CREATING HIGH QUALITY TISSUE MICROARRAYS USING MANUAL AND AUTOMATED SYSTEMS WITHIN THE HUMAN PROTEIN ATLAS

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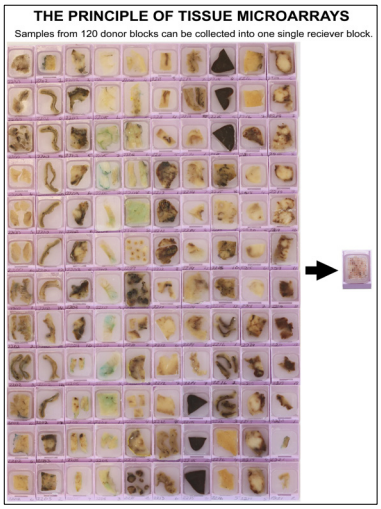
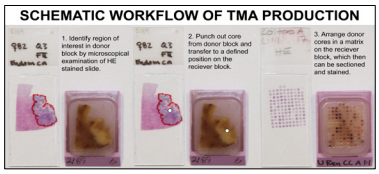
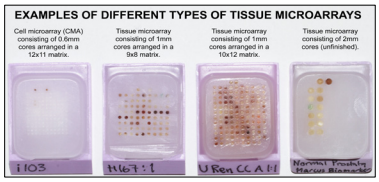
Background to the tissue microarray technology

The tissue microarray (TMA) technology enables high-throughput analysis of multiple tissue and/or cell samples. The advantage is that large amounts of data rapidly can be obtained in a single experimental run, while avoiding experimental variability and facilitating direct comparisons. Importantly, only limited amount of valuable tissue is needed for TMA production, and the number and size of cores in a TMA block can vary from forty (2mm cores) to hundreds (0.6mm cores). The TMA technique is used within the Human Protein Atlas (HPA) for global analysis of protein expression patterns in normal human tissues, cancer and cell lines using immunohistochemistry (IHC). Over 1500 TMAs and 200 cell microarrays have been thus far been generated within HPA.



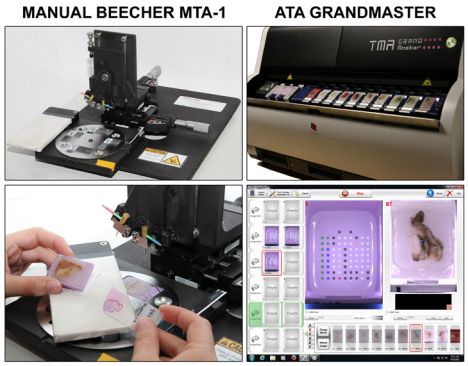




Two systems of TMA production

Here we compare the assembly of TMAs using two different systems available at the SciLifeLab Tissue Profiling Center: The manual Beecher MTA-1 system and the automated ATA Grandmaster system. The advantage of a fully automated system is that it is much faster and could be left unsupervised, whereas the manual arrayer is slower and dependent on an experienced lab technician's work hours. On the other hand the manual system gives the user more control when punching since the applied pressure can vary depending of the hardness of the tissue. Conversely, the automated systems run the risk of damaging valuable or scarce material when human control over the punching process is lost. The manual system is also capable of handling all sorts of tissues, whereas the automated system is not optimal for use with tough tissues like the skin or thyroid. However, the automated arrayer has the possibility of being integrated with other systems and softwares and does not require the same level of hands-on tissue experience to operate as the manual system does. Thus, depending on tissue composition and quality, the successful production of high quality TMAs are in many aspects influenced by the choice of TMA production system.

Comparing production systems

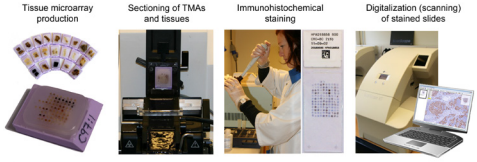


	Beecher MTA-1	ATA Grandmaster
Operation	Manual operation	Fully automated
Output	Slow. 4 TMAs /8 hours (0.5/h)	Very fast. 12 TMAs /3 hours (4/h)
Punching cores from donor blocks	High precision is dependent on technician's experience, however there is more freedom to adjust for irregular samples.	High precision due to mechanics. Human control over precision while programming coordinates, but less ability to compensate for irregularities.
Matrix precision in reciever block	Less precision in creating a linear matrix in the reciever block since reciever holes are punched manually.	High precision in creating a linear matrix in the reciever block, which facilitates later analyses and handling.
Risk for sample damage	Manual handling allows for adjusting the lenght and pressure when punching cores, thus lowering the risk of sample damage.	Automated handling increase the risk of damage to the samples since the robot preforms the same operation for every sample.
Operator	Requires a lab technician with hands-on experience and knowledge of tissues.	Requires a lab technichian with software training. Less tissue knowledge required.
Time	Dependent on lab technician work hours.	Can be left unsupervised to operate alone. Liberates work hours.
Tissue limitations	Can hande all tissue types.	Not suitable for processing tough tissues, like skin samples.
Other	Workflow is more flexible since the work can be interupted, TMA design changed, donor blocks replaced, etc. in the work process.	Can be integrated with other systems and softwares for digitalization of the workflow (scanner, bar codes, etc).
Main usefulness	When human experience matters, when samples are scarce or heterogenous, or when a limited number of samples are to be processed.	When there are many samples to process, when samples are ample and mainly homogenous, or when speed is important or technician hours are limiting.

The SciLifeLab Tissue Profiling Center

Combining the TMA technology with IHC is a powerful strategy for generating protein expression data on a large scale and allows for the simultaneous analysis of samples from eg. large patient cohorts, while saving valuable material and ensuring more reproducible experiments. Moreover, the use of TMAs saves costs and laboratory processing time. The SciLifeLab Tissue Profiling Center is a national resource that offer scientists and institutions not only TMA production service, but also sectioning of TMAs and paraffin embedded tissues, standardized and automated histological and immunohistochemical staining, as well as high resolution scanning (up to 400x) of stained TMA or tissue slides into digital image files.

SciLifeLab Tissue Profiling Center



For more information

Kampf C, Olsson I, Ryberg U, Sjöstedt E, Pontén F: Production of tissue microarrays, immunohistochemistry staining and digitalization within the human protein atlas. *J Vis Exp. 2012 May 31;(63).*

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