Histological dissection: landmarks and pointers past, present and future

The story of histological dissection and the development of understandings of human anatomy and physiology spans the past centuries and has always been linked to the history of medicine itself. Here, Guy Orchard looks at the latest laboratory equipment in this area.

A glance at the history books tells us a great deal. Let's begin with the word 'dissection' derived from the Latin 'dissecare' meaning 'to cut to pieces'. This is perhaps quite a blunt description of what we now understand by modern dissection; however, it reflects the key premise of the act to dissect.

Dissection was used primarily as a process to explore and evaluate anatomy and later improve understanding of physiology. Early reports suggest that human dissection was carried out by the Greek physicians Herophilus of Chalcedon and Erasistratus of Chios in the early part of the 3rd century BC. The Romans had a significant role to play in the development of medicine and were largely acknowledged for the development and division of specialisation within medicine, most notably ophthalmology and urology. The most widely recognised practitioner of the time was Galen (129 CE), who was originally of Greek descent but moved to Rome in 162 CE, where he lectured, wrote and exhibited extensively on anatomy and the value of dissection as a learning tool. It was Galen who largely adapted and refined the work of his predecessor, Hippocrates. Indeed, Galen once wrote that a physician "must be skilled at reasoning about the problems presented to him, must understand the nature and function of the body within the physician world and must practise temperance and despite all money".

Despite strong resistance to the practice of human dissection, the Greeks were keen to establish a hub of medical knowledge, and the government of the time supported its practice. Resistance to human histological dissection was not just something experienced in Greece, and became a taboo subject around the globe. This was as a result of religious beliefs merged with fear and trepidation about what might happen to the preservation of the human soul if dissection was performed on corpses.

This resistance continued in the UK up until 1832 when the First Human Anatomy Act was passed. Up to this point, it was an outlawed practice and medical professionals of the time would go to great lengths to acquire the cadavers required to study human anatomy. This spawned the era of the 'body snatchers', brought to life by the tales of Burke and Hare, the two most famous villains of the time. The passing of the Human Anatomy Act paved the way for the modern-day study of anatomy and physiology, and gave licence to doctors, teachers of anatomy and bona fide medical students to dissect donated bodies.

Further back in time, the issue of dissection was recorded in religious works. One of the 12 Apostles of Jesus, St Bartholomew, was reputed to have met an unpleasant end. In works of art he is often depicted holding a large knife, or, as in The Last Judgment by Michelangelo, with his own skin hanging over his arm (Fig 1). Tradition holds that in Armenia he was flayed alive and then crucified upside down. What then have been the significant advances in terms of the practice and equipment used for medical practice and more specifically histological dissection? Again, the Romans made significant strides forward in this area, with the development of a wide range of surgical instruments, many of which are still used today. Many of these instruments have been unearthed at archaeological excavations and are referenced in the Roman medical literature. The most widely known example is the scalpel. Made mainly from bronze or steel, arguably this is the most valuable dissection instrument for incisional, deep or long cutting of tissue, and the almost identical form is retained in scalpels used today. Other
examples include bone drills, bone forceps, male catheters, vaginal specula, spatulas and the surgical saw.

Advances in cellular pathology
Modern-day dissection, which continues to rely heavily on the traditional tools discussed above, surprisingly has not progressed significantly over time. Our understanding of anatomy and physiology has progressed but our methods of assessing or evaluating macroscopic dissection procedures has relived mainly on surgical instruments used in the operating theatre, rather than improving on dissection instrumentation at the cut-up bench.

The discipline of cellular pathology has advanced tremendously and we have seen some very impressive improvements in the developing technologies. Some examples include the introduction of enclosed tissue processing machines, sophisticated paraffin embedding equipment, and improved microtomes for precision in section cutting. Most significantly, we have seen the rise of automation with the introduction of a plethora of variations on staining machines for routine haematoxylin and eosin (H&E) staining, special staining and immunocytochemical (ICC) staining procedures, and also have automated coverslipping machines. The growing developments in molecular technology and equipment also looks set to be an area of great expansion in the future.

We have, perhaps, spent a great deal of time perfecting and improving on new technologies without necessarily working out the parameters that ensure that the tissue we assess is optimal for the procedures we need to investigate. A classic case in point is the massive explosion of publications on the use of ICC in cellular pathology during the 1980s and 90s. There was great interest in developing automated platforms and also improving sensitivity for the detection of ever-smaller antigenic epitopes. However, as we attempted to identify an ever-increasing panel of antibodies to work on paraffin sections, recognition dawned that optimising tissue fixation and processing was more important to the final results than was originally believed. At this point we took tissue fixation and processing more seriously and also introduced the antigen retrieval procedures with which we are familiar today. But the first procedure undertaken on tissue in the cellular pathology laboratory is dissection.

Initial tissue dissection
Information in the scientific literature on the importance of initial dissection and how accuracy and precision are achieved is hardly discussed. To an enthusiastic observer it appears a gaping omission! We have traditionally viewed histological dissection as quite a labour-intensive, fundamentally basic, yet highly skilled (in terms of those who perform it) practice. Yet we have not studied the variables of practice that contribute to inaccuracy and lack of precision.

The devices used traditionally to measure tissue at the cut-up bench have included the weighing scales and the metric ruler. There is very little consideration given to the need to ensure perpendicular sectioning of tissue and to ensure optimal tissue thickness (Fig 2). Thus, the appearance of tissue slices that have been measured by eye and by the metric rule can quite often be inaccurate and not perpendicular to the cutting face. This affects processing and embedding procedures, impacts on microscopy procedures, and also can affect ICC procedures and molecular investigations.

True cutting
While standing at the delicatessen of my local supermarket, I watched a customer being served by the assistant; he lifted a large ham from the display counter, placed it on a bacon slicer, and cut several slices from the joint. He was unsure about how thin he could cut slices, but a glance at the Parma ham slices in the display in front of me told me what I needed to know.

Later I read about the bacon slicer and also about the guillotine, used popularly during the French Revolution for beheading and as the instrument of the death penalty prior to abolition of capital punishment in France. What was evident was how successful these devices had been, the reason being that they were perfectly constructed for the purpose.

The next day I started drawing some constructions and pondered on how something that was not dissimilar to a guillotine or bacon slicer could be used for histological dissection, the biggest issue being how to ensure precision and accuracy. The best option appeared to be adapting the devices on which we already rely (i.e. the microtome and micrometer) and modifying them for this purpose.

With this in mind I approached a commercial company (CellPath) and we discussed designs and formats. The literature in this area is not extensive and covers a wide spectrum of different approaches to tackling the needs of histological investigation. Some of the key factors that can affect accuracy and precision for histological dissection need to be appreciated, and include:

- flat uniformity perpendicular to the specimen cutting face
- appropriate immobilisation of the tissue specimen during grossing
- good visualisation of the cutting tissue face
- sharp knives with associated grossing equipment fit for purpose
- grossing knife action.

Designs were constructed that attempted to take into account these factors. What ensued were considerations of not just final designs but also the materials to be used in construction of these devices. Trials of two devices were performed by staff at Viapath's St John's Histopathology Department (Fig 3) and in histopathology departments located at Guy's and St Thomas' NHS Trust.

These two devices were named TruSlice and TruSlice Digital (Figs 4a and 4b). TruSlice relies on the insertion of reinforced plastic inserts with defined recessed depths of 2, 3, 4 and 6 mm. The TruSlice Digital relies on the use of an attached micrometer. Both used a guillotine-like construction with a knife plate configuration that ensured perpendicular action of the blade.

Preliminary trials were extremely positive with good recordings of accuracy and precision. The findings were presented at last year's ISMS Biomedical Science Congress as a short paper and also were published in the British Journal of Biomedical Science.1
Following these encouraging results, I requested that we embark on a five-site trial to determine if these initial findings were mirrored elsewhere, and also to see how feedback could improve the devices.

The use of a micrometer (TruSlice Digital) to set tissue slice thickness is innovative and its use on this device reminds us about how traditionally we have defined measurement and accuracy in the microscopy of histological sections from paraffin blocks. Clearly, in developing these devices, we have not reinvented the wheel but applied the concepts of well-trusted methodology to a different area of histological assessment.

There is a need, however, to compare and contrast the most promising devices in this area of investigation, simply to determine which will provide the best overall options for routine histological dissection. This is something that has not been performed to date. Owing to the complexity of, and variation in, tissue types dealt with in the modern histopathology laboratory, a single device that suits every need and eventually with regard to dissection is perhaps an idealistic goal, but that is not an excuse for not trying, as Thomas Huxley said: "Science is simply common sense at its best.".

References

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