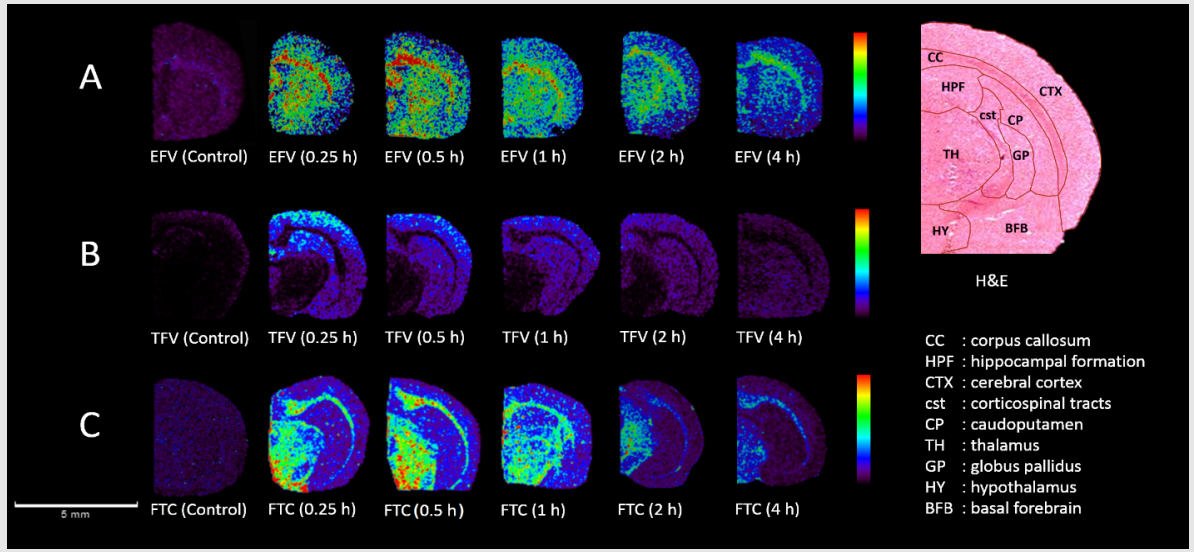
Technological advances in mass spectrometry imaging driving preclinical drug development

Sooraj Baijnath (PhD)

University of KwaZulu-Natal/ Uppsala University

What is mass spectrometry imaging?

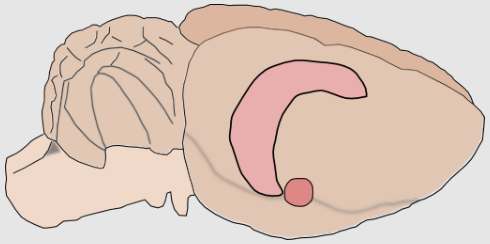
- Combines the power of mass spectrometry with histology
- Traditional histology methods are limited – no distribution information
- Traditional drug imaging modalities require radiolabeled analytes



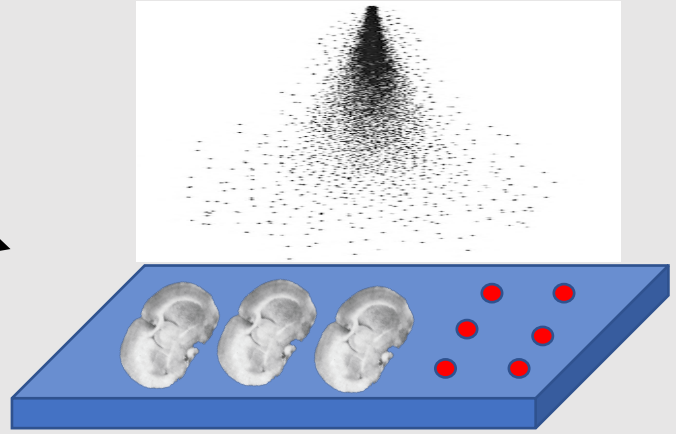
ACS omega, *4*(25), pp.21169-21177.

Basic MSI workflow

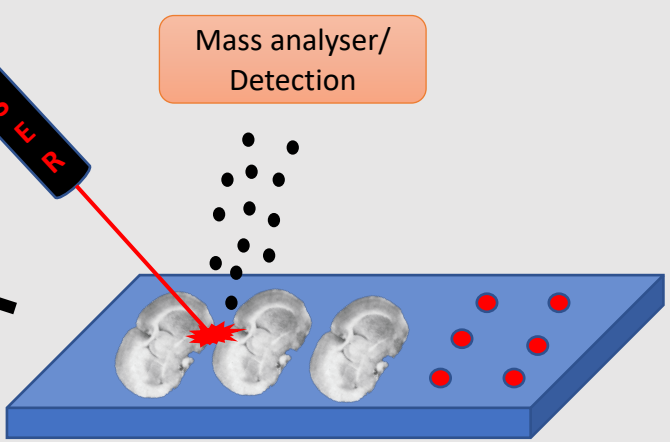
In vivo drug administration



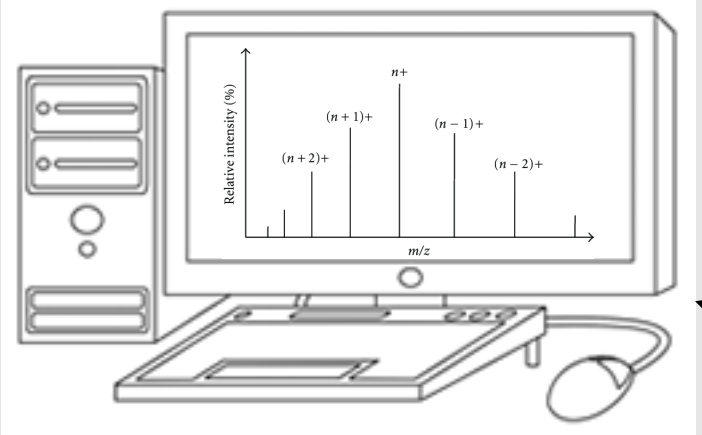
Tissue collection/
Sample preparation



Matrix application



Data collection/
Instrumentation

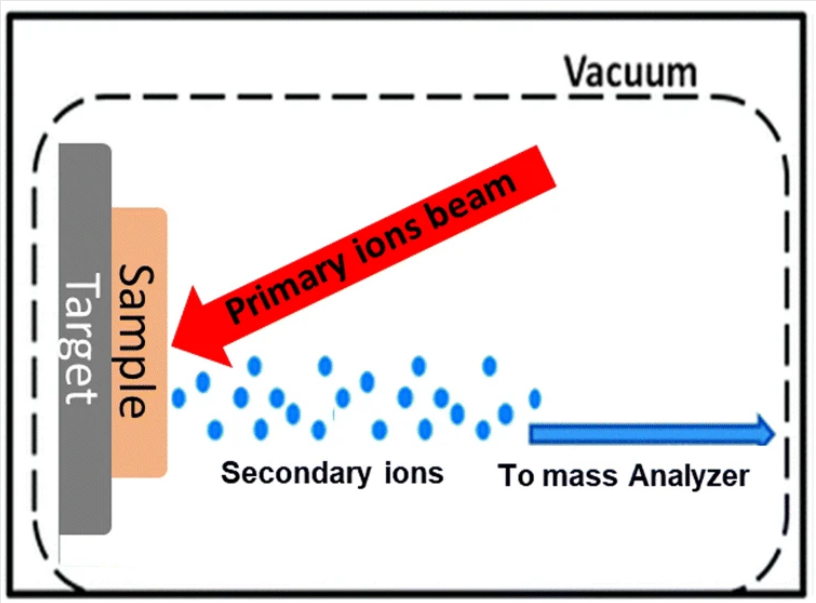


Data analysis

SIMS

Secondary Ion Mass Spectrometry

- Primary ion beam > secondary ions
- Primary ion beam (monoatomic [Au^+, Cs^+,O^-]; polyatomic [C_{60}^+]; liquid metal guns; gas cluster ion beams)
- Mass range – 1000 *m/z*

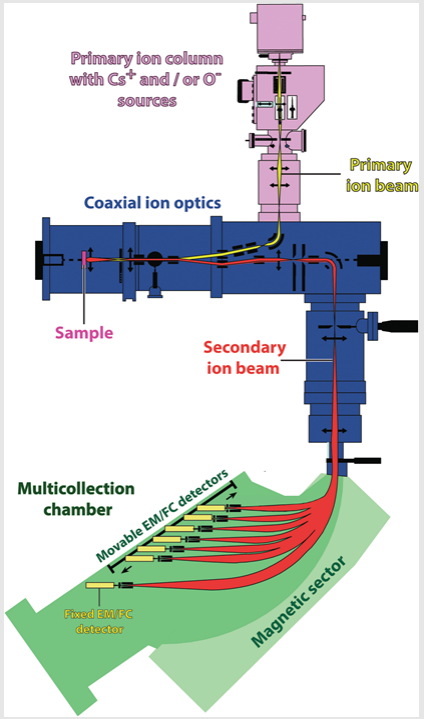


Mol Imaging Biol (2018) 20:888Y901

SIMS

Secondary Ion Mass Spectrometry

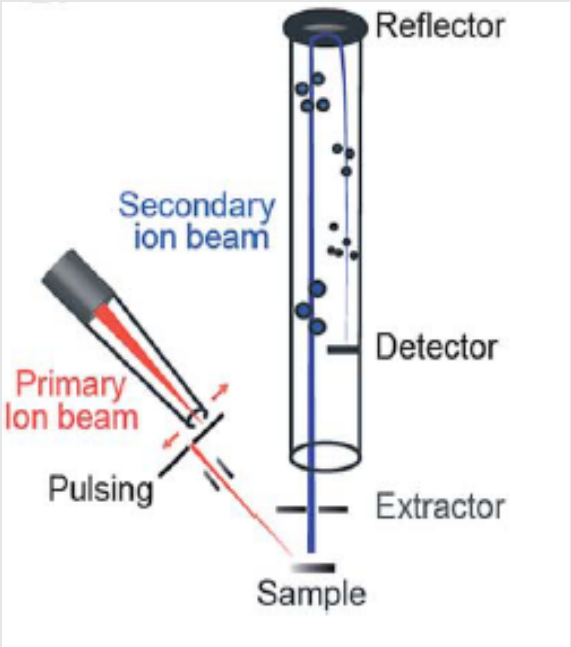
- Primary ion beam > secondary ions
- Primary ion beam (monoatomic [Au^+, Cs^+,O^-]; polyatomic [C_{60}^+]; liquid metal guns; gas cluster ion beams)
- Mass range – 1000 *m/z*
- Nano SIMS
  - Multiple secondary ions
  - Spatial resolution - 50nm



SIMS

Secondary Ion Mass Spectrometry

- Primary ion beam > secondary ions
- Primary ion beam (monoatomic [Au^+, Cs^+,O^-]; polyatomic [C_{60}^+]; liquid metal guns; gas cluster ion beams)
- Mass range – 1000 *m/z*
- Nano SIMS
  - Multiple secondary ions
  - Spatial resolution - 50nm
- ToF SIMS
  - ToF mass analyzer
  - Pulsed primary ion beam
  - Spatial resolution – 250 nm
- FT-ICR SIMS

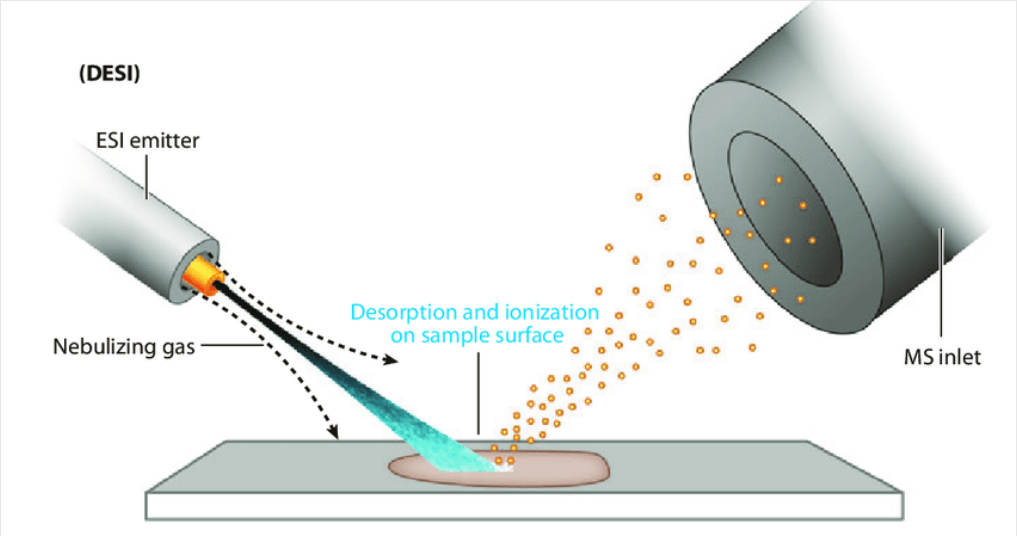


J. Anal. At. Spectrom., 2019,34, 1355

DESI

Desorption Electrospray Ionisation

- Electrospray emitter > generate charged microdroplets
- Solvents – MeOH:H_2O (1:1); DMF; EtOH
- Limited mass range – 2000 *m/z*
- Spatial resolution – 50µm
- Nano-DESI
  - Low ID silica capillaries
  - Nanospray
  - Spatial resolution – 10µm

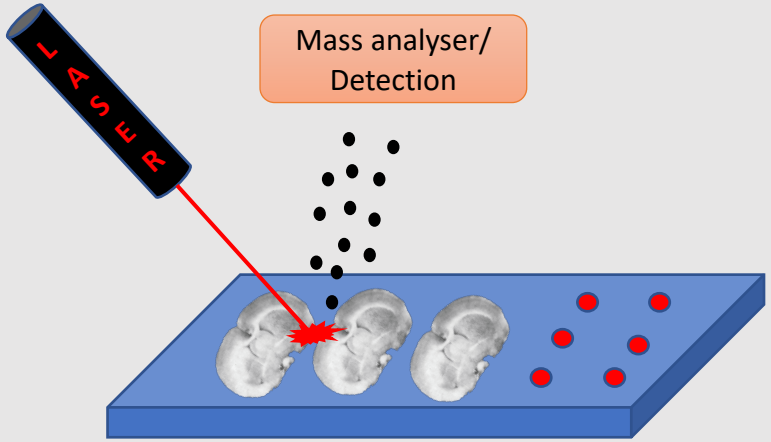


Mass spectrometry reviews, *35*(1), pp.147-169.

MALDI

Matrix-assisted laser desorption ionisation

- Sample coated with a small molecule matrix
- Matrix co-crystallizes with analytes
- Analtyes desorbed from tissue surface
- Mass range – 100 000 *m/z*
- Spatial resolution – 20 µm



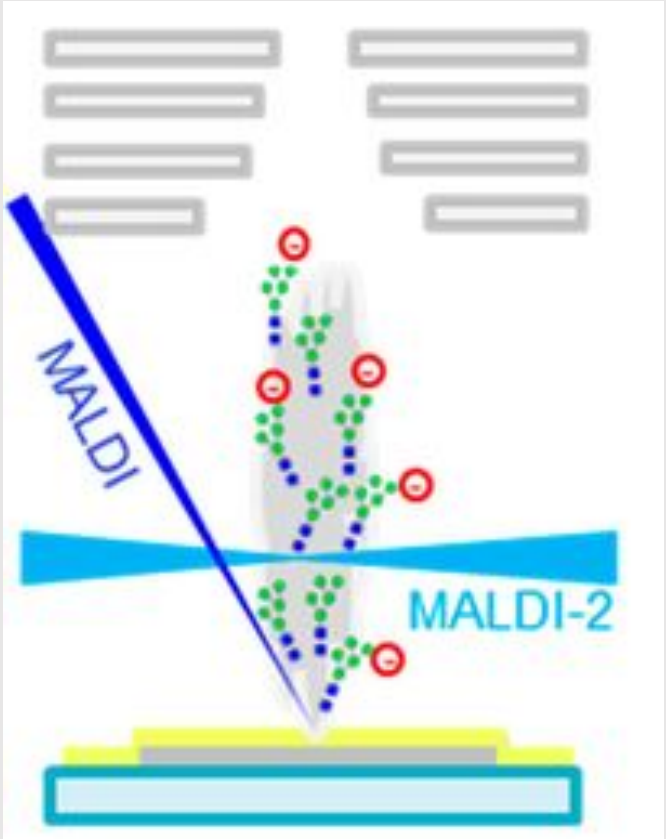
Data collection/
Instrumentation

Mass spectrometry reviews, *35*(1), pp.147-169.

MALDI

Matrix-assisted laser desorption ionisation

- Sample coated with a small molecule matrix
- Matrix co-crystallizes with analytes
- Analtyes desorbed from tissue surface
- Mass range – 100 000 *m/z*
- Spatial resolution – 20 µm
- Newer MALDI configurations
  - MALDI-2
    - Higher number of analytes ionized
  - Tranmission MALDI-2
    - 600 nm spatial resolution



Nature Methods,(6) pp. 925–931

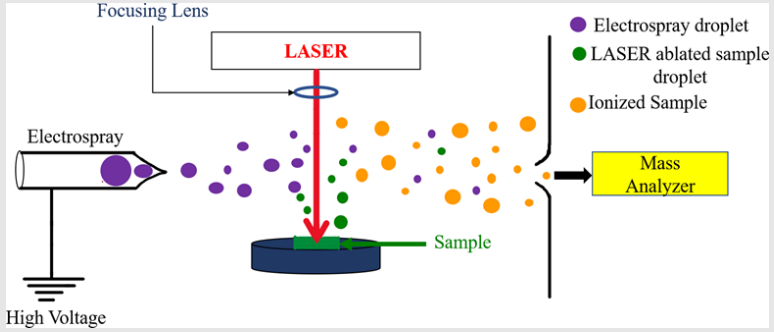
Alternative ionisation methods

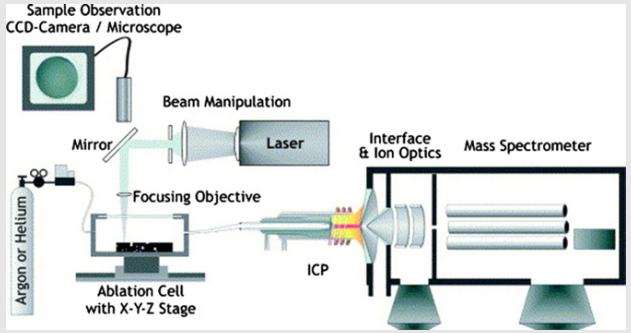
LA-ESI
Laser Ablation Electrospray Ionization

- Infrared laser
- Sample moisture acts as a matrix
- Resolution – 200 µm
- Range – 0-200 *m/z*

LA ICP MS
Laser Ablation Iductively Coupled Plasma Mass Spectrometry

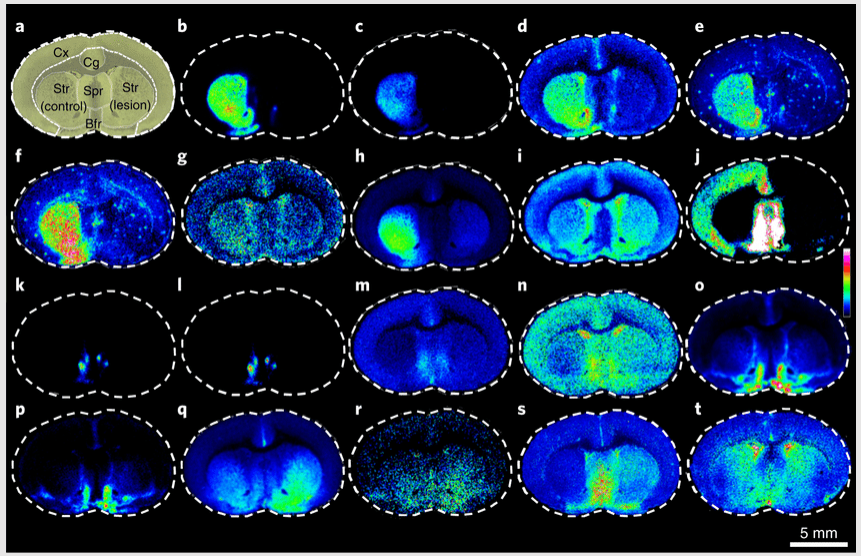
- Elemental analysis on tissue surface
- UV laser and carrier argon gas
- Resolution – 10-100 µm
- Range – 0-250 *m/z*





Conclusion

- Mass spectrometry imaging – established technique
- Ability to advance drug development and reduce the time expended
- Wide range of applications
- Allows for the detection of a wide array of analytes
- Beyond drug distribution – lipids, proteins, functional molecules



Nature Methods 16(10):1-8

Thank you

- I would sincerely like to thank:
  - Dr Sanil Singh
  - Naamah Maundrell & Naomi Baba
  - Ngan Nguyen (Waters Corporation)
  - Catalysis and Peptide Research Unit (UKZN)
  - National Research Foundation (South Africa)