FAQs.

Will the chip dry out once opened? Yes, you should avoid leaving the chip exposed for too long as it may become dry. If this happens the BxChip™ can be remoistened with sterile saline or your fixative. This will facilitate the adhesion of the cores into the channels.

Is the chip X-ray transparent? Yes. The BxChip™ material will not interfere with X-ray imaging.

Can you decalcify the BxChip™ (i.e., for breast core biopsies)? Yes. The material used to create the BxChip™ does not degrade during the decalcification protocols employed in pathology laboratories.

Do I need specialist cassettes or biopsy pads to process the BxChip™? No, the BxChip™ can be processed using any user validated combination of cassettes/biopsy pads (however, cassettes with small holes are not recommended). One or two pads per chip (depending on BxChip™ gauge) are provided and validated for use by the manufacturer. These can be used for transporting the chip to the laboratory before transfer to a new printed cassette.

How should the BxChip™ be handled? It is recommended to treat the BxChip™ as carefully as a similarly sized piece of tissue. The flexible material can be punctured or torn if roughly handled which will make it impossible to process correctly. Cores should be loaded into the BxChip™ without damaging the matrix. If this happens, transfer the biopsies into a fresh BxChip™**.**

What does the chip look like through a microscope? Both the BxChip™ and the cores change colour after staining, however it will be immediately obvious which material is the tissue core.

Do I need to use tissue marking dye on cores in the BxChip™? No, the orientation aids engraved in the matrix such as arrows, numbers and channel markers are eliminating the need for marking or measuring each core. The BxChip™ may also be marked directly with tissue dyes if additional orientation information is desired.

How should the BxChip™ be handled before and during sectioning? Blocks containing BxChip™ must be kept dry and cold in order to achieve good quality ribbons. If the BxChip™ becomes wet, it will swell, and tissue cores may dislodge from the channels. In order to prevent BxChip™ swelling during cooling it is recommended that blocks are kept in the mould to prevent direct contact with the cold plate/ice block or without any precautions if using LUMEA BxCOOL!™.

What techniques is the BxChip™ validated for? The BxChip™ is validated for immunohistochemistry (IHC), tissue microarrays (TMA), fluorescence in-situ hybridisation (FISH) and next generation sequencing (NGS). You should conduct your own validation of any processes you wish to use the chip with.

Are alternative BxChip™ designs available? Yes, please contact Themis Pathology to discuss your requirements for alternative core gauge sizes, number of channels, pack sizes and coding colours. The BxChip™ is available to fit various core biopsies (kidney, spleen, liver, lung, brain, bone marrow, soft parts, etc.) of the following gauges: 7, 8, 10, 12, 14, 16, 18, and 20. Up to 16 channels/groves per individual BxChip™ have been successfully used (for Gauge 18). For larger diameters of the biopsies the maximum number of biopsies that can be multiplexed in one single BxChip™ is smaller (e.g., 10 biopsies for Gauge 16, 6 biopsies for Gauge 14, etc.).

SELECTED BxChip™ REFERENCES

Tomosoiu RB et al (2022) *Rev Rom Urol (in press)*
Ștefan AE et al (2021) *Rev Rom Med Vet* **31**(3):12-16
Ștefan AE et al (2020) *RJME* **61**(4):1077–1083
Murugan P et al (2019) *AJCP,* **152**(6):757–765
Wojno KJ, et al (2016) *J Urol (Suppl)*, **195**(4S):e168
Radavoi D, et al (2014) *Eur Urol*, **13** (1):e745
Farcas CP, et al (2014) *Rev Rom Urol*, **3**(13):9-16
Farcas CP, et al (2012) *Rev Rom Urol*, **80**(3):278
Jinga V et al (2012) *Eur Urol Suppl* **11**(4):124
Musat S, et al. (2011) *ROMURO*:v2.4

Manufactured in EU by
Themis Pathology SRL
EN ISO 13485:2016
EN ISO/CEI 17067:2014

Themis Pathology is a wholly owned subsidiary of LUMEA Inc.

themispathology@lumea.net
+40371 377 150
lumea_bxchip
Themis Pathology

Instructions for Use

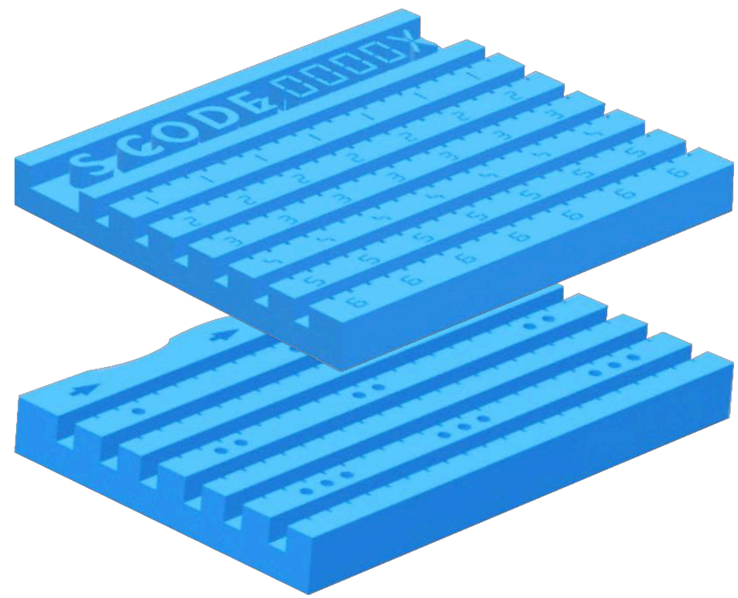
CE

LUMEA BxChip™

US PAT: 9,851,349 B2; 10,670,593 B2; 10,734,100 B2, D836,796 S, D914,238 S, 11,935,632 B2

Sectionable matrix for core biopsies

GMDN 63436: Organic polymer embedding medium IVD



STERILE R *or* *4% Formaldehyde*

LUMEA

IN THIS PACK

The BxChip™ is delivered double sealed in aluminized pouch/plastic blister packages with one or two companion reticulated sponges (depending on BxChip™ gauge).

Materials required but not provided: tissue cassettes and container with Neutral Buffered Formalin (or other suitable histological fixative).

INTENDED USE:

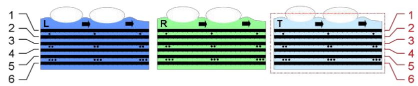
For professional use only.

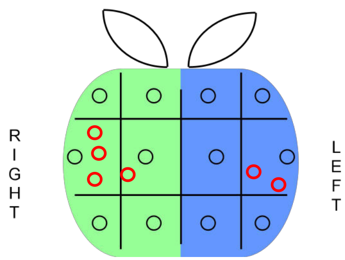
The BxChip™ is a sectionable planar matrix made from a biomimetic organic polymer that allows the creation of tissue microarrays for routine clinical diagnostics at the point of care. The BxChip™ virtually eliminates core fragmentation by protecting delicate tissue cores and reduces the need for tissue manipulation. Processing and sectioning tissue cores in parallel significantly increases the tissue yield of every core and cancer detection rate.

Fresh biopsy samples can be loaded into the site-specific channels of the BxChip™ in the operating room (sterile matrices). Alternatively, pre-fixed biopsies that arrive in the Pathology laboratory can be loaded in non-sterile matrices. The partitions between the channels are marked unambiguously either with numbers or with dots.

IMPORTANT: The BxChip™ should be validated and verified in your laboratory prior to routine use.

LOADING THE BXCHIP™





Example of diagram for fusion prostatic biopsy

○ =12 core systematic biopsies ○ =Targeted biopsies

In the operating room: The plastic blister is removed from the aluminized pouch by dropping it onto the surgical table and opened by peeling off the transparent film from the elongated corner. The BxChip™ is unloaded face up.

The biopsy cores are placed one by one into the channels according to your protocol. Supporting the biopsy needle approximately 8-10 cm from the pointed end will help in keeping the needle tremor free. The location of each core in the BxChip™ should be recorded according to your procedure/policy for identification.

When finished, loose ends and protruding tissue can be re-positioned into the channels with tweezers. The loaded BxChip™ is transferred into the tissue cassette and a sponge is placed over it. The lid of the tissue cassette must be securely locked, without pinching the BxChip™.

The cassette is placed in a container with sufficient fixative to cover the cassette(s) completely, even if tilted or flipped over and sent to the Pathology laboratory. After opening, the BxChip™ should not be stored in Neutral Buffered Formalin for longer than 4 days.

In the Pathology laboratory: The BxChip™ is removed from the plastic blister, placed onto the grossing table and loaded with fixed biopsy samples. Fixed cores will be stiffer than fresh tissue and will require careful manipulation.

PROCESSING THE BXCHIP™

When the BxChip™ arrives in the Pathology laboratory: *i)* remove it from the transport cassette, place it into a new cassette, pre-printed if required, with soaked biopsy pads **or** *ii)* start tissue processing according to your protocols.

The BxChip™ can be processed using any proven protocol in current use, including microwave assisted and/or hybrid. Protocols at room temperature (dehydration and clarification) perform better than those with heating. During processing ensure the cassette containing the BxChip™ cannot float freely and is aligned vertically, if possible.

The paraffin block can be prepared with the BxChip™ face up in the base mould - this will give the histotechnologist ample time to adjust the plane of sectioning during facing the block in order to obtain full sections and not losing precious patient tissue. After the learning curve is completed, the histotechnologist can choose to prepare the paraffin block with the BxChip™ face down.

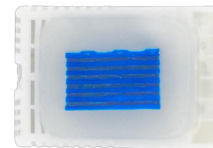
Choose appropriately sized base moulds which allow a minimum of 2 mm paraffin rim surrounding the specimen on all sides. If the moulds are too large, trim the excess paraffin.

Recommended processing protocol for 18G BxChip™ (fluid transfer tissue processors):

	NBF	Ethanol							Xylene		Paraffin			
	I	70%	95%	95%	95%	100%	100%	100%	I	II	I	II	III	IV
Time (min)	15	15	15	15	10	15	15	10	15	15	10	15	15	15
Temp (^oC)	40	40	40	40	40	40	40	40	40	40	58	58	58	58

Length of protocol and number of pads should be adjusted depending on the thickness of the BxChip™

Gauge		**12**	**14**	**16**	**18**
Thickness (mm)		3	2.7	2.2	2.2
Number of sponges	Above	1	1	1	1
	Bellow	0	0	1	1



BxChip™

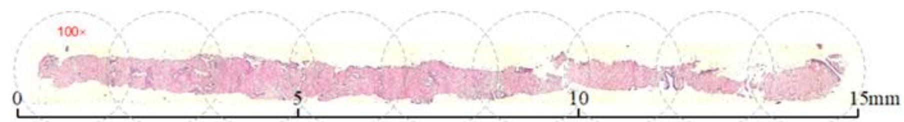
Paraffin

block

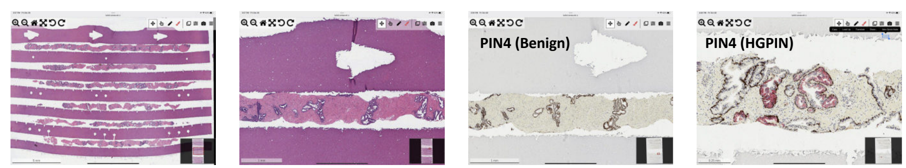
SECTIONING AND STAINING THE BXCHIP™

In order to section, the paraffin block must be cold. Cool the block by placing it in the base mould on a cold plate. As the BxChip™ is thin, trim the block in small increments (no more than 10 micrometers per step).

When floating sections, the water in the flotation bath should not exceed 42°C.



First prostate core biopsy using the BxChip™ (2011). Microphotography (100×) courtesy of Central Military Hospital Dr. Carol Davila, Bucharest, Romania



Imaging of H&E and IHC staining of prostate biopsies using the BxLink diagnostic information system (LUMEA Inc., Lehi, UT, USA)