

Advion is a leader in mass spectrometry & synthesis solutions. The **expression** CMS is a high performance, compact, affordable single quad mass spectrometer. Its compact size allows it to fit in space-limited labs for direct access and immediate results for chemists requiring mass confirmation, reaction monitoring, quality control and purity analysis.

## Routine detection and identification of PET radiopharmaceuticals Using Compact Mass Spectrometry

### Introduction

The rapid identification of radiolabeled compounds would clearly be beneficial for applied clinical and preclinical tracers used for imaging with positron emission tomography (PET). The limited uptake of mass spectrometry in the imaging field has been due arguably to several factors including concerns regarding adequate sensitivity, instrument footprint in the highly constrained space requirements for the majority of labs and high initial capital costs plus high ongoing maintenance costs.

The introduction of the **expression** Compact Mass Spectrometer (CMS) at the 2012 Spring ACS National Meeting addressed for the first time three of the concerns, space, capital cost and maintenance costs. Only the question of adequate sensitivity remained to be answered.

An evaluation at Stanford University under the guidance of Dr. Frederick T. Chin was therefore undertaken using the **expression** CMS plus Cerno Biosciences spectrum analytical software to determine if the limits of detection and the spectral accuracy were sufficient to enable identification of PET radiopharmaceuticals and/or their respective carrier compounds made by carrier-added (CA)  $^{18}\text{F}$ -fluorination, no-carrier-added (NCA)  $^{18}\text{F}$ -fluorination and  $^{11}\text{C}$ -methylation.



The evaluation comprised eighteen  $^{19}\text{F}$  or  $^{12}\text{C}$  reference compounds of tracers commonly used for PET imaging. These were tested with the **expression** CMS system (ESI or APCI) with 0.1% formic acid or 0.03% ammonium hydroxide in methanol/water as solvent. Spectrum analysis was used to confirm the elemental components of the reference compound parent ion peaks with mDa spectral accuracy. ESI/MS conditions were employed for confirmation of radiotracers.

## Results

Eighteen reference compounds were detected at low mass levels (pg to ng) with ESI/MS and confirmed with >95% spectral accuracy.

Eleven tracers (2 CA <sup>18</sup>F-labeled compounds, 6 NCA <sup>18</sup>F-labeled compounds, 3 <sup>11</sup>C-methylated compounds) were collected and tested after HPLC purification.

Eight of these tracers 3 <sup>11</sup>C-methylated compounds (<sup>11</sup>C-SA4503, <sup>11</sup>C-PIB, <sup>11</sup>C-Raclopride), 2 CA <sup>18</sup>F labeled compounds (<sup>18</sup>F-EF5, <sup>18</sup>F-TFSB) and 3 NCA <sup>18</sup>F-labeled compounds (<sup>18</sup>F-FTC-146, <sup>18</sup>F-P3BZA, <sup>18</sup>F-FBPA, SR 1~3 Ci/umol), could be detected by mass identification of respective parent ions of <sup>19</sup>F and/or <sup>12</sup>C carrier compounds following HPLC elution.

### Mass confirmation of 18 PET radiopharmaceutical standards

Standards	Predicted m/z	Observed m/z	Minimum Detection Level
<sup>12</sup> C-PIB	+257.1	+257.1	500 pg
<sup>12</sup> C-Raclopride	+347.1	+347.2	10 pg
<sup>12</sup> C-SA4503	+369.2	+369.2	50 pg
<sup>19</sup> F-EF5	+303.0	+302.9	2.5 ng
<sup>19</sup> F-FAZA	-282.2	-282.1	1 ng
<sup>19</sup> F-FBPA	-217.1	-217.1	500 pg
<sup>19</sup> F-FEAU	-237.2	-237.2	100 pg
<sup>19</sup> F-FHBG	+256.1	+256.2	1 ng
<sup>19</sup> F-FLT	-242.1	-243.2	1ng
<sup>19</sup> F-FPPRGD2	+807.5	+807.9	2 ng
<sup>19</sup> F-FSPG	-206.1	-206.2	5 ng
<sup>19</sup> F-FTC-146	+337.2	+337.2	10 pg
<sup>19</sup> F-FU	-129.1	-129.2	100 pg
<sup>19</sup> F-P3BZA	+240.2	+240.3	50 pg
<sup>19</sup> F-SPARQ	+451.1	+451.2	200 pg
<sup>19</sup> F-TFSB	-347.0	-347.1	2.5 ng
6- <sup>19</sup> F-fluoro-dopamine	+172.2	+172.1	1 ng
6- <sup>19</sup> F-fluoro-L-DOPA	+216.1	+216.2	1 ng

## Summary

- The expression CMS single quadrupole LC/MS with spectrum analysis is a sensitive and fast approach that enables mass identification of small molecules within minutes.
- Detection and identification of CA <sup>18</sup>F-labeled and tertiary amino compounds was straightforward.
- Ionization and chromatographic condition optimization is still required for some of the tracers evaluated.