue are apparent.

G. Dispose of the excess water by using a Pipette with a fine tip, sucking the water from the well wall/ surface joining area.

ⓘ ***Note:*** *Different blood types will require either prolongated or shorter washing cycles, depending on the blood viscosity.*

Fig. 6-15: Washing the well

H. using a Pasture Pipette add May Grunwald stain solution to the washed well.

⇩ The stain should fill at least half of the well.

I. Wait for about 1 minute and completely suck the stain out using a Pipette with a fine tip.

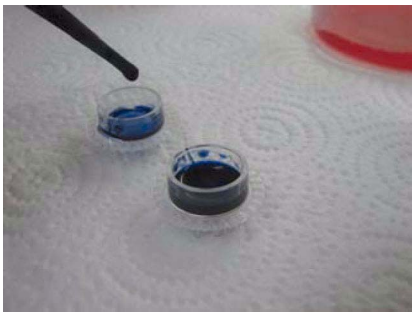


Fig. 6-16: Adding stain solution

☞ ***Recommendation:*** *Make sure that the Pipette does not touch the inspection area at the bottom of the well.*

J. Leave the well to dry for about 1 minute and until there are no visible residues of liquid on the surface.

☞ ***Recommendation:*** *Wait at least 3-4 minutes in a normal temperature and humidity environment before attempting to read the well.*

K. Read the stained well as described in chapter “6.2.3 Image Analysis” on page 46.

6.2.3 Image Analysis

A. Insert the stained wells in the CMM sample tray.

B. Capture the first image by clicking on the ***Capture*** (5) button.

C. Rotate the well until the tray stops at the first notch («click» sound) to capture the second image. Repeat this step another 5 times turning the tray clockwise until a total of 7 images are captures. After completing the capture of 7 images, the Impact-R automatically computes and presents a report with the computed values on the screen.

D. Perform the ***Image - Analyze Saved Images*** command.

The program analyzes the captured images, purging the 4 least readable and calculating the average of the remaining 3.

See section "4.2.2.1 «Impact-R Test results» form" on page 28.

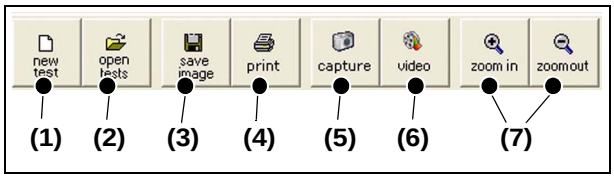


Fig. 6-17: Image Analysis tool bar

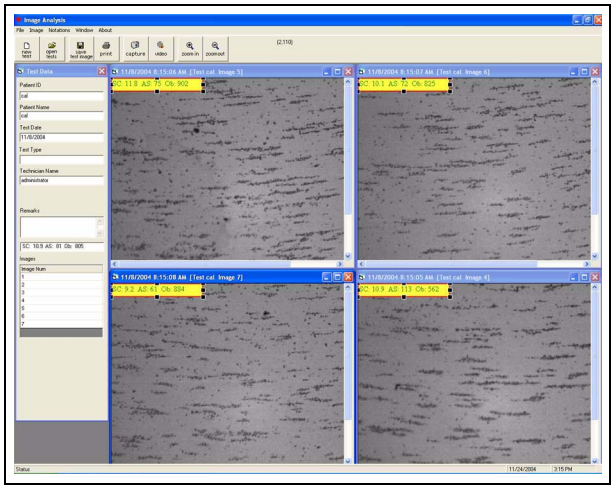


Fig. 6-18: Image Analysis pictures

6.3 Using the archive

A. From the toolbar, click on ***open tests*** icon (1).

Fig. 6-19: Image Analysis tool bar

Note: *You also can launch the* ***File - Open Test*** *command.*

See section "4.2.1 File menu" on page 20.

See section "4.3 Image Analysis tool bar" on page 31.

The ***Tests Archive*** window appears.

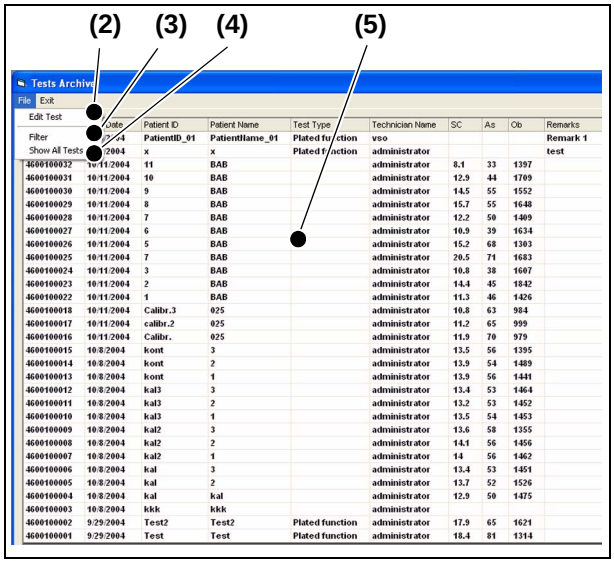


Fig. 6-20: Tests archive

6.3.1 General

Each test has been given a unique number. This number is based upon the system activation code and a test serial number. As mentioned, this number is unique to a test and cannot be duplicated and it is used also to better identify a test while exporting or importing tests from another system.

Displaying the archive, the current user can change the display order by clicking on the column name box (bars) located on the upper side of each column. This will change the order of TestID (Ascending/Descending), Test Date (Ascending/ Descending), Patient ID (By first letter or number Ascending/Descending), Test type (By first letter), technician name (By first letter), SC/AS/Ob (By numbers Ascending/Descending).

6.3.2 Archive management

Note: *To better demonstrate the system capability, the administrator access will be explained first and differences from regular user access will follow.*

Tests are divided with 3 visual cues to distinct them apart :

- regular letters - locked tests. No further analysis is possible;
- bold letters - unlocked tests. Altering the test is still possible;
- light blue background - imported tests (Regular or highlighted letters also apply).

See section "4.2.1.3 Tests archive (administrator mode)" on page 23 for more information about the commands for an administrator.

See section "4.2.1.4 Tests archive (user mode)" on page 24 for more information about the commands for a user.

6.3.3 Searching an existing test

A. Perform the ***File - Filter*** command (3).

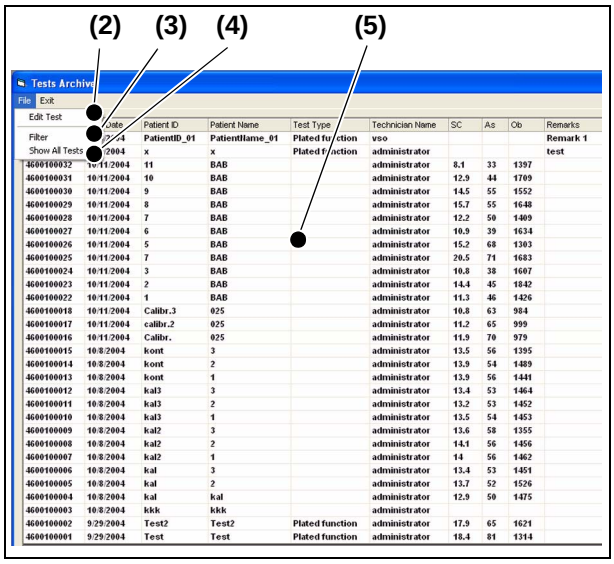


Fig. 6-21: Tests archive

A window is displayed to filter the saved tests using a criteria.

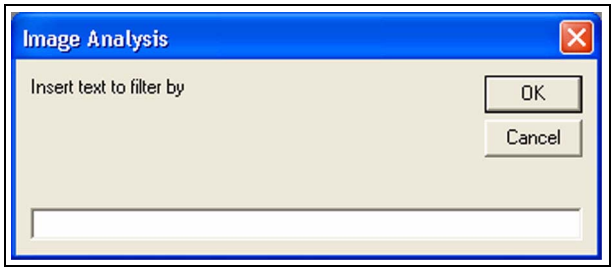


Fig. 6-22: Test archive filter

B. Type the searched criteria in the field.

C. Click on ***OK***.

Note: *Perform the* ***File - Show All Tests*** *command (4) to disactive the filter and display the complete archive again.*

6.3.4 Opening an existing test

A. Double-click on the desired test (5).

The test is loaded.

Note: *The corresponding images are loaded respecting the* ***Automatic loading of test images*** *option.*

See section "4.2.1.7 Options" on page 25.

6.3.5 Editing an existing test

A. Click on the desired test (5) to select it.

B. Perform the ***File - Edit Test*** command (2).

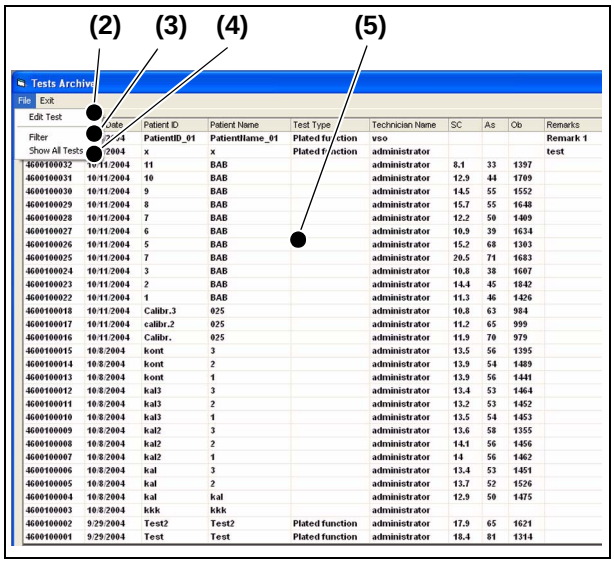


Fig. 6-23: Tests archive

The ***Edit Test*** window appears.

C. Modify the information data you want to change.

D. Click on ***OK***.

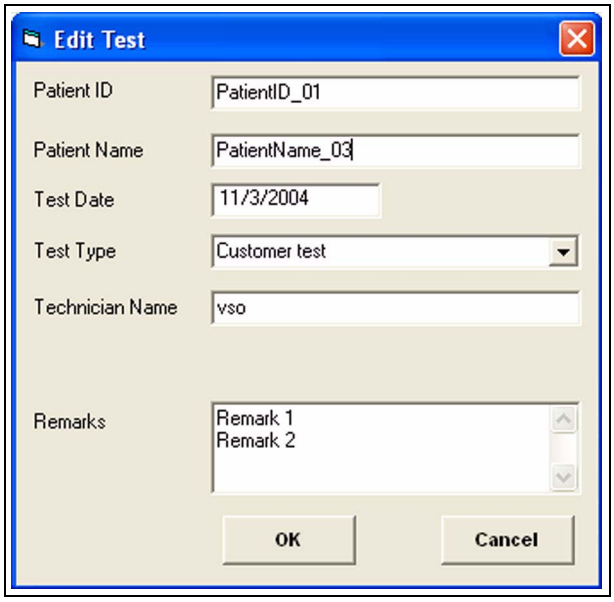


Fig. 6-24: Test archive edit

6.3.6 Deleting an existing test

A. Open an existing test.

See section "6.3.4 Opening an existing test" on page 49

B. Perform the ***File - Delete Test*** command.

See section "4.2.1 File menu" on page 20

6.4 Password management

6.4.1 Administrator

The "Administrator" (most probably the person in-charge of the laboratory) is the person who is managing the system access (assigning users) and can also further manipulate, duplicate and alter a test or a single image (Thus affecting results).

While accessing the system via a regular user logon the only ability of the user is to change his / her own password.

See section "6.4.2 Modify the password for the current operator" on page 52

The "User" level allow its user to perform a full test, enter patient information, analyze tests, manage the archive and produce reports.

Accessing the system via the "Administrator" logon will give the administrator the ability to manage other users access and passwords. The administrator menu is presented in Fig. 6-25.

Fig. 6-25: Password management

Recommendation: *Always log on to the system using your assigned username and password. Undoing so might lead to a false information in the test results.*

6.4.2 Modify the password for the current operator

The command ***File - Users*** permits to the administrator to manage the operators and their passwords.

See section "6.4.1 Administrator" on page 51 and Service Manual for more information.

Furthermore, it permits to the current operator to modify its password. To do this, follow the procedure below :

A. Perform the ***File - Users*** command.

See section "4.2.1 File menu" on page 20

The ***Users*** window appears.

B. Click on the ***Set password for 'current user'*** button (1).

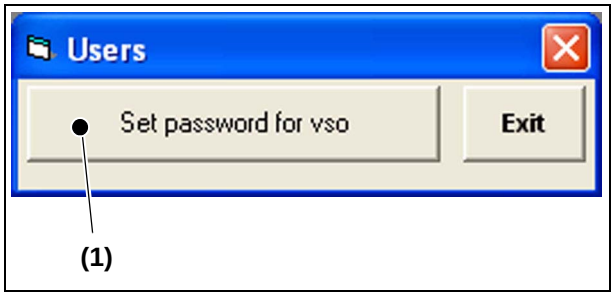


Fig. 6-26: Modify the password of the user, first step

The ***Set Password*** window appears.

C. Type your password in the ***Current Password*** field (3).

D. Type your new password in the ***New Password*** field (4).

E. Type your new password again in the ***Retype Password*** field (5).

F. Confirm your modification with ***OK*** (2).

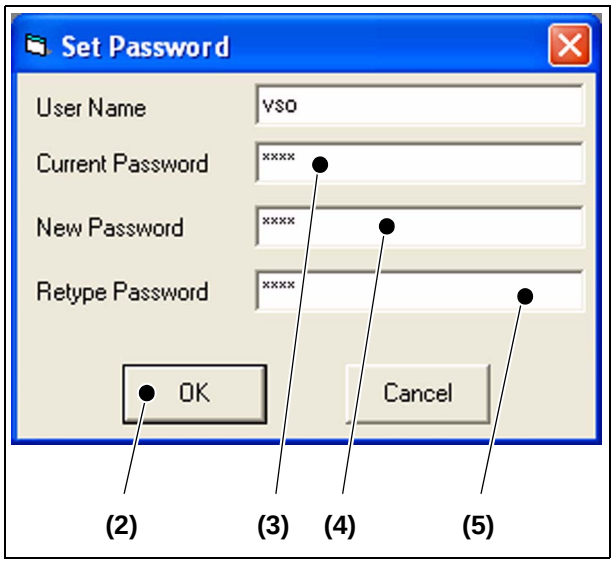


Fig. 6-27: Modify the password of the user, 2nd step

Note: *The password must comprise at least 4 characters. Otherwise, the error message beside appears.*

Recommendation: *Always log on to the system using your assigned username and password. Undoing so might lead to a false information in the test results.*

Fig. 6-28: Incorrect password

6.5 Live Video

The live video mode enables the user to receive a full image of a sample section with quick rotation to bypass the regular still sampling.

While in video mode, there is no sample analysis and no picture reading is made, the user can make a better assessment of the sample in hand. It can also be used to adjust CMM focus, when required.

See section "5.1.2 Focus adjustment" on page 35.

Live video mode is activated by using the same procedure as preparing a sample for analysis but without activating the ***Image Analysis*** function.

A. Place the sample well under the CMM. Make sure the sample sits firmly in the CMM sample tray.

B. Activate the live video mode by clicking on the ***Video*** icon (6) or by launching the ***Image - Show Video*** command.

See section "4.2.2 Image menu" on page 27.

⇨ A window will appear showing a live video image of the sample in the CMM sample tray. Rotate the well as needed to see various areas of the well.

Note: *By pressing the mouse left button the user can open a menu, which will allow a partial manipulation of the picture.*

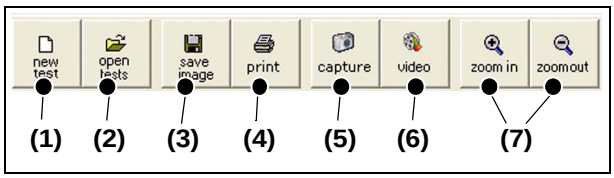


Fig. 6-29: Image Analysis tool bar

6.5.1 Video controls

(1) Exposure :
To modify the USB camera shutter settings.

(2) Presets :
To modify the settings for creating - saving picture according to user preferences.

(3) Resolution :
The user can switch between regular view or full screen by changing the format.

Note: *Changing resolution may affect system performance (slows down).*

(4) Color Depth :
Changes picture colour 8bit gray - 24 bit color.

(5) Gain :
Picture manipulation using light enhancement.

Note: *Changing picture settings in live video WILL NOT change the pre-defined settings for image analysis.*

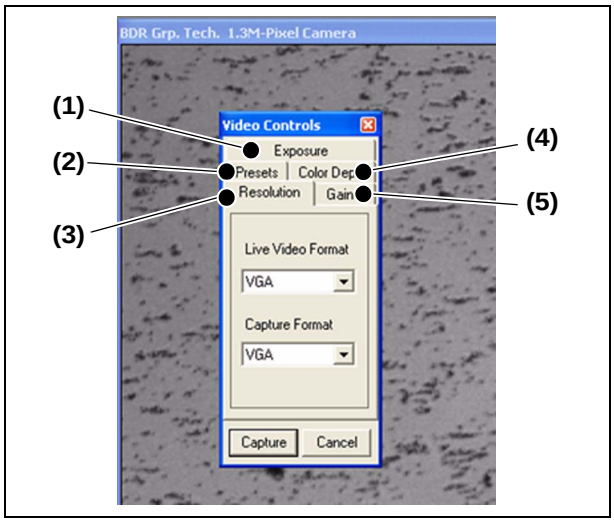


Fig. 6-30: Image Analysis, video controls

6.6 Tubes mixer

6.6.1 Setting the tube rotator

A. Press ***2*** (2) to activate motor 2 (blood mix).

B. Type <10> (rotation rate in RPM).

C. Press ***B*** (4) to go to the next field.

D. Type <60> (time in SEC).

E. Press ***C*** (5) twice.

Note: *Your device has left the QC line with the above setting pre-selected into the memory (10 RPM for 60 seconds).*

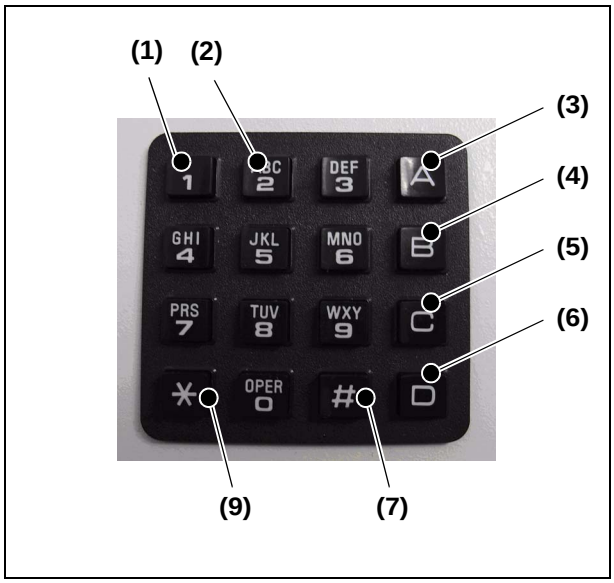


Fig. 6-31: Impact-R keypad

6.6.2 Operation

A. Insert tubes, with stoppers (10), into the tube holder (11).

B. Press ***B*** (4) (Repeat last set motor 2).

⇨ The motor will run on the pre-selected parameters).

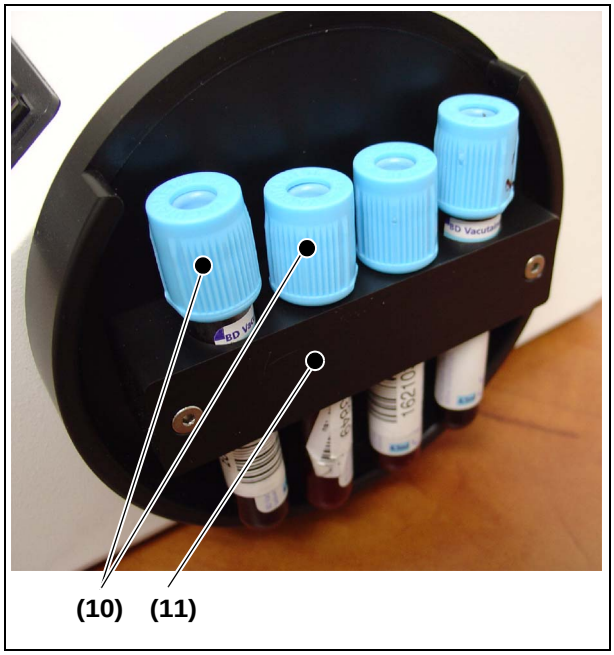


Fig. 6-32: Motor 2 with 4 PT Tubs

7.1 Publications

Note: *All studies cited bellow were done using a kit consisted of a polystyrene 4-well plate (Nunc, Roskilde, Denmark) and a special Teflon cone designed to fit the well.*

7.1.1 Review article

(1) D. Varon, N. Savion.
Cone and Plate(let) Analyzer.
In: Platelets (A.D. Michelson, ed.), Academic Press, p. 337-345, 2002.

7.1.2 Original articles

(1) Y. Hagaya, J. Lahav, A. Levanon, D. Varon, A. Brill, A. Panet.
Molecular characterization of an human monoclonal antibody that interacts with a sulfated tyrosine-containing epitope of the GPIb receptor and inhibits platelet functions.
Molecular Immunology 43:443–453, 2006.

(2) F. Hermann, L.E. Spieker, F. Ruschitzka, I. Sudano, M. Hermann, C. Binggeli, T.F. Lüscher, W. Riesen, G. Noll, R. Corti.
Dark chocolate improves endothelial and platelet function.
Heart 92;119-120, 2006.

(3) Y. Levy, B. Shenkman, I. Tamarin, R. Pauzner, Y. Shoenfeld, P. Langevirtz, N. Savion, D. Varon.
Increased platelet deposition on extracellular matrix under flow conditions in patients with antiphospholipid syndrome who experience thrombotic events.
Arthritis & Rheum., 52:4011-4017, 2005.

(4) G. Spectre, A. Brill, A. Gural, B. Shenkman, N. Turetzky, N. Savion, D. Varon.
A new point-of-care method for monitoring anti-platelet therapy: application of the Cone and Plate(let) Analyzer.
Platelets, 16: 293-299, 2005.

(5) EIB Peerschke, RT Silver, B Weksler, SE Grigg, N Savion, D Varon.
Ex vivo evaluation of erythrocytosis-enhanced platelet thrombus formation using the cone and plate(let) analyzer: effect of platelet antagonists.
Bri.t J. Haematol, 127, 195–203, 2004.

(6) R. Gerrah, E. Snir, A. Brill, D. Varon.
Platelet Function Changes as Monitored by Cone and Plate(let) Analyzer during Beating Heart Surgery.
Heart Surgery Forum 7 (3): E191-E195, 2004.

(7) Spieker LE, Ruschitzka F, Badimon JJ, Noll G, Corti R.
Shear stress-dependent platelet function after LDL cholesterol apheresis.
Thromb. Res. 113 (6): 395-398, 2004

(8) S. Matetzky, B. Shenkman, V. Guetta, M. Shechter, R. Bienart, I. Goldenberg, I. Novikov, H. Pres, N. Savion, D. Varon, H. Hod.
Clopidogrel Resistance Is Associated With Increased Risk of Recurrent Atherothrombotic Events in Patients With Acute Myocardial Infarction.
Circulation 109:3171-3175, 2004.

(9) S. Wolberg, Z. Hong Meng, D.M. Monroe III, M. Hoffman.
A Systematic Evaluation of the Effect of Temperature on Coagulation Enzyme Activity and Platelet Function.
J Trauma. 56:1221–1228, 2004.

(10) B. Shenkman, A. Brill, G. Brill, O. Lider, N. Savion, D. Varon.
Differential response of platelets to chemokines: RANTES non-competitively inhibits stimulatory effect of SDF-1α
J. Thromb. Haemost., 2:154-160, 2004.

(11) H. Hu, D. Varon, P. Hjemdahl, N. Savion, S. Schulman, N. Li.
Platelet-leukocyte aggregation under shear stress: Differential involvement of selectins and integrins.
Thromb. Haemost., 90: 697-687, 2003.

(12) K. Jurk, K. J. Clemetson, P. G. de Groot, M. F. Brodde, M. Steiner, N. Savion, D. Varon, J. J. Sixma, H. Van Aken, B. E. Kehrel.
Thrombospondin-1 mediates platelet adhesion at high shear via glycoprotein Ib (GPIb): an alternative/backup mechanism to von Willebrand factor.
FASEB J. 17: U254-U271, 2003.

(13) B. Shenkman, A. Inbal, I. Tamarin, A. Lubetsky, N. Savion, D. Varon.
Diagnosis of thrombotic thrombocytopenic purpura based on modulation by patient plasma of normal platelet adhesion under flow condition.
Brit. J. Haematol. 120: 597-604, 2003.

(14) R. Dardik, N. Savion, N. Gal, D. Varon.
Flow conditions modulate homocysteine induced changes in the expression of endothelial cell genes associated with cell-cell interaction and cytoskeletal rearrangement.
Thromb. Haemost. 88: 1047-1053, 2002.

(15) X.K. Wang, R.T. Dorsam, A. Lauver, H. Wang, F.A. Barbera, S. Gibbs, D. Varon, N. Savion, S.M. Friedman, G.Z. Feuerstein.
Comparative analysis of various platelet glycoprotein IIb/IIIa antagonists on shear-induced platelet activation and adhesion.
J. Pharmacol. Exp. Ther. 303: 1114-1120, 2002.

(16) B. Shenkman, D. Varon, I. Tamarin, R. Dardik, M. Peisachov, N. Savion, E. Rubinstein.
Role of agr (RNAIII) in Staphylococcus aureus adherence to fibrinogen, fibronectin, platelets and endothelial cells under static and flow conditions.
J. Med. Microbiol. 51: 747-754, 2002.

(17) C. Fallgren, A. Ljungh, B. Shenkman, D. Varon, N. Savion.
Venous shear stress enhances platelet mediated staphylococcal adhesion to artificial and damaged biological surfaces.
Biomaterials 23: 4581-4589, 2002.

(18) Y. Finkelstein, B. Shenkman, L. Sirota, T.H. Vishne, R. Dardik, D. Varon, N. Linder.
Whole blood platelet deposition on extracellular matrix under flow conditions in preterm neonatal sepsis.
Eur J Pediatr 161: 270-274, 2002.

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Deposition of whole blood platelets on extracellular matrix under flow conditions in preterm infants.
Arch. Dis. Child. 86: F127-F130, 2002.

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Administration of abciximab to patients receiving tirofiban or eptifibatide: Effect on platelet function.
J. Am. Coll. Cardio. 37: 847-855, 2001.

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Testing platelet activation with a shear-dependent platelet function test versus aggregation-based tests - Relevance for monitoring long-term glycoprotein IIb/IIIa inhibition.
Circulation 103: 1488-1491, 2001.

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Adherence properties of Staphylococcus aureus under static and flow conditions: Roles of agr and sar loci, platelets, and plasma ligands.
Infec. Immun. 69: 4473-4478, 2001.

(23) B. Shenkman, J. Schneiderman, I. Tamarin, S. Kotev-Emeth, N. Savion, D. Varon.
Testing the effect of GPIIb-IIIa antagonist in patients undergoing carotid stenting: Correlation between standard aggregometry, flow cytometry and the cone and plate(let) analyzer (CPA) methods.
Thromb. Res. 102: 311-317, 2001.

(24) N. Savion, B. Shenkman, I. Tamarin, R. Dardik, D. Varon.
Transient adhesion refractoriness of platelets under flow conditions: The role of partial activation and microaggregate formation in controlling thrombus expansion.
Brit. J. Haematol. 112: 1055-1061, 2001.

(25) B. Shenkman, N. Savion, R. Dardik, I. Tamarin, D. Varon.
Testing of platelet deposition on polystyrene surface under flow conditions by the cone and plate(let) analyzer: Role of platelet activation, fibrinogen and von Willebrand factor.
Thromb. Res. 99: 353-361, 2000.

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Blood irradiation by He-Ne laser induces a decrease in platelet responses to physiological agonists and an increase in platelet cyclic GMP.
Platelets 11: 87-93, 2000.

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Staphylococcus aureus adherence to thrombin-treated endothelial cells is mediated by fibrinogen but not by platelets.
J. Lab. Clin. Med. 135: 43-51, 2000.

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Homocysteine and oxidized low density lipoprotein enhance platelet adhesion to endothelial cells under flow conditions: Distinct mechanisms of thrombogenic modulation.
Thromb. Haemost. 83: 338-344, 2000.

(29) C. Yosefy, J.R. Viskoper, A. Laszt, R. Priluk, E. Guita, D. Varon, Z. Illan, E.M. Berry, N. Savion, Y. Adan, G. Lugassy, R. Schneider, A. Raz.
The effect of fish oil on hypertension, plasma lipids and hemostasis in hypertensive, obese, dyslipidemic patients with and without diabetes mellitus.
Prostaglandins Leukotrienes and Essential Fatty Acids 61: 83-87, 1999.

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Increased neonatal platelet deposition on subendothelium under flow conditions: The role of plasma von Willebrand factor.
Pediatr. Res. 45: 270-275, 1999.

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Activated platelets mediate Staphylococcus aureus deposition on subendothelial extracellular matrix: the possibe role of glycoprotein Ib.
Platelets 10: 36-44, 1999.

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Shear-induced platelet adhesion and aggregation on subendothelium are increased in diabetic patients.
Thromb. Res. 90: 181-190,1998.

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Brit. J. Cancer 77: 2069-2075, 1998.

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Cone and plate-let Analyzer (CPA): a new tool for the prediction of bleeding among thrombocytopenic patients.
Brit. J. Haematol. 101: 225-259, 1998.

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7.2 Feedback

Note: *Your feedback is welcome !*

In the process of developing new technologies there is always room for improvements.

If you note any omisions or unsatisfying information or you just have a suggetion for upgrading this system, please let us know…

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