



Application of large format tissue processing in the histology laboratory

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ABSTRACT

In clinical, research and veterinary laboratories of North America, large format histology has more recently been improved with newer equipment and better methodology. Large tissue specimens are frequently sliced in the grossing room and processed in multiple smaller, standard size tissue cassettes. Justifiably, submitting more blocks inherently lends itself to a greater confidence in the accuracy of the diagnosis, yet guidelines for tissue sampling often suggest taking fewer samples. For example, large tumor specimen protocols recommend taking one standard-sized tissue block for each cm diameter of tumor. However, cancers are the culmination of many complex changes in cell metabolism and often appear dissimilar at different tissue locations. As these changes have an uncertain behavior, many other tissue samples are often taken from areas that appear to have either a variable texture or color. Consequently, at microscopy, the complete tissue sample may need to be reassembled like a jigsaw puzzle as the stained sections are frequently presented over many slides. This problem has easily been overcome by using large format cassettes since the entire cross-section of the tissue sample can often be viewed on a single slide. Because these cassettes can effectively hold up to 10 times the volume of conventional standard size cassettes, they are a more efficient way of assessing large areas of tissue samples. This system is easily adapted for all tissue types and has become the established method for assessing large tissue samples in many laboratory settings.

KEYWORDS

Large format histology; mega blocks; supa mega; whole mounts; whole slide images

Introduction

For decades, large format technology has been established for both research and specialty work where it often utilized an embedding medium other than paraffin wax [1]. In more recent times, large format, supa mega (SM) cassettes specifically designed for paraffin processing of larger specimens up to a maximum thickness of 12 mm have been introduced. Presently, large format histology refers to surgical tissue samples that are mounted on double-wide (75 mm × 50 mm) glass microscope slides. Large format histology, also known as whole mounts, is not suited to every laboratory, and several factors need to be considered before using this method. Primarily, it should meet the need for pathologists, especially for those attending interdisciplinary tumor board meetings. In addition, the expense and time of processing entire tissue samples should be balanced against the risk of missing important prognostic parameters. Lastly, the benefits of implementing such a system should be cost-effective.

In response to these factors, there are several advantages of using large format histology [2]. For instance, the grossing of large surgical samples would be performed much faster as it eliminates slicing the tissue into multiple blocks and reduces the length of time attributed to

rendering a gross description. Furthermore, complete cross sections of large tissues allow for better visualization of the tumor and its resection margins and eliminates the need to reconstruct multiple-stained tissue sections like a jigsaw puzzle. The large format system is a more efficient way of assessing wide areas of tissue and helps to avoid undersampling of cancer specimens [3,4]. Consequently, this not only enables validation of any residual tumor but would also help identify what may have been previously unsuspected significant findings [5]. Large format histology is suitable for resected tissues and whole organs such as breast, prostate and gastrointestinal tract in both clinical and research settings [3,6–9]. In the laboratory, migration from conventional to large format histology requires very little additional equipment. The large format essentials include microtome cassette clamps, SM tissue cassettes, embedding molds, slides, and staining rack adapters (Figure 1). With archive filing trays and boxes completing this outfitting, the total outlay for initial setup could cost less than 2,000 USA dollars. Vendors and details for all large format products and accessories are found in Tables 1–6.

In large format histology, the SM tissue processing cassette plays a pivotal role (Figure 2). There are several



Figure 1. Essentials required for setting up large format include [1] slides and staining rack with adapters [2], cassette clamp [3], embedding molds and [4] processing cassettes.

Table 1. Vendors of equipment used for large format histology.

Brain Research Laboratories, Waban, MA, USA
Cancer Diagnostics Inc, Morrisville, NC, USA
CellPath Ltd, Newtown, UK
Electron Microscopy Sciences (EMS), Hatfield, PA, USA
General Data Company Inc, Cincinnati, OH, USA
Huron Digital Pathology, St. Jacobs, Ontario, Canada
Lab Storage Systems Inc, Saint Peters, MO, USA
Leica Biosystems Inc, Buffalo Grove, IL, USA
Medite GmbH, Burgdorf, Germany
Milestone Medical, Sorisole (BG), Italy
Sakura Finetek USA, Inc, Torrance, CA, USA
Ted Pella Inc, Redding, CA, USA
ThermoFisher Scientific, Waltham, MA, USA

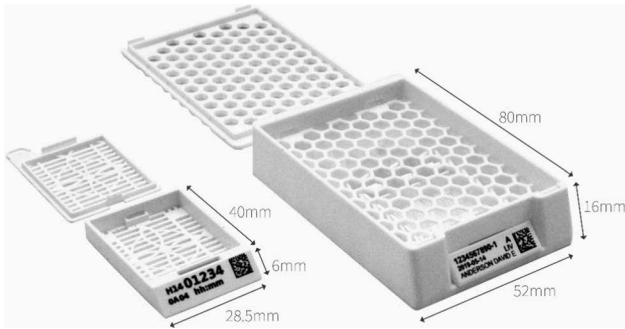


Figure 2. Comparison of a large format processing cassette with one of standard size to show an increased capacity by the larger cassette. Dimensions are shown in mm.

cassette styles available, each having external measurements of 75 mm \times 52 mm with a variable internal depth of between 6 mm and 15 mm depending on the cassette type (Figure 3). The traditional design of the standard SM cassette had an internal depth of up to 15 mm with an open pore area of 20%. However, the latest slotted, hexagonal designs have open pore areas of approximately 67% (Figure 4). This increased open pore area not only offers an improved flow of reagents for more consistent processing but also ensures greater



Figure 3. Large format cassettes showing standard (white), slim (blue), and mothership style (yellow). SM mothership mold with SM mothership cassette (bright pink) is in the background.

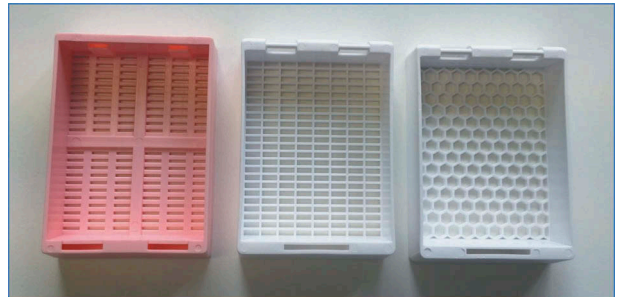


Figure 4. Large format cassette designs showing the traditional-slotted cassette (left, pink), the most recent larger slotted cassette (center, white) and the hexagonal open pore designs (right, white) to increase the flow of processing reagents and paraffin infiltration.

adhesion of the paraffin block to the cassette during sectioning. This also minimizes the risk of the paraffin block being sheared off the rear of the cassette when sectioning fibrous or difficult tissues.

Just like the standard SM cassette, the SM slim cassette has a hexagonal open pore design but with a reduced internal depth of 6 mm (Figure 5). This reduction in internal depth ensures tissues are consistently grossed to 5 mm thickness and that the samples remain flat, preventing distortion of tissue. Consequently, the reduced thickness of the grossed specimen will not only enable improved turnaround times due to the significantly reduced processing time but will also allow for more consistent processing, thereby decreasing the number of specimens that require reprocessing.

Additionally, SM mothership cassettes are available which have hexagonal pores and similar external dimensions to the standard SM cassettes (Figure 6). Although mothership cassettes allow for a standard-sized cassette printed with an identifier, and then

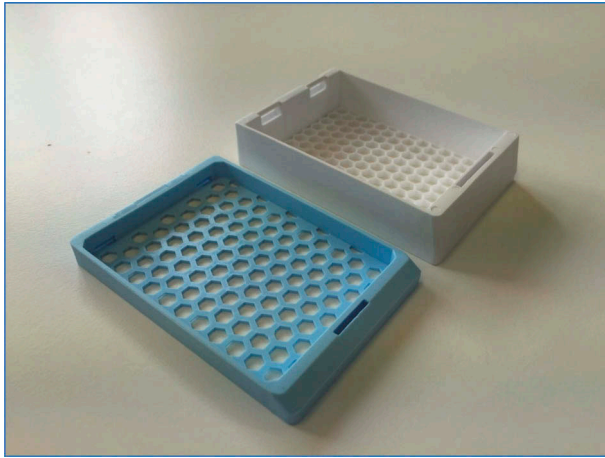


Figure 5. Image compares the depth of the large format cassette (white) with the reduced depth of the slim SM cassette (blue). Both cassettes have the hexagonal open pore design for improved reagent flow.

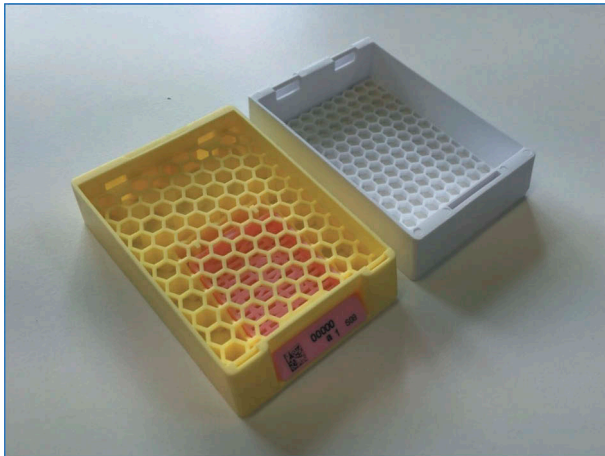


Figure 6. The mothership cassette (yellow) has the same external but a shallower internal dimension above the small patient identifier cassette (pink) when compared to the conventional large-format cassette (white).

inserted into the mothership cassette, care must be taken to ensure that the standard-sized cassette bearing the patient identifier is inserted correctly to allow scanning of the barcode (Figure 7). This system eliminates risks of transcription errors since the 2D barcodes printed on the identifier cassettes enable tracking and traceability. Similar to the SM slim, the mothership cassettes have an internal depth of 6 mm, and the reduced grossed specimen thickness also allows consistent processing with improved turnaround times.

However, as with all sizes of processing cassettes and if tissues are trimmed too thick, the hexagonal pores can leave imprints on the tissues, which requires extra trimming at microtomy. This can be avoided by simply grossing tissues consistently to a 5 mm thickness when using

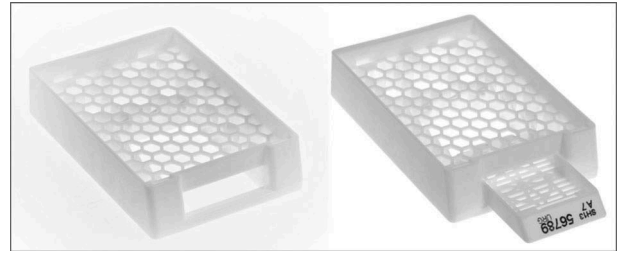


Figure 7. Mothership cassette before and after insertion of a standard size processing cassette complete with the patient identifier.

slim and mothership cassettes. Alternatively, tissues may be grossed and thin metal spacer plates laid on top of the tissues in the cassette to prevent imprints appearing. All SM cassette types can be used for processing large tissue samples, but if tissues are soft and friable, sponge biopsy pads should be implemented (Figure 8, Table 2). These pads help to eliminate carryover by ensuring that no tissue fragments escape from the cassette during processing. Spacers for use with standard 15 mm depth SM cassettes are available in various thicknesses and help reduce the well depth to 5 mm (Figure 9, Table 2). This ensures that tissues remain distortion-free to provide consistent, high-quality tissue processing. The cassette spacers are re-usable and suitable for use in both conventional and microwave tissue processors.

Methods and materials

Grossing of tissue

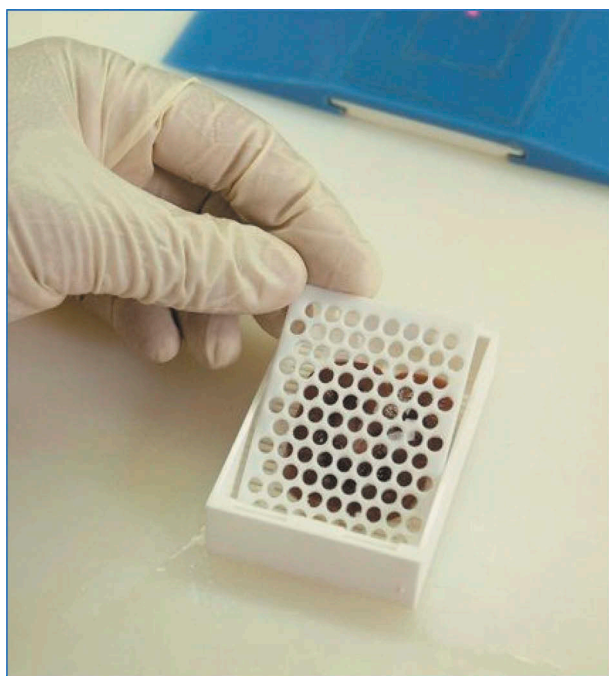
The grossing room is where tissue sample selection and dissection take place. The most common method of grossing large tumor samples is the 'bread-loafing' technique



Figure 8. Large format sponge biopsy pads for containing friable tissue samples.

Table 2. Large format cassettes and grossing accessories.

Product	Vendor	Part #
SM Cassette (Hex Pore)	Ted Pella	27198-1
SM Cassette (Hex Pore)	EMS	70065-W
SM Cassette (Hex Pore)	CellPath	EAG-0102-00A
Super Cassette (Slotted)	Leica Biosystems	38VSP59060
Large Cassette (Slotted)	Cancer Diagnostics	LPC1000
SM Cassette	Sakura Finetek USA	7820
SM Slim Cassette (Hex Pore)	Ted Pella	27199-1
SM Slim Cassette (Hex Pore)	EMS	62510-W
SM Slim Cassette (Hex Pore)	CellPath	EAN-0102-02A
SM Mothership Cassette	Cancer Diagnostics	KLPC1000
SM Mothership Cassette	EMS	62511-W
SM Mothership Cassette	CellPath	EA0-0102-02A
SM Biopsy Pad – Black	CellPath	EBA-0201-02A
Spacers for SM Cassettes (2, 3 and 5 mm thickness)	Milestone Medical	SM-SPACER
TruSlice Specimen Grossing System	CellPath	CBA-0100-00A
TruSlice Grossing Board	CellPath	CBA-0100-00B
TruSlice Steel Calibrated Ruler 300 mm/12 in.	CellPath	QAA-0100-00A
ProCUT XL5 Grossing System	Milestone Medical	PROCUT-XL5

**Figure 9.** Large format cassette spacers help tissue remain distortion free without compression artifact on tissue surface during processing.

which allows serial slices to be made through tissue samples. The method permits the determination of both tumor extent and assessment of surgical resection margins. An alternative to this more traditional practice of tissue dissection is the technique known as multisite tumor sampling, a simple method that clearly improves routine detection of complex changes in tumors [10]. The method is based on a divide-and-conquer (DAC) algorithm which involves selecting certain areas of the tumor with the goal that these areas are representative of the entire tumor. This strategy has been used to solve complex problems by selecting the most appropriate tissue areas for analysis, making it

especially important for large tumors which often have a propensity for incomplete sampling. The practice of multisite tumor sampling is carried out by applying a cutting grid to the tumor slice to obtain multiple smaller tissue samples. Several of these relatively smaller samples are then placed into a standard-sized tissue cassette in readiness for processing [2]. This procedure has proven to be cost effective by limiting the quantity of standard cassettes used while increasing the number of sampled tumor areas. However, irrespective of which grossing method is employed, the total number of cassettes is dramatically reduced when using large format histology.

Although grossing to 5 mm thickness is preferred for improving the processing times of all tissues when using large format, this is not always possible due to the type and consistency of certain tissues. In these instances, thicker slices of fixed tissues can be taken and re-trimmed to 5 mm following treatment in alcohol for 1 h to firm up the tissue. Likewise, this treatment also reduces the need for reprocessing difficult and fatty tissue which may prove troublesome. If tissues are fatty at the outset, then treatment in fat removing solvents such as acetone or alcoholic formalin could be used prior to grossing. However, these solutions may prove detrimental if immunohistochemical or molecular studies are required at a later date. Extended processing times may also be required if ethanol is used as the dehydrating agent though isopropanol can be used as an alternative since it is a superior fat solvent. The availability and convenience of using grossing aids such as the ProCUT slicing device (Milestone Medical) and the TruSlice specimen cut-up system (CellPath) allow consistency when dissecting either fresh or fixed tissue samples, particularly when handling large tissue specimens (Figures 10 and 11). All product details and vendor information for this section are found in Tables 1 and 2.



Figure 10. The ProCUT grossing system (Milestone Medical). The images show the tissue on the base prior to grossing (left). Application of a dome large enough to accommodate and hold the tissue during slicing (center). Sliced tissue following grossing (right).



Figure 11. The TruSlice grossing system (CellPath) shows a sharp blade used for slicing the specimen and SM mothership cassettes containing selected tissue samples.

Tissue processing and embedding

SM cassettes in large format histology are compatible with all modern automated enclosed, open and microwave tissue processors. The tissue cassettes can either be layered or stacked in the processor racks and baskets which allow up to 32 SM or 64 slim cassettes, depending upon the processor capacity. All routine tissue processors can be adapted for large format cassettes whether the tissue processing schedules are incorporating ethanol and xylene, isopropyl alcohol (with or without xylene) or xylene substitutes. Processing times can be adjusted accordingly and will depend upon the final tissue sample thickness and style of SM cassette employed (standard, mothership or slim). In practice, processing times under 8 h can be achieved for 5 mm thick tissue samples using microwave-assisted processing.

Following processing, the paraffin-infiltrated tissues are transferred to the embedding station where they are embedded using either metal or plastic SM base molds designed to accommodate all large format cassette styles (Figure 12). As with conventional histology systems, specimen orientation at embedding must be performed depending on instructions from the pathologists and



Figure 12. Image shows various sizes of deep metal, large format embedding molds.

pathologist assistants. Although cut surfaces are generally placed face down in a mold, the tissue must be properly orientated in the correct plane if it has been inked to indicate the margins. Embedding tampers such as the CellCeps Plus (CellPath) may be used to flatten tissues in the mold during the embedding process, and these should be heated to allow a constant working temperature. Solidifying paraffin blocks at -5°C can vary, since blocks in plastic molds take longer to harden and be released from the mold due to the insulating properties of the plastic. Tissue blocks in metal SM molds take around an hour to harden and be released from the mold, while tissue blocks in mothership and slim molds harden much quicker (Figure 13). A paraffin build-up during embedding on the mothership cassette can often obstruct the identification (ID) cassette. Removal of this excess paraffin is required and can be performed manually by either scraping or preferably with the heated paraffin trimmer such as the Block Trimmer Plus (CellPath), leaving a crisp, undamaged barcode label on the ID cassette available for scanning. All product details



Figure 13. Tissue blocks in deeper metal SM molds take up to an hour for paraffin to harden completely (white). Paraffin blocks for mothership and slim molds (red) will solidify much quicker.

and vendor information for this section are found in [Tables 1](#) and [3](#).

Microtomy

Microtomy of large format blocks is compatible with most modern rotary and sliding microtomes. Although attachment of a quick release or vice clamp to individual microtomes is necessary for microtomy of large format blocks, most laboratories will dedicate microtomes for large block sectioning ([Figures 14](#) and [15](#)). However, it is up to each laboratory to ensure that their microtomes are compatible with the sectioning of large format blocks. Quick release clamps are easy to switch between standard and SM cassettes although there are several issues that need to be considered before purchasing these clamps. For example, while the Super cassette clamp (Leica Biosystems) can only be used in

vertical orientation, the Microm adjustable clamp (Thermo Fisher Scientific) and SM universal cassette clamp (CellPath) can be used in both the vertical and horizontal positions.

It is essential to check the length of the downward stroke of a microtome prior to commencing sectioning SM blocks. If the stroke length is less than 70 mm, this will be too short to section SM blocks which are orientated vertically and microtomists will be unable to section completely through the length of the block. For microtomes with a stroke length less than 70 mm, it is recommended that SM blocks are sectioned with the block orientated horizontally in the clamp. In addition, users should check for any signs of collision between the base of the blade holder and the lower jaw of the SM clamp while sectioning. This is particularly important as the microtomist sections deeper into the block as this will have a negative effect on section quality and may actually prevent a section from being cut.

Collision between the base of the blade holder and the lower jaw of the clamp has occurred with some older models of RM2200 series rotary microtomes (Leica Biosystems) when used with their Super cassette clamp. These collisions can be prevented by removing the plastic cover located at the base of the knife holder, thereby allowing greater clearance between the knife holder and this clamp. However, the impact becomes apparent very quickly when sectioning SM slim and mothership blocks embedded in shallower 8 mm deep molds since the clamp jaw is much closer to the knife holder base when holding blocks embedded in slimmer molds. For these reasons and when using the Leica Biosystems Super cassette clamp, it is recommended that SM blocks are embedded using deeper 15 mm SM molds. To utilize 8 mm deep molds, users of this

Table 3. Large format embedding molds and accessories.

Product	Vendor	Part #
SM Mold 60 mm × 45 mm × 15 mm	Ted Pella	27197-1
SM Mold 36 mm × 36 mm × 15 mm	Ted Pella	27197-2
SM Slim Mold 60 mm × 45 mm × 8 mm	Ted Pella	27197-3
SM Base Mold 60 mm × 45 mm × 15 mm	CellPath	GBC-6014-05A
SM Base Mold 36 mm × 36 mm × 15 mm	CellPath	GBC-3614-05A
SM Slim Base Mold 60 mm × 45 mm × 8 mm	CellPath	GBC-6014-05B
SM Mothership Base Mold 60 mm × 45 mm × 8 mm	CellPath	GBC-6014-05C
Super Cassette Base Mold	Leica Biosystems	38VSP58166
SM SS base Mold 36 mm × 26 mm × 15 mm	EMS	62354-36
SM SS base Mold 60 mm × 45 mm × 15 mm	EMS	62354-60
SM Slim SS base Mold 60 mm × 45 mm × 8 mm	EMS	62354-37
SM Mothership SS base Mold 60 mm × 45 mm × 8 mm	EMS	62354-61
Mold disposable, Super large cassette	Cancer Diagnostics	LBM5550-P
CellCeps+ Heated Tweezer System (Includes 1 mm + 2 mm Serrated Jaw Tweezers, Controller + PSU)	CellPath	GZG-0100-00A
CellCeps+ Heated Tamper 28 mm × 25 mm (Blue)	CellPath	GZJ-0100-00A
CellCeps+ Heated Tamper 8 mm × 8 mm (Red)	CellPath	GZJ-0300-00A
Block Trimmer Plus – Wax Trimmer	CellPath	JAZ-0100-00A



Figure 14. Three styles of SM quick release clamps used for microtomy.



Figure 15. Sectioning large format blocks in the laboratory using a dedicated microtome.

clamp are advised to either have the lower jaw of their clamp adjusted by their engineering department or alternatively use the compatible SM universal cassette clamp (CellPath). If tissues have been processed and embedded using SM slim cassettes, aluminum spacer blocks are available which allow compatibility with quick release SM clamps and vice clamps available in the market (Table 4).

With the Microm adjustable clamp (Thermo Fisher Scientific), care needs to be taken when setting the jaw distance on the clamp with the screw fitting. If the distance between the jaws is set too short, this can apply too much pressure to the ends of the cassette causing it to

bend and result in a cracked paraffin block. When sectioning fibrous specimens with the clamp in the horizontal position, the cassette and block can pivot on the factory-fitted support plates. However, longer support plates which prevent this pivoting action are available from suppliers such as CellPath (Figure 16).

Unlike quick release clamps, vice clamps are slower to use. If SM blocks need to be recut or re-cooled, it is more difficult to reposition blocks returned to the microtome (Figure 17). Consequently, more refacing of blocks is required as compared to blocks sectioned using the clamps specifically designed for SM cassettes. In order to address this issue, blocks are often chilled *in-situ* in the clamp using freeze sprays, although there is the potential risk to crack and fracture blocks with embedded tissue specimens. Vice clamps have limited use and often do not allow blocks to be cut in either the horizontal or the vertical position. Another issue to consider when using vice clamps is the draft angle, i.e. the sloped side of the cassette (Figure 18). The draft angle makes it easier to remove the plastic cassettes from injection molds during cassette manufacture. If the draft angle is good, the sides of the cassette will be drawn into the clamp by the jaws and provide stability. However, if the draft angle is not optimized, the cassette will be pushed out of the clamp as the jaws travel down the slope of the cassette. If tissues have been embedded in SM slim cassettes, thinner spacer blocks are available for use with vice clamps. The spacer block enables the vice clamp to grasp a larger

Table 4. Microtome SM cassette clamps and accessories.

Product	Vendor	Part #
Spacer Block for SM Hex Slim Cassettes	Ted Pella	27199
SM Slim Microtome Chuck Spacer Block	CellPath	JFA-0100-00A
SM Slim Microtome Chuck Spacer (Vice Clamps)	CellPath	JFA-0100-00B
SM Universal Cassette Clamp	Ted Pella	27198
Universal SM Cassette Clamp	EMS	70065-01
Super Cassette Clamp	Leica Biosystems	14050238967
Microm Adjustable Universal Cassette Clamp	ThermoFisher Scientific	716120
Shandon Finesse Vice Clamp 60 mm × 55 mm	ThermoFisher Scientific	77510167
SM Universal Cassette Clamp	CellPath	JFB-0100-00A
SM Support Plates for Microm HM microtomes	CellPath	JFA-0200-63A



Figure 16. Longer replacement support plates for the Microm adjustable universal macro-cassette clamp. Note the silver arms shown on top of the clamp holding the SM cassette with paraffin block. These arms on the longer plate provide improved stability for SM blocks during sectioning when the clamp is in the horizontal position as shown.

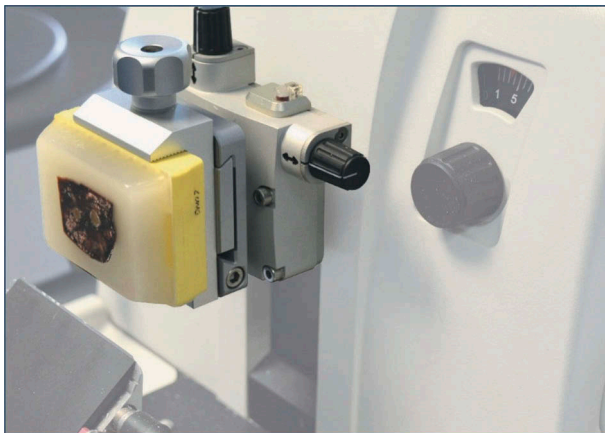


Figure 17. Vice clamps with a large metal screw for SM cassettes are slower to use than quick release clamps. If blocks need to be recut or recooled, it takes practice to return them to the same position and not waste tissue.

area on the side of a slim cassette in order to hold it firmly for more block stability. The spacers also provide additional paraffin cooling prior to sectioning if blocks are pre-cooled on a cold plate. All product details and vendor information for this section are found in [Tables 1](#) and [4](#).

Staining

Following microtomy, the large format sections are floated onto a water bath and mounted onto 3 in. × 2 in. glass slides. These slides are obtainable as plain, twin-frost (with ground 5 mm wide color-frosted writing area) and available as positively charged for keeping problem sections attached to the slides during routine and special staining, including immunohistochemistry. Because the

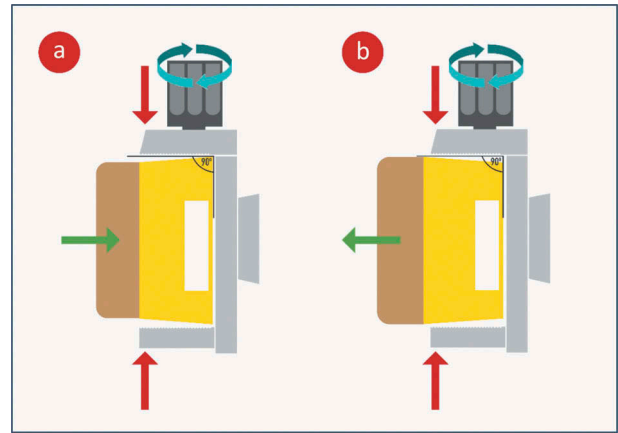


Figure 18. In both images, the SM cassette (yellow) is clamped in a horizontal position. The blue arrows show the knob of the clamp closing the jaws onto the cassette. Red arrows indicate the direction of the jaws pressing on the cassette, and the green arrows show the direction the cassette moves as the jaws tighten. In (a) the cassette has a good draft angle and is pulled into the clamp (green arrow) as the jaws close and grip the cassette walls. In (b), a cassette with a bad draft angle is forced out of the clamp as the jaws tighten onto the cassette walls (green arrow).

slides are twice the width of conventional 3 in. × 1 in. microscope slides, slide rack adapters are available for most makes of automated stainers, i.e. produced by Sakura Finetek, Leica Biosystems, ThermoFisher Scientific, Medite and General Data ([Table 1](#)). These adapters are able to carry five SM slides per rack and can be positioned in the rack to accommodate different width slides ([Figure 19](#)). As each adapter has a ledge to support the edge of the slide, there is no requirement for slide supports in the base of these racks.

Currently, no platforms are available for SM slides for immunohistochemical (IHC) staining. Additionally, if large format blocks must be sent away for further analysis, many external laboratories do not have the capability for sectioning these blocks. Nonetheless, these problems can be overcome in one of the several ways. If IHC staining is a pre-requirement for a particular specimen at grossing, it is sometimes beneficial to prepare an additional smaller representative tissue block and process it in a conventional-sized, standard cassette. However, since the region of interest (ROI) is often uncertain, it would be preferable to process the whole tissue sample in large format cassettes. This will allow the pathologist to highlight the ROI on the slide for either IHC or molecular testing. In the laboratory, the chosen area is selected by floating the large format section onto a water bath and with forceps, cut out the area marked by the pathologist on the original stained slide ([Figure 20](#)). The new section is then re-floated onto a standard positively charged glass

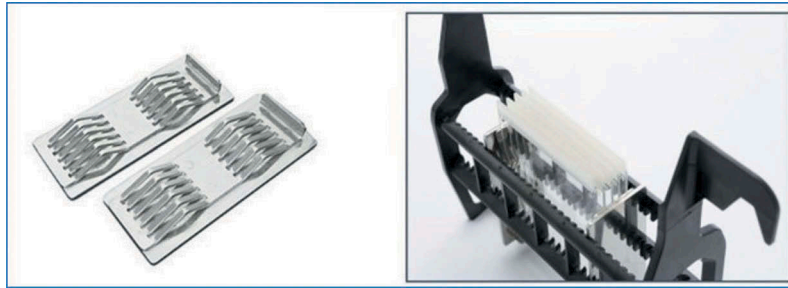


Figure 19. Slide rack adapters for large format microscope slides (left). Adapter with slides positioned in a staining rack in readiness for automated staining (right).

slide and the process repeated for each ancillary test required. Alternatively, the area to be evaluated can be excised from the SM paraffin block with a bladed instrument and re-embedded in a conventional-sized cassette. This would allow smaller sections within a region of interest to be cut and mounted onto standard positively charged slides in readiness for IHC staining. With IHC playing such a leading role in cancer diagnostics, it is assumed that automated immunostaining platforms could soon become available to support large format histology. Until then, the current IHC systems need to be modified and adapted in order to manage the staining of large format sections.

Following staining, coverslipping large format sections is usually performed manually under chemical fume hoods. Coverslips for large sections are available in several sizes and fit the dimensions of larger slides. Additional drying time is often required following mounting and slides can either be left overnight at room temperature or placed in an oven at 65°C for 1 h. Slide labeling is best performed following coverslipping, and there are label printers such as the Cognitive Printer CXT2-1300 (General Data) currently available for SM slides which can print on 1.75 in. x 0.375 in. labels. Examination of stained slides is carried out using laboratory microscopes (with standard or large

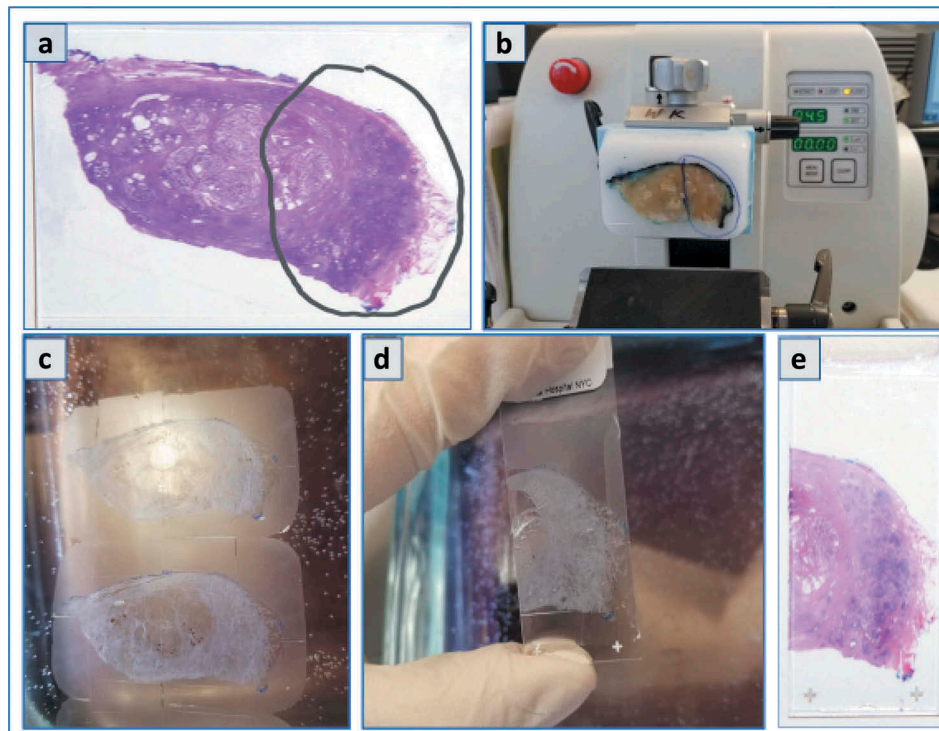


Figure 20. Large format sectioning for a small region of interest in a tissue. (a) Large format section stained with hematoxylin and eosin (H&E) with ROI circled. (b) Same ROI outlined on SM block in preparation for re-cut. (c) Paraffin sections cut from ROI on block (a) are floated onto a water bath. (d) The selected ROI section is separated with forceps and picked up onto a regular, positive charged microscope slide. (e) The new ROI section stained with H&E and examined prior to IHC staining.

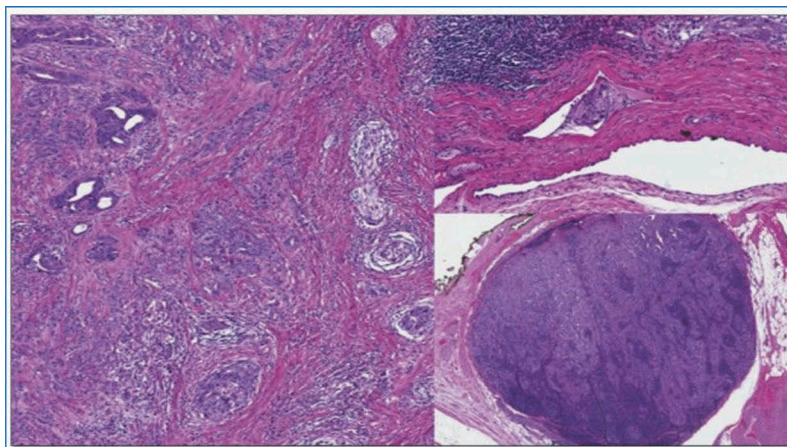


Figure 21. Large format, digitized section of prostatic cancer showing lymphovascular invasion (on left) and lymph node metastases (on right) (Reproduced from [11] with permission).

slide platforms) and slide scanners such as the TissueScope CF (Huron Digital Pathology) capable of digitizing large format sections (Figure 21, Reference [11]). All product details and vendor information for this section are found in Tables 1 and 5.

Filing and archiving

Transporting large format sections around or away from the laboratory is easily achieved using dedicated slide trays, boxes, and mailers available from numerous vendors. Filing and archiving of large format slides and blocks is managed using stackable metal or non-metal boxes, drawers, and cabinets. The removal of central dividers in conventional filing systems often allows suitable storage for large format slides and blocks. Many archiving systems are modular, interchangeable and compatible with those offered by other vendors and can often

be stacked with standard size block and slide cabinets. All product details and vendor information for this section are found in Tables 1 and 6.

Clinical laboratory benefits

Large format sections may be used for radical prostatectomies and rectal specimens containing rectum and mesorectum. For radical prostatectomies, the large format sections allow sampling of the entire gland which will decrease the number of samples in routine size cassettes submitted from a grossing room. The easy anatomic orientation provided by large format sections enables pathologists to map the exact tumor location, rather than the reconstruction of sections which were cut into quadrants. Large format section becomes a helpful tool for easy determination of the greatest tumor dimension, as required by the College of

Table 5. Large format microscope slides and staining accessories.

Product	Vendor	Part #
HiQa SM Twinfrost Microscope Slide	EMS	71881-30
HiQa SM Cover Slips No.1, 50 mm × 64 mm	EMS	71881-90
Histobond+ SM Slides	EMS	71881-60
Microscope Slides 51 mm × 75 mm	Brain Research Labs	5075-PLUS
Cover glass 50 mm × 75 mm	Brain Research Labs	5075-1
Corning Large Glass Slide 50 mm × 75 mm	Ted Pella	26005
Large Plain Slide 2 in. × 3 in.	Ted Pella	260439
Adhesion Superfrost+ 51 mm × 75 mm (2 in. × 3 in.)	Ted Pella	260239
Cover Glass No.1, 48 mm × 65 mm	Ted Pella	260365
Cover Glass No.1, 50 mm × 75 mm	Ted Pella	260462
HiQa SM Twinfrost Microscope Slide	CellPath	MAD-1400-02A
HiQa SM Cover Slips No. 1, 50 mm × 64 mm	CellPath	SAF-5064-02A
Histobond+ SM Slides	CellPath	MAD-1402-02A
Slide Rack Adapters	Ted Pella	21055
Slide Rack Adapters	EMS	70065-30
Slide Rack Adapters	Brain Research Labs	5055
Slide Rack Adapters, Stainless Steel	CellPath	RMC-2000-63A
Cognitive Printer CXT2-1300	General Data	C9-204-2130
TissueScope CF Slide Scanner	Huron Digital Pathology	TissueScope CF

Table 6. Large format archive boxes and cabinets.

Product	Vendor	Part #
BlocFile 1 for SM Blocks/Slides	EMS	63290-03
BlocStor 3 SM Archive Box for Blocks/Slides	EMS	63290-01
Filoslide 100 SM Slide Box Plastic (Tall – Blue)	EMS	71659-19
Tall Slide Box, 100 slides (2 in. × 3 in. slides)	Ted Pella	2197
Tall Slide Box, 25 slides (2 in. × 3 in. slides)	Ted Pella	2195
BlocFile 1 SM Cassette/Slide box	CellPath	WCB-1100-08F
BlocStor 3 SM Cassette/Slide box	CellPath	WCB-0500-08F
OmniStor 4 Standard	CellPath	WEA-0700-08F
OmniStor SM Cabinet – Blue	CellPath	WEA-1305-00A
OmniStor Base Plinth (Wheeled) – Black	CellPath	WEA-0601-00A
OmniStor Base Plinth (Static) – Black	CellPath	WEA-0501-00A
LABSTACK Multi-Purpose Filing Cabinet	Lab Storage Systems	L-7FC-BL
Base Stand	Lab Storage Systems	L-BS
Base Stand (Wheeled)	Lab Storage Systems	L-HDWB
Lab Archive Unit – 7 Drawers	Leica Biosystems	14037560001

American Pathologists (CAP) guidelines (www.cap.org). In addition, pathologists can easily identify the location and extent of extracapsular margin status when sections are presented in large formats. Similar to the benefits seen with prostate specimens, the use of large format specimens in colorectal cancer allows for exact mapping of all lymph nodes present in the mesorectum as well as providing pathologists with

highly detailed spatial information on any lymphovascular invasion.

In conclusion, large format histology has proven to be cost-effective and able to meet the needs of the modern histology laboratory, particularly for a multidisciplinary approach to cancer diagnosis [3,12–15]. Stained large format sections can be photographed either macroscopically or at low magnification then compared with macro

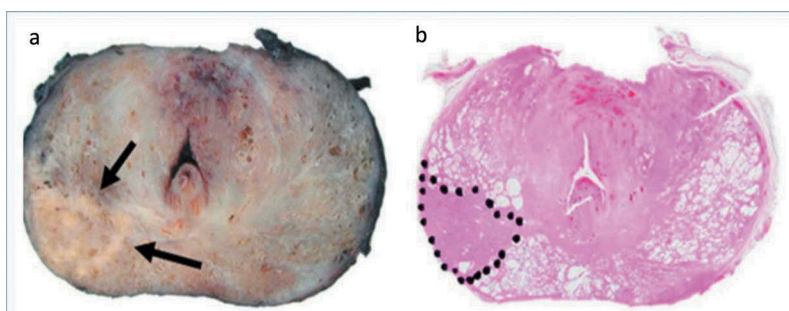


Figure 22. Macroscopic slice of prostate with tumor (a). Pale tumor is shown in gross sample (arrows) and compared to (b) H&E-stained large format section from the same sample. Dotted lines indicate the area of the tumor (Reproduced from [15] with permission).

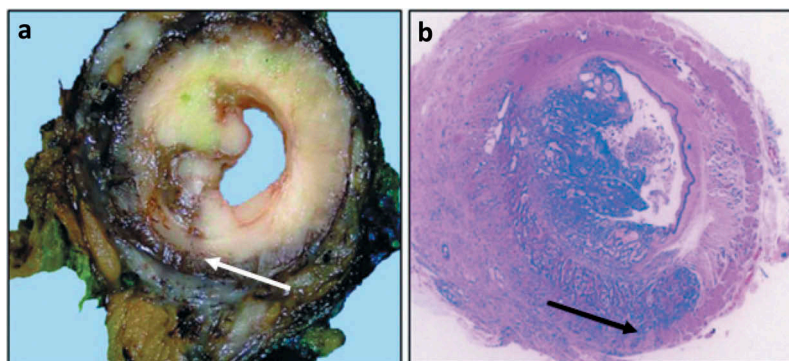


Figure 23. Macroscopic slice through an esophageal tumor (a) compared with (b) H&E-stained large format section from the same slice. The white arrow in (a) shows extent of the tumor while the black arrow in (b) indicates the proximity of the tumor to the resection margin (Reproduced from [3] with permission).

images taken at the time of grossing (Figure 22, Reference [15]; Figure 23, Reference [3]). Furthermore, the system has shown it can aid in detecting clinically significant pathology that is often absent on standard format slides [5]. Large format histology is dependent upon the needs of both the pathologist and the laboratory. Any shortcomings however can be significantly outweighed by the clinical benefits that the large format system brings to the histology laboratory.

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Disclosure statement

Dr Neil Haine is employed by CellPath Limited. No potential conflict of interest was reported by the other authors.

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