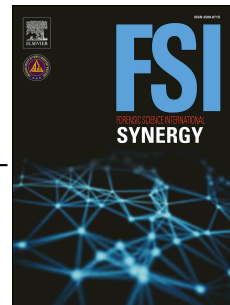# Journal Pre-proof

Exploring a route to a selective and sensitive portable system for explosive detection–swab spray ionisation coupled to of high-field assisted waveform ion mobility spectrometry (FAIMS)

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Exploring a Route to a Selective and Sensitive Portable System for Explosive Detection– Swab Spray Ionisation Coupled to of high-field assisted waveform ion mobility spectrometry (FAIMS)

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1 **Abstract**

2 Paper spray mass spectrometry is a rapid and sensitive tool for explosives detection but has

3 so far only been demonstrated using high resolution mass spectrometry, which bears too high

4 a cost for many practical applications. Here we explore the potential for paper spray to be

5 implemented in field applications with portable mass spectrometry. This involved (a)

6 replacing the paper substrate with a swabbing material (which we call "swab spray") for

7 compatibility with standard collection materials; (b) collection of explosives from surfaces;

8 (c) an exploration of interferences within a +/- 0.5 m/z window; and (d) demonstration of the

9 use of high-field assisted waveform ion mobility spectrometer (FAIMS) for enhanced

10 selectivity. We show that paper and Nomex® are viable collection materials, with Nomex

11 providing cleaner spectra and therefore greater potential for integration with portable mass

12 spectrometers. We show that sensitive detection using swab spray will require a mass

13 spectrometer with a mass resolving power of 4,000 or more. We show that by coupling the

14 swab spray ionisation source with FAIMS, it is possible to reduce background interferences,

15 thereby facilitating the use of a low resolving power (e.g. quadrupole) mass spectrometer.

16 **Keywords:** Explosives, Swab Spray, Mass Spectrometry, FAIMS

17

Introduction

18

19 Screening techniques capable of rapidly detecting explosive compounds play an essential

20 safeguarding role in areas recognised as being at "high-risk" of terrorist activities. Current

21 methods that are widely implemented for screening explosives are based on thermal

22 desorption coupled to ion mobility spectrometry (TD-IMS) [1-4]. The thermal desorption

23 process, however, can offer unsatisfactory performance for thermally labile compounds of

24 interest which break down upon heating [4-7]. We have previously shown how paper spray,

25 a rapid ionisation technique previously used in the analysis of biofluids [8-19], ink [20] and

26 foodstuffs [21-25] can be used as an effective and efficient alternative to TD-IMS for the

27 analysis of explosive compounds at ultra-trace levels (25 pg) [26]. Paper spray can detect

28 multiple explosive compounds including trinitrotoluene (TNT), 1,3,5-trinitroperhydro-1,3,5-

29 triazine (RDX), octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX), pentaerythritol

30 tetranitrate (PETN), tetryl, nitroglycerin (NG), tetryl, picric acid (PA) and hexamethylene

31 triperoxide diamine (HMTD) [26].

32 During paper spray, samples are deposited directly on to a triangular-shaped paper substrate.

33 A voltage and a drop of solvent are applied to the back end of the paper, which extracts and

34 sweeps analytes from the substrate and induces a spray which is directed into a mass

35 spectrometer for detection. It has been demonstrated by other groups that the substrate from

36 which the spray is induced does not necessarily need to be paper. Alteration of the substrate

37 has previously provided many other techniques, which are similar to paper spray such as leaf

38 spray [27, 28] or tissue spray (from a needle tip) [29], which are far more suited to their

39 desired application.

40 Current techniques for the screening of explosives generally involve swabbing of the surface

41 with a collection material such as cotton, Nomex® or Teflon coated fibreglass. These

42 materials are employed in explosives screening because they are known to be efficient at

43 picking up relevant materials from surfaces [30]. Bain *et al.* [31] have recently shown that

44 swab touch spray (using a cotton swab) can be used to pick up explosives from surfaces such

45 as gloves and human skin. Swab touch spray utilises a different substrate, geometry and

46 solvent delivery system to what is described here. Rather than introduce a new swabbing

47 material as per Bain *et al.* [31], we explore the potential to integrate materials that are

48 currently used in explosives screening for this application, with the aim of easing integration

49 into the operational workflow. In our previous work [26] only a paper substrate was

50 considered. Here we consider the use of other collection materials (Nomex, Teflon coated

51 fibre glass and cotton) that are currently employed in security screening programmes.

52 Research to date on paper spray for explosives detection [26, 32, 33], has only considered

53 laboratory-based mass spectrometers. However, many operational scenarios (e.g. airports,

54 military checkpoints) cannot afford the associated high acquisition cost or footprint of such

55 instruments. Miniature mass spectrometers are now available at a fraction of the cost of

56 laboratory based instruments, but with a lower mass resolution [34]. Therefore, in this paper

57 we use a high-resolution mass spectrometer to explore interferences within a ± 0.5 *m/z* range

58 of analyte peaks to facilitate integration with portable mass spectrometry. We also explore

59 the use of high-field assisted waveform ion mobility spectrometer (FAIMS) [35] to improve

60 the selectivity of the analytical method.

Experimental

62 A paper spray source was designed and built in-house as described previously [26]. This

63 source was coupled to a Thermo Scientific™ Q Exactive™ Hybrid Quadrupole-Orbitrap™

64 mass spectrometer (Thermo Scientific, Bremen, Germany). Data was acquired in full scan

65   mode (*m/z* 100-500) with a resolution of 280,000 at *m/z* 200 and analysed using Xcalibur

66   2.10 software (Thermo Fisher Scientific, Bremen, Germany).

67   Paper spray measurements used Whatman Grade I chromatography paper as a substrate.

68   Nomex® (meta-aramid swabs, 200 ct), teflon coated fibreglass (PTFE coated trap, 100 ct) and

69   cotton gloves were obtained from DSA Detection (St Albans, UK) and investigated as

70   alternative substrates. All substrates were cut into triangles (1.6×2.1 cm, b × h). Aluminium

71   foil was folded around the base of the substrate to prevent contamination of the clip

72   supplying the voltage. The substrate was placed on a pre-cut glass slide to prevent

73   contamination of the sample holder.

74   Swabbing experiments used Solmedia glass slides (Shrewsbury, UK), a generic Dell

75   keyboard (Berkshire, UK) used in an explosive-free environment and a new "Classicline"

76   keyboard (Trust, Netherlands) as deposition surfaces.

77   Explosive standards were prepared from certified reference materials of trinitrotoluene

78   (TNT), 1,3,5-trinitroperhydro-1,3,5-triazine (RDX), octahydro-1,3,5,7-tetranitro-1,3,5,7-

79   tetrazocine (HMX), pentaerythritol tetranitrate (PETN), tetryl, nitroglycerin (NG), tetryl,

80   picric acid (PA) and hexamethylene triperoxide diamine (HMTD), which were obtained from

81   AccuStandard through Kinesis (St Neots, UK). Chloramphenicol (CAM) was obtained from

82   Sigma Aldrich (Poole, UK). Optima™ LC-MS grade solvents, methanol (MeOH) and

83   acetonitrile (ACN), were used to prepare all solutions and solvent mixtures (Fisher Scientific,

84   Loughborough, UK). Sodium chloride (NaCl; Sigma Aldrich, Poole, UK) and ammonium

85   nitrate (NH_4NO_3; Fisher Scientific, Loughborough, UK) were used as additives to the spray

86   solvent.

87   Adducts determined and in previous work [26] were used for detection of relevant analytes.

88   The analysis method involved the addition of the analytes to the paper, followed by the

89 addition of 5 μL of 500 ng/ml (2.5 ng) solution of CAM (prepared in MeOH), spray solvent

90 (50 μL; 0.1 mM NH₄NO₃/NaCl in 100% MeOH) and the application of a 2.0 kV spray

91 voltage. As per our previous publication, CAM (at 2500 pg) was used as a spray monitoring

92 tool to prevent false negative events. The internal standard threshold was set at 1×10^5 counts

93 (based on the sum intensity of CAM peaks). Any replicate measurement below this threshold

94 was considered a failed spray [26].

95   The MS was operated at a capillary temperature of 90 °C and S-lens RF level of 80 in

96 negative mode for the detection of TNT, RDX, HMX, PETN, NG, tetryl and PA. Operational

97 parameters for HMTD were identical except for the spray voltage, which was increased to 3.5

98 kV.

99 To explore the possibility of reducing interferences in a ± 0.5 *m/z* range, a FAIMS system

100 (Owlstone, Cambridge, UK) was coupled to the Q-Exactive™ Plus Orbitrap mass

101 spectrometer. Samples containing TNT, RDX, HMX, PETN, Tetryl, NG and PA (500 ng/mL

102 in 0.1 mM NH₄NO₃/NaCl 100% MeOH) were introduced using ESI infusion (flow rate,

103 5 μL/min) and the dispersion and compensation voltages (DV and CV) of the FAIMS were

104 swept across their range to produce a number of 2D scans. The parameters for the

105 UltraFAIMS were set using a software interface provided by Owlstone (UltraFAIMS Control

106 Software V2.00.0.00-r0) with the hardware settings fixed at an analytical gap width of

107 100 μm, trench length of 96 mm and chip thickness 700 μm. The chip region temperature was

108 set to 100 °C and the bias voltage was set to 0 V.

109 A 2D scan was carried out over the dispersion field (DF) range of 200-300 Td and a

110 compensation field (CF) range of -10-10 Td with a CF sweep duration of 30 s. The sensitivity

111 for each explosive compound peaked between a DF of 210-220 Td and clear separation was

112 observed at DF values > 270 Td. 1D sweeps were then carried out at a fixed DF (200-300 Td)

113 and CF of -2 to 2 Td with a CF sweep time of 300 s, allowing for optimum CF values to be

114 clearly identified.

Results and Discussion

116 ### Substrate compatibility

117 Substrates made from Whatman grade 1 chromatography paper, cotton, Nomex® and

118 teflon-coated fibreglass were spiked with 2, 10, 20, 50, 100 and 200 pg of analyte and tested

119 for suitability. Various volumes (20-100 μL) of spray solvent (0.1 mM NH_4NO_3/NaCl in

120 MeOH) and clip voltages (1-5 kV) were investigated for compatibility. None of the analytes

121 could be detected using either the cotton or teflon-coated fibreglass substrates. However,

122 analytes were readily detected using Nomex® and thus Nomex® was a viable alternative to

123 paper. From this point forward, paper spray refers to the use of Whatman Grade I

124 chromatography paper and "swab spray" refers to the use of Nomex®.

125 ### Detection of HMTD

126 To show applicability of a peroxide explosive for this type of analysis, the swab spray

127 method was modified for the detection of HMTD, which produces positive ions. The same

128 experimental conditions were used as for the detection of the remaining seven explosives in

129 negative ion mode, with the exception of the applied voltage, which was raised to 3.5 kV.

130 HMTD was detected at m/z 229.0431 ([HMTD-2H+Na]$^+$), as shown in Figure 1.
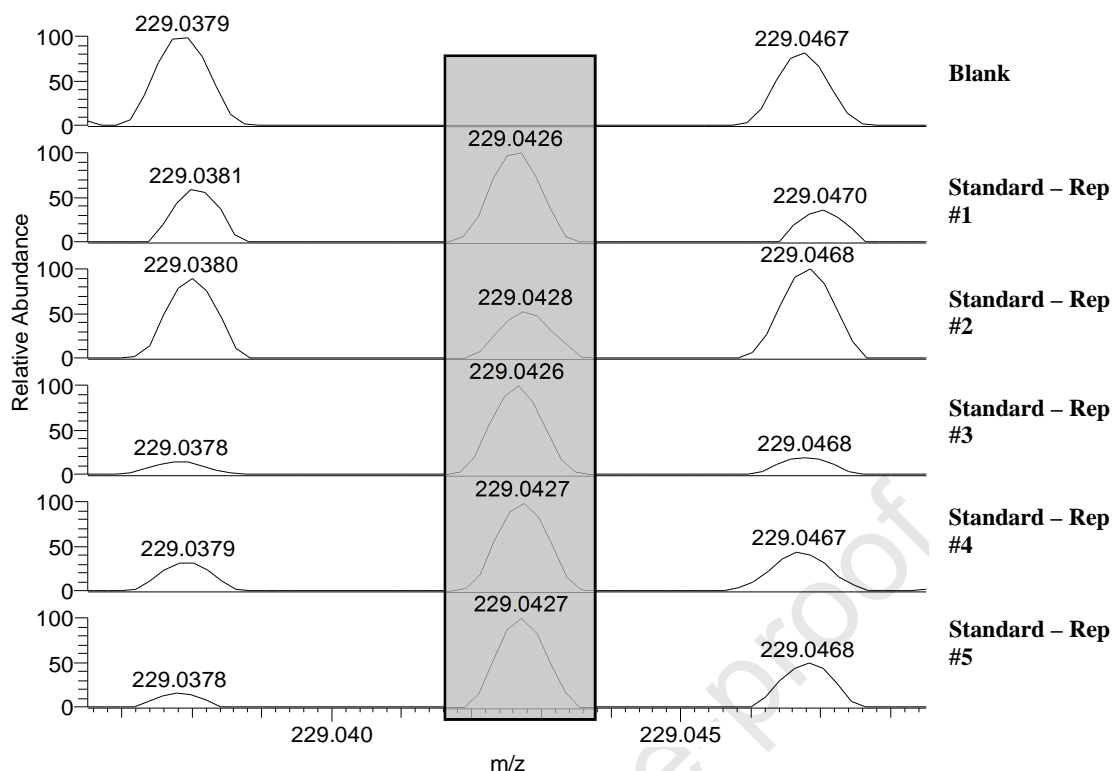
Figure 1. Example spectra showing the HMTD signal [HMTD-2H+Na]$^+$ in blank measurements (top spectrum) and 5 replicate standard measurements using SS-MS. 2500 pg of HMTD were deposited on the substrate for analysis (5 µL of 500 ng/mL)

Comparison of swab spray and paper spray

Solutions containing the analytes were prepared over a range of concentrations (5-180 ng/mL). The standard solutions were drop deposited (5 µL) onto the substrate and allowed to dry (c.a. 1 min)before analysis using the protocol described above.

Due to the high variability observed with paper spray [26, 36], estimation of limits of detection in the absence of an isotopically labelled internal standard is not trivial. As such, for this publication we report on the lowest mass detected. This is defined as follows: in addition to the internal standard cut-off discussed above, successful detection of the analytes required a minimum of 500 counts (peak height) on at least 3 replicate measurements.

145   Table 1 reports the lowest detected mass for both substrates investigated (this is based on the

146   most abundant ion for each analyte) [26]. From Table 1 it is clear that replacing the paper

147   substrate for a swab does not result in a loss of sensitivity, with the exception of NG.

148   **Table 1. Lowest mass detected in all replicate measurements for each explosive material for swab spray**
149   **and paper spray for a 30 s acquisition.**

	Lowest detected mass (pg)	
	Paper Spray	**Swab Spray**
TNT	25	25
RDX	25	25
HMX	25	25
PETN	25	25
Tetryl	25	25
NG	25	50
PA	25	25

150

151   **Surface swabbing**

152   An investigation was carried out to demonstrate the feasibility of collecting explosives from a

153   surface and analysing with both paper spray and swab spray. Known masses of explosives

154   were drop deposited (10 and 25 ng)onto glass slides). The solutions were left to dry until no

155   residue could be observed. The surface was then swabbed using Whatman grade 1 paper or

156   Nomex, the internal standard was added (and allowed to dry) and the substrate was mounted

157   in the source holder for analysis. The data was considered in the same way as described

158   above. Swab spray performed slightly better than paper spray; this is presumably due to the

159   superiority of the swab in picking up explosive compounds from the glass surface. Thus, any

160   further swabbing experiment was carried out using Nomex as a substrate. In Table 2, the

161   results are also compared to Tsai *et al.* [33], which also used paper to collect explosives from

162   glass slides. The method developed here demonstrates detection of explosives at two orders

163   of magnitude than those obtained in previous work and for a wider range of explosives [33].

164 Bain *et al.* [31] recovered explosives from gloves and hands, so no direct comparison can be

165 made, however, we have target other analytes such as tetryl, NG and PA.

166 **Table 2. The lowest mass of explosives detected in each replicate measurement from various surfaces.**
167 **Key: N/D = not detected.**

	Lowest detected mass (ng)				
	Tsai *et al.*, [33] recovery from glass slide	This work, recovery from glass slide		Clean keyboard	Used keyboard
	Paper spray	Paper Spray	Swab Spray	Swab Spray	Swab Spray
TNT	800	N/D	N/D	ND	Partial at 25
RDX	100	25	10	10	10
HMX	600	25	10	Partial at 10	10
PETN	100	25	10	Partial at 10	10
Tetryl	-	25	10	Partial at 10	10
NG	-	N/D	N/D	ND	25
PA	-	10	10	10	10

168

169 The same methodology was used to analyse explosives drop deposited onto individual keys

170 of a clean keyboard at two different masses (10 and 25 ng) using swab spray. Both TNT and

171 NG were not detected at the two masses tested here and both RDX and PA were detected at 1

172 ng/ Conversely, HMX, PETN and tetryl were only detected in 2 out of 3 replicate swabbing

173 experiments and were therefore defined as partially detected.

174 The same experiment was also carried out using a used keyboard and the data is shown in

175 Table 2. With the exception of TNT (partially detected at 25 ng) and NG (detected at 25 ng),

176 all analytes were successfully detected at 10 ng of material. The more successful detection

177 can be rationalised by the higher recovery of analytes caused by the presence of dirt on the

178 keyboard changing the surface adhesion. It was also observed that the background signals of

179   the samples collected from the dirty keyboard were higher than those collected from the clean

180   keyboard, as shown in Figure 2.

181
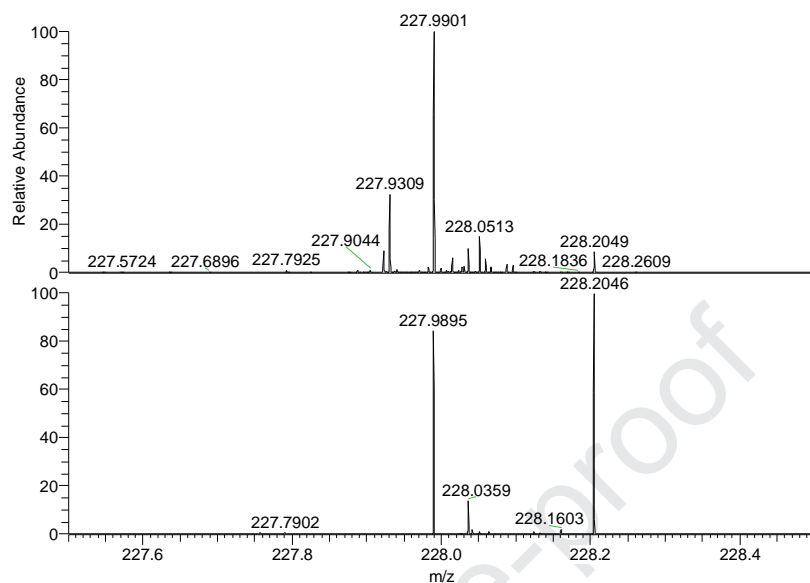
Figure 2. Mass spectra showing 500 pg of PA (*m/z* 227.9894) after swabbing a dirty keyboard key (top) and a clean keyboard key (bottom).

184   **Mass interferences**

185   In order to produce a field-deployable technique, the mass spectrometer that the swab spray

186   ionisation source is coupled to must be of a compact size and low cost compared with

187   laboratory instruments. The portable MS instruments currently available are not capable of

188   reaching the high mass resolving power of 280,000 (at *m/z* 200) used here, with the best

189   available portable mass spectrometers only providing resolving powers in the order of 6,000

190   [37-40].

191   As a next step towards a portable system for explosives detection, we have explored the mass

192   resolving power that is required to resolve background interferences from analyte signal for

193   both swab spray and paper spray. To this, we have estimated the mass resolving power that

194   would be required in order for 200 pg of analyte to be distinguished from the background at a

195   3:1 ratio (see Table 3).

196 **Table 3. Estimated resolution required to separate the analyte signal from background peaks (>3:1) for**
197 **samples containing 200 pg of each explosive compound.**

Explosive	Paper Spray	Swab Spray
TNT	3,400	3,400
RDX	1,200	1,700
HMX	17,500	2,800
PETN	8,300	3,350
Tetryl	6,600	1,300
NG	1,750	2,500
PA	4,900	1,350

198

199 Generally, swab spray gave cleaner background than paper spray (see Figure 3 and Figure 4).

200 For swab spray, it was found that a mass resolving power of greater than 3,350 was required

201 to separate all analyte peaks from their background, compared with 17,500 for paper spray.

202 Ion trap or ToF systems [37-39, 41, 42] do therefore appear to have sufficient mass resolution

203 to enable detection of low levels of the explosives considered here on clean Nomex swabs. It

204 might be expected that swabbing from a dirty surface would attract more background

205 interferences and thereby increase the mass resolution required to distinguish analytes from

206 their background. However, Figure 2 shows that although for a dirty keyboard the

207 background is higher than for a clean keyboard, the closest interference to picric acid is 0.06

208 m/z away from the $[M-H]^-$ peak, and so in this case a mass spectrometer with a resolution of

209 3,800 should be able to resolve the analyte from the background. Of course, the mass

210 resolution that would be required to discriminate all explosives without any false alarms on

211 any dirty swab can only be determined through pseudo operational trials, because there is no

212 "standard" dirty swab. This should be the subject of further work.

213
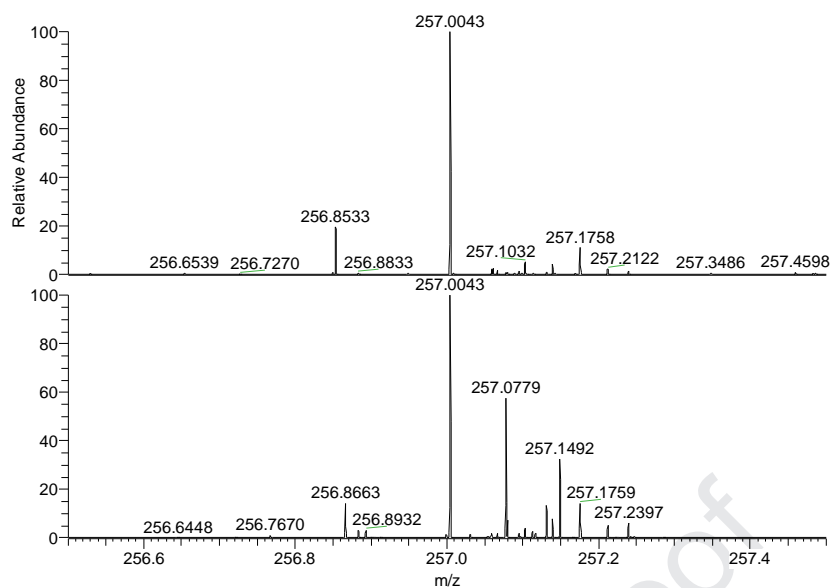
Figure 3. Mass spectra for RDX (200 pg, m/z +/- 0.05 m/z) sprayed using swab spray (top) and paper

spray (bottom).

216
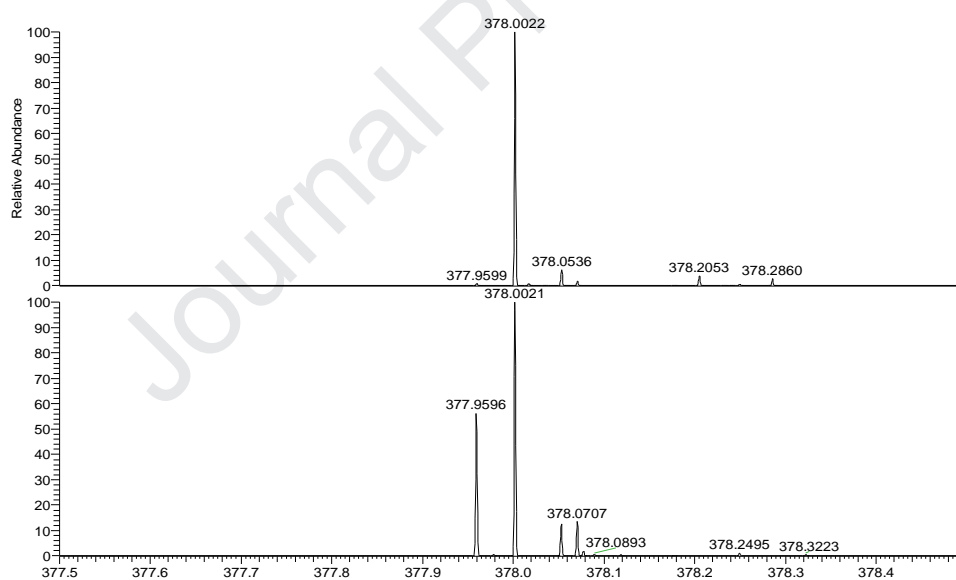
Figure 4. Mass spectra for PETN (200 pg, m/z +/- 0.05 m/z) sprayed using swab spray (top) and

paper spray (bottom).

219   Whilst mass spectrometers with mass resolutions of 4,000 or more do exist, the more

220   affordable and field deployable types employ quadrupoles with only unit mass resolution [41,

221   43]. Therefore we investigate whether pre-filtering of ions using FAIMS can be carried out to

222   allow possible integration with a lower resolution system.

223   **Integration of FAIMS**

224   Samples containing 500 pg of explosives were run using swab spray at a DF of

225   220 and 280 Td and at a fixed CF of 0.6 Td. These results were compared to swab spray

226   results which were collected with no FAIMS attachment. An example is presented in Figure 5

227   below, and shows complete elimination of the background signals around the signal for RDX

228   at m/z 257.0043 (second panel).

229   The data presented here clearly shows that with the right FAIMS settings, the background can

230   be virtually eliminated from swab spray spectra. Therefore integration of FAIMS-MS offers

231   considerable promise for further exploitation, to enable low resolution mass spectrometry

232   from a swab spray source.
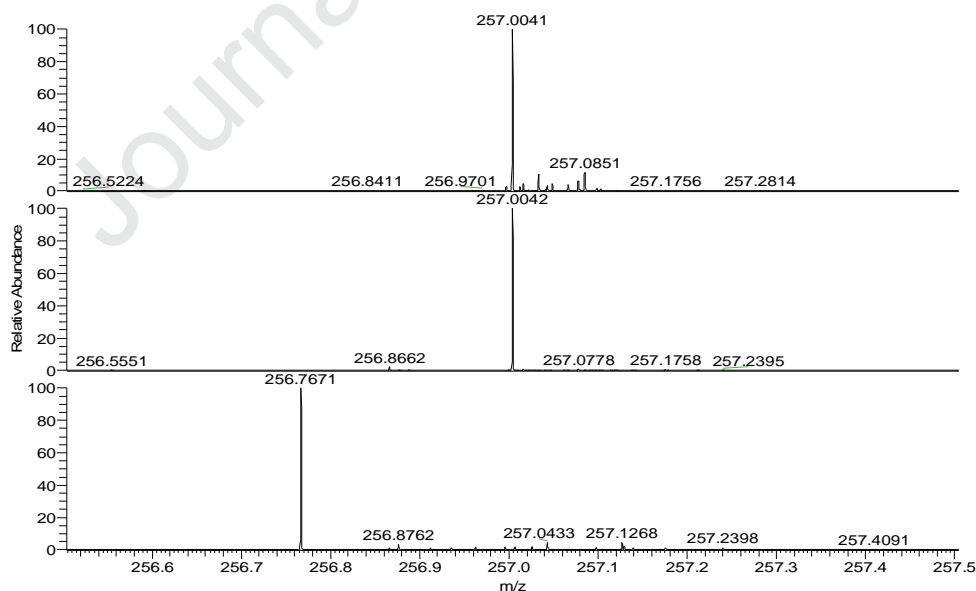
233

234   **Figure 5. Top, swab spray-FAIMS-MS (DF 280 Td, CF 0.5 Td); Middle, swab spray-FAIMS-MS (DF 220**

235   **Td, CF 0.6); Bottom swab spray-MS of [RDX+^{35}Cl]$^-$ (500 pg, m/z 257.0037+/- 0.5).**

Conclusions

Swab spray coupled to a high-resolution mass spectrometer was successfully used to detect explosive compounds including TNT, RDX, HMX, PETN, tetryl, NG and PA with the lowest detected mass below 50 pg. The lowest detected mass of HMTD was 2.5 ng. The recovery and detection of trace quantities of explosives from glass slides showed enhanced sensitivity compared with previously published work. This was extended to other surfaces, including clean and dirty keyboards, during which >25 ng of explosives could be observed, an operationally relevant sensitivity. Interferences in a ±0.5 *m/z* range were also explored in order to specify the resolution required of a field deployable mass spectrometer; this was determined to be <4,000. It was also shown that coupling with FAIMS to the swab spray source, interferences with a ± 0.5 *m/z* range for the analytes of interest can be eliminated. This opens up the opportunity of using a lower resolution and thus more affordable portable quadrupole mass spectrometer for this application.

249 **Acknowledgments**

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