

Recent Advances in Ambient Mass Spectrometry of Trace Explosives†

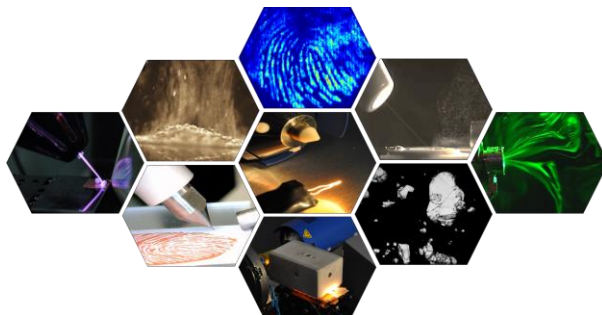
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TOC Image



Abstract

Ambient mass spectrometry has evolved rapidly over the past decade, yielding a plethora of platforms and demonstrating scientific advancements across a range of fields from biological imaging to rapid quality control. These techniques have enabled real-time detection of target analytes in an open environment with no sample preparation and can be coupled to any mass analyzer with an atmospheric pressure interface; capabilities of clear interest to the defense, customs and border control, transportation security, and forensic science communities. This review aims to showcase and critically discuss advances in ambient mass spectrometry for the trace detection of explosives.

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1. Introduction

The steady increase in terrorist attacks across the globe highlights the vital need for instrumentation to sensitively detect trace explosives.¹ The security sector, including national defense, customs and border control, and transportation security often operate in a high-throughput screening setting, targeting energetic materials, material synthesis precursors, and other related compounds. Complementary to screening applications are the identification and characterization of device signatures, post-blast and degradation products, and trace contaminants for attribution and investigative purposes by the forensic science and environmental monitoring communities. These compounds may be found in a range of chemical forms, including particulate material, residue, liquid, emulsion, vapor, or aerosol species. Currently, the appealing size, weight, and power (SWaP), combined with rapid analysis and good sensitivity have led to extensive deployment of ion mobility spectrometry (IMS) at screening points for transportation security.²⁻⁹ Similarly, colorimetric techniques also provide rapid analysis in a very portable field deployable platform; however, they are often hindered by poor specificity.¹⁰⁻¹² Alternatively, mass spectrometric techniques provide superior sensitivity and specificity, and are often employed with an upstream separation (*e.g.*, gas or liquid

chromatography (GC or LC)) or tandem mass spectrometry (MS) capabilities providing structural information.¹³⁻¹⁶ These beneficial qualities have led to the utilization of MS across forensic and investigative laboratories. Some of the more restrictive aspects of GC/MS and LC/MS, such as extensive sample preparation and lengthy run times, have led to the evolution of ambient mass spectrometry. Ambient MS is a collection of techniques requiring no or minimal sample preparation, enabling analysis within seconds, and allowing for direct coupling to mass spectrometers with atmospheric pressure interfaces.

The detection of explosives has been an integral application of ambient mass spectrometry since the field's origins with desorption electrospray ionization (DESI)¹⁷ and direct analysis in real time (DART)¹⁸ over a decade ago. Since this introduction, a plethora of techniques and platforms for the sampling and ionization of compounds under ambient conditions have been presented. A wide range of review articles, collections, and themed issues have been published summarizing and categorizing these techniques.¹⁹⁻²⁴ Likewise, more specific reviews have focused on ambient MS in high-throughput screening,²⁵ ambient MS in forensics,^{26, 27} forensic applications of DESI,²⁸ and DART in forensic and security applications.²⁹ Ambient MS methods provide a range of capabilities of clear interest for the trace detection of explosives, including direct coupling a wide range of miniature and field portable mass spectrometers.³⁰⁻³⁵ The combination of ambient ionization and field portable mass analyzers provides an appealing avenue toward high sensitivity and specificity on-site detection of explosives.

The primary focus of this review is to showcase advances in ambient MS of trace explosives and to discuss critically what advances have been made and what hurdles still exist. The content within is not meant to be an exhaustive list of platforms demonstrating explosive detection, but an evaluation and discussion of those providing unique benefits or interesting results to the security or forensic science communities. We provide a brief background on explosives and classical detection techniques, as well as ambient sampling/ionization mass spectrometry, followed by detailed discussion of advances in the detection of organic nitrate-based, organic peroxide, and inorganic explosives. In addition, we briefly summarize notable developments in closely related security and forensic applications and provide a general discussion of future prospects and directions.

2. Traditional Mass Spectrometry Chemical Analysis of Explosive Materials

Trace detection of explosives is complicated by an ever-expanding list of explosives materials. The 2016 Annual List of Explosive Materials by the United States Bureau of Alcohol, Tobacco, Firearms and Explosives included close to 240 compounds and mixtures.³⁶ These energetic materials can generally be classified based on a number of properties – performance (low order/deflagration vs high order/detonation), sensitivity/output (primary, secondary, and tertiary), or as is often of direct significance to detection by analytical instrumentation, the chemical nature (nitroaromatic, nitramine, nitrate ester, peroxide, fuel-oxidizer mixture, etc.). Likewise, explosives are often grouped into traditional military-grade explosives such as TNT (trinitrotoluene) and RDX (cyclotrimethylene trinitramine), or homemade explosives such as TATP (triacetone triperoxide) and ANFO (ammonium nitrate fuel oil). The evolution of homemade explosives (HMEs), improvised explosive devices (IEDs), and even radiological dispersion devices (RDDs) has only further expanded the target compound list. The open source Global Terrorism Database^{37, 38} provided by the National Consortium for the Study of Terrorism and Responses to Terrorism reveals a surge in attacks using homemade explosives in recent years.¹

The wide variety of chemical classes making up explosive devices and their signatures, readily explains the vast list of analytical methods and instrumentation commonly employed for their detection.³⁹⁻⁴² These analytical techniques include chemical separations such as ion mobility spectrometry (IMS),²⁻⁹ capillary electrophoresis (CE),⁴³⁻⁴⁵ ion chromatography (IC),⁴⁶⁻⁴⁸ gas chromatography (GC),⁴⁹ and liquid chromatography (LC),^{50, 51} optical spectroscopies such as Raman, surface enhanced Raman,^{52, 53} and Fourier transform infrared (FTIR),^{54, 55} mass spectrometry (MS) such as electrospray (ESI)-MS,⁵⁶⁻⁵⁸ secondary ion mass spectrometry (SIMS),⁵⁹⁻⁶¹ and inductively coupled plasma (ICP)-MS;⁶² and hyphenated techniques such as GC/MS, LC/MS, and CE/MS.^{13-16, 63} In addition to these classical analytical methods, a wide range of sensor platforms based on various physicochemical phenomena such as electrochemical,⁶⁴ colorimetric,¹⁰⁻¹² fluorescence quenching,^{65, 66} immunochemical/immunoassay,^{67, 68} and functionalized

nanomaterials^{69, 70} have been developed.⁷¹ These techniques vary widely in capability, size, and amenable compounds.

From this vast list of analytical techniques, those most commonly used by the forensic science field for the identification and confirmation of trace explosives have a mass spectrometry component. While optical-based techniques (such as Raman and FTIR) are useful in making preliminary identifications, they often require bulk (visible) amounts of material. They also exhibit difficulties analyzing low percentage components in mixtures, especially when complex background matrices are present. Currently, the most prevalent tool for trace identification of a suspected organic explosive material is a chromatography-based mass spectrometry system (GC/MS or LC/MS). Significant research exists on the development of the optimal instrumental and sample preparation methods for these techniques.

Analysis of trace explosive by GC/MS goes back to the 1970s,^{72, 73} and has most commonly focused on the detection of nitro compounds and organic nitrates. The power of chromatographic separation, combined with mass spectral identification, has led to broad ranging applications from identification of synthesis or manufacturing impurities,^{49, 74} to detection in complex matrices such as soil,¹⁴ wastewater,⁷⁵ sea-water,⁷⁶ and plant material. While traditional GC/MS analysis utilizes electron impact (EI) ionization, explosives analysis is typically aided by the use of chemical ionization (CI)⁷⁷ to reduce fragmentation and increase sensitivity. The versatility of the GC platform allows for sample introduction via a liquid injection (typically from a solvent extraction) or a vapor injection, such as headspace sampling⁷⁸ or solid phase microextraction (SPME).⁷⁹ In addition to nitrated organics and nitro-containing explosives, GC/MS has demonstrated the detection of peroxide based explosive residues, both pre- and post-detonation.^{80, 81} The analysis of these volatile species typically involves a vapor sampling introduction technique like SPME. While GC/MS is a powerful tool that has been widely deployed in laboratory settings, it does have several drawbacks, including potentially complex sample preparation and extraction procedures, the need for solution phase or thermally desorbed vial-based samples, and often lengthy analysis times. GC/MS also typically requires high purity gases which take up valuable space and weight, introducing constraints for field deployable

applications. In addition, GC/MS largely cannot detect inorganic components and is generally less sensitive than the derivative hyphenated technique, LC/MS.

The LC/MS analysis of explosives⁸² has incorporated a variety of different ionization techniques including CI,^{82, 83} ESI,⁸⁴ and APCI.⁸⁵ Due to its prevalence in analytical laboratories, reversed phase separation is often employed. LC/MS has demonstrated the detection of a range of organic explosives, from nitrated compounds to peroxides. The softer ionization techniques employed by LC/MS typically reduce thermal decomposition and fragmentation of labile analytes. This allows for the detection of intact molecular or adduct ions in most instances. LC/MS also enables the detection of low volatility explosives, such as HMX (cyclotetramethylene tetranitramine) and PYX (2,6-Bis(picrylamino)-3,5-dinitropyridine), which are difficult to detect by GC/MS. As with GC/MS, LC/MS has demonstrated the detection of trace explosive in complex matrices⁸⁴ and those extracted directly from hands.¹⁶ While sensitivities of LC/MS (typically ng mL⁻¹) exceed that of GC/MS, LC/MS also requires lengthy analysis times, large volumes of high purity solvents, and substantial infrastructure. Detection of the inorganic components is typically not completed.

Other hyphenated techniques have also been employed to detect trace explosives, including CE/MS^{63, 86} and IC/MS.⁸⁷ Notably, CE/MS⁸⁶ has demonstrated the analysis of both organic and inorganic explosives with sensitivities comparable to GC/MS. IC/MS is a superior technique for the detection of inorganic explosives such as ammonium nitrate and potassium chlorate. However, both techniques, like LC/MS, require multi-step solvent dissolution sample preparation processes, followed by lengthy analysis times. Other mass spectrometry techniques such as SIMS and ICP-MS, have demonstrated explosives detection, but have not been widely adopted by the community.

The evolution of ambient MS has introduced a suite of tools capable of addressing many of the issues that arise with traditional analyses. Ambient MS techniques do not require extensive sample preparation or utilize chromatographic separations, drastically reducing analysis times to seconds. Sensitive detection (*e.g.*, nanogram-to-sub-nanogram) is achievable *in situ*, providing rapid preliminary or confirmatory

analyses. The field of ambient MS and the many derived platforms, as well as their implementation for trace explosives detection, will be detailed in the following sections.

3. Advances in Ambient Mass Spectrometry

As presented above, the field of ambient MS blossomed with the introduction of DESI¹⁷ and DART¹⁸ in the early-to-mid 2000s. DESI, DART, and the wide range of techniques that have followed in the years since, offer unique capabilities inaccessible by classical MS platforms.¹⁹⁻²⁴ Ambient MS removes the enclosure constraints common to electrospray ionization (ESI) and matrix assisted laser desorption/ionization (MALDI) techniques. This enables the direct analysis of sample surfaces – even from uniquely shaped or sized substrates – without prior sample preparation. By their nature, ambient MS methods are rapid and allow for high-throughput screening. Samples extending from wipe collections to post-blast shrapnel and debris can be readily analyzed by ambient MS for trace explosives and related compounds. Direct sample interrogation has also opened the door to visualizing spatial distribution of chemicals across surfaces, including explosives within latent fingerprints and colocalization of species across wipe collections.⁸⁸⁻⁹⁰ In several instances, non-proximate or remote interfaces have been developed in conjunction with ambient ionization sources for the sampling of large or cumbersome substrates and surfaces that cannot be easily positioned at the mass spectrometer inlet.⁹¹⁻¹⁰⁰ A variety of flow control methods have been employed for these interfaces to generate the transport of neutrals and ions, including vacuum pumps and Venturi-based components. Ambient MS also permits the coupling of these methods to just about any mass spectrometer with an atmospheric pressure interface. This aspect has led to the thriving field of miniature and portable mass spectrometers incorporating ambient sampling and ionization platforms,³⁰⁻³⁴ as well as interchangeable and swappable ion sources.³⁵

Ambient MS techniques have generally demonstrated soft ionization, imparting internal energy to analytes equal to or less than classical ESI or MALDI platforms, minimizing fragmentation of most

molecules, unlike, for example, EI.^{101, 102} The ease with which ionization mechanisms and pathways can be manipulated through the addition of dopants or reactant ions provides unique control over the ionization of analytes.¹⁰³⁻¹⁰⁶ Largely, ambient MS techniques have demonstrated sensitive detection in the nanogram-to-sub-nanogram range for typically square centimeter surface areas, however, it should be noted that sensitivity is strongly dependent on a range of parameters (*e.g.*, substrate surface) and the performance of the mass spectrometer in use. Quantitative and semiquantitative analyses are also possible with ambient MS techniques, however, special care must be taken when selecting an appropriate internal standard (IS) and the method of its incorporation.^{107, 108} Similar to a number of classical MS platforms, ambient MS techniques enable the simultaneous or near-simultaneous detection of both organic and inorganic species.^{89, 109-111} This aspect becomes vital in the consideration of explosives detection, specifically with homemade fuel-oxidizer mixtures and improvised explosive devices.

3.1. Ambient Ionization Sources & Classification

The field has expanded rapidly, leading to a wide range of techniques and countless acronyms. Yet, for the most part, these platforms can be classified based on a number of physical phenomena behind their desorption and ionization processes. Ambient MS techniques have been categorized and classified in several recent reviews,^{19, 20, 24} however, given this is not an exhaustive review of ambient MS, we will condense the main categories here for simplicity. In general, techniques will be discussed in the context of (1) solid-liquid extraction-based, (2) plasma-based, (3) laser-based, and (4) all two-step, multimode, or hybrid methods. Typically, these hybrid or multimode techniques will be discussed in the context of their components.

Solid-liquid extraction techniques use a liquid or liquid-based vapor to directly desorb analytes from a substrate surface. Analyte desorption is most frequently followed by classical electrospray ionization (ESI) mechanisms, however, other atmospheric pressure ionization schemes such as sonic spray ionization (SSI) or atmospheric pressure photoionization (APPI) have been implemented. Solid-liquid extraction platforms

include techniques such as desorption electrospray ionization (DESI), transmission mode (TM)-DESI, desorption atmospheric pressure photoionization (DAPPI), desorption electro-flow focusing ionization (DEFFI), easy ambient sonic spray ionization (EASI), and paperspray ionization (PSI). A DESI source consists of a pneumatically-assisted ESI sprayer directed at a surface in an off-axis (with respect to the inlet axis) configuration.¹⁷ The spray is charged by a kilovolt range potential and is focused at the surface by a nebulizing gas flow. The charged spray of primary droplets generates a thin film that extracts analytes from the surface and carries them to the mass spectrometer inlet in secondary droplets.¹¹² TM-DESI represents an alternative configuration in which the DESI source is positioned on-axis with the instrument inlet and samples through a porous substrate.¹¹³ DEFFI,¹¹⁴ a similar technique to DESI, incorporates electro-flow focusing¹¹⁵ in a desorption-style configuration. In this platform, a low pressure laminar gas, flowing concentrically, focuses a solvent stream from a recessed capillary through a small orifice. This “flow focusing”¹¹⁶ phenomena results in a small diameter liquid jet ($\approx 1\ \mu\text{m}$ to $5\ \mu\text{m}$) that is charged through a potential difference between the solvent and orifice plate. The significant reduction in distance between potentials, enables high electric fields to be generated at low potentials.¹¹⁷ Though the physics of jet formation are altered, DEFFI also generates charged secondary droplets that result in electrospray ionization mechanisms.

Like DESI, EASI also utilizes a high pressure nebulizing gas to assist solvent flow to a substrate surface, however, no potential is applied for droplet charging.¹¹⁸ Here, droplet charging and ionization are achieved through sonic spray ionization (SSI) mechanisms.¹¹⁹ The spray current in EASI is a function of the supersonic gas velocity, generated by nebulizing pressures multiple times greater than classical DESI. The voltage-free, supersonic charged droplet spray enables superior matrix penetration and a reduction in solvent clusters and adducts relative to DESI.¹¹⁸ Another technique incorporating alternative ionization mechanisms, DAPPI, uses a nebulized solvent vapor directed toward a surface for analyte desorption coupled with atmospheric pressure photoionization.¹²⁰ PSI includes a high voltage applied to a solvent and sample laden piece of paper or other substrate, which generates electrospray formation from a tip.^{121, 122} Techniques such as PSI incorporate some level of sample preparation or separation prior to analysis. It

should be noted that a number of platforms discussed within this review (*e.g.*, PSI) may not fit within the strict definition of ambient MS, but provide relevant results to the overall theme of ambient sampling and ionization of explosives theme.

Plasma-based techniques either chemically sputter or thermally desorb neutrals from substrate surfaces. Depending on the configuration and aspects of the thermal component, various techniques may also fall into the multimode or hybrid classification. The discussion of plasma-based sources in this review will encompass a wide range of gas discharges, including direct current (*e.g.*, glow, corona, and hollow cathode discharges) and alternating current discharges (*e.g.*, dielectric barrier, radio frequency, and microwave discharges). For the most part, gas discharges in use for ambient MS can also be categorized as low temperature plasmas (based on thermodynamic properties), including glow, corona, dielectric barrier, and RF discharges. Given their simplicity and lack of solvents, plasma-based techniques have provided appealing platforms for field deployable explosives detection. Plasma-based techniques highlighted in this review include direct analysis in real time (DART), low temperature plasma (LTP), dielectric barrier discharge ionization (DBDI), flowing atmospheric pressure afterglow (FAPA), desorption atmospheric pressure chemical ionization (DAPCI), helium plasma ionization (HePI), atmospheric pressure glow discharge (APGD), and microwave plasma torch (MPT).

The utility and commercial availability of DART has led to considerable research into its use for explosives detection and other related forensic applications. DART incorporates a low current DC discharge within the source to generate a flowing plasma, from which the majority of ions are filtered by grid electrodes, typically leaving only metastable species.¹⁸ These metastable species are directed at the surface within a heated gas stream for thermal desorption and ionization. Extensive research exists on various ionization pathways and phenomena demonstrated by DART.^{105, 123} Both DBDI and LTP utilize an AC dielectric barrier discharge, however, LTP incorporates the counter electrode within the source, providing a more direct platform for surface sampling.^{124, 125} The simplicity of the LTP configuration has led to miniaturized versions and implementations coupled with portable and backpack mass spectrometers.^{98, 126}

All of the ions generated by the LTP plasma are emitted and interrogate the surface (*i.e.*, there are no filtering grid electrodes as employed by DART).

FAPA incorporates a similar configuration to DART with a DC discharge, however, high currents are used, generating Joule heating of the gas stream.¹²⁷ This thermal component aids in desorption of surface laden analytes. Similar to LTP, no filtering of the ionic plasma species is completed. HePI is another DC discharge based plasma technique that uses a repurposed ESI emitter with a helium discharge gas instead of solvent.¹²⁸ The kilovolt potential generates a plasma through which gaseous samples are driven. The MPT technique incorporates a higher power microwave plasma (GHz range) that requires high gas flow rates to maintain reasonable plasma temperatures.¹²⁹ The non-resonant MPT geometry eliminates the typical frequency sensitivity, enabling stable operation. The MPT technique discussed in this review incorporates an argon discharge gas.¹³⁰ Finally, the DAPCI platform differs from the previously discussed plasma sources in that it incorporates a solvent.¹⁰⁴ A corona discharge within the source ionizes a gaseous solvent that impinges the surface of interest. The resulting charged gas phase solvent species chemically sputter the analyte and yield ions and spectra similar to DESI.

Laser-based mass spectrometry techniques gained popularity for organic analysis with the advent of matrix assisted laser desorption/ionization (MALDI) platforms, which included a matrix for enhanced energy absorption and ionization. Platforms incorporating lasers have evolved to exploit various benefits of ambient and atmospheric pressure ionization methods. The only solely laser-based technique discussed in this review is LDI, which employs nanosecond Nd:YAG lasers to ablate and ionize samples.¹³¹ Ambient pressure laser desorption single photon ionization (APLD-SPI), AP LD-chemical ionization (CI), and laser electrospray mass spectrometry (LEMS) represent laser-based hybrid techniques that incorporate a secondary ionization step. The AP LD technique deploys a nanosecond Nd:YAG laser with pulses at maximum energy of 6 mJ, all within a handheld endoscope sampling probe.¹³² The handheld unit connects to the ionization technique and mass spectrometer through a 1.5 m heated transfer line. The handheld AP LD probe is interchangeable between instruments and has been demonstrated with both photoionization/time-of-flight and chemical ionization/ion trap mass spectrometry. LEMS couples a non-resonant femtosecond

laser vaporization with electrospray-based ionization.¹³³ The 1.5 mJ to 2.5 mJ pulses eliminate the need for matrix and first-order resonant absorption.

A range of additional hybrid or multimode techniques have demonstrated interesting explosives detection, including thermal desorption (TD)-DART, TD-APCI, Joule heating thermal desorption (JHTD)-DART, infrared thermal desorption (IRTD)-APCI, IRTD-DART, dopant-assisted reactive (DAR)LTP, neutral desorption extractive electrospray (ND-EESI), and ultrasonic nebulization (USN)-EESI. As introduced for the hybrid laser technique, LEMS, the decoupling of sample desorption or vaporization from sample ionization is often completed to take advantage of specific aspects of each component. In the instance of LEMS, the benefits of femtosecond laser vaporization are coupled with ESI mechanisms, enabling easy dopant addition for targeted ionization pathways and generation of multiply-charged species.

Several of the hybrid platforms implemented for trace explosives detection incorporate thermal desorption coupled with a vapor-phase plasma-based ionization scheme. This exhibits parallels to sample introduction for many classical and next generation commercial explosives trace detectors based on IMS, MS, or molecular sensing, which rely on thermal desorption for the vaporization of analytes from collection media (*e.g.*, wipes, traps, swabs). For example, TD-APCI couples the thermal desorption of swab samples with corona discharge-based atmospheric pressure chemical ionization.¹³⁴ TD-APCI also takes advantage of gas-phase dopants to target specific ion pathways and adduct formation. Similarly, the DARLTP technique incorporates a halogen lamp for discrete (*i.e.*, 3 s intervals) non-contact thermal desorption of analytes from a polytetrafluoroethylene (PTFE) swab, with dopant-based reactive LTP ionization.¹⁰³ More recently, a series of hybrid platforms have coupled both thermal desorption (TD),¹³⁵ infrared thermal desorption (IRTD),¹³⁶ and Joule heating thermal desorption (JHTD)¹¹⁰ components with APCI and DART ionization techniques. TD-DART and IRTD-APCI incorporate heating units designed to accommodate the direct insertion of commercially available wipes used for trace sample collection in screening and check-point arenas.

ND-EESI is a hybrid technique that uses nitrogen gas to desorb neutral analyte compounds from surfaces and carry them through an ESI plume for extractive electrospray ionization (EESI). This enables

solvent-free surface interrogation while still reaping the advantages of solvent-based ionization.¹³⁷ In a similar manner, USN-EESI, includes nominally neutral droplets (droplets will acquire minimal net charging due to electric fields resulting from piezoelectric actuation and differences in ion mobility of charge carrying species) interacting with a charged electrospray plume.¹³⁸

Another class of hybrid platforms discussed in this review encompasses coupling vapor collection and transport with ambient ionization, including aerodynamic assisted thermal desorption (AATD)-APCI, Venturi-assisted entrainment and ionization (VENTI), and atmospheric flow tube (AFT)-DBDI. The AATD-APCI platform uses a heated gas jet for the thermal desorption of analytes, which is coupled with aerodynamically-assisted vapor collection and transport through a corona discharge. The large gas jet enables a relatively large sampling area of 324 cm².¹³⁹ The VENTI platform incorporates multiple Venturi-based components for the collection and transport of vapors and aerosols from non-proximate locations through a multi-meter sampling probe for real-time APCI-MS analysis.⁹⁵ The air amplifier used for sample entrainment within the VENTI platform takes advantage of the Coandă effect to preferentially recycle the supply gas back into the environment while transferring the collected sample to the remote sampling probe. The VENTI system enables an enhancement in the aerodynamic reach of vapor and aerosol collection by 3-fold over simple suction.⁹⁵ The AFT-DBDI system aerodynamically samples vapors through a DBDI region followed by an approximately 70 cm flow.^{140, 141} The multi-second residence time in the flow tube enables efficient ion/analyte interaction and reduces chemical noise and background.

The above introduction to ambient MS techniques is not a comprehensive list of those discussed in this review, however, it does touch on the main categories implemented for trace explosives detection. A number of additional techniques and platforms may be discussed below. In addition, given traditional definitions of ambient MS, this review will also touch on vapor sampling with ambient ionization; other sources not strictly meeting the definition of ambient MS, but developed with the same goals of rapid real-time analysis at atmospheric pressure; and related platforms and applications. Table 1 displays a list of the main ambient MS techniques discussed here and the classes of explosives that detection has been demonstrated for.

Table 1. List of ambient MS techniques, abbreviations, and select references demonstrating the detection of explosive classes.

Abbreviation	Technique	Selected References for Explosive Classes Detected				
		Nitramines	Nitro-aromatics	Nitrate Esters	Peroxides	Inorganics
<i>Solid-Liquid Extraction-Based Techniques</i>						
DESI	desorption electrospray ionization	104, 142	104, 142	104, 142	143, 144	111
TM-DESI	transmission mode-DESI	109				109
DAPPI	desorption atmospheric pressure photoionization	145	145	145		
DEFFI	desorption electro-flow focusing ionization	89, 114	89, 114	89, 114	89	89
EASI	easy ambient sonic spray ionization				146	147
PSI	paperspray ionization	148	148	148		
<i>Plasma-Based Techniques</i>						
DART	direct analysis in real time	18, 149	18, 149	18, 149	18, 150	18
LTP	low temperature plasma	151, 152	151, 152	151, 152	151	
DBDI	dielectric barrier discharge ionization	153, 154	153, 154	154		
DAPCI	desorption atmospheric pressure chemical ionization	104	104, 155		144	
FAPA	flowing atmospheric pressure afterglow	156	156	156		
HePI	helium plasma ionization	157	157			
APGD	atmospheric pressure glow discharge	158	158	158		
MPT	microwave plasma torch	130				130
<i>Laser-Based Techniques</i>						
LDI	laser desorption/ionization					131
<i>Hybrid or Multimode Techniques</i>						
TD-DART	thermal desorption-DART	159	159	159	159	159
TD-APCI	thermal desorption-APCI	134	134	134		
LEMS	laser electrospray mass spectrometry	160			160	161
JHTD-DART	Joule heating thermal desorption-DART	110	110	110	110	110
IRTD-DART	infrared thermal desorption-DART	136, 162	136, 162	136, 162	136, 162	136, 162
DAPNe-DART	direct analyte-probed nanoextraction-DART	163	163			
DAPNe-NSI	DAPNe-nanospray ionization	164	164	164	164	164
ND-EESI	neutral desorption extractive electrospray ionization	137	137	137	137	
USN-EESI	ultrasonic nebulization-EESI					138
APLD-SPI	ambient pressure laser desorption-single photon ionization		132	132		
APLD-CI	APLD-chemical ionization		132	132		
DARLTP	dopant-assisted reactive LTP	103	103	103		
AATD-APCI	aerodynamic assisted thermal desorption-APCI	139	139			

VENTI	Venturi-assisted entrainment and ionization		95	95	95	
AFT-DBDI	atmospheric flow tube-DBDI	140, 141	141	141		

4. Organic Nitrate-Based Explosives

Much of the research on trace detection of explosives, in general and within ambient MS, has focused on common military-grade organic nitrated explosives. The most frequently demonstrated nitroaromatic, nitramine, and nitrate ester explosives have been 2,4,6-trinitrotoluene (TNT), cyclotrimethylenetrinitramine (RDX), and pentaerythritol tetranitrate (PETN), respectively. However, other commonly investigated nitrate-based explosives include 2,4,6-trinitrophenylmethylnitramine (Tetryl, nitroaromatic) and 2,4-dinitrotoluene (DNT, nitroaromatic), cyclotetramethylene tetranitramine (HMX, nitramine), nitroglycerin (NG, nitrate ester), ethylene glycol dinitrate (EGDN, nitrate ester), and erythritol tetranitrate (ETN, nitrate ester). Detection of these compounds has been extensively investigated using solid-liquid extraction-based platforms, most notably, DESI-MS. DESI-MS has demonstrated the detection of explosives from numerous surfaces, including paper, plastic, stainless steel, glass, nitrile gloves, fabrics (polyester, fleece, cotton, linen, denim, and silk), and even skin.^{104, 112, 142, 165, 166} The flexibility offered by ambient MS to analyze target compounds directly from native surfaces was established early on and remains one of the field's most appealing capabilities. These early works focused mainly on TNT, RDX, PETN, and HMX, however, Cotte-Rodriguez *et al.* also included the detection from complex mixtures, such as plastic-bonded explosives (*e.g.*, C-4, Semtex, and Detasheet), and in the presence of interferents such as diesel, vinegar, Windex, WD-40, Clorox, and explosives from fingerprints.¹⁰⁴

DESI has also demonstrated explosives detection coupled with portable mass spectrometers, providing an avenue for field deployable sampling and detection.^{167, 168} Exploiting the geometry and physics of the “flow focusing”¹¹⁶ technique for jet formation, DEFFI enabled a decrease in the required gas and power for electrospray generation relative to classical DESI, seeking to reduce consumables for fieldable

instrumentation.^{89, 114} However, in both cases (*i.e.*, DESI and DEFFI) the need for solvents, flow control, and pressurized gas, present hurdles to widely deploying these techniques in the field.

Other solid-liquid extraction techniques that incorporate ionization mechanisms other than electrospray ionization-based mechanisms, such as DAPPI, have been demonstrated. While DAPPI performs well with nitroaromatics, it exhibits difficulties with nitrate esters and nitramines.¹⁴⁵ Nevertheless, ambient MS also enables manipulation of the ion chemistry, which is often exploited by adding reagents or dopants. Common nitramines and nitrate esters typically ionize by adduct formation, an aspect Kuappila *et al.* employed to enhance sensitivity for the detection of these compounds by adding dopants to the DAPPI spray solvent.¹⁴⁵ Manipulation of ion chemistry is used widely for a range of ambient MS platforms. Improvements in sensitivity of DESI-MS for nitrate based explosives has been increased up to an order of magnitude in cases, down to tens of picograms,¹⁰⁴ through the addition of chloride containing species in the spray solvent (Figure 1).^{100, 104, 169, 170} Compounds such as RDX and HMX have demonstrated a strong affinity for the chlorine anion, creating a preferential ionization pathway, which in turn aids in sensitivity improvement.¹⁰⁴ Dopants often include various ionic species from salts or acids. For example, the addition of ammonium nitrate to the spray solvent in PSI (paperspray ionization) led to enhancements of the nitrate adducts that surpassed enhancements from a chloride containing additive.¹⁴⁸ Szakal and Brewer presented an in-depth investigation into the ion chemistry of RDX in DESI-MS, identifying a range of parameters (*e.g.*, local analyte concentration, tip voltage, and acquisition time) which directly affect the ionization pathways and dimerization frequency.¹⁶⁹

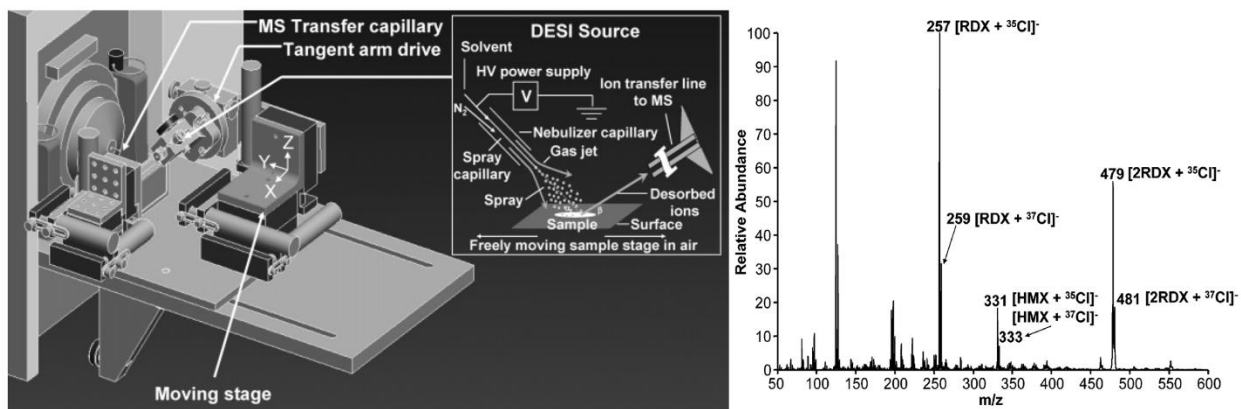


Figure 1. Schematic representation of DESI configuration and representative negative ion DESI mass spectrum of C4 explosive from a metal surface using a HCl (0.05 %) reactive dopant in a methanol/water (1/1 (vol/vol)) spray solvent. Adapted with permission from reference ¹⁰⁴. Copyright 2005 American Chemical Society.

The sensitivity of a range of solid-liquid extraction-based techniques has been demonstrated down to the single to tens of picograms range, however, it is important to recognize the sensitivity of spray-based techniques (*e.g.*, DESI and DEFFI) is dependent on the analyte, surface analyzed, and the presence of additional matrices. For example, the physicochemical nature of the substrate surface directly affects the interactions between the surface and liquid spray, as well as between the surface and free charge carriers. Non-porous and hydrophobic surfaces typically demonstrate good sensitivity by providing direct analyte desorption, secondary droplet formation, and efficient charge transfer to secondary droplets. Porous substrates lead to solvent absorption and wicking, reducing overall secondary droplet formation.¹⁴² In addition, insulating materials exhibit long charge relaxation timescales, leading to optimal current carried by the secondary droplet stream. Alternatively, conductive surfaces (*e.g.*, metallic) exhibit very fast charge relaxation timescales, which leads to near instantaneous loss of charge from primary droplets as they impact the surface, yielding low current carried by secondary droplets and inefficient analyte ionization.¹¹⁷

While ambient MS provides the ability to directly sample substrate surfaces, there are applications for which this may not be feasible, for example screening of individuals at checkpoints for transportation or security arenas. Justes *et al.* demonstrated the unique and interesting capability of DESI for direct sampling and detection of explosives from skin,¹⁶⁶ while Chen *et al.* cleverly eliminated the need for solvent exposure

by using neutral desorption of explosives from skin, followed by extractive electrospray ionization (ND-EESI).¹³⁷ However, the applicability, safety, and presumed legal issues of accomplishing this in practice are unavoidable. For these applications, including a range of forensic and security arenas, dry wipe sample collection remains standard operating procedure. In this instance, a wipe, swab, or trap material (*e.g.*, Nomex, PTFE-coated fiberglass weave, or paper) is swiped across the target surfaces, including luggage, personal belongs, vehicles, hands, persons, etc. and subsequently analyzed. However, many ambient ionization platforms only interrogate a small surface area. For example, when operated under traditional parameters, DESI only addresses an approximately 1.5 mm² to 2.0 mm² area.¹⁷¹ Soparawalla *et al.* offered a unique adaptation of DESI developed for large-area sampling.¹⁷¹ This configuration, displayed in Figure 2, generated a larger spray plume and increased the desorption area near 200 times that of conventional DESI sources, allowing for efficient sampling across large surfaces. The enclosed large-area DESI platform also allowed for the direct analysis of large collection areas from wipe sampling substrates. The below discussion of plasma-based hybrid techniques will expand on the analysis of wipe-based collections.

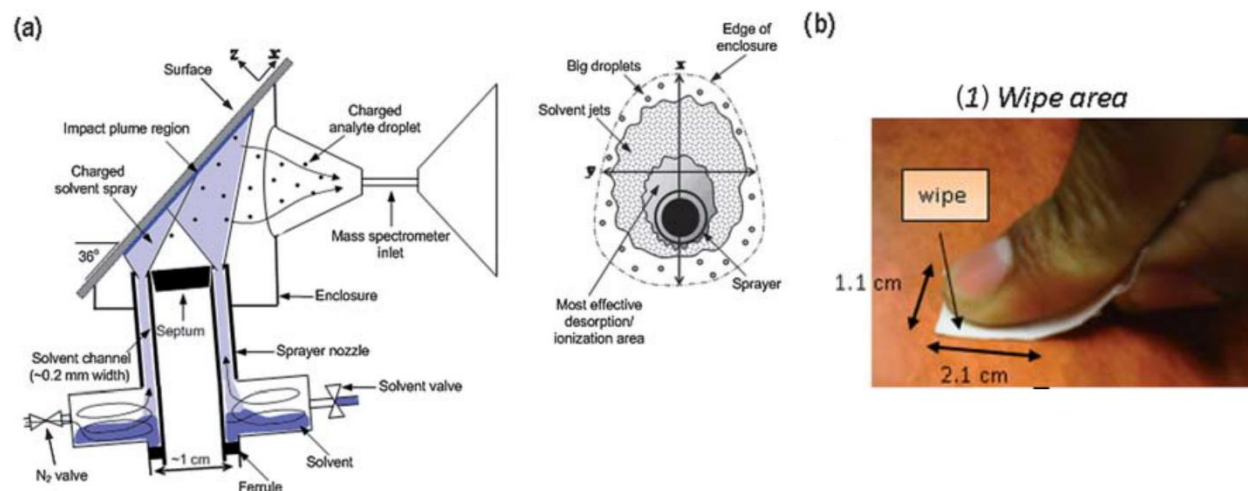


Figure 2. Schematic representation of the (a) large-area DESI configuration for the analysis of larger surface areas and (b) wipe-based sampling analysis. Adapted from reference ¹⁷¹ with permission from The Royal Society of Chemistry.

Solid-liquid extraction techniques have also demonstrated robust chemical imaging capabilities, providing detection across a larger area and still maintaining spatial distribution information. Forbes and

Sisco demonstrated DEFFI-MS imaging of multiple explosive species off a Nomex swab collection of residues from an aluminum surface. The colocalization and separation of individual device chemical constituents were observed from the chemical images of elemental inorganic and organic species.⁸⁹ Similarly, Ifa *et al.*⁹⁰ and Forbes and Sisco^{88, 89} have demonstrated the chemical imaging and spatial resolution of nitrate-based explosive residues within latent fingerprints from plastic and forensic lift tape by DESI and DEFFI, respectively.^{88, 90}

Plasma-based techniques have also been widely employed for the trace detection of nitrated explosive materials, including LTP,¹⁵² DART,¹⁴⁹ DBDI,^{153, 154} HePI,¹⁵⁷ DAPCI,¹⁵⁵ FAPA,¹⁵⁶ and APGD.¹⁵⁸ Typically, these plasma-based ambient MS techniques are operated with helium discharge gas, however, argon, nitrogen, and air have also been demonstrated. A number of early investigations on DART,¹⁸ DBDI,¹⁵⁴ and LTP¹²⁵ provided preliminary demonstrations of nitrate-based explosives detection and were followed up by more in-depth works.^{149, 151, 152, 172} Zhang *et al.* demonstrated improved sensitivity (single picogram to sub-picogram) for LTP over the spray-based DESI and similar plasma-based DBDI for TNT, PETN, and RDX.¹⁵² Both DBDI and LTP utilize a dielectric barrier discharge, however, LTP incorporates the counter electrode within the source. This feature enables direct analysis from any surface, including explosives from glass, paper, PTFE, latex, and fabric.¹⁵¹ Similarly, DART incorporates a discharge within the source, allowing for trace detection of explosives from a range of common substrates, including glass, asphalt, foam, metal, wood, tape, Nomex, and PTFE.^{106, 149}

In the basic configuration of LTP, the discharge gas is not heated, however, Garcia-Reyes *et al.* demonstrated that heating the sample substrate improved desorption and overall limits of detection.¹⁵¹ A number of similar multimode or hybrid techniques have taken advantage of decoupling thermal desorption from the ionization processes, providing more direct control over each. These include an LTP platform incorporating non-contact heating of the target surface by a halogen lamp,¹⁰³ as well as thermal desorption of swab collections,¹³⁴ infrared thermal desorption (IRTD) of wipe collections,¹³⁶ and aerodynamic assisted thermal desorption,¹³⁹ all coupled to implementations of corona discharge ionization.

Alternatively, DART directly incorporates a heated discharge gas, which can be used to manipulate the thermal desorption of analytes based on their physicochemical properties.^{106, 172} Extensive research has been conducted on characterizing and validating the use of DART for explosives detection.^{18, 106, 149, 163, 172-176} Early investigations into the use of DART-MS for explosives detection and screening by Nilles *et al.*¹⁴⁹ and Swider¹⁷⁵ considered sets of 75 explosive-surface combinations and 22 explosive compounds, respectively. Nilles *et al.* also expanded on the common ambient MS approach for dopant addition, targeting chlorine-adducts similar to early DESI demonstrations.¹⁴⁹ In addition to the range of substrate surfaces demonstrated in earlier works, Roswell *et al.* investigated the detection of nitrated explosives directly from latent fingerprints without sample preparation.¹⁷⁴ Sisco *et al.* performed an in-depth validation and parametric optimization study for 24 explosives, characterizing various parameters, dopants and providing comparisons to alternative screening platforms.¹⁷² A recent study by Bridoux *et al.* combined Raman spectroscopy and DART-MS to generate orthogonal signatures of explosive, binder, plasticizers, and other organic additives from 15 defused devices (*e.g.*, rockets, mines, and mortars).¹⁷⁷ Residues and particles were collected by sampling and prepared for analysis with the use of a vacuum impactor. Though this requires some sample preparation, the combined Raman spectroscopy and high resolution MS analysis of individual target particles demonstrates a unique capability for the laboratory-based investigation of explosive device signatures.¹⁷⁷

In addition to the thermally-based multimode platforms discussed above, plasma techniques have been coupled with initial extraction methods, for example, direct analyte-probed nanoextraction (DAPNe) targeting single particles of TNT and RDX,¹⁶³ and sorbent-coated wire mesh collecting vapors from nitro-based smokeless powders.¹⁷⁸ Clemons *et al.* introduced DAPNe as a platform for single particle analysis coupling a nanomanipulator and bright-field microscopy with DART-MS.¹⁶³ This platform enabled precise analysis of forensic samples without disturbing surrounding fingerprints or particles. Li *et al.* demonstrated another multimode technique that targeted vapor collection and DART-MS of nitrate-based smokeless powder components and additives found in IEDs.¹⁷⁸ The platform demonstrated the analysis of chemical

attribute signatures and provided an avenue for field analysis when combined with portable vacuum and heating components.

Additional plasma-, discharge-, and hybrid-based platforms have also found success in the direct sampling, ionization, and detection of nitrate-based explosive vapors and aerosols.^{95, 139, 153, 157} Ma *et al.* used an APGD source for the direct analysis of RDX and TNT vapors from complex soil samples.¹⁵³ Other vapor sampling platforms have developed avenues for enhancing the aerodynamic reach (distance at which vapors and aerosols can be sampled),⁹⁵ reducing chemical noise and background,^{140, 141} or aerodynamically-assisting vapor collection.^{95, 139} The VENTI platform introduced by Forbes and Staymates, demonstrated enhanced aerodynamic sampling of TNT, DNT, NG, and EGDN vapors from remote (*i.e.*, multiple meters) locations.⁹⁵ The aerodynamic entrainment generated by VENTI enabled both vapor and particulate aerosol sampling of TNT from a carry on suitcase. In an alternative configuration, VENTI demonstrated continuous real-time monitoring of a large laboratory (approximately 570 m³) and detection of a surrogate chemical warfare agent release.⁹⁵ Similarly, Ewing *et al.* incorporated aerodynamic suction for sampling RDX, PETN, NG, and Tetryl vapors by AFT-DBDI.^{140, 141} The extended distance between the DBDI point of ionization and mass analyzer inlet (*i.e.*, the aerodynamic flow tube) yielded efficient mixing of the nitrate reactant ions and explosive vapors and reduction in chemical noise. Alternatively, the AATD-APCI platform developed by Zhao *et al.* used a heated gas jet for both thermal desorption and transport of RDX and TNT from large items (*e.g.*, luggage) to the mass analyzer at distances of 0.65 m.¹³⁹

The recent surge in the use of homemade explosives has led to an increased interest in their detection. One of the new classes of HMEs, homemade nitrate ester explosives, has been the focus of several recent DART-MS publications.^{106, 173, 176} These explosives are synthesized through the nitration of common sugar alcohols, a class of artificial or alternative sweeteners ubiquitous in everyday life. Common sugar alcohols such as erythritol, xylitol, inositol, sorbitol, mannitol, and maltitol can be found in sugar free chewing gum and candy, vitamins, and drinks. Ostrinskaya *et al.* provided a recent in-depth mass spectral characterization of a number of these compounds by APCI-MS.¹⁷⁹ Sisco and Forbes demonstrated trace detection of the precursor sugar alcohols, nitrate ester explosives, and partially-nitrated and dimerized by-

products from a range of substrate surfaces in a series of investigations.^{106, 173, 176} For these studies, an off-axis DART-MS configuration was incorporated, coupled to the mass spectrometer by the commercial Vapur hydrodynamic-assist interface (Figure 3). The nature of the substrate surface played an important role in detection, much the same way it did for DESI-MS studies. Thermally conductive substrates (*e.g.*, metals) quickly distributed the heat from the DART gas stream, heating a larger area than insulating surfaces and increasing signal. Similarly, porous and rough surfaces disrupted the gas stream, decreasing signals.¹⁰⁶ Importantly, this series of investigations considered the effects that confounding species (*i.e.*, precursors and by-products) had on the detection of the nitrate ester explosives in mixtures.^{106, 173, 176} Figure 3 demonstrates the detection of both sugar alcohol precursors and corresponding nitrate ester explosives in binary mixtures as a function of increasing mass of the corresponding molecule (*i.e.*, erythritol/ETN and pentaerythritol/PETN). In both mixtures, sensitivity for the explosive compound remained nearly constant in the presence of increasing amounts of the corresponding sugar alcohol. The differences in chemical properties (*e.g.*, vapor pressure and volatility) and ionization pathway (sugar alcohols: deprotonation, nitrated species: nitrate adduct formation) allowed for sensitive detection of the nitrate ester explosive in the presence of several orders of magnitude more corresponding sugar alcohol (Figure 3).^{106, 173} However, as the extent of nitration on partially-nitrated by-products increased, the level of competitive ionization and signal suppression of the nitrate ester also increased.¹⁷⁶ This highlights the importance complex matrices can play in detection sensitivity by ambient MS techniques. In addition, given the explosive nature of many of these synthesis by-products, they should also be considered of interest for various deployed detection schemes.

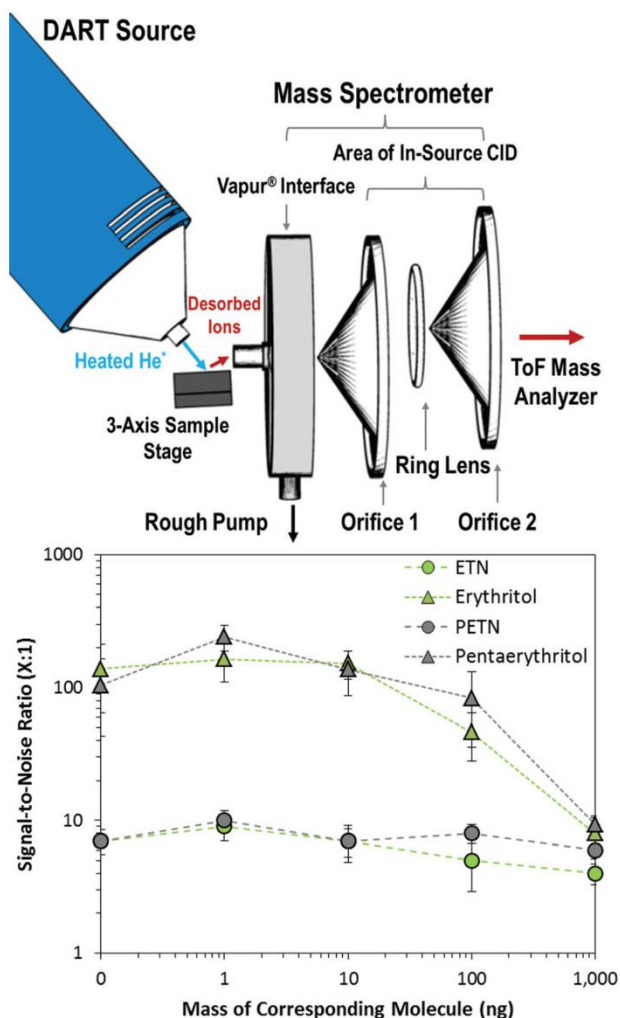


Figure 3. Schematic representation of the off-axis DART-MS configuration with demonstration of sugar alcohol and nitrate ester explosive detection in the presence of varying levels of the corresponding molecule from binary mixtures. Uncertainty represents the standard deviation of four replicate measurements. Reproduced from reference ¹⁰⁶ with permission from the Royal Society of Chemistry.

A number of interesting portable and handheld plasma-based systems have also been developed. Dalgleish *et al.* introduced a miniature LTP source operated with air provided by a small diaphragm pump leading to 4-fold less gas consumption than classical LTP.¹²⁶ The miniature LTP source was coupled with a Mini 11.5 ion trap mass spectrometer through a discontinuous atmospheric pressure interface (DAPI). The DAPI system efficiently maintains vacuum by only periodically introducing ions from the ambient MS source. The overall system demonstrated single nanogram to 10 nanogram detection sensitivities of RDX, PETN, and Teteryl.¹²⁶ A subsequent incarnation of this system, the Mini S (Figure 4), comprised of a hand-

held LTP unit for direct surface sampling coupled to a backpack ion trap mass spectrometer by a 76 cm transfer line and DAPI valve.⁹⁸ This system demonstrated the detection of TNT, PETN, and RDX from glass at sampling distances of 1 mm to 5 mm. To achieve efficient desorption of the lower vapor pressure compounds (*i.e.*, PETN and RDX) the input power for the plasma was elevated to increase the overall plasma temperature (Figure 4).⁹⁸ Finally, the related technique, DAPCI,¹⁰⁴ which utilizes a corona discharge and gaseous solvent vapor jet directed at a surface to generate ions and spectra similar to DESI was developed into a hand-held platform by Jjunju *et al.*¹⁵⁵ The hand-held DAPCI source incorporated the necessary battery power, circuitry, and a small diaphragm pump. Though coupled with a benchtop linear ion trap mass spectrometer for this demonstration, hand-held DAPCI demonstrated sensitive detection from nanograms down to picograms for nitroaromatic explosives.¹⁵⁵

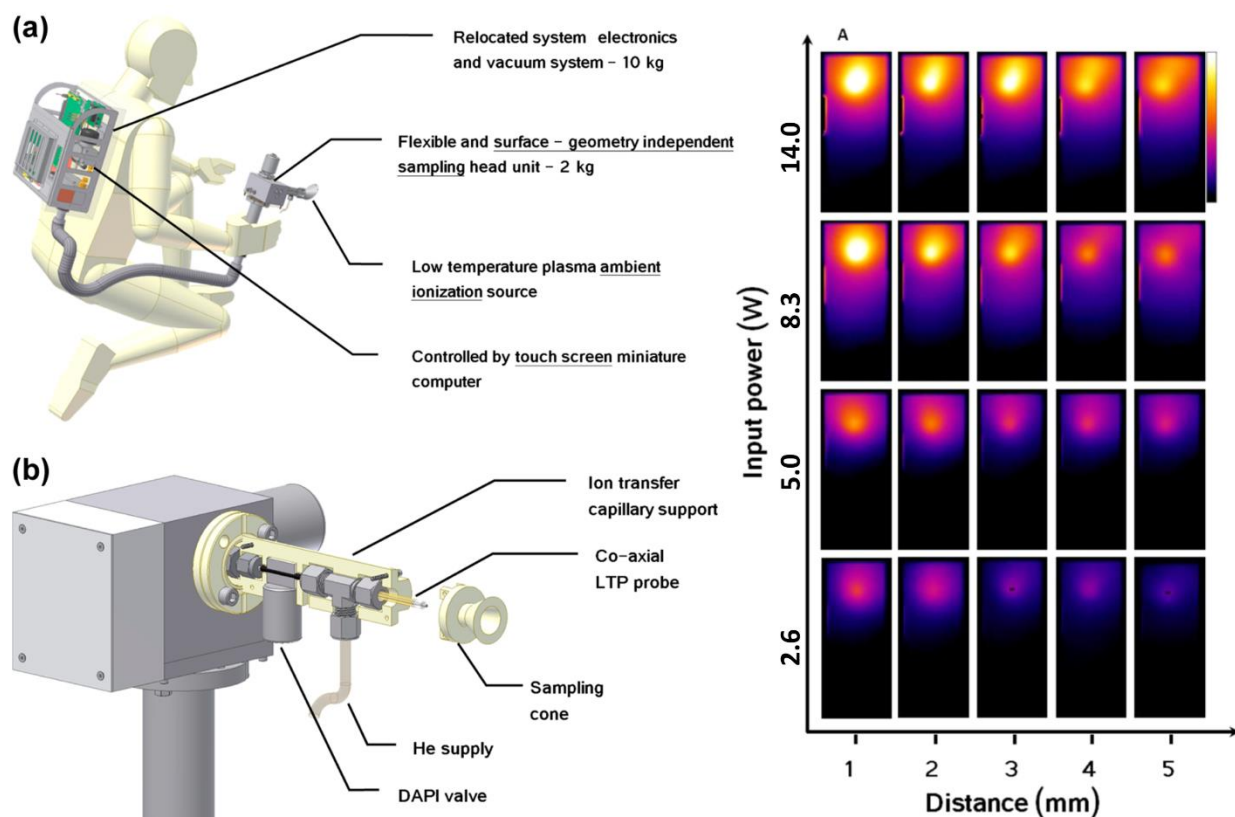


Figure 4. Schematic representation of the miniature backpack mass spectrometer and hand-held LTP sampling unit, with thermographic images of the source at varying power and stand-off distances. Adapted with permission from reference ⁹⁸. Copyright 2014 American Chemical Society.

Given obvious safety considerations and necessary equipment, laser-based platforms have not been as prevalent for the trace detection of explosives in screening type settings, however, a couple interesting examples are provided here. Ehlert *et al.* developed a hybrid platform that coupled ambient pressure laser desorption (APLD) into a handheld sampling probe that utilized a 1.5 m long heated sniffing transfer line with either photoionization or chemical ionization for MS detection of explosives (Figure 5).¹³² The APLD platform was coupled with both time-of-flight (ToF) and ion trap mass spectrometers (ITMS) for evaluation under laboratory conditions and deployed to the German Federal Criminal Police Office. The APLD desorption probe was based on a compact Nd:YAG laser operated at 532 nm with 4 ns to 10 ns pulse widths at 6 mJ. The source demonstrated soft desorption and ionization for both single photon ionization (APLD-SPI) and chemical ionization (APLD-CI) with minimal fragmentation. Samples were interrogated from aluminum, stainless steel, polystyrene, paper, and fiberglass, yielding sensitivities for a range of nitrated explosives down to the single nanogram level. The deployed APLD-ITMS system demonstrated trace level detection of TNT from a leather suitcase as well as TNT and Teteryl from metal pliers used at the explosion test ground (Figure 5).¹³² Brady *et al.* introduced another hybrid laser-based platform, LEMS, demonstrating the detection of RDX and a corresponding taggant.¹⁶⁰ The LEMS system included a femtosecond laser for sample vaporization coupled with electrospray ionization. This decoupling of vaporization and ionization enabled the benefits of both to be incorporated, including the use of dopants in the spray solution – specifically sodium chloride and potassium chloride. In this study, the authors investigated detection in positive mode, targeting the sodium and potassium adducts. Brady *et al.*¹⁶⁰ also demonstrated the detection of RDX in the presence of plasticizers and binders, as well as homemade peroxide explosives, TATP and HMTD, the class of explosives focused on in the next section.

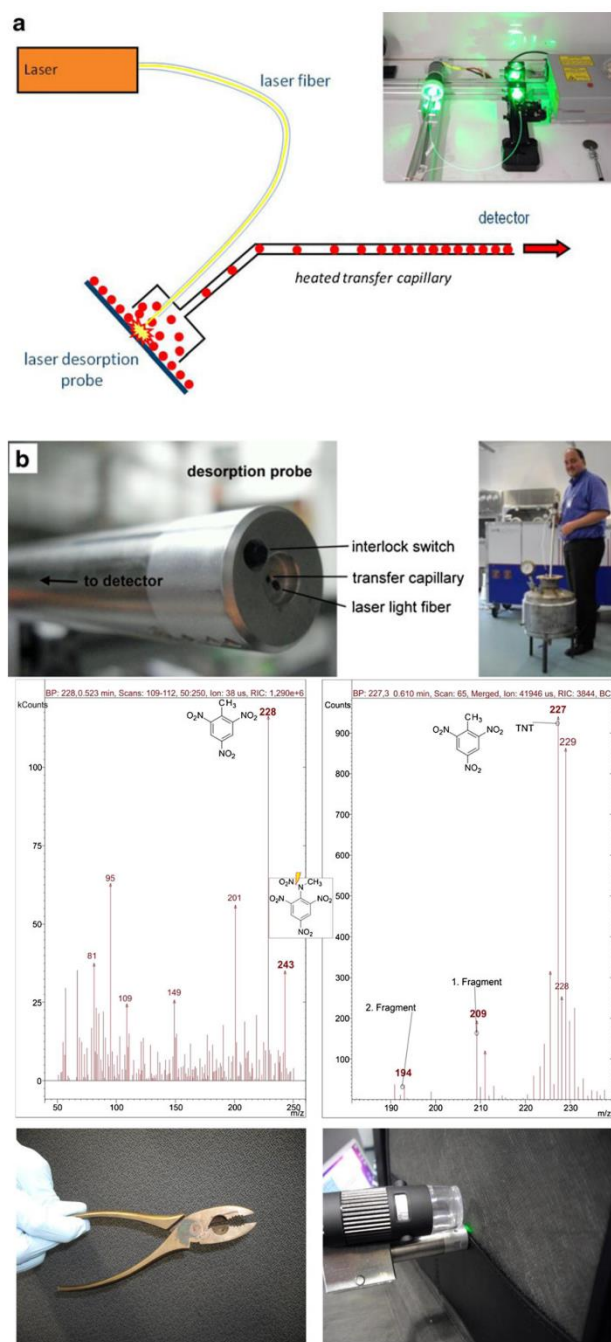


Figure 5. Schematic representation and photographs of APLD endoscope sampling probe. Associated mass spectra of TNT and Tetryl from pliers in positive mode (left) and TNT from a briefcase in negative mode (right). Adapted from reference ¹³² with permission from Springer.

5. Organic Peroxide Explosives

The increased use of homemade explosives in recent years has demonstrated the ongoing need for advancements in their detection. In the previous section, we discussed previous and ongoing work for the detection of homemade nitrate ester explosives based on the nitration of common sugar alcohols. Here, we focus on ambient MS developments targeting the detection of peroxide-based HMEs, such as diacetone diperoxide (DADP), triacetone triperoxide (TATP), tetracetone tetraperoxide (TrATrP), hexamethylene triperoxide diamine (HMTD), hexamethylene diperoxide diamine (HMDD), and methyl ethyl ketone peroxide (MEKP). As introduced above, the detection of peroxide-based explosives presents a number of hurdles due to their instability, sensitivity to insult (*e.g.*, impact, heat, friction, and electrical shock), and labile nature. The inherent soft ionization of most ambient MS techniques enables the direct detection of these explosives with minimal fragmentation.

Early DESI-MS studies demonstrated the trace detection of peroxide explosives, specifically, TATP, along with the suite of nitrate-based explosives.¹⁰⁰ Cotte-Rodriguez *et al.*¹⁴³ conducted a more focused evaluation of reactive DESI for the detection of TATP from a number of complex matrices, including methanol, diesel, lubricant, window cleaner, and vinegar from paper, metal, and brick substrates. Peroxides generally form positively charged ions and similar to the salts added to the spray solvent for generating anion adducts in negative mode, the corresponding cations (alkali metals) formed adducts with TATP in positive mode. Single to tens of nanogram sensitivities were demonstrated, even from these complex matrices and non-ideal surfaces.¹⁴³ A follow-up work by Cotte-Rodriguez *et al.*¹⁴⁴ investigated both DESI and DAPCI for the detection of HMTD, TATP, and TrATrP. Similar to their previous paper, a series of substrate surfaces and reactive cation additives were considered. Dopant addition to the DESI solvent led to an order of magnitude increase in signal intensity of peroxide-based explosives and overall low nanogram sensitivities. An in-depth investigation of peroxide adduct fragmentation patterns was also conducted.¹⁴⁴ EASI, a similar technique not requiring an applied potential, achieves ionization by sonic spray ionization (SSI).¹¹⁹ Nascimento Correa *et al.* employed EASI for the detection of TATP and DADP directly off of

banknotes collected from an automated teller machine (ATM) explosion.¹⁴⁶ Sodium cation adducts were observed for peroxide explosives in addition to multiple domestic synthesis chemical markers. Forbes and Sisco also provided demonstration of select peroxide-based explosive detection by DEFFI.⁸⁹ In addition, Clemons *et al.* used a solid-liquid extraction-based hybrid technique, DAPNe-nanospray ionization (NSI) for the detection of a range of nitrate-based and peroxide-based explosives, including TATP, HMTD, and MEKP.¹⁶⁴ Interestingly, for the solvent composition selected (2:1 acetonitrile/water (vol/vol) with 1 % acetic acid and 1 % dextrose), these peroxides were observed in negative ion mode.

Demonstrations of peroxide-based explosives by plasma-based ambient MS techniques includes DART,^{18, 174} LTP,¹⁵¹ DAPCI,¹⁴⁴ DBDI,¹⁸⁰ and IRTD-APCI.¹³⁶ DAPCI, with the inclusion of a dopant gas (*i.e.*, ammonium acetate), exhibited sensitive detection (tens of nanograms) for TATP and HMTD adducts with ammonia.¹⁴⁴ This DAPCI configuration demonstrated comparable performance to DESI. Multiple studies have also taken a deeper look at peroxide detection by DART-MS. In their thorough parametric optimization of explosive detection, Sisco *et al.* covered both nitrated and peroxide explosives.¹⁷² Lower optimal DART gas stream temperature (125 °C) and reduced declustering or in-source collision induced dissociation (CID) potentials were observed for the labile peroxides relative to nitro-explosives. In addition, one of the dopants investigated, ammonium hydroxide, led to significant decreases in both TATP and HMTD detection. The optimized method developed in this work yielded 10 ng sensitivities for both compounds.¹⁷² Newsome *et al.* conducted a focused investigation into the effects of humidity on DART-MS detection of HMTD (Figure 6).¹⁵⁰ An enclosed DART platform with controlled atmosphere was employed to investigate documented seasonal variability in HMTD spectra. Most notably, the spectra and peak distribution varied significantly with humidity (Figure 6). Though increasing the DART gas temperature minimized this effect, it led to increased fragmentation.¹⁵⁰ This study demonstrates the trade-off between the utility of open access and detrimental effects of some environmental conditions, an aspect important for the field deployment of ambient MS platforms.

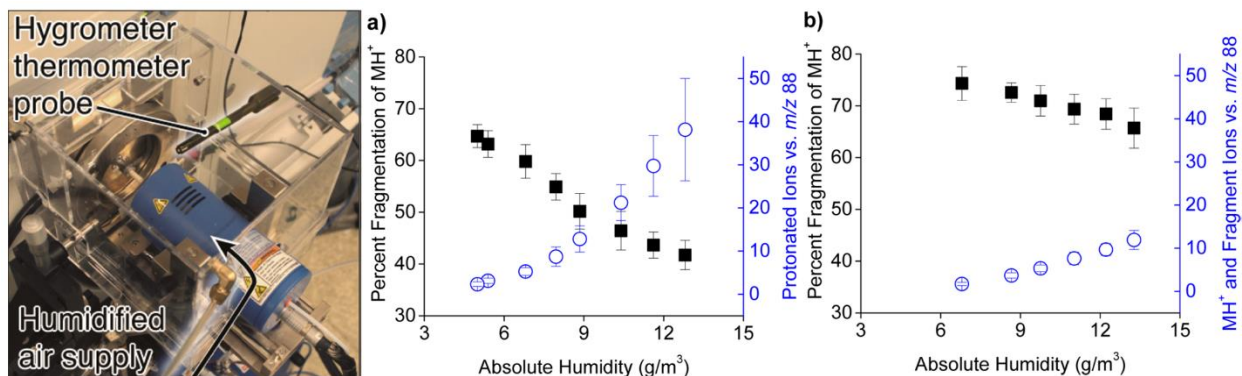


Figure 6. Photograph of humidity controlled enclosure for DART-MS analysis and HMTD signal as a function of absolute humidity for (a) 150 °C and (b) 350 °C DART gas stream temperatures. Adapted with permission from reference.¹⁵⁰ Uncertainty represents standard deviation of replicate measurements. Copyright 2014 American Chemical Society.

DBDI was also recently investigated for the detection of TATP and DADP from glass, paper, brick, and fabric surfaces.¹⁸⁰ Ammonia adducts were observed as the dominant ions in the majority of cases considered. DBDI-MS also demonstrated differences in the mass spectra and extent of fragmentation based on the carrier solvent used to deposit TATP for analysis. For most ambient MS investigations not considering actual real-world samples, explosive analytes are maintained and stored in solution, deposited onto surfaces, and the solvent allowed to evaporate prior to analysis. Here, Hagenhoff *et al.* demonstrated that using a chloroform solvent yielded spectra matching that of direct solid TATP, however, using acetonitrile as the solvent led to significant fragmentation and a more diverse ion distribution (Figure 7).¹⁸⁰ The effects of the carrier solvent on the chemical composition, dried crystal morphology, and desorption profile must be considered in ambient MS experiments. In addition, the effects of matrix species on the mass spectra and ion distribution must be well understood for the effective development of explosive signature libraries. Hagenhoff *et al.* also demonstrated quantitative analysis of TATP using an isotopically labeled TATP internal standard.¹⁸⁰

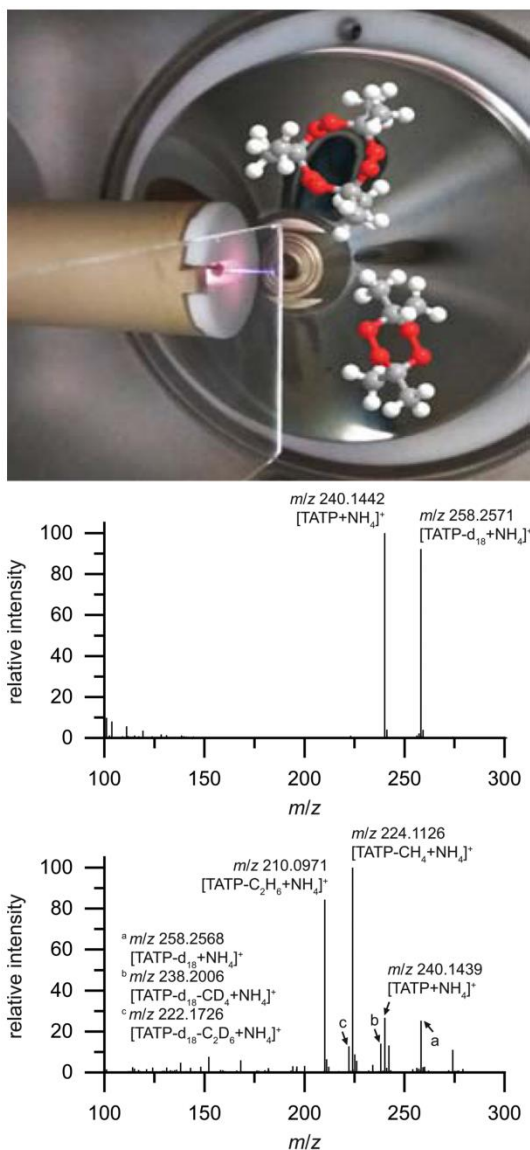


Figure 7. Image of DBDI-MS analysis of TATP from glass slide with associated mass spectra for depositions with chloroform (top) and acetonitrile (bottom) solvents. Adapted with permission from reference ¹⁸⁰. Copyright 2017 American Chemical Society.

In a corona discharge-based multimode platform, IRTD-APCI, Forbes *et al.* coupled an infrared heater for thermal desorption of wipe collected peroxide explosives with APCI-MS.¹³⁶ The IRTD enabled rapid and discrete (5 s duration) heating ramps of the wipe material, enabling analytes of variable volatility to be thermally desorbed at each's optimal temperature. This aspect allowed for thermal desorption and ionization of HMTD and HMDD without fragmentation, while still achieving elevated temperatures needed for the thermal desorption of less volatile organic¹³⁶ and inorganic explosives.¹⁶² As introduced in the

discussion of nitrated explosives detection, Brady *et al.* also demonstrated the detection of the peroxide explosives TATP and HMTD with the hybrid technique, LEMS, coupling laser ablation and electrospray ionization mechanisms.¹⁶⁰ Sodium and potassium additives were included in the ESI solvent for direct adduct formation, however, significant fragmentation of TATP and HMTD were observed, even with the inclusion of a femtosecond laser.¹⁶⁰

6. Inorganic Explosives and Device Components

Expanding on the classes of homemade explosives discussed in the previous sections, we now consider inorganic explosives and device components. Inorganic explosives commonly encompass fuel-oxidizer mixtures, self-initiating mixtures, azides, and will be expanded here to include the inorganic components of radiological dispersion devices (RDDs). These explosive device components include oxidizers such as nitrite, nitrate, chlorate, and perchlorate salts, elemental fuels such as aluminum, magnesium, or zinc, and explosives such as lead azide. Many of these compounds introduce unique difficulties due to their physicochemical properties (*e.g.*, low vapor pressures causing difficulties with thermal desorption avenues and a propensity for forming adducts and larger clusters with available organics) convoluting the mass spectrum. Solid-liquid extraction-based techniques avoid the thermal desorption difficulty by using solvent-based desorption. For example, Sokol *et al.* demonstrated trace detection of chlorate, perchlorate, nitrate, and sulfate inorganic oxidizers from surfaces including glass, wood, metal, cotton, filter paper, and PTFE by DESI-MS.¹¹¹ Sub-nanogram sensitivities were achieved for sodium chlorate and sodium perchlorate on the majority of non-porous surfaces.¹¹¹ Similar to the implementation for peroxide-based explosive detection, Hernandez *et al.* used EASI to detect ANFO (ammonium nitrate-fuel oil) fuel-oxidizer mixtures and rhodamine B-based antitheft device markers directly off of banknotes from simulated and actual ATM explosion thefts (Figure 8).¹⁴⁷ Unique markers from the ANFO were observed in negative mode, specifically, $^{24}\text{Mg}(\text{NO}_3)_3^-$, and confirmed by high resolution ESI-FTMS (Fourier transform mass

spectrometry). The magnesium contaminant was attributed to either a common coating used by ammonium nitrate manufacturers to reduce agglomeration or inclusion as a fuel enhancement.¹⁴⁷

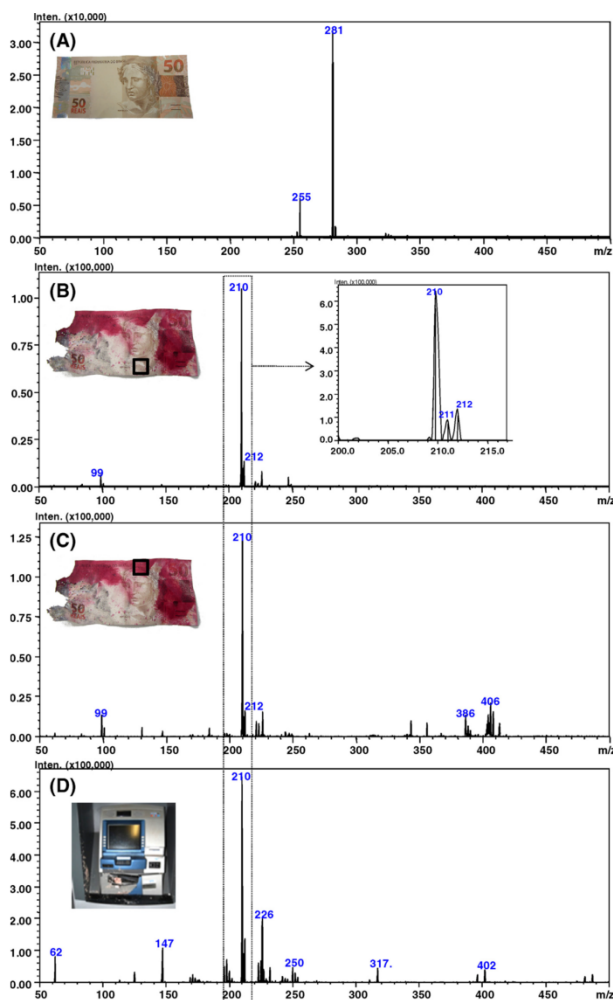


Figure 8. EASI mass spectra from (A) Brazilian banknote, (B) and (C) multiple locations on banknote following ANFO explosion, and (D) extracted ANFO from ATM crime scene – m/z 210 identified as $^{24}\text{Mg}(\text{NO}_3)_3^-$. Reprinted from reference ¹⁴⁷ with permission from Elsevier.

Solid-liquid extraction-based techniques not only offer desolvation and ionization of molecular inorganic species, but also enable detection of elemental species. The detection of elemental inorganic species is important for the identification of elemental fuels (*e.g.*, Al, Zn, Mg), elemental components of explosives, primers and fireworks (*e.g.*, Pb (lead azide), Sr (strontium nitrate), Ba (barium nitrate)), and attribution by unique elemental contaminants. In addition to explosives, the detection and isotope analysis of radionuclides from RDDs (*i.e.*, “dirty bombs”) necessitates the sensitive measurement of elemental

species. These elemental species may include accessible industrial radionuclides such as cobalt-60, strontium-90, or cesium-137. The nature of electrospray-based ionization mechanisms results in these elemental ions frequently forming adducts or clusters with solvent species or organic species present in the sample. Through the manipulation of in-source collision induced dissociation (CID), sensitive detection (tens of nanograms to sub-nanogram) and isotopic analysis of elemental and molecular inorganic species is achievable.^{89, 109, 138} In-source CID typically occurs at a stage within the differentially pumped region of atmospheric pressure inlet mass spectrometers. In this region, ions are accelerated, increasing the energy and frequency of collisions with remaining ambient gas molecules. These collisions lead to fragmentation of more labile organic compounds and “declustering” of larger adducts. In-source CID is often used in proteomics for reducing water clusters and was first employed for ambient MS of elemental species by Evans-Nguyen *et al.*¹⁰⁹ Here, samples were analyzed by DESI from both metal mesh and swab collections in a transmission mode configuration. TM-DESI demonstrated the detection of elemental inorganic, molecular inorganic (oxidizers), and organic (RDX) components of explosive devices.¹⁰⁹

The framework for implementing in-source CID for inorganic analysis was further expanded to DEFFI, USN, LDI, MPT, and JHTD-DART.^{89, 110, 130, 131, 138} Through in-source CID optimization, Forbes and Sisco achieved sub-nanogram sensitivities for organic (TNT, NG, PETN, RDX, HMDD) and molecular inorganic (ClO_3^-) explosives, while enabling nanogram to sub-nanogram sensitivities for elemental inorganic species (Pb, K, Cs, Co) with DEFFI-MS.⁸⁹ DEFFI was also deployed for chemical imaging of inorganic and organic species from wipe collected samples and latent fingerprints from forensic lift tape (Figure 9).⁸⁹ Likewise, USN-EESI of elemental species used in-source CID to control the transition from ligand loss of hydrate clusters to charge reduction (doubly charged to singly charged) regimes. USN-EESI also demonstrated trace detection of inorganic primers and analogue radionuclides from particulate-laden sediment and fingerprint matrices.¹³⁸

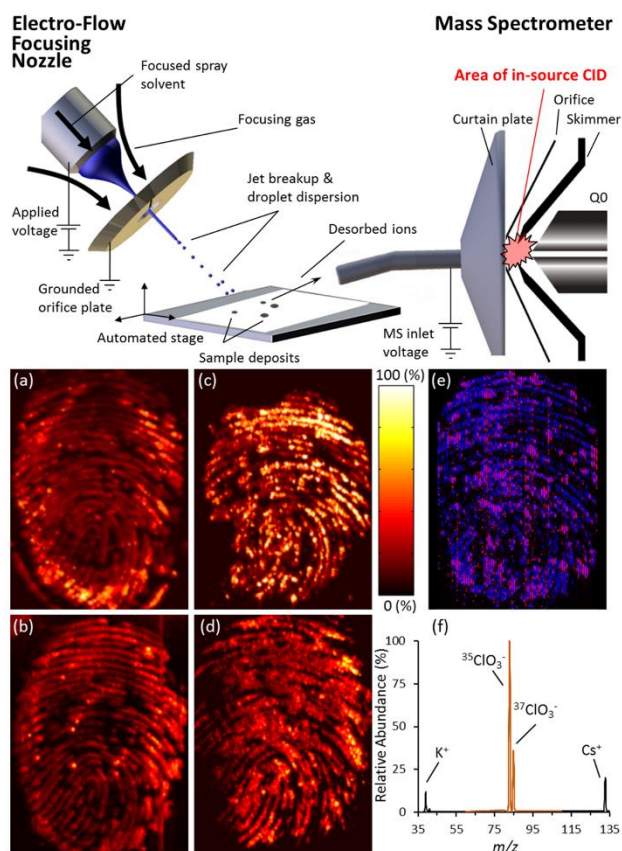


Figure 9. Schematic representation of DEFFI-MS and associated images of exogenous organic and inorganic compounds from artificial fingerprints: (a) HMX, (b) hand lotion, (c) chlorate, and (d) cesium. (e)-(f) MS image and spectra of chlorate (blue) and cesium (red) alternating rows between negative and positive mode. Adapted with permission from reference ⁸⁹. Copyright 2014 American Chemical Society.

Ambient MS techniques not incorporating a solution-based dissolution of inorganic species must rely on elevated temperatures (thermal desorption methods), sufficient energy for chemical sputtering (high(er) power plasma-based platforms), or direct ablation (laser-based techniques). In the original work on DART, Cody *et al.* demonstrated the detection of ammonium nitrate, sodium azide, and sodium perchlorate.¹⁸ Ammonium nitrate and sodium azide exhibit reasonable vapor pressures at room temperature, enabling thermal desorption; however, given the rapid cooling of the DART gas stream as it moves away from the source, achieving the elevated temperatures required for effective thermal desorption of refractory perchlorate salts remains a hurdle. Recent hybrid ambient MS developments have been aimed at increasing the achievable temperatures for thermal desorption of inorganic oxidizers. One such multimode platform coupled resistive heating through a metallic mesh or wire to DART ionization.^{110, 181} The resistive Joule

heating generated by driving current through the metal material enhanced thermal desorption of inorganic oxidizers, including chlorates and perchlorates. One such platform, JHTD-DART, provided a rapid heating ramp from room temperature up to temperatures as high as 750 °C within seconds, allowing for the thermal desorption of organic and inorganic species, each at their respective optimal temperatures.¹¹⁰ Unfortunately, the nature of the JHTD-DART configuration restricts direct surface analysis, a main goal of ambient MS platforms.

Similarly, Forbes *et al.* implemented infrared thermal desorption (IRTD) for generating rapid heating ramps on the order of seconds, coupled with APCI and DART ionization platforms.¹³⁶ Like JHTD, IRTD-APCI enabled species to thermally desorb at their optimal temperature, yielding nanogram to sub-nanogram sensitivities for explosives from volatile peroxides to nitrate-based to inorganic nitrate salts.¹³⁶ Recent work has coupled the IRTD platform with DART (Figure 10), extending capabilities to the thermal desorption and detection of refractory chlorate and perchlorate salts at nanogram levels.¹⁶² While these IRTD iterations focused on thermal desorption from wipe based sample collections, IRTD has also exhibited capabilities for direct surface sampling. However, care must be taken as the infrared energy absorption is dependent on the material and some materials may strongly absorb energy in the emission range of the heater, leading to significantly higher temperatures than surrounding materials. Though not specifically deployed for ambient MS, acidic reagent-based chemical conversion of chlorate and perchlorate salts has been confirmed to enable thermal desorption of the resulting chloric and perchloric acids at more reasonable temperatures (<250 °C) for APCI-MS and IMS.^{182, 183} This avenue has demonstrated interesting results that could be employed for ambient MS platforms, however, it would be a step away from the goal of no sample preparation.

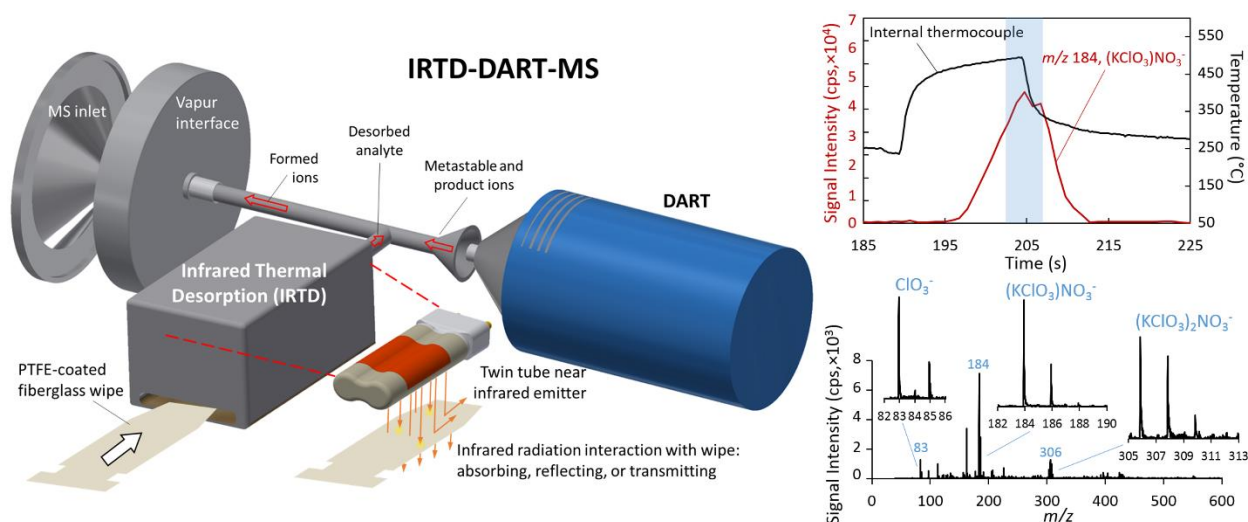


Figure 10. Schematic representation of IRTD-DART-MS platform for the detection of explosives from wipe-based sample collections, including representative internal temperature profile and potassium chlorate extracted ion chromatogram and associated mass spectrum.

Plasma- and laser-based techniques have also demonstrated interesting investigations into the detection and analysis of inorganic explosives and device components. Evans-Nguyen *et al.* developed a microwave plasma torch (MPT) platform that exhibited efficient desorption and ionization of elemental inorganics relevant to explosive device detection, including fuels: Zn and Al; surrogate radionuclides: Cs, Sr, U, and Co; and organic explosives: RDX.¹³⁰ The MPT technique was coupled with an ion trap mass spectrometer demonstrating the potential for field deployability, however, elevated argon flow rates (up to 68 L/min) were needed to reduce the overall temperature of the plasma to the point necessary for surface analysis. In addition, organic explosives were fragmented, introducing an added level of complexity to consider.¹³⁰ Forbes and Sisco provided an in-depth characterization of the effects of in-source CID on inorganic oxidizers using LDI.¹³¹ Manipulation of the extent of in-source CID identified the transition from a regime of salt ionic bond fragmentation, in which increased CID led to increased molecular anion signal, to a regime of molecular anion fragmentation, in which the molecular anion signals steadily decreased. Optimization of this parameter led to a 10-fold to 100-fold increase in the oxidizer anion signal. Chemical imaging of oxidizer particles from latent fingerprints, as well as quantification from tape collections, were also demonstrated. However, the uncertainty in quantification using LDI was significantly larger than

compared techniques, ICP-MS and IC.¹³¹ Finally, Flanigan *et al.* employed the hybrid technique LEMS to characterize IED signatures, including inorganic oxidizers, sugar fuel, and black powders.¹⁶¹ The hybrid nature of LEMS enabled the vaporization of low vapor pressure chlorate and perchlorate oxidizers, while simultaneously taking advantage of adding complexing dopants to the electrospray ionization. These complexing agents enabled the simultaneous detection of nominally cations, anions, and neutrals. Principal component analysis (PCA) was employed to demonstrate accurate classification of IED signatures by LEMS.¹⁶¹

7. Related Security and Forensic Science Applications

Ambient MS techniques offer the potential to add additional capabilities to the security and forensic science sectors. There are a number of applications, ranging from narcotics detection to the analysis of chemical warfare agents, which help to illustrate the breadth of potential uses of these techniques. In addition, with the introduction of miniaturized or field-portable mass spectrometers, it is becoming increasingly possible for sensitive *in situ* analysis – a concept which has been shown in several instances over the past few years. This section intends to highlight both related applications for ambient MS technologies and the potential applications that miniaturization can address.

While many ambient MS techniques have been shown to readily detect trace explosive residues, substantial research exists highlighting the capabilities of these technologies to detect a much wider range of security and forensically relevant compounds. Perhaps the largest body of research is in the detection of narcotic compounds. Narcotics represent a vast and increasingly more complicated set of compounds for detection. They span many different classes and include stimulants, barbiturates, opioids, cannabinoids, and cathinones, to name a few. In addition, in recent years, synthetic novel psychoactive substances (NPS) are appearing at alarming rates in efforts to skirt drug scheduling laws. Much like trace explosives detection, trace narcotics is well suited for analysis by ambient MS due to the need for high fidelity rapid turnaround

of potential complex mixtures. Most narcotics will readily undergo protonation and can be detected at levels similar to or better than explosives. Many ambient MS techniques have already shown promise for the rapid detection of related compounds with substantial work completed by DART-MS,¹⁸⁴⁻¹⁸⁸ TD-DART-MS,^{135, 189} DESI-MS,^{28, 190, 191} DEFFI-MS,^{88, 114} and LTP-MS¹⁹² for the analysis of both seized drugs and toxicological samples. The use of portable mass spectrometers has even been demonstrated in the vehicle-mounted spatial analysis of covert drug labs.¹⁹³ Several reviews have provided in-depth discussion of various applications for ambient MS narcotics detection.^{19, 26, 194}

As synthetic NPSs become more potent, they begin to blur the line between illicit narcotic and potential chemical warfare agent. Traditional chemical warfare agents represent another application where ambient MS analysis has been widely demonstrated and investigated. Chemical warfare agents are typically volatile compounds which easily undergo protonation to form readily detected ions. Detection of these agents and/or their simulants has been demonstrated on a number of platforms including DESI,¹⁰⁰ DART,¹⁹⁵ DBDI,¹⁹⁶ and SESI.¹⁹⁶ Applications for on-site^{197, 198} and remote sensing,¹⁰⁰ detection using miniaturized mass spectrometers,^{33, 199, 200} and detection within bodily fluids²⁰¹ have also been shown.

Another application for forensics and security with close ties to explosives detection is the detection of gunshot residue. Gunpowders, both black and smokeless, are commonly used in IEDs and therefore could be considered an important analyte of interest for explosives detection. Much like traditional explosives, gunshot residues can have both an organic and inorganic constituent depending on whether black powder (organic and inorganic) or smokeless powder (organic) are analyzed. A number of recent papers have looked at ambient MS analysis of gunshot residues using platforms such as DESI,^{202, 203} DAPNe-NSI,²⁰⁴ USN-EESI,¹³⁸ DART,¹⁷⁸ and MPT.²⁰⁵ While the majority of the work has focused on detection of organic constituents such as methyl centralite and diphenylamine, the works by Forbes¹³⁸ and Wan *et al.*²⁰⁵ show that detection of the inorganic species can be accomplished.

One of the major capabilities of ambient MS platforms, unachievable by traditional hyphenated mass spectrometry techniques, is the ability to chemically image a surface of interest, generating spatial distribution information. This opens a range of possible applications to forensic and security arenas,

enabling higher fidelity information than could be obtained by bulk extraction of a surface. The collection and analysis of latent fingerprints has long been a staple for forensic investigations. The spatial analysis of latent fingerprints by ambient MS enables the detection of drugs and/or explosives, while simultaneously obtaining fingerprint ridge detail for identification. Imaging of drugs, their metabolites, and explosives in fingerprints has been completed using several platforms including DESI^{90, 206, 207} and DEFFI.^{88, 89} Chemical imaging can also be used to detect lotions and lubricants within fingerprints to relate back to potential sexual assault cases.²⁰⁸ While the chemical images produced do give enough spatial resolution to obtain the ridge detail, obtaining the tertiary pore structure is often not possible using the current ambient state-of-the-art. Other forensic applications of chemical imaging and detection include imaging of fibers for differentiation on tape pulls,²⁰⁹ analysis of inks on paper,²¹⁰⁻²¹⁴ documents,²¹⁵ and banknotes,²¹⁶ analysis of artwork,²¹⁷ and imaging of plant tissues,²¹⁸ by techniques such as DESI, DART, LTP, and EASI. Recent reviews have covered several other applications of ambient MS in the forensic and security sectors.^{28, 29, 219, 220}

8. General Discussion, Future Prospects, and Major Hurdles

The application of ambient MS for the trace detection of explosives has provided an array of platforms demonstrating sensitive (*i.e.*, nanogram to sub-nanogram) analysis. Yet, as with any ambient ionization scheme, sensitivity levels are strongly dependent on the presence of confounding species and matrices. The needs of various sectors seeking explosives identification and attribution have expanded the configurations and direct utility of many ambient MS techniques. Dopants and reactive species specifically targeting nitrate-based explosives have been employed, soft ionization schemes have minimized labile peroxide explosive fragmentation, and platforms enabling the introduction of wipe-based sample collections have been developed. Given the many advantages of ambient MS, a number of general difficulties still exist. Absolute quantification remains problematic given matrix effects, incomplete sample consumption, and unknown or variable transmission and ionization efficiencies. The implementation of appropriate internal

standards requires prior knowledge of the sample composition (or at least target compound) and suitable incorporation into the system or sample. Often the reproducibility and inter-laboratory repeatability of ambient MS analysis can be inconsistent based on environmental conditions, sample geometry and makeup, and even user operational or platform configuration differences. The Versailles Project on Advanced Materials and Standards (VAMAS) has conducted an inter-laboratory investigation on DESI²²¹ and is currently completing a similar inter-laboratory analysis of general ambient ionization MS, considering within batch repeatability, day-to-day repeatability, matrix tolerance, and both intra- and inter-technique comparisons. Many of the appealing aspects (*e.g.*, open and unconstrained analysis for a wide range of sample sizes and shapes) also have detrimental effects on reproducibility. Ambient MS techniques also demonstrate varying degrees of susceptibility to matrix effects from complex mixtures.

As stated in the introduction, ambient MS provides benefits to two main detection arenas, specifically, 1) high-throughput screening or field detection and 2) investigative identification and attribution. The first encompasses security check-point screening, efficiency in traditional forensic laboratories, and field deployable detection of explosives on-site. The capabilities of portable and miniature mass spectrometers and associated technology continue to advance. This trend in conjunction with the miniaturization and reduction in consumables (solvents, gases, etc.) of ambient MS platforms, aims to provide potential next generation field deployable systems for *in situ* real-time analysis of target analytes. However, in their classical configuration for direct surface sampling, most ambient MS techniques would have difficulty screening large areas without prior knowledge of sample locations, for example, screening a piece of luggage or a vehicle. Current screening arenas often incorporate wipe-based sample collection procedures to circumvent this hurdle. Recent hybrid platforms have sought to expand the utility of these systems for screening applications by coupling wipe-based sample collection with various ionization schemes. Techniques that integrate wipe-based sample introduction or direct vapor analysis will provide the most value to screening applications. In addition, advances in automation and machine learning provide interesting avenues for ongoing and future research, investigating semi-autonomous sampling and monitoring. Explosive identification and analysis for investigative applications includes detection of pre-

and post-detonation materials. These, often laboratory-based, applications have relaxed requirements for portability and SWaP, allowing the unique advantages of ambient MS techniques to be implemented with powerful and sensitive mass analyzers.

Finally, as homemade explosives continue to expand and the list of target compounds increases, the enhancement in selectivity provided by MS (relative to current deployed IMS technology) will be imperative. While a number of commercial, institutional, and government run databases exist, there is currently no inclusive database for ambient MS explosives spectra. Further development and advancement of mass spectral libraries for explosives based on sample introduction, ionization, and mass analyzer combination is needed, similar to the DART Forensics Library maintained by NIST (http://chemdata.nist.gov/mass-spc/ms-search/DART_Forensic.html). The importance of collecting and maintaining such information will also become more important as homemade explosive continue to expand and the list of target compounds increases. These databases and the enhancement in selectivity provided by MS aim to enhance accurate identification and reduce false positive detection.

Conflicts of Interest

The authors declare no competing financial interests.

Acknowledgments

Certain commercial products are identified in order to adequately specify the procedure; this does not imply endorsement or recommendation by NIST, nor does it imply that such products are necessarily the best available for the purpose.

Notes and References

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