Leica LMD6500
Leica LMD7000

Laser Microdissection Systems

Living up to Life

Leica
MICROSYSTEMS

Ultimate Perfection!

Laser microdissection (LMD) is the ultimate tool for perfection. LMD makes it possible to obtain homogenous, ultrapure samples from heterogenous starting material. A researcher can selectively and routinely analyze regions of interest down to single cells to obtain results that are reproducible, and specific.

Laser microdissection uses a microscope to visualize individual cells or cell clusters. Regions of interest are selected by software, excised from the surrounding tissue by a laser, and collected by gravity into specialized devices for analysis.

There has been enormous progress in the development of laser microdissection instrumentation in recent years. The driving force in this area is the development of laser microdissection systems by Leica Microsystems.

At the forefront of laser microdissection technology,
only the Leica LMD6500 and Leica LMD7000 offer:

- Laser beam movement via optics – fast and precise cuts
- Specimen collection by gravity – contact- and contamination-free
- Dedicated objectives for LMD – highest possible laser power
- Adjustable laser – for thick, thin, soft, and hard tissue

Specimen Collection by Gravity

Benefits:

- Contact- and contamination-free collection
- Fast and reliable specimen collection
- Dissect all specimen shapes and sizes
- Pool unlimited amounts of specimen
- Use standard consumables

The three slide holder allows simultaneous work on up to three slides. Several holders for different applications are available.

Convenient handling of the collectors due to the automatically movable tray. The tray takes customized devices as well.

LMD uses a UV laser to isolate microscopic regions from samples. Leica Microsystems applies the most gentle technique for specimen collection – gravity.

Contact- and contamination-free
Gravity is the most sensible method of specimen collection. Once the region of interest is excised, it gently falls into the collection vessel. No additional steps or complicated methods are necessary. Most importantly, the specimens are not touched. This makes specimen collection by gravity a contamination-free procedure.

Transfer dissectates of any size or shape
Gravity is the ideal tool to collect dissectates of any size or shape – round and compact, or long and thin – it simply falls into the collection device. Large areas up to several mm^2 are excised in one step. No subdivision into smaller transportable sections is required. This ensures the complete recovery of the sample without the loss of tissue due to additional cut lines.

Collect directly into reaction buffer
Collection by gravity is the fastest way to progress from tissue section to reaction buffer. The collection vessel may contain medium or buffer. Additionally, unlimited amounts of specimen can be pooled.

Most comprehensive method
Leica Microsystems offers a wide range of specially designed membrane systems for the best specimen preparations from tissue sections, over cell cultures, bacteria suspensions, plant materials, and many more. Samples and membranes are simultaneously cut by the laser. Specimen preparation has to be adapted to the experimental needs, and with gravity as the motor for collection, the indispensable flexibility is provided.

Laser Beam Movement via Optics

When a high-energy laser pulse hits the sample a fast reaction limited to the focus of the laser light called “cold ablation” occurs. Surrounding tissue is not impaired or heated.

Only Leica Microsystems uses high-precision optics to direct the laser beam along the desired cutting line.

Highest precision
Precision is the prerequisite to obtain homogenous material for downstream analysis and reliable results. The unique laser beam movement of the Leica LMD7000 and LMD6500 is controlled by patented* high precision optics, while the microscope stage and the sample are stationary. The cutting precision is unmatched and far superior to using a fixed laser beam and moving the sample.

Maximal speed
Quick and reliable material collection for downstream analysis is of highest importance. By moving only small optical parts during the cutting process, Leica Microsystems’ approach allows precise cutting at high magnifications, and fast cutting speeds at low magnifications. This technique ensures rapid capture, minimizing degradation of the specimen.

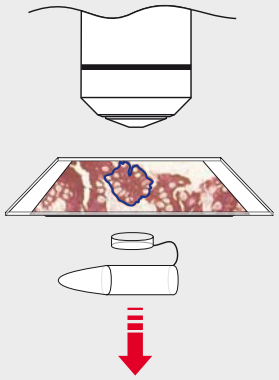
Real-time laser cutting
A smart software tool allows live, on-the-fly dissections. The unique function is especially beneficial for specimens that are difficult to cut. This tool can also be used for real-time ablation of tissue. An important effect of laser beam movement is the ability to conveniently document the dissection with movies. The image remains fixed and only the laser beam moves – just the way our eyes are used to.

* Patented EP 1276586 B1, US 7035004 B2, JP 3996773 B2, TW 486566 B

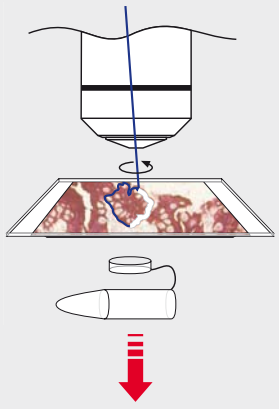
Benefits:

- Highest possible precision
- Maximal speed
- Real-time laser cutting
- Convenient movie documentation
- Maintenance free

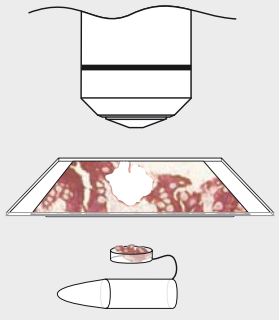
Step 1: Define region of interest

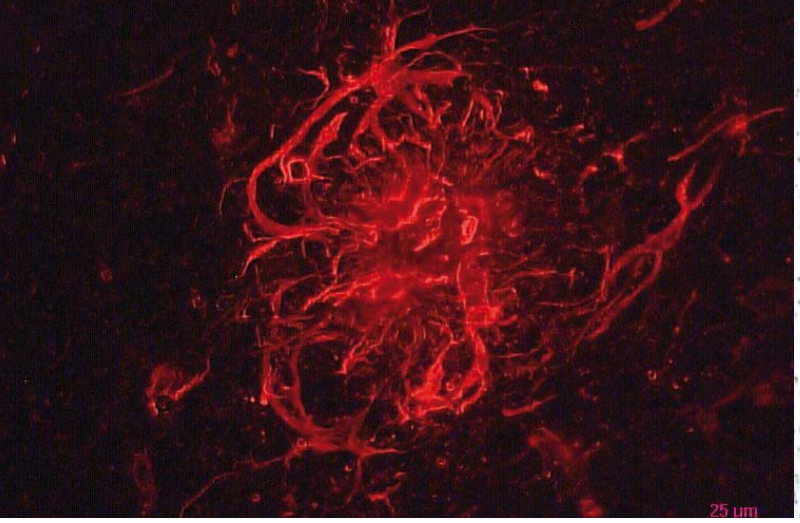


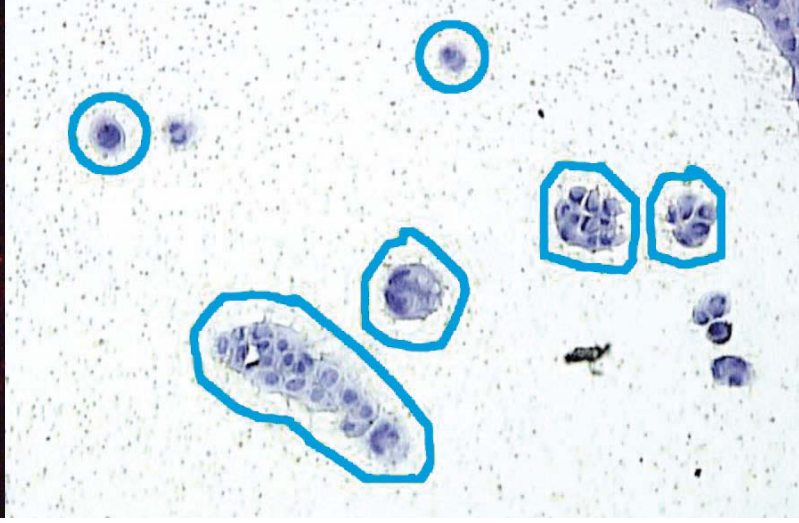
Step 2: Laser beam steered by optics along the cut line

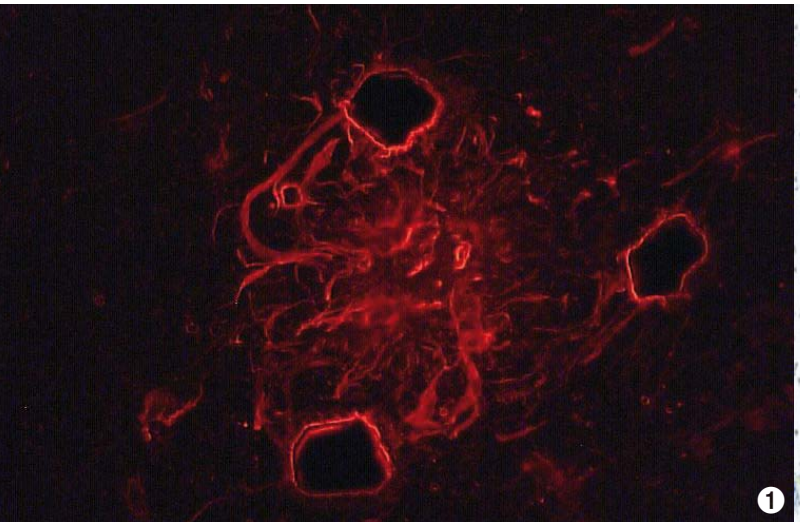


Step 3: Specimen collection by gravity




25 µm

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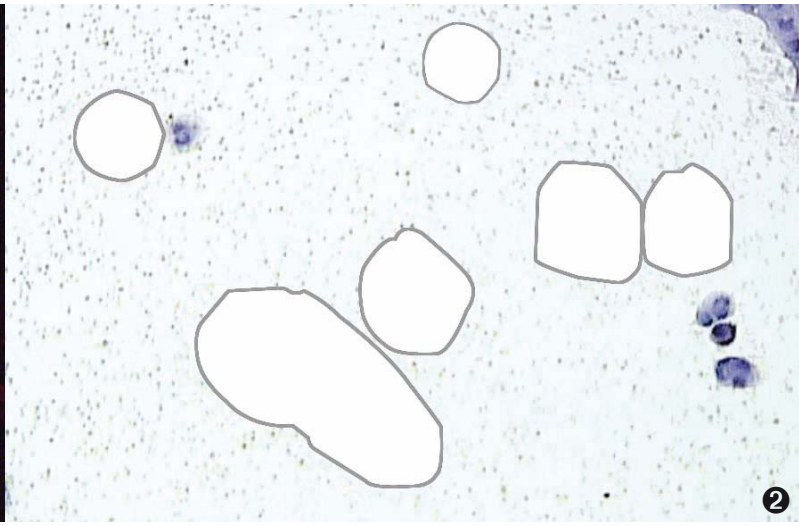
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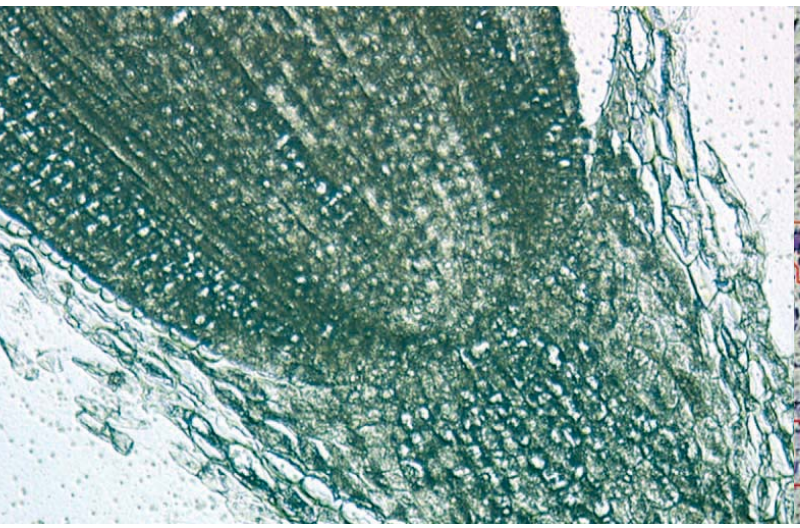

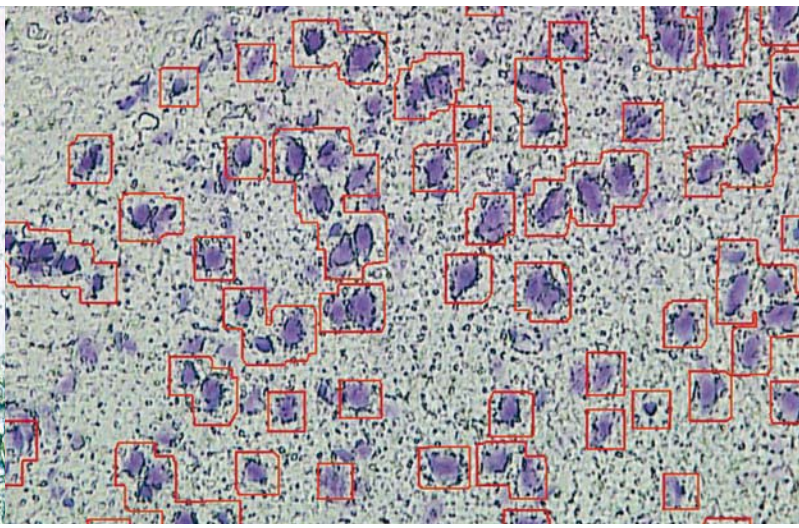

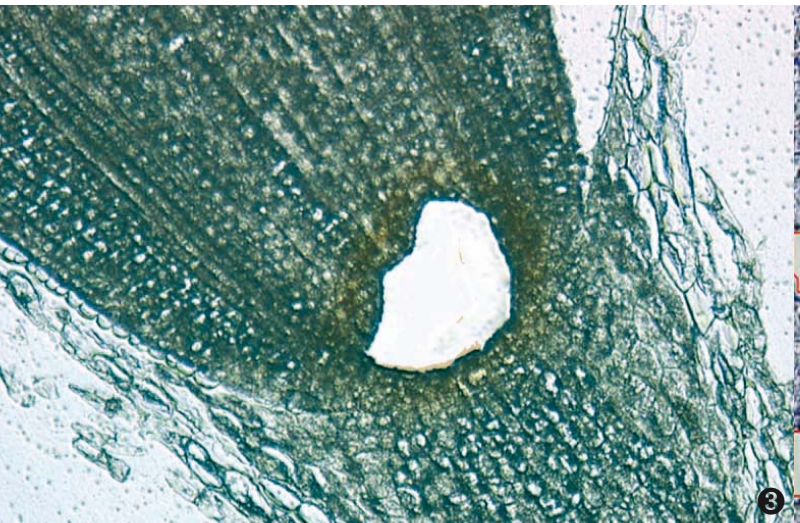
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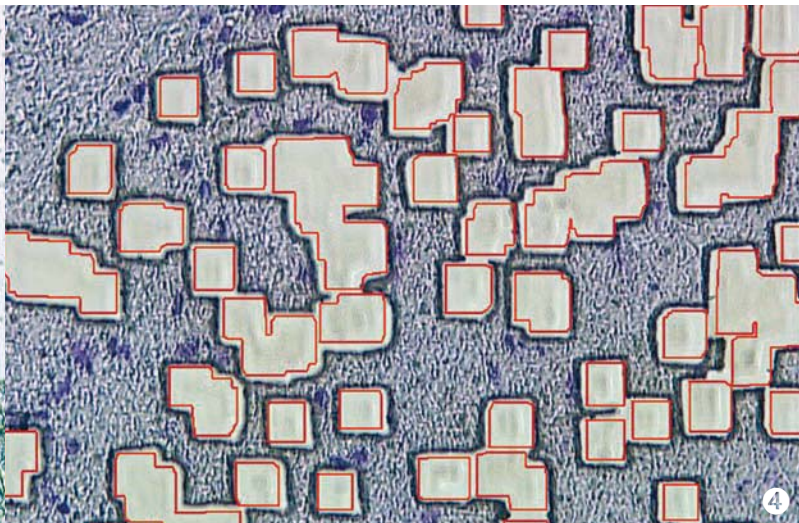

4

Leading-edge Laser Technology

The laser is the core part of a laser microdissection system. The two key features of a laser are pulse energy and pulse frequency. The combination of these features within a LMD system was realized by Leica Microsystems for the first time.

Adapt the laser to the specimen
The Leica LMD7000 allows the control of laser pulse energy and frequency. Adjust the laser according to the specimen and make narrow, powerful, and fast cuts within a single system. Leica Microsystems' LMD systems provide the flexibility to align the UV offset with respect to the focus of the visible light for the most precise cutting performance, for thick or thin samples, and ablation.

Control the thickness of the cutting line
The aperture control enables the adjustment of the width of the cutting line. Combined with the high repetition rate, the narrowest cuts are possible. The laser aperture settings can be stored individually for each objective.

Longlife, solid state laser
Leica Microsystems uses diode-pumped, solid state lasers. These state-of-the-art lasers are maintenance free and reliable, ensuring long lifetimes.

Choose the laser according to your needs: the Leica LMD6500 offers a pulse energy of 50 µJ and a fixed repetition rate, whereas the Leica LMD7000 provides a pulse energy of up to 120 µJ and the unique flexibility to adjust power and frequency.

Please visit www.leica-microsystems.com/lmd
for more images and movies, application letters, etc.

Benefits:

- Control the pulse energy and frequency (for Leica LMD7000)
- Adjust the width of the cutting line
- Control the UV offset
- Maintenance free solid state laser

LMD Laser Systems	Leica LMD7000	Leica LMD6500
Max. pulse energy	120 µJ	50 µJ
Repetition rate	Single pulse to 5000 Hz	80 Hz
Adjustable repetition rate	Yes	No
Wavelength	349 nm	355 nm
Laser aperture control	Yes	Yes

Fig. 1: Brain, frozen section of GFAP-immunopositive astrocytes. Courtesy of G.J. Burbach, MD, and T. Deller, MD, Institute of Clinical Neuroanatomy, J.W. Goethe University, Frankfurt, Germany.

Fig. 2: Primary cell culture from pancreatic adenocarcinoma (PDAC) stained with hematoxylin, objective 10x (before cutting, after cutting and inspection). Courtesy of N. Funel, Department of Oncology, University of Pisa, Italy

Fig. 3: Maize root meristem. Courtesy of L. Feldman, University of California, Berkeley, USA

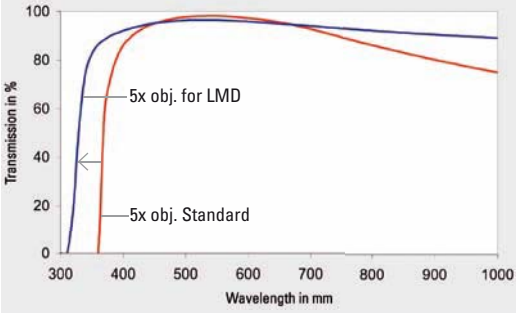
Fig. 4: Brain section, stained with thionin. Courtesy of Axaron Bioscience AG, Heidelberg, Germany

System Integration

Benefits:

- Fully automated DIC
- Motorized fluorescence axis with 5- or 8-position filter cube turret
- Fluorescence intensity manager (FIM)
- Motorized Excitation Manager and fast Internal Filter Wheel (IFW)
- Convenient Leica SmartTouch touchscreen for controlling the automated modules

Leica Microsystems offers a wide range of objectives (from 5x–150x) dedicated for laser microdissection.



The specially designed objectives for laser microdissection provide a much higher UV transmission than standard objectives, and therefore, provide more laser power on the sample.

All components of the Leica LMD systems are fully integrated and act in concert, building a winning team greater than the sum of its components.

High-end Leica DM6000 B research microscope
The foundation of every Leica LMD system is the high-end Leica DM6000 B upright research microscope, which is suitable for all types of life science research. Excellent optical performance, intelligent automation, and user-friendly operation make this fully automated microscope the perfect tool for microscopic research.

Specially designed optics for laser microdissection
Leica Microsystems' dedicated LMD objectives feature the highest possible UV transmission and outstanding imaging performance – the Leica SmartCut series. With SmartCut objectives, thicker tissue can be cut faster. The unique high magnification 150x dry objective enables the dissection of even the smallest areas without using oil.

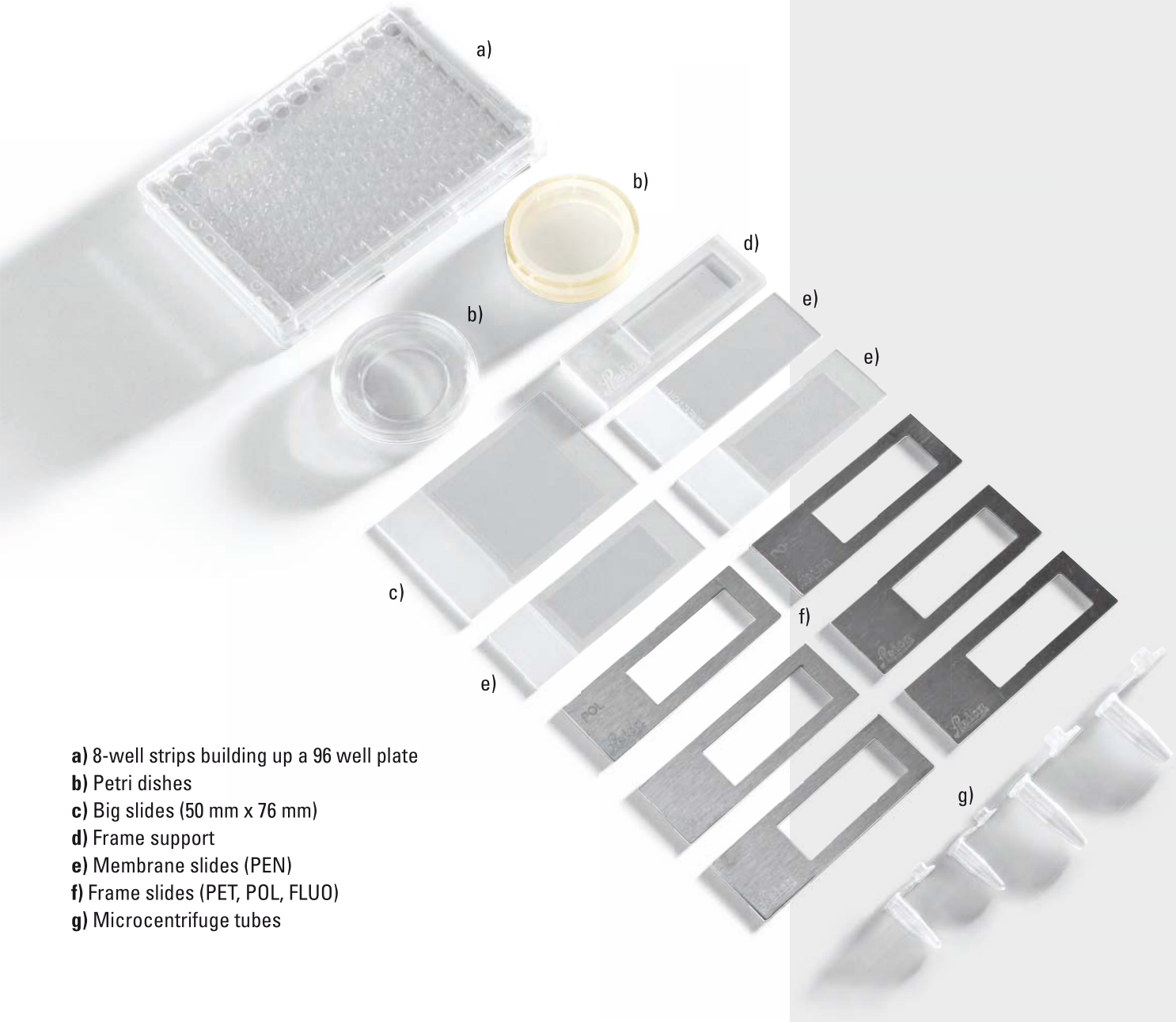
User-friendly software
Leica Microsystems' LMD software is very easy to use, yet powerful without being complicated. A workflow guides the user through the dissection process and intuitively provides all control elements where they are needed. The software contains all features for dissection, such as serial section cutting, an optional database, and fully integrated and automated cell recognition.

With the Leica SmartTouch all automated functions are easily controlled.

Application specific consumables for laser microdissection
Leica Microsystems offers four different types of metal frames, glass slides and Petri dishes in different sizes. Whether the user needs slides that show no autofluorescence, or uses DIC contrast to reveal the specimen areas – Leica Microsystems has the right solution for any application.

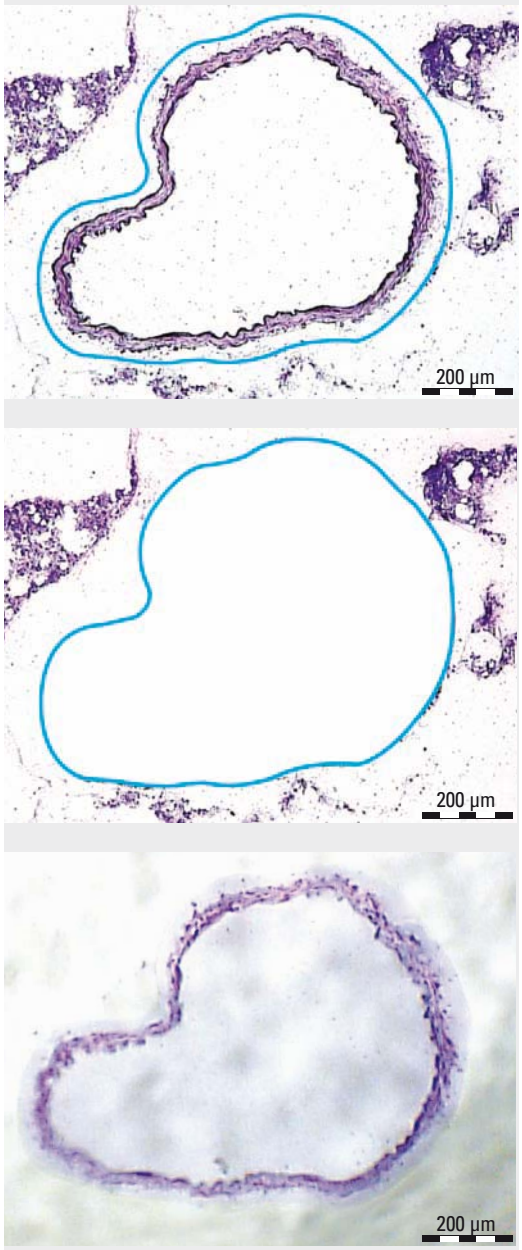
Benefits:

- High-end Leica DM6000 B
- Specially designed optics
- User-friendly software
- Application specific consumables



a) 8-well strips building up a 96 well plate
b) Petri dishes
c) Big slides (50 mm x 76 mm)
d) Frame support
e) Membrane slides (PEN)
f) Frame slides (PET, POL, FLUO)
g) Microcentrifuge tubes

Solutions for Advanced Applications



Frozen section (10 µm) of a mouse aorta (whole vessel) stained with cresyl violet on a POL frame slide. Courtesy of K. Beuerlein, Rudolf-Buchheim-Institut für Pharmakologie, Justus-Liebig-Universität Giessen.

Cancer research

Cancer research requires visualization of morphologically altered cell populations and their subsequent isolation.

- Contamination-free dissection by gravity
- Fast dissection of areas of any size or shape
- Collect directly into buffer
- Fully integrated database option for automated documentation

Single cells

The fastest possible dissection, the highest precision combined with narrow cutting lines, are the prerequisite for expression analysis of single cells.

- Laser movement via optics for fast and precise lasing
- Pen-screens for the most accurate drawing of cutting lines
- Leica SmartCut objectives with the highest UV transmission
- The unique 150x dry objective with the highest magnification available for laser microdissection

Proteomics

For proteomics analysis, either very sensitive analysis methods or large amounts of protein are necessary for analysis.

- Auto vision control (AVC) for fast and fully automated cell recognition and dissection
- Semi-automated cell recognition for assisted dissection
- Pool unlimited quantities of dissectates

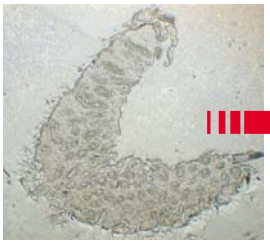
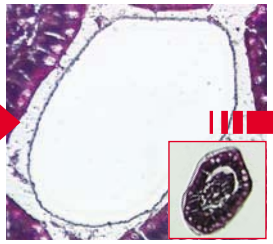
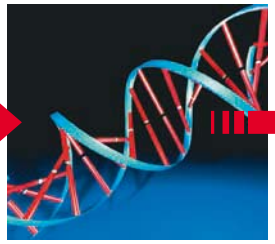
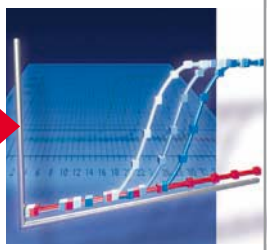
Live cell cutting

Laser microdissection of living cells enables the separation of single cells and cell clusters for recultivation or analysis.

- Unique, integrated consumables for sterile dissections
- Dissect non-adherent cells or bacteria
- Optional incubator
- Special sputtered GFP and BGR cubes for lasing in fluorescence
- Fully automated fluorescence axis with 5- or 8-position filter cube turret

Ablation and multi-dimensional imaging
Directly after the targeted ablation in a living structure, the imaging of the induced processes is important.

- Time lapse series with different fluorescence channels, using Leica AF6000 (Advanced Fluorescence) software and LMD at the same time
- Convenient movie documentation
- Real-time lasing for direct ablation

Specimen Preparation	Staining	Microdissection	Extraction	Analysis
				
Section and prepare biological specimens – Histological specimens (formalin-fixed/ paraffin-embedded or cryo sections) – Living cells and cell cultures – Chromosome spreads – Smears – Cytospins – Plant material – Sperm and other forensic preparations	**Visualize regions of interest** Brightfield: – HE (hematoxylin-eosin) – Cresyl violet – Toluidin blue – Thionin – Immunohistochemistry Fluorescence: – Secondary antibodies – Acridine-orange – FISH	**Selectively dissect regions of interest** – Contact-free – Contamination-free – Any size from cell compartments of a few µm² to several mm² – Any shape	**Extract and prepare important molecules** – DNA – RNA – Proteins – Metabolites – Biomarkers	**Obtain reproducible and specific results** – PCR – Quantitative real-time PCR – Microarrays – Expression profiling – Genetic fingerprinting – LOH – FISH – LC-MS/MS – 2-D PAGE – SELDI – MALDI

4

11888829
Condenser BF
mot. condenser head

11888830
Condenser DIC (suitable for BF, PH, DF, ICT)
mot. condenser head,
with mot. condenser disk (7 pos.),
with mot. polarizer

ICT condenser prisms
(K1–K15)

11521505
Light ring set

3

11504133
HBO Lamp Adapter

11504070
Lamp housing LH 106z
12 V 100 W halogen lamp
4-lens collector
0.55 m connection

11504114
Lamp housing
LH 106z Hg 100 W,
1" 6-lens collector

11500325
Supply unit
Hg 100 W

11504117
1" fiber-optics
adapter

11504116
Liquid light guide, 2 m

11504115
External light
source EL6000

C-Mount
HC 0.70x

12730203
Leica DFC400 FX

11547000
Leica DFC360 FX

11547002
Leica DFC310 FX

11501450
Hitachi HV-D20P

5

11518146
Objective 5x/0.12
Microdissection

11518145
Objective 6.3x/0.13
Microdissection

11506208
Objective 40x/0.60 XT
Microdissection

11506222
Objective 63x/0.70 XT
Microdissection

11506214
Objective 150x/0.90 XT
Microdissection

Objective series BF

11505161
Tube attachment
with 1 camera port

11505223
Tube attachment
with 2 camera ports
selectable 100:100, manual
(LMD6500 only)

11505146
BDT 25+ V 100/50/0
Documentation tube
with documentation port
with variable beam splitting

11505202
Imaging module
beam splitting: 100%:0%
with integrated and centrable
C-mount (0.7x)
(LMD7000 only)

5 11888828
Stand top without fluorescence axis,
with 7-position objective turret M25, mot.

5 3 11888831
Stand top with fluorescence axis,
with 5-position filter turret, mot.,
with 7-position objective turret M25, mot.

5 3 11888832
Stand top with fluorescence axis,
with 8-position filter turret, mot.,
with 7-position objective turret M25, mot.

1

11600184
Holder for 1 slide
25 x 76 mm

11505214
Holder for big slide
50 x 76 mm

11505257
Holder for Petri dish

11888826
Motorized Stage
1
4

11888827
Scanning Stage
2
4

2

11505226
Holder for 3 slides
25 x 76 mm

11505227
Holder for Petri dish and
big slide 50 x 76 mm

11505255
Holder for 18-well
double stack ibidi slide

1

11505131
Lever for
4 x 0.2 ml PCR-tube

11505130
Lever for
4 x 0.5 ml PCR-tube

11505258
Lever for
1 x 8-well strips

2

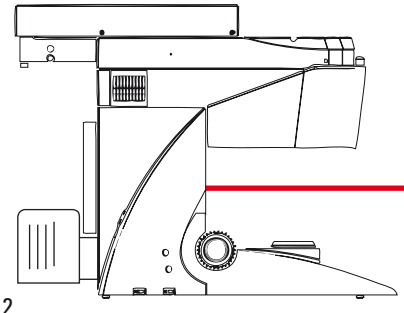
11505229
Collector for
4 x 0.2 ml PCR-tube

11505228
Collector for
4 x 0.5 ml PCR-tube

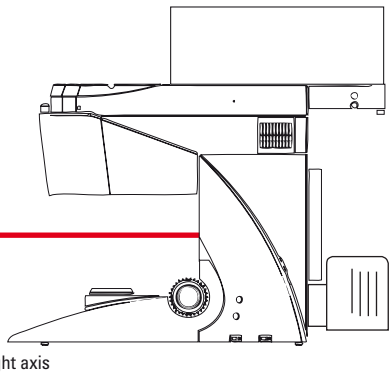
11505230
Collector for
2 x 8-well strips

11501255
Leica STP6000
SmartTouch Panel

11505180
Remote Control
Smart Move



11888825
Leica LMD6500
max. 50 µJ laser
Basic stand without
stage and transmitted light axis



11888834
Leica LMD7000
max. 120 µJ laser
Basic stand without
stage and transmitted light axis

Highlights of the Leica LMD Systems

Specimen collection by gravity

- Contact- and contamination-free specimen collection
- Collect all specimen shapes and sizes directly into reaction buffer
- Pool unlimited amounts of specimen
- Use standard consumables for collection
- No additional laser pulses are needed for collection

Laser movement via optics

- Highest possible precision and speed
- Real-time laser cutting
- Convenient movie documentation

Leading-edge laser technology

- Control the pulse energy and frequency for thick, thin, hard and soft tissues
- Control the width of the cutting line using the laser aperture
- Maintenance-free, longlife, solid state laser
- Control the UV offset for thicker samples or ablation

Fully automated high-end Leica DM6000 B research microscope

- Fully automated DIC
- Unique Fluorescence Intensity Manager (FIM)
- Motorized excitation manager and fast internal filterwheel
- Constant color intensity control

Specially designed optics for laser microdissection

- Wide range of LMD objectives, from 5x to 150x
- Higher UV transmission than standard objectives
- Use the unique 150x dry objective for the most precise dissection

Lasing within fluorescence

- Special GFP and BGR cubes
- See three fluorescence channels (such as DAPI, FITC, TxRed) at a glance through the eyepieces
- Use the internal filter wheel to visualize a single fluorochrome
- Non-fluorescent FLUO-frame slides

Intuitive software

- Workflow based and time saving
- Fully integrated database
- Overview images for navigation
- Serial section cutting
- Automated cell recognition

Flexibility to use a variety of dissection devices

- Adapt the collection devices to specific research needs
- Use metal frames or glass slides, with or without membrane (PEN, PET, POL, FLUO)
- Sterile dissection of living cells out of Petri dishes, stackable membrane rings or 18-well membrane slides
- Use a sandwich of two metal frames for dissecting non-adherent cells or bacteria

Features and Specifications

Laser	Leica LMD7000	Leica LMD6500
Type	Diode pumped, solid state	Diode pumped, solid state
Wavelength	349 nm	355 nm
Maximum pulse energy	120 µJ	50 µJ
Repetition rate	Single pulse to 5000 Hz	80 Hz
Adjustable repetition rate	Yes	No
Laser aperture control	Yes, continuously adjustable	Yes, continuously adjustable
Free intensity control	1-100%	1-100%
UV offset freely adjustable and specific objective saved	Yes	Yes
Laser beam movement	Via optics	

Microscope		
Transmitted light axis	Contrast methods	BF, optional PH, DF, POL, DIC (fully automated)
	Illumination	12 V 100 W halogen lamp
	Automation	Automated illumination manager Automated contrast manager Constant color intensity control (CCIC)
	Condenser	Condenser head S28, 0.55 NA Motorized 7x condenser disk Motorized polarizer
Fluorescence axis	Filter cube turret	Motorized 5x or 8x
	Automation	Fluorescence intensity manager (FIM) for brightness adjustment Circular and rectangular field diaphragms for eyepiece or camera viewing Internal filter wheel and motorized Excitation Manager
	Illumination	Leica EL6000 (120 W metal halide) or 100 W HBO
	Cubes	All cubes size k Special cubes for simultaneous fluorescence and cutting e.g. – LMD-BGR – LMD-GFP
Operation	Focus	Motorized: – 5 electronic ratios – Includes parfocal function Memory function for two z-positions
	Objective turret	Motorized 7x M25 thread including dry and immersion modes
	Controls	6 programmable function buttons
		Leica SmartMove Controls for z (focus) movement and x, y (stage) movement 4 programmable function buttons
		Optional Leica STP6000 Controls for z (coarse and fine focus) and x, y (stage) movement 11 programmable function buttons Touchscreen with information and control panels
Stand	Display	With integrated touchscreen Leica SmartTouch
	Interfaces	2 x USB 2.0, 2 x I^2C
	Dimensions	With scanning stage: 649.6 mm height, 512.0 mm width, 596.5 mm depth

Dissection	Dissection and Collection Unit Based on Scanning Stage	Dissection and Collection Unit Based on Motorized Stage
Specimen Collection	Contact- and contamination-free	
Dissection modes	Draw & Cut Move & Cut (direct online cutting) Draw & Scan (dot dissection scan)	
Serial section cutting	Yes	No
Stage precision	± 2 µm	> ± 5 µm
Holding devices	3x standard slides (25 mm x 76 mm) Optional 1x big slide (50 mm x 76 mm) Optional Petri dish (50 mm) Optional 18-well slide stack	1x standard slide (25 mm x 76 mm) Optional 1x big slide Optional Petri dish (50 mm)
Collection devices	4x 0.2 ml standard PCR tubes 4x 0.5 ml standard PCR tubes Petri dish (50 mm) Optional 2x 8-well strips building up a 96-well plate	4x 0.2 ml standard PCR tubes 4x 0.5 ml standard PCR tubes Optional 1x 8-well strips building up a 96-well plate
Power supply	CTR6500	CTR6000

System software		
Package includes	Dissection	Automated collection devices and positioning of the PCR tubes Fully automated inspection mode Multi-cutting over the entire slide Save and load drawn shapes
	User guidance	Workflow based graphical user interface Free scaling drawn shapes Saving user profiles Overview images in BF and Fluorescence
	Control	Full laser control Control software for the microscope Laser and illumination settings are linked to objectives
	Interfaces	Export of shape list data for Microsoft Excel or OpenOffice Integrated database interface to transfer all relevant data (laser, microscope and camera; database itself as option)
Optional software packages		Automated vision control (AVC) for automated cell recognition within field of view (standard version) or fully automated or semi automated over freely defined area (professional version) Database Leica IM500 or Leica IM1000

Camera	Leica DFC310 FX	Leica DFC360 FX	Leica DFC400	Hitachi HV-D20P
Type	High sensitivity digital color	High sensitivity digital monochrome	High sensitivity digital color	High sensitivity analog 3 CCD color
Cooled	Yes, -20°K to ambient	Yes, -20°K to ambient	No	No
Resolution	1392 x 1040	1392 x 1040	1392 x 1040	795 x 596 (x 3)
Pixel size	6.45 µm x 6.45 µm	6.45 µm x 6.45 µm	4.65 µm x 4.65 µm	8.00 µm x 8.00 µm
Speed	20 fps at 1392 x 1040 71 fps at 348 x 260	20 fps at 1392 x 1040 39 fps at 696 x 520	20 fps at 1392 x 1040 39 fps at 696 x 520	25 fps
Electronic interface	Single FireWire b cable (IEEE1394b)	Single FireWire b cable (IEEE1394b)	Single FireWire b cable (IEEE1394b)	PCI board

“With the user, for the user”
Leica Microsystems

Leica Microsystems operates globally in four divisions, where we rank with the market leaders.

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The Leica Microsystems Life Science Division supports the imaging needs of the scientific community with advanced innovation and technical expertise for the visualization, measurement, and analysis of microstructures. Our strong focus on understanding scientific applications puts Leica Microsystems’ customers at the leading edge of science.

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