

Technical Note # 018

A New Matrix Application Device for MALDI Tissue Imaging

The ImagePrep™ station introduces preparation QC for maximum performance at highest reproducibility in a push-button process.

ImagePrep™ provides highly reproducible matrix preparations for MALDI tissue imaging in a fully automated process. On tissue, high quality spectra are obtained from these preparations at a lateral resolution of 50 μm . The quality of MALDI tissue imaging analyses is dependent on the matrix application protocol. Current protocols have several disadvantages, including lack of reproducibility and analyte delocalization from pneumatic spray, and limited spatial resolution from time consuming nano spotting. Both techniques require experience or time consuming maintenance efforts. The ImagePrep technique is a new approach that consistently provides high resolution images at high speed with superb spectra quality without user intervention.

Gentle Matrix Application

In the ImagePrep station, a matrix aerosol is created by vibrational vaporization under controlled conditions that is gently deposited onto tissue sections.

An average droplet size of $\sim 20 \mu\text{m}$ is generated with all droplet diameters being smaller than $50 \mu\text{m}$.

Preparation occurs in cycles in a fully automated process :

1. deposit droplet layer
2. incubate in saturated atmosphere
3. allow partial or complete drying.

Multiple sections on a microscope slide can be homogeneously matrix-coated in one run, typically with 30-100 cycles within 1 hr (Fig.1).

Real Time Preparation Quality Control

An optical sensor monitors scattered light from the matrix layer that allows controlling all relevant preparation parameters in real-time: deposition periods, intervals, matrix layer thickness, wetness, drying rate, etc. During the wetting period the scattered light intensity fades due to refractive index matching. Upon drying, the signal, again, increases due to formation of new crystals. At complete dryness, the signal is a direct measure of the thickness of the matrix layer.

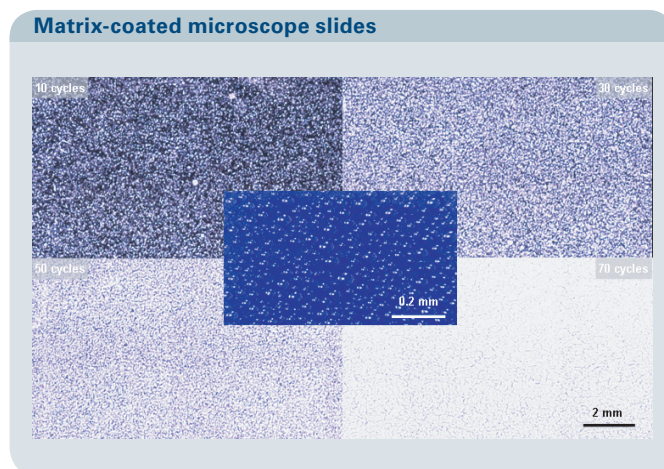


Fig. 1: Density of MALDI matrix layer as a function of the number of spray cycles.

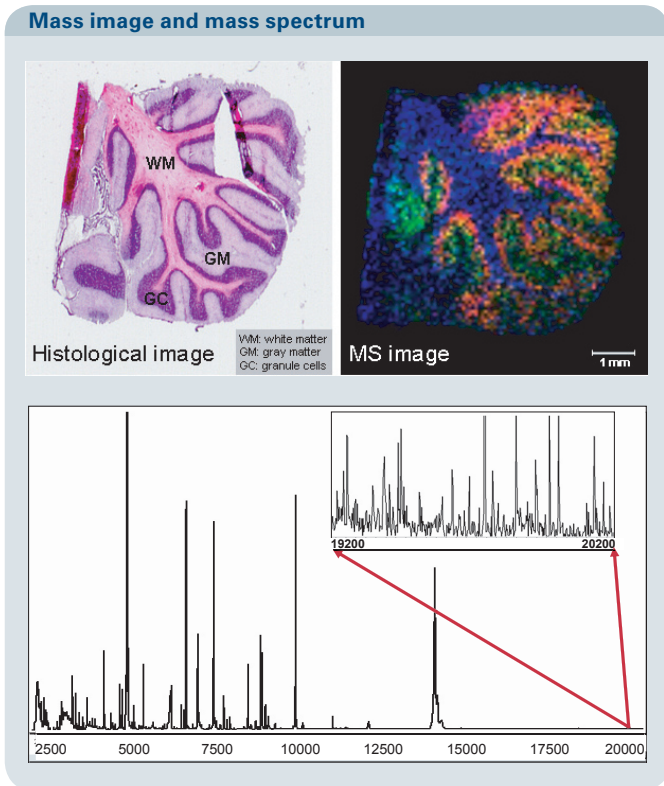


Fig. 2: 70 μm image of rat cerebellum after ImagePrep preparation and sum spectrum of all positions showing >700 individual peaks.

This QC process built into the preparation cycles provides high reproducibility over several slides and at different days. In a complex workflow, the sample is kept wet for 90 % of the time. Every 10th cycle, complete drying is permitted to determine the thickness of the matrix layer and to terminate the preparation after a pre-defined thickness is reached. User intervention is not required in the fully automated process.

Acquire High Quality Spectra

Typically, tissue images are obtained that combine an unmatched high spectrum quality with many peptide/protein signals and a high spatial resolution comparable to pneumatic spraying (Fig 2). A lateral resolution of 50 μm was observed in an Alzheimer rat model (Fig.3), identical to the spot raster used. This result suggests that even higher resolutions can be achieved.

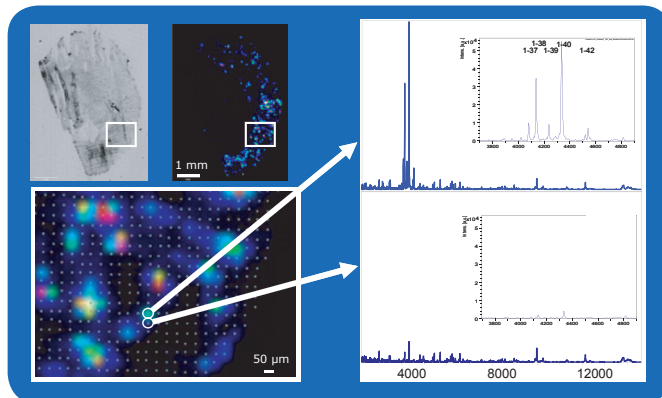


Fig. 3: Amyloid plaques in rat brain: Spectra taken 50 μm next to a plaque (bottom right) do not show significant amyloid peptides (top right).

ImagePrep completes Bruker Daltonics MALDI Molecular Imager suite

The ImagePrep station completes the MALDI Imaging solution from Bruker Daltonics consisting of a high performance MALDI-TOF/TOF system with 200 Hz smartbeam™ laser technology and PAN™ mass resolution, an electrically conductive glass slide assembly, the most advanced flexImaging software delivering full integration from data acquisition to image analysis and ClassImaging for tissue classification.

Conclusion

- The ImagePrep station operates in a fully automated process.
- Highly reproducible preparations are achieved by the sophisticated QC process.
- A lateral resolution of 50 μm is achieved.
- ImagePrep enables an unmatched high spectra quality.
- Easy push-button operation for walk-up users.

Acknowledgement

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