

Intraoperative molecular analysis of human brain tumors using desorption electrospray ionization – mass spectrometry

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Human brain tumors can lead to a significant source of morbidity and mortality. The primary treatment option is surgical resection, the extent of which is associated with length of survival. Unfortunately, intraoperative tools for rapid diagnosis are lacking – particularly those based on molecular information. The current standard for obtaining pathologic information during surgical resection is frozen section and smear histopathology, taking upwards of 20 minutes per sample. Ambient ionization - mass spectrometry (MS) allows for rapid and direct biomolecule detection from unmodified biological samples, and can provide surgeons with near real-time pathologic information.

Ambient ionization, generation of ions at atmospheric conditions, allows for direct analysis of biological samples with minimal to no sample preparation – overcoming one major obstacle for MS implementation for intraoperative analysis. Desorption electrospray ionization (DESI) – MS is one such method by which biomolecules are analyzed from surfaces via thin-film extraction and subsequent sputtering. Tissue biopsies taken for standard histopathology are rapidly analyzed (<2 mins) by DESI-MS acquiring biomolecular information characteristic of cancer, namely membrane phospholipids and oncometabolites. The biomolecular information, *i.e.* profiles, is then analyzed by multivariate statistics to provide diagnostic predictions. The ability to differentiate brain parenchyma and glioma exceeds 95%, while different brain tumors (*i.e.* glioma, meningioma, and pituitary tumors) are differentiated at >99%. In addition to providing surgeons with pathologic information, DESI-MS could guide resection of the tumor at the difficult to detect peritumoral borders.

Here we present the fundamental aspects of DESI-MS and describe its evolution from laboratory-based DESI-MS imaging of frozen tissue sections to intraoperative DESI-MS analysis of fresh tissue smears.