Automation in the histology department

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Introduction

Transforming a tissue specimen from fixed material to stained sections is a multiple step process which began as separate manual tasks. Indeed, histology in the last century has been the slowest of the laboratory medicine departments to innovate and keep pace with the speed required for a modern dynamic hospital. Whereas the availability of high-throughput analyzers has made same-day results the expected norm in the blood sciences, histology, with its labor-intensive preparations and processes usually sees result turnaround time (TAT) for biopsies and surgical samples being counted in days or weeks rather than hours or minutes.

Historically the lengthy TATs of the histopathology laboratory have been unavoidable due to the technical requirements and the multiple manual stages involved from tissue handling through to the preparation of slides. However, alongside the demands of modern medicine many laboratories have introduced new semi and fully automated processes and tracking systems designed to enable rapid, accurate and safe histopathology reporting.

The modern manipulations to deliver these tissue handling steps are covered in the various chapters of this book, but increasingly this is an automated and standardized reality. Histology automation is perceived as a relatively recent movement, but examples began to be seen as far back as 1945 (Titford, 2006). This chapter will deal with various components of laboratory activity and the automation which currently exists. Whilst there are many companies and systems to facilitate these automated solutions to histology laboratory practice, only some illustrative examples are given and the discussion cannot be all-encompassing. Indeed, one must look at this evolving technology arena regularly in order to to keep up to date with the companies which serve this aspect of laboratory practice and their equipment.

The drivers for change

Drivers for the automation of histology processing are various, but principally hinge on two elements: financial budgets (generally constrained) and the need for rapid sample analysis (patient and clinician led). The increase and availability of preventative medicine such as screening protocols, and the development of specific testing for personalized medicine within an aging population, have all contributed to an increase in histology workload. Globally, laboratories are expected to be more efficient than ever. The trend being seen in terms of economies of scale and diagnostic national and international guidelines has pushed towards a minimum number of samples for laboratory efficiency. There are fewer, larger laboratories processing thousands of specimens per month.

The changing nature of laboratory accreditation is another driver to the introduction of automation. The required standards for an accredited laboratory have been expanded to include the validation and verification of all processes, as well as standardizing the equipment and reagents used. The innate production of this type of process normalization and audit information is one of the strengths of an automated procedure.

Technology now exists which, combined with adaptations to work practices, allows results to be available within 24 hours of a biopsy being taken for small and straightforward samples. This should lead

to an improved clinical response and patient outcome without an increase in cost. The goal of introducing a more automated process into histology is to enable a leaner, more efficient process which benefits staff, patients and the service user/s.

Finally there are subsidiary drivers to be considered. For example, looking at processing, one can appreciate that tissue samples needing to move from fixative to paraffin wax requires transfer between multiple solvents and impregnation periods at each stage; this normally takes several hours. Automation of this stage reduces the requirement for manual intervention and allows the process to occur faster or overnight, assisting TATs. Other beneficial outcomes to these systems include the increased safety of the user as the process occurs in an enclosed environment with minimal reagent handling. This has significant health and safety benefits.

Barcode technology and automated sample tracking

A laboratory's responsibility for a specimen (and the laboratory's TAT) begins as soon as the tissue has been removed from the patient. It is from here automation and tracking can begin. Systems such as the Menerini Tissue SAFE are available. These record the time the specimen was taken, when formaldehyde was added and the temperature at which the specimen was transported to the laboratory, therefore maintaining standardization. This allows comprehensive verifiable data on the pre-analysis handling of the specimen (Menerini, 2016).

Sample tracking continues once the specimen is received and passes through all the laboratory processes, ultimately producing a diagnostic report and recording both the disposal of excess material, and specimen storage. The production of an audit trail and the associated chain of custody can be a labor intensive process both to complete and interrogate. Indeed, this mundane task of the completion of an audit trail can account for a significant portion of the departmental workload, the majority of which is the responsibility of the laboratory staff.

In many laboratories the creation of this audit trail has been constructed piecemeal over a period of time, with each step often recorded in a different format and the records often stored in separate physical locations within the laboratory. As a result, laboratories have a plethora of different systems in use including (but not limited to) colored slides and beads, lists of specimens, log books, worksheets and initials here, there and everywhere! This approach arises as a result of the different requirements for the histology material as the specimen moves through the histology process. It is not easy to capture all the required information in a centralized location and there has been a lack of computer software designed specifically for this task.

A comprehensive computer system which records key aspects of the process, such as who has booked in, dissected, embedded, trimmed, cut and checked a specimen can be a useful information management tool.

Barcoding specimens on receipt and integrating this into the laboratory information management system (LIMS) can help facilitate tracking through the laboratory processes. Printing corresponding barcodes onto all of the forms, blocks and slides associated with the specimen and scanning at every station in the laboratory process can provide a comprehensive tracking system from the time a specimen enters the laboratory, right up to the time the sample analysis is concluded. Using purpose-built software with user identification, this kind of minute-by-minute, station-to-station tracking can also provide a detailed record of the personnel involved at each step, detailed data on which equipment was used (where applicable), and the overall laboratory efficiency.

Not only does this automation create the audit trail with a fraction of the user time currently required, it also integrates this information and displays it in an easy-to-use dashboard format. This information can easily and quickly be interrogated to provide workflow, error identification and quality indication information. This is simply not possible with conventional manual systems.

The other advantage of barcode technology is that it enables the automation of the transcription of information from one medium to another. For example, slides can be automatically printed with the laboratory accession number, patient name and

stain generated by the LIMS system and driven directly from the block barcode. This makes the process much faster, safer and more reliable than error-prone manual transcription by humans. At the same time the audit trail attached to the block can be automatically updated with details such as the microtome used and microtomist performing the task.

Many laboratories currently manually transcribe tens of thousands of digits per day and the potential adverse impact of any transcription error necessitates several checks to ensure that the manual transcription of information is correct. The appeal of automating this step wherever possible can be readily appreciated. Providers claim that the correct use of a proprietary system of this kind can reduce the chance of transcription error to almost zero (Roche, 2011).

Implementation of these error reducing automated steps can significantly minimize the risk of adverse events reducing reliance on vigilance at each process step. This permits streaming of the complex array of double and triple checks, thereby significantly improving productivity. There is also an improvement in the ability to access relevant information at each point in the workflow from block or slide.

Automated sample transcription and tracking can either be achieved via in-house development or purchased as whole tracking systems, such as the Leica CEREBRO system, Dako's True Positive ID or VENTANA/Roche's VANTAGE. Some of the advantages and disadvantages associated with each method are outlined in Table 11.1.

Dissection/grossing

Dissection remains a hands-on area of the laboratory with knowledge and training the main requirements for best practice. However, the implementation of macroscopic photography and videography equipment can assist in both of these aspects.

Photographs can be used to store images of forms, blocks and pot labeling and other relevant information e.g. where certain blocks have been taken from a macro specimen. These images can be stored and annotated, improving the record of the macroscopy and dissection of complex specimens. The images can then be made available to the pathologist at the time of reporting and during future discussions, e.g. multidisciplinary team (MDT) meetings.

Table 11.1 The advantages and disadvantages of in-house and commercially available specimen tracking systems

In-house	Commercial
Cheaper initial costs	Requires additional funding
Flexible	Service contract provided
Bespoke solution	Single joined-up solution
Expert support in-house	On-going development and software updates
Asset creation	Try before buy
Requires in-house skills	Expensive, but costs may be offset with other service contract commitments
Difficult to join up components	Tied in to single provider
Requires time to develop	Closed system – requires engineer response
Requires IT resource commitment	Ongoing support costs
Works around your departmental needs	May require adaption of whole laboratory process to correlate with system upon implementation

Their use allows dissection images to be taken which can be used as training tools, to write standard operating procedures (SOP's) in a video format, or to live stream an unusual case for pathologists to discuss. Their use can also allow for remote pathology, with real-time guidance given to the dissector by off-site pathologists viewing the dissection over a video link or web-based systems.

Many systems now exist which fulfill this role and can be permanently mounted over the dissection table. Examples currently include the Menerini MACROpath and Cirdan's Pathlite Macro Camera Station.

Processing

To take a tissue specimen from fixative to paraffin wax requires transfer between multiple solvents and impregnation periods, often taking many hours. This is one of the most commonly automated stages in any histology laboratory, reducing the requirement for manual intervention and allows the process to occur overnight. The length of processing schedules can be reduced with automation, as it becomes possible to use heat and vacuum-assisted impregnation techniques. Other beneficial outcomes to these systems include the increased safety of the user as a result of the process occurring in an enclosed environment, with minimal reagent handling.

Specimen processing was the original automated procedure in histology and remains possibly the most widespread example of histology automation today. The first examples of automated processing in histology involved a dish into which samples were placed. This then revolved through the processing chemicals; a predecessor to the current carousel type tissue processors.

The majority are now stationary chamber processors, where tissue samples are placed into a retort into which the reagents are pumped in and drained out according to a processing schedule. Early advances on this design resulted in the option to use a vacuum and/or convection style heat exchange to encourage rapid solution permeation and hence improved, faster, more reliable tissue processing. With conventional processors of this type, smaller tissue samples can be processed in under 2 hours, allowing them to be run continuously throughout the day. To ensure adequate processing, however, the majority of blocks are still restricted to a processing schedule in excess of 8 hours. In practice this means overnight processing of larger tissue blocks, leads to a minimum of 1 day delay in slide production and the batching of the majority of the following day's workload.

Shortening the processing procedure has been successfully achieved by replacing or enhancing the convection heating methods with microwave heating. This shortens the processing schedule and can remove the need for hazardous chemicals such as xylene and, in some cases, formalin. Despite the proven benefits, such as the production of high quality staining and reduced tissue shrinkage, with shorter process times and reduced reagent costs over conventional methods, microwave processing has been slow to catch on (Metgud et al., 2013). This may partly be due to concerns to antigen preservation as a result of the irregular distribution of energy due to reflection and interference within the chamber. Many systems incorporate a platform or other device to facilitate uniform heat exposure. Two examples of processors which can use microwave technology to reduce processing times are the Leica PELORIS and the Sakura Finetek Tissue-Tek® Xpress®.

The Tissue-Tek® Xpress® (Fig. 11.1) is a microwave unit with reaction chambers designed for uniform distribution of electromagnetic waves to uniformly heat the samples. All samples must be cut to a uniform thickness of no more than 2 mm which allows both biopsies and larger specimens to be processed on the same run. Up to 40 blocks can be added to the processor every 20 minutes in a continuous process, which promotes LEAN workflow by eliminating batching (Sakura Finetek, 2014).

Reagents must be purchased ready-to-use, and the system is xylene and formalin free. A pre-processing step is required, consisting of fixation with Tissue-Tek® Xpress® Molecular Fixative to ensure the preservation of DNA, RNA and proteins in the paraffin wax block.

The Leica PELORIS (Fig. 11.2) is a dual retort processor capable of traditional or xylene-free processing. Xylene-free protocols use two sets of

Fig. 11.1 Sakura Finetec Tissue-Tek® Xpress®.

dehydrants: industrial denatured alcohol (IDA) and isopropyl alcohol (IPA) rather than separate dehydration and clearing steps. This allows the use of higher temperature paraffin wax impregnation steps leading to faster processing.

Each retort can be run separately and hold 300 cassettes across 3 baskets. This scheduling flexibility together with faster xylene-free programming can aid in a laboratory's LEAN workflow. One-, two- and four-hour programs allow almost all diagnostic biopsies and many other small specimens within a department to be processed through the day, greatly improving turnaround times, and leading to a continual flow process. As a result, small biopsies can be processed during the day, and as the embedding of blocks processed overnight finishes, these rapid runs become available for embedding and sectioning. Staggering the loading of each retort throughout the day ensures continuous flow.

The Leica PELORIS also features automated reagent management, monitoring reagent usage and alerting the user when reagent purity has dropped below a pre-set prescribed limit. This ensures that processing quality is maintained at an acceptable standard and reduces reagent usage and associated costs (Leica Biosystems, 2016).

Fig. 11.2 Leica Biosystems PELORIS.

Recent trends in enclosed, automated processor design show the increased awareness and the responsibility that the laboratory has to the health and safety of their staff. These concerns have led to a new generation of processors which have minimized hazardous reagent handling. Processors such as the Thermo Fisher EXCELSIOR and Milestone LOGOS are designed to accept the original reagent transport containers which are stored in the base of the machine. This removes the need to transfer reagents between containers, minimizing operator exposure to the reagents and also reducing reagent change times.

Embedding

This has always been the first task at the start of the day for the laboratory staff. Even with continuous processing, all blocks requiring an extended

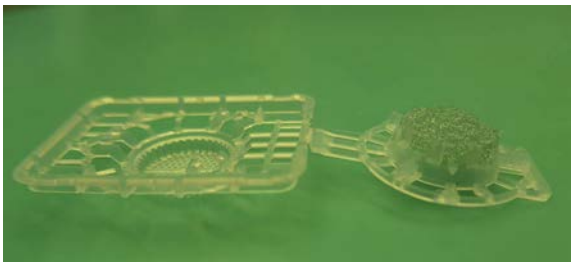

Fig. 11.3 Sakura Finetek Paraform cassette.

processing schedule tend to become available to embed as a single large batch at the beginning of the day, and in some departments the embedding of this batch may take the entire day.

Automated embedding equipment now exists which involves orienting the tissue at dissection and processing it in the mold/capsule it will be embedded in. This removes any requirement for orientation at the embedding stage and enables this step to be automated, freeing up the personnel to do other tasks. Two examples of automated embedding equipment are the Sakura Finetek Tissue-Tek® AutoTEC® and Milestone's SYNERGY system.

The Sakura Finetek system, the Tissue-Tek® AutoTEC® uses Paraform cassettes which hold the orientation of tissue placed into them at dissection. The auto-embedder then embeds the entire Paraform cassette holding the tissue in the retained orientation (Fig. 11.3).

The Paraform cassettes' plastic mesh is the same density as the solid paraffin so the resulting block can be sectioned using routine microtomy techniques. The system is capable of embedding up to 120 cassettes per hour with continuous loading of 4 magazines (Sakura Finetek, 2016).

Milestone has introduced their SYNERGY system which they describe as an all-in-one processing and embedding method. This involves placing the tissue into disposable molds prior to processing which are then kept in place with sponge and the printed cassette. Post-processing the mold/cassette unit is transferred to a cold plate to set, after which the blocks can be removed for microtomy.

Auto-embedding technology is still in its infancy, and there are currently several limitations to its use. When looking to purchase an auto-embedder, careful consideration must be given to the ongoing cost of the product and its required consumables, balanced against the cost of the laboratory personnel it may replace. As the precision of the tissue orientation with automated systems is currently poor, thought must be given to the proportion of the laboratory workload for which it which would be appropriate. For example, it would not be possible to continue to orient GI biopsies, which some laboratories routinely position to ensure mucosal cross-section.

With this in mind, the question to address is whether the auto-embedder may deal with sufficient embedding to significantly improve the work-flow and free up sufficient personnel to make an advantageous change to the TATs. Finally, in this arena, one has to address the issue of what back-up will exist if the auto-embedder is broken.

Trimming and microtomy

Microtomy is another area where full automation is yet to be realized, as it depends on the judgement of the microtomist to both trim the tissue to the required depth, and determine when an adequate section has been produced. This is not to say that the process cannot be improved by the introduction of automated ancillary elements. As discussed briefly above workflow, accountability and safety in this area all have the potential to be significantly improved with the use of barcoded cassettes producing labels or printed slides at the microtomy station (Fig. 11.4).

Manual transcription of numbers from block to slide is still a common sight in the majority of laboratories, despite significant opportunities for error. As workloads increase, double or triple checks became required to detect these potential errors and the quality assurance process becomes time consuming.

The use of a barcoded cassette, barcode reader and slide printer at each microtome station removes the need for many of these QA steps by automatically producing a barcoded slide or slide label at the point of production. Done correctly this results in a reduction in human transcription error, an increase

Fig. 11.4 Microtomy station showing barcode reader and label printer.

in patient safety and a saving of many staff hours in checking and rechecking of numbers. Some of the potential effects upon the workflow resulting from the introduction of this type of system are indicated in (Table 11.2).

Hematoxylin and eosin

Alongside tissue processing, the H&E stain is another major component of histology which is automated in a majority of laboratories. Traditional dip-and-dunk automated H&E stainers come in two basic forms.

The first is the linear style of stainer where the slides progress along a conveyor individually, or within a rack being submerged in various solvent and dye pots. The time in each container is constant, and the stain can be optimized by adapting the number of pots for each solvent and stain (Fig. 11.5).

The streamline design enables a LEAN, first-in-first-out system, and the limited mechanical complexity makes these stainers robust. However, the ability to tailor the staining is limited by the predetermined number of seconds per pot and pot number. Additionally the constant use of the same reagent pots can lead to variation in staining as the day progresses and frequent reagent changes or monitoring may be required. These systems are frequently not fully enclosed, and issues arising from evaporation, humidity and increased user contact with the chemicals can also prove disadvantageous.

The second type is the X-Y stainer design. This is usually enclosed and can attach to ovens and/or a cover slipper. These machines feature a robotic arm which moves the rack along, following a predesigned protocol (Fig. 11.6). Protocols can be designed by dictating the sequence of reagents, and the time in each can be modified independently, allowing multiple stains to be performed on a single unit. User contact with the chemicals can be minimized as the rack can be loaded into an empty input area. For a small number of racks these systems can be quick. One disadvantage of these systems is that unless programs are carefully designed, bottlenecks commonly occur once a certain threshold has been reached. This is because racks are held in a queue for limited heater spaces, or to allow previous racks to complete lengthy staining steps. As a result of this in a larger laboratory these stainers can cause batching of work and delay.

The new generation of automated H&E stainers, such as the Dako Coverstainer and the Roche Symphony, seek to provide a complete integrated system from slide drying to staining and coverslipping. Emphasis is placed upon the reduction of carryover, consistency of staining, LEAN workflow and capacity. Slide racks are typically smaller than those of previous machines, and slides are held flat, side-by-side to reduce carryover and simplify the mechanics of coverslipping. These tend to be 'closed' systems. They require proprietary reagents to be purchased from the manufacturer, but there is the possibility of linking into specimen tracking systems to extend the audit trail.

Table 11.2 The effect of slide transcription automation upon workflow

Stage	Without transcription automation	With transcription automation
Microtomy	Check block. Transcribe block number to slide in pencil. Initial slide. Indicate intended stain on slide. Cut block and mount section on slide. Check transcribed number.	Check and scan block. Cut block and mount section(s) on slide(s) generated.
Post stain labelling	Check handwritten slide number against block number and tissue. Find LIMS generated printed label. Label slide with printed label.	N/A
Post stain quality assurance step	Check label against block. Check slide for section depth and defects. Check slides against request form and compile case. Check slides and form against LIMS system. Release to Pathologists.	Check slide for section depth and defects. Check slides against request form and compile case. Check slides and form against LIMS system. Release to Pathologists.
Audit	Who embedded? – check bead in cassette. Which embedder? – guess work. Who trimmed? – check logbook. Which trimming microtome? – Unknown. Who cut? – check slide. Which microtome? – Unknown. Who checked? – check request form audit trail.	Interrogate database

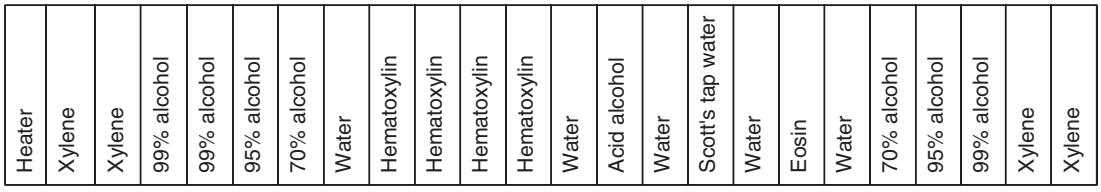

Fig. 11.5 Typical arrangement of reagents in a linear stainer. Slides travel from left to right at a constant speed.

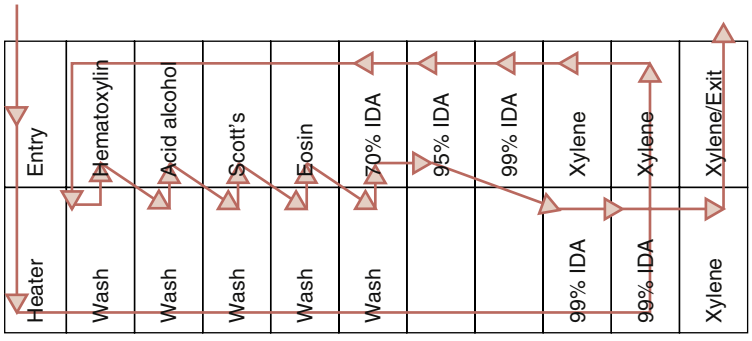

Fig. 11.6 A typical arrangement of reagents in an X-Y stainer. One possible programmed path is shown by the red line.

With so many automated H&E systems available on the market it may be useful to consider the following options when choosing which is right for your laboratory and its workflow:

- Extraction vs. filtration of solvent fumes.
- Speed of single rack vs. speed of 5+ racks.
- Fully autonomous vs. speed of multiple rack.
- 1 stain vs. 2-3 stains in one unit.
- Cost of equipment vs. predicted time savings.
- Compatibility with existing laboratory hardware/software.

Tinctorial staining

Manual staining is a time consuming process which requires at least one trained individual to spend a large proportion of the day juggling timers, stains and rinse steps, often having to adapt the protocol due to tissue type, humidity, dye variation or other variable. If individuals are on a rota through this section, some of the less common stains may not be performed by an individual for months or more, making standardization and competency hard to maintain.

With the increasing need to categorically demonstrate the validity of results, the standardized, same day result which is produced by a tinctorial autostainer can be a great asset to a laboratory. Many of these automated tinctorial staining systems are capable of being customized. Individual slide heaters and the ability to produce a custom protocol enables consistency, whilst also catering to established pathologist preferences.

The overall TAT for individual stains is frequently longer than the bench equivalent (with a few notable exceptions), but the true saving is that of personnel, who are only required to load, unload and maintain the machine. As well as being less labor intensive, these steps do not require the same experience level or length of training as bench staining itself does, reducing the training burden on the laboratory and enabling staff to become competent in the section in a reduced timeframe. As always, a back-up has to be considered in case of technical failure.

There is also the potential for remote requesting: many systems when used together with 3D barcodes and an LIMS system enable the pathologist to request further work from remote workstations. These systems can also resolve some commonly found poor practice, such as the need for illegible paper slips to request further work, stains being missed, or re-labelling of slides by automatically adding requests to both the pending label printing software and pending staining protocols worksheet. Once the barcode labelled slide is added to the stainer it proceeds to confirm and log which stain is required and if the required reagents are both available and in date, information which forms part of the comprehensive audit trail.

Two widely used histochemical stainers are the Dako Artisan Link System (Fig. 11.7) and the Ventana Benchmark SS, both of which use proprietary reagents, individual heating plates and the ability to perform multiple stains in a single run (Roche 2013a; Dako, 2016).

In both cases the emphasis is placed upon the quality and reproducibility of the staining. Reagent management and validation is simplified with the use of barcoded IVD marked reagents. The drawbacks of tinctorial stain automation at present include the limited range of stains available, and the comparatively high cost per slide of automated staining when compared to the conventional manual approach (Table 11.3).

Immunohistochemistry

Immunohistochemistry (IHC) staining (see Chapter 19) revolves around sequential, well-defined steps, time intervals and prescribed temperatures so the whole process is ideal for automation. Indeed, in most laboratories this now happens in one form or another. Many different systems exist which can perform some, or all of the multistep process.

The instruments are a combination delivery system with or without heat, controlled by computer software. Slides may be stationary or mobile and either in a linear or rotary fashion, whilst reagents are delivered via pipettes from reagent containers/pre-packed cartridges. Some platforms also include deparaffinization, multiple antigen retrieval options and counterstain. All of these enable a wide range of immunohistochemical stains to be produced.

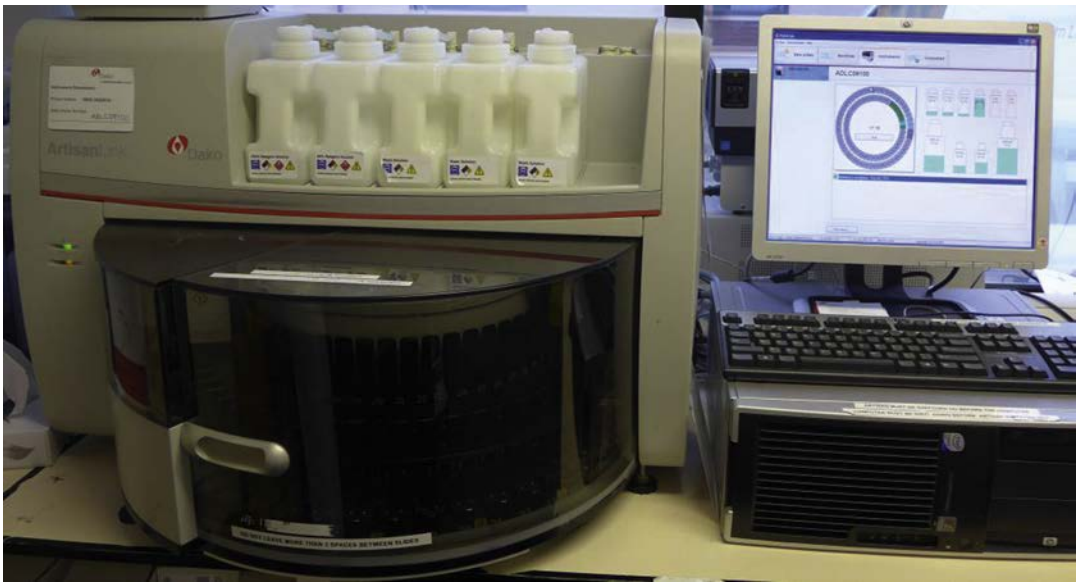

Fig. 11.7 Dako's Artisan Link.

Table 11.3 A comparison of two commercially available automated tinctorial staining platforms to manual staining

	Manual	Bench Mark SS	Artisan
Slide capacity	Limited by space, time and reproducibility	1-20	1-48
Reagent capacity	Limited by space and safety	25	50
Unmanned runs	No	Yes	Requires advance deparaffinization of section
Overnight runs	No	Yes	Yes, but reduces life span of reagents recommended to be refrigerated
Reduces contact with harmful components	No	Yes	Yes

Automation of immunohistochemical techniques has been a major step in improving quality efficiency and reproducibility of results. Most IHC automated systems include flexibility for continuous flow and user defined steps. Some are capable of performing all the steps within the process, making them a true 'walk-away' system requiring far fewer man hours than previous manual or partly automated systems. Workflow features such as independent slide draws and reagent racks are essential if a 'first-in-first-out' workflow system is desired, and work can be continuously added and sent out.

Integration of the platform's software with the LIMS system can allow a full patient tracking package and remote requesting options whilst also removing the need for constant re-labelling of slides. More advanced platforms are available with an expanded range of functions, such as in situ hybridization and direct immunofluorescence.

Examples of IHC platforms on the market include the DAKO Autostainer plus, Labvision Autostainer 720, Ventana Benchmark and Vision Biosystems Bondmax.

Molecular techniques

In-situ hybridization (ISH) and other molecular tests (see Chapter 20) are increasingly used techniques, where specific nucleic acids are targeted within formalin-fixed tissue sections. Individual gain/loss of gene expression can be viewed with both temporal and spatial information, and the targets can either be RNA or DNA.

Many similarities exist in the process of staining to that of IHC. ISH requires timed incubation periods, unique slide reagent management, and rinsing at specified intervals. Additionally a controlled heat application is needed to denature and anneal the nucleic acids, making automation the obvious choice.

Various instruments exist on the market with a range of capacities and abilities and the following are examples. The BioGenex Xmatrix Infinity is a staining system which can provide either IHC, ISH, SS, IF or multiplex staining, as well as slide-based PCR and miRNA. This system fully automates the run from dewax to final coverslip, producing up to 100 slides per day. The Ventana Benchmark ULTRA can provide simultaneous IHC, ISH, SISH, Dual Stain and FITC slide processing, and titration. The latter features individual slide drawers and continuous access to slides, processing up to 90 slides in 8 hours, or 120 slides with an overnight run (BioGenex, 2015; Roche, 2013b).

Slide digitization

Digital images are a common part of daily life, but it is only relatively recently that technology allows the digitalization of an image with sufficient resolution for diagnostic use, and the potential to remove the microscope from the reporting process. This is discussed in more detail in Chapter 22.

In most laboratories tissue slides have to be physically taken to the pathologist, or the pathologist has to travel to view them. This results in potential delays and the added risk of slides being damaged or lost. For a second opinion this process must be repeated with only a single copy of the slide.

Once a slide has been produced and stained, automated slide scanners can scan it and produce high resolution images, as vivid as those seen down a microscope. The hardware and software to perform this is an emerging market, and is becoming available from a growing range of manufacturers, including, for example, Nikon, GE and Hamamatsu.

Currently the storage of the resulting image is a stumbling block to the routine use of digitization. To produce a scanned image, it is necessary to either identify an area of interest in a low-power scan and re-scan these areas at a higher power, or undergo a space-consuming 'whole slide' high-power scan. To compound the issue, most software and hardware can be used to scan at multiple levels, allowing 'z-stacking' of images to duplicate the effect of focusing up and down through the tissue.

GE have released the Omnyx flatbed scanner with a 'load-and-go' operation which enables continuous scanning (overnight if required) to produce images in a timely manner, allowing their potential use for a diagnosis to become realistic for the first time (Fig. 11.8).

Whichever way the images are produced, the ability to view a sample in high resolution on a computer screen removes many of the current limitations:

- Slide images are instantly available anywhere
  - They cannot be left in another office or at another site.
  - They cannot be lost or broken in transit on their way for a second opinion.
  - They do not need to wait for a specialist pathologist to be on site.
- They can be viewed by multiple people at once so they do not miss this week's MTD meeting whilst in transit for the second opinion.
- A patient's records from radiology through to histology can be viewed with ease at MDTs, even those across sites via video conference.
- Pathologists do not need to be on site to report urgent cases.
- Pathologists do not need to wait for an old case to be searched for in an off-site storage facility, they can access it in minutes and do side by side comparisons with the up to date case.

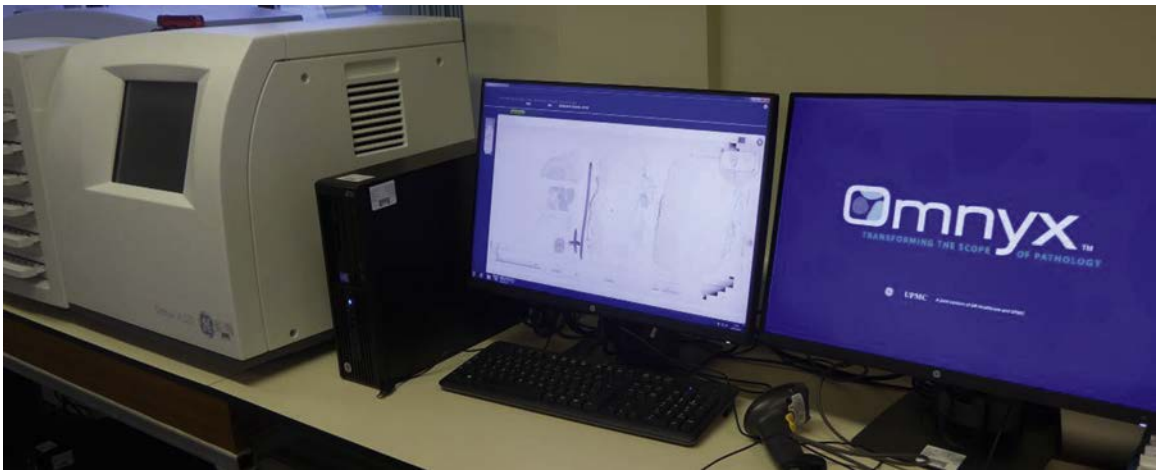

Fig. 11.8 GE's Omnyx flatbed scanner.

Computer algorithms are also under development designed to assist with quantitative and qualitative tasks currently done by eye, such as tumor grading and IHC scoring.

Automated block filing/ archiving

The potential for automation does not stop with the final report. For example, the UK RCPath guidelines recommend that all surgical blocks are kept for up to 30 years. This means that archiving is an expensive and time-consuming problem in many institutions.

There are two approaches to automated archiving of blocks. In the first, the block is scanned and a computer system identifies the next available position for storage. The block is then archived in this position, either using robotic placers or manual placement. The second approach, such as that seen in the Thermo Fisher Arcos system is to mount a scanner above the block file tray, and scan whole racks of barcoded blocks into file. The archive database software then stores the location of each block (Thermo Scientific, 2016).

Similar to other specimen tracking systems, automation of the archival process can be achieved either by development of an in-house IT system or purchased as an off-the-shelf commercial solution. A key feature of these systems is that filing is chronological, NOT numerical. Not only does this reduce the time spent sorting and organizing the archive, it also removes a drawback which has been observed since the onset of electronic requesting systems such as order-comms, where laboratories may be receiving requests already numbered in a non-sequential fashion. With automated archiving there would be no need to relabel these specimens with additional numbers.

The future of automation in histology

What does the future of histology hold? With the current healthcare environment putting cost pressures upon histopathology laboratories to improve efficiency and consolidate resources, the scalability of many processes currently carried out seems likely to be placed under increasing pressure.

Increasing the size of a laboratory and streamlining its workload without also investing in developing the infrastructure underpinning the service, often results in a decline in efficiency and performance. It has been known for some time in many fields that the scalability of a system is often related to the proportion of processes within the system which can be automated. Automation can drive growth, quality, efficiency and standardization of processes whilst increasing the overall capacity of the system (Adler et al., 1995).

Completely integrated systems covering the histology process from receipt to reporting are already on the way, and slide scanning is developing

towards a point where it will soon be conceivable to use and store digital images in place of glass slides. Techniques and software such as telepathology, voice recognition and macroscopic imaging can all be combined and made available to the reporting pathologist alongside the digital slide to produce an integrated reporting platform which can be remotely accessed by multiple users simultaneously.

The laboratory process itself can be streamlined, with sample tracking, automated transcription and remote test requesting increasing patient safety, whilst reducing the workload.

Reproducibility, consistency and reagent management can be improved and recorded through use of automated processing and staining platforms. These techniques can produce audit data which can be used to identify bottlenecks, target inefficiencies and monitor workflows visible in real time on 'dashboard' style displays.

All this is currently theoretically possible and elements have been in use in some laboratories for over a decade. However, the uptake of these technologies has been slow in many laboratories and must not be seen as a quick fix.

The automated instrumentation and workflow patterns must work synergistically together and address the following:

- Will a stainer with attached heater stations release a scientist from the need to load slides onto a stainer or delay slides if the workload is greater than the heater's capacity?
- Will the limited repertoire of tinctorial stains provided by an automated system streamline the process, or result in the need to run two systems in parallel?
- Will being tied into a closed system where reagents can only be purchased from one supplier result in increased cost, or does the known standardization and release of staff from making these reagents lead to an overall saving?

If a task can be done manually more consistently, faster and at reduced cost to an automated system then automation in that instance is often not the preferred outcome.

It is also worth considering that laboratory automation is rarely a low cost initiative. As a result, it is often introduced in a fragmentary fashion as funding becomes available and equipment requires replacement. This piecemeal introduction can be particularly inefficient and frustrating when it is considered that the largest benefits of automation are realized when each element is linked together to form a cohesive system.

It is the role of the laboratory management team to bear in mind the holistic vision and overall objective of the department when considering such replacements to ensure unified and efficient adoption of improvements in technology. Each component must be selected to both add value in itself, but also represent a step towards a long-term goal of an integrated system. Automation as a service development is dauntingly expensive in terms of resource commitment, requiring large amounts of funding and/or time to be invested in the process. Despite this the ever-increasing potential for the realization of improvements in efficiency, economy, quality and safety which is offered by the intelligent use of automation in histology makes it a significant option for a modern laboratory.

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