

**INCREASED SELECTIVITY FOR THE ION MAPPING OF SYNTHETIC  
ANTAGONISTS OF DOPAMINE RECEPTORS IN RAT BRAIN SPECIMENS USING  
MS/MS ON A MALDI Q-TOF MASS SPECTROMETER**

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Imaging the spatial distribution of molecules in tissue using MALDI mass spectrometers is a rapidly developing technique. The acquisition of accurate mass data in this type of experiment can be hampered in axial MALDI ToF systems. It has long been recognised that even small changes in sample position and laser energy in the source region of this type of mass spectrometer affect mass measurement accuracy and mass spectral resolution. Here, we show how the use of an orthogonal ToF MALDI mass spectrometer circumvents these problems by decoupling the MALDI source from the mass analyser

Imaging data are acquired on a MALDI Q-ToF mass spectrometer. The tissue sections are mounted on a target plate and moved in a raster pattern relative to the laser. To reduce interference from the biological matrix and enhance specificity the instrument is operated in MS/MS mode, a quadrupole is used for precise precursor ion selection. The sensitivity of specific ions can be further enhanced by synchronising the high voltage push of the ToF mass analyser with the arrival of ions of appropriate  $m/z$  in the acceleration region.

Raclopride is retained in tissue as a result of binding to a neurotransmitter receptor. Raclopride is a selective dopamine antagonist with a high affinity for dopamine type 2

(D<sub>2</sub>) receptors. Since the neurotransmitter dopamine may be involved in various neuropsychiatric diseases, the in vivo binding of raclopride to dopamine receptors in the striatum can be measured by positron emission tomography (PET) with radiolabeled raclopride used as a tracer. Raclopride C 11 is rapidly cleared from both plasma and whole blood, and crosses the blood-brain barrier. After intravenous administration, raclopride C 11 localizes in the basal ganglia, a region with a high density of dopamine receptors. PET images show stereoselective concentration of raclopride C 11 in the region of the putamen relative to the rest of the brain.

MALDI imaging information has been obtained from thin sections of rat brain from animals doped with the well studied D<sub>2</sub>/D<sub>3</sub> dopamine receptor antagonist Raclopride. Data obtained on the spatial distribution of Raclopride and endogenous adenosine monophosphate will be presented. Challenges and future directions with MALDI imaging sample preparation are discussed.