MALDESI was the first hybrid ionization source combining laser ablation and electrospray post-ionization using a resonantly excited matrix (endogenous or exogenous) to enhance the desorption of neutral analyte molecules. In IR-MALDESI (2.94 µm), exogenous water in the form of ice can also be used as a matrix to improve the desorption of neutrals. MALDESI combines characteristics of ESI such as its ambient nature and capability to generate multiply charged ions as well features of MALDI such as high resistance to salts and capability to spatially resolve sample collection over a surface. The later characteristic enabled the development of an IR-MALDESI mass spectrometry imaging source. The engineered device was coupled to a high mass resolving power LTQ-FT-ICR instrument and offered multi-shot capability and full control over the repetition rate and the scanning cycle. A novel flash shadowgraphy system which has the capability to simultaneously collect images of the plume of ablated material and record the IR-MALDESI mass spectrum associated with that same plume was implemented. The system was used to investigate the fundamentals of the IR-MALDESI ablation/ionization process and optimize the source for the imaging of biological tissue using ice as a matrix by nearly 10 folds. The source has recently been coupled to a faster Orbitrap instrument (Thermo Q-Exactive Series) and MSI can is now routinely performed at 1.6 scan/s. High throughput MSI using high resolving power instruments generates extremely large sets of data. MSiReader, a vendor neutral interface was developed to view and process the MS imaging data generated.