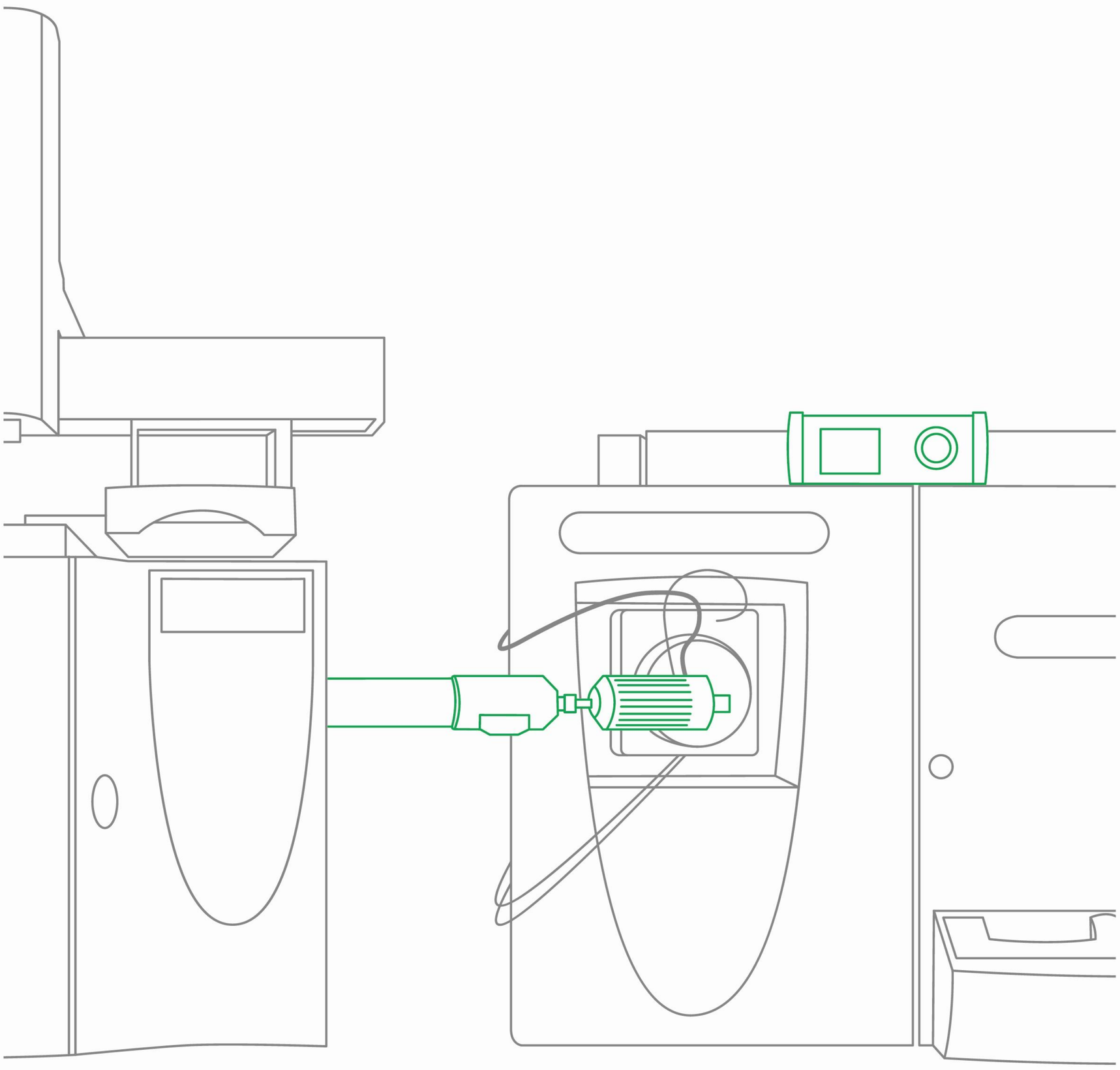
Sicrit
technology

A new dimension in massspectrometry

Content

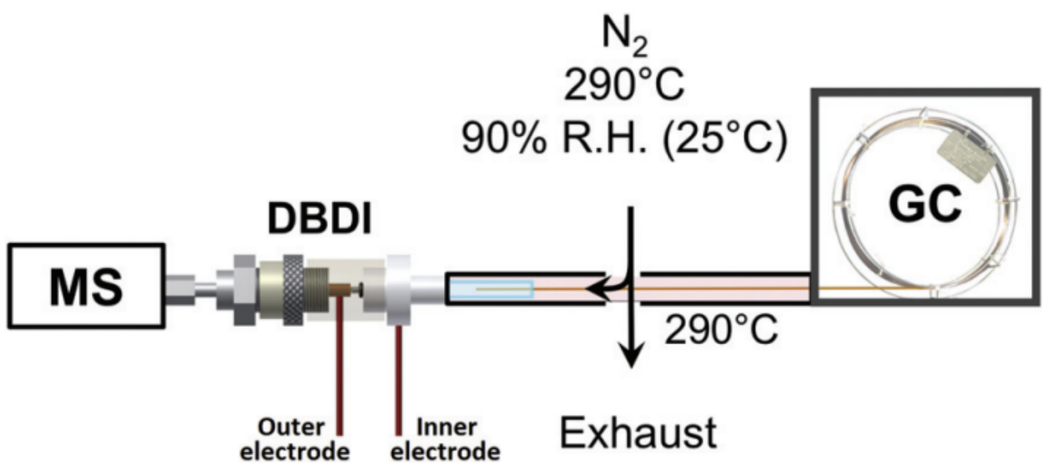
Chromatography coupling

With SICRIT® GC-MS coupling you will get both extraordinary separation delivered by GC and mass spectrometry analysis, ideally in high-resolution mode (HRMS). Long-established paradigm of instrumentally strictly divided LC/GC-MS is being disrupted whilst such a seamless coupling is always being carried out on LC-interfaced mass spectrometry system. Furthermore, SICRIT® GC-MS coupling increases sensitivity and provides molecular information by soft ionization mechanism. Alongside with HRMS it’s a powerful tool for target and especially non-target analyses.



Atmospheric pressure soft ionization for gas chromatography with dielectric barrier discharge ionization-mass spectrometry (GC-DBDI-MS)

Mario F. Mirabelli, Jan-Christoph Wolf, Renato Zenobi



A B S T R A C T

In this study, a gas chromatography (GC) system was interfaced to a high-resolution Orbitrap mass spectrometer by means of an active capillary plasma ionization source, based on dielectric barrier discharge ionization (DBDI). This allowed highly efficient soft ionization of gas-phase, chromatographically resolved compounds at ambient pressure. Several pesticides and illicit drugs were analyzed, and the limits of detections (LODs) were as low as 30 pg mL−1 for the GC-DBDI-MS coupling (corresponding to 60 fg on-column sensitivity) and 30 fg mL−1 for SPME-GC-DBDI-MS.

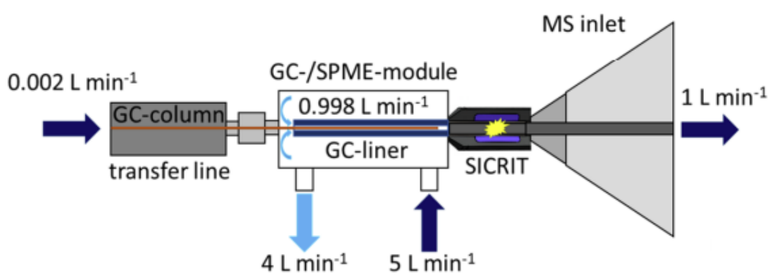
C O N C L U S I O N S

The reported coupling of GC to MS using a capillary DBDI source was demonstrated to be very effective in the determination of pesticides and drugs at pg mL−1 level. These figures of merit clearly show the superior sensitivity of our approach compared to conventional GC-MS, with LODs that could be lowered further, to the fg mL−1 range, with SPME-GC. The workflow can be easily automated with existing solutions, and integrated in routine analytical laboratories. There are several advantages of coupling a GC system to DBDI. Among these, the fact that API MS instruments (generally employed in combination with LC) can be used as well for GC, without the requirement of dedicated vacuum interface instruments is considered of high practical importance. Furthermore, the ionization is soft, with little to no fragmentation observed. This gives more flexibility in the quantification of compounds based on their [M + H]+ ion signal. In this regard, the use of high resolution MS instruments represents a perfect combination, giving the ability to perform non-targeted analysis of unknown samples. The use of SPME also allows to further improve LODs and reduce the matrix complexity by a simultaneous clean-up and up-concentration of the samples. Another advantage is the simplicity of the proposed approach, and the absence of geometric parameters requirements to interface the GC column to the DBDI source.

DOI: https://doi.org/10.1039/C7AN00245A

Gas Chromatography−Atmospheric Pressure Inlet−Mass Spectrometer Utilizing Plasma-Based Soft Ionization for the Analysis of Saturated, Aliphatic Hydrocarbons

Markus Weber, Jan-Christoph Wolf, Christoph Haisch



A B S T R A C T

Soft ionization by a chemical reaction in transfer (SICRIT) is applied to couple gas chromatography (GC) to a high-resolution atmospheric pressure inlet mass spectrometer. These instruments are generally used in combination with LC-MS. Ionization of alkanes is not possible here with conventional electrospray ionization. Alternatively, separate GC-EI-MS is employed for the analysis of nonpolar substances like alkanes, however, with the inherent challenge of strong fragmentation. In the case of alkanes, the determination of molecular masses becomes nearly impossible in complex hydrocarbon mixtures because of the wealth of similar fragment ions and the absence of the molecular ion signal. SICRIT, a soft ionization technique based on dielectric barrier discharge (DBDI), produces characteristic oxidized cations from alkanes that can be directly correlated to their molecular mass. Isotope labeling experiments reveal an ionization mechanism via hydride abstraction and reaction with water. Soft ionization for iso- and n-alkanes enables the determination of their molecular mass. Calibrations for n-alkanes from C10 to C30 were performed exhibiting high linearity, reproducibility, and sensitivity with an average LOD of 69 pg (on column). Measurements of diesel fuel samples are compared to traditional GC-EI-MS. The presented method combines sensitivity and easy handling of a GC-EI-MS with the determination of molecular mass commonly by using existing and highly optimized mass spectrometers commonly coupled with LC. Additionally, many other analytes such as (alkylated-) PAHs could be detected simultaneously in the diesel sample.

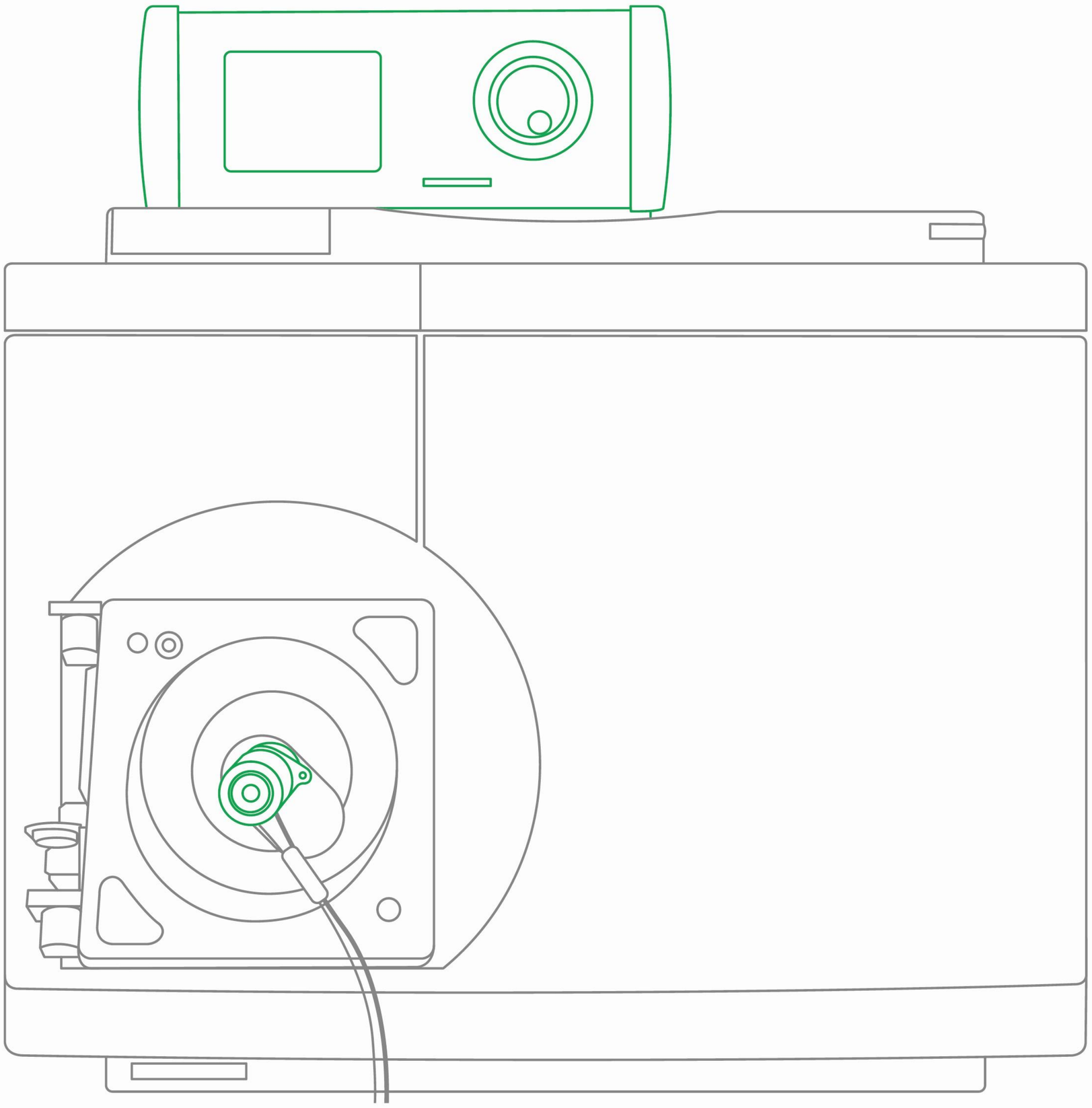
C O N C L U S I O N S

This study discusses the coupling of a GC by SICRIT, a commercial DBDI based soft ionization technique, with a high resolution atmospheric pressure inlet MS for the analysis of alkanes. Characteristic oxidized ions with the generic formula $[M- (2n + 1)H + mO]^+$ are generated with minimal fragmentation. The oxidized ions can be assigned directly to the molecular mass of the alkane. Isotope labeling experiments reveal that the oxidation most probably occurs via hydride abstraction and subsequent reaction with water in the carrier gas. The ionization can be applied to iso-alkanes as well as n-alkanes, although with varying ionization efficiency. The minor fragments of iso-alkanes can be used to gain structural information, due to increased fragmentation adjacent to branches. Calibration curves for n-alkanes from decane to triacontane show high linearity, reproducibility, and LODs in the low ppb range. To the best of our knowledge, these are the lowest LODs achieved with an atmospheric pressure inlet mass spectrometer for alkanes so far. The quantitative results achieved for n-alkanes with the new method applied to a diesel fuel sample match with traditional GC-EI-MS results. Additionally, it allows for the identification of iso-alkanes and further unknown components. Our results show that GC-SICRIT-HRMS is a valuable alternative to GC-EI-MS for the measurement of alkanes. It significantly reduces the amount of unresolved complex mixture found, e.g., in diesel samples and enables a search for specific alkanes in GC nontarget screening, employing established LC-MS workflows. This finding might be relevant also for other applications, such as lubricant analysis, packaging material characterization, or food analysis, where alkane analysis is mainly limited to sum parameters like MOSH so far.

DOI: https://doi.org/10.1021/jasms.0c00476?rel=cite-as&ref=PDF&jav=VoR

Online detection

Volatile Organic Compounds (VOCs) analysis by mass spectrometry has never been easier. By simply placing the sample in front of the SICRIT you will get the desired results instantaneously. This enables sensitive aroma profiling, product classification, detection of trace contaminants or breath analysis. Direct and quantitative measurements of solids, liquids, and gaseous samples (e.g. by headspace sampling or using SPME fibres) may be performed manually or completely automated in combination with a CTC PAL system.



Direct gas-phase detection of nerve and blister warfare agents utilizing active capillary plasma ionization mass spectrometry

Jan-Christoph Wolf, Martin Schaer, Peter Siegenthaler, Renato Zenobi

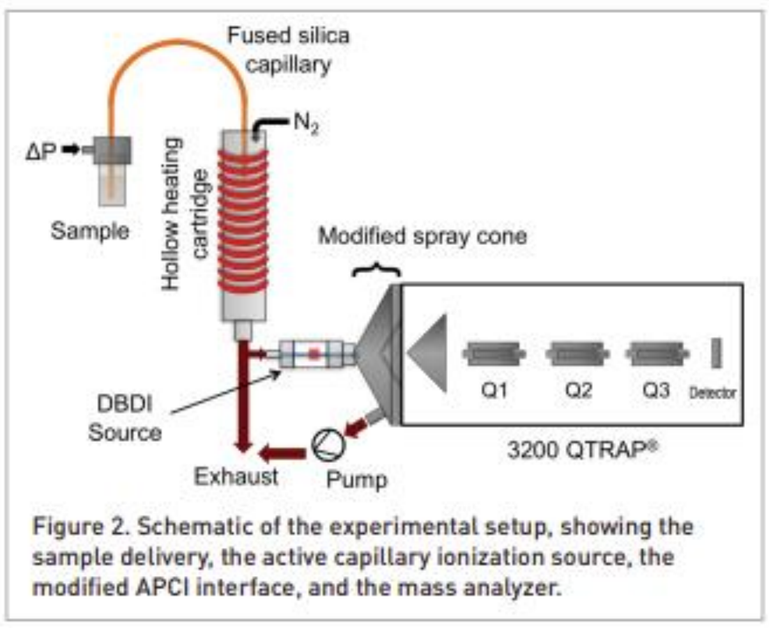


Figure 2. Schematic of the experimental setup, showing the sample delivery, the active capillary ionization source, the modified APCI interface, and the mass analyzer.

A B S T R A C T

Ultrasensitive direct gas-phase detection of chemical warfare agents (CWAs) is demonstrated utilizing active capillary plasma ionization and triple quadrupole mass spectrometry (MS) instrumentation. Four G-agents, two V-agents, and various blistering agents [including sulfur mustard (HD)] were detected directly in the gas phase with limits of detection in the low parts per trillion (ngm–3) range. The direct detection of HD was shown for dry carrier gas conditions, but signals vanished when humidity was present, indicating a possible direct detection of HD after sufficient gas-phase pretreatment. The method provided sufficient sensitivity to monitor directly the investigated volatile CWAs way below their corresponding minimal effect dose, and in most cases even below the eight hours worker exposure concentration. In general, the ionization is very soft, with little to no in-source fragmentation. Especially for the G-agents, some dimer formation occurred at higher concentrations. This adds complexity, but also further selectivity, to the corresponding mass spectra. Our results show that the active capillary plasma ionization is a robust, sensitive, “plug and play” ambient ionization source suited (but not exclusively) to the very sensitive detection of CWAs. It has the potential to be used with portable MS instrumentation

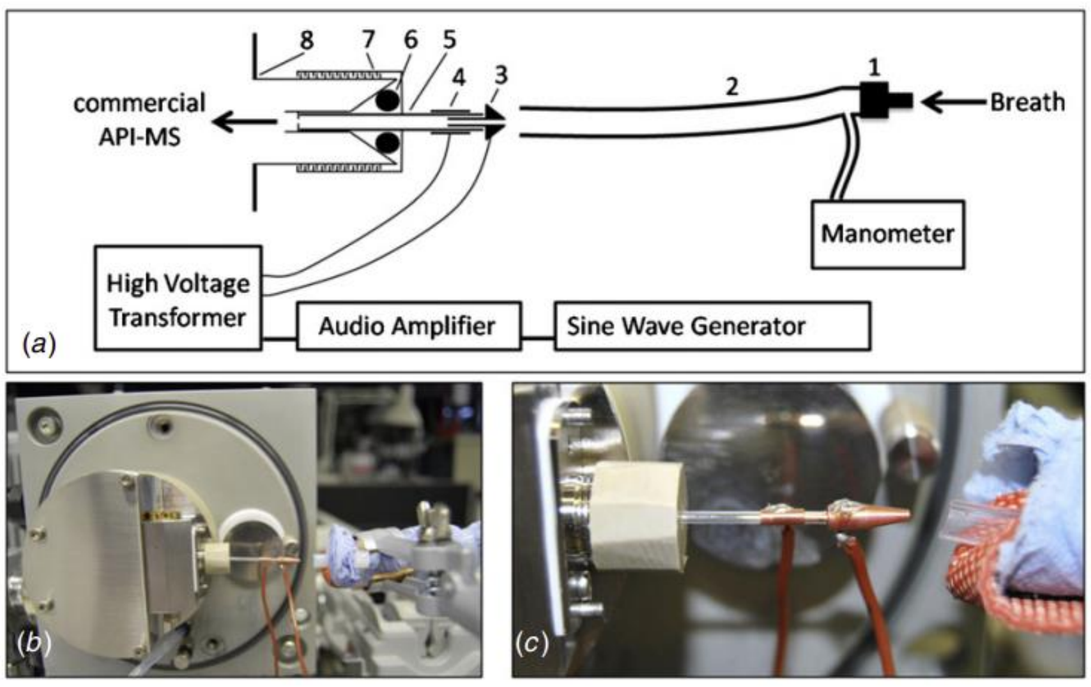
C O N C L U S I O N S

The ultrasensitive and selective direct gas-phase detection of 10 CWAs was achieved using active capillary plasma ionization in combination with a triple quadrupole MS run in the MRM mode. We showed the detection capabilities for G- and V-agents as well as various blistering agents, including HD. The LODs achieved (0.009 µg m–3 to 0.33 µg m–3) were significantly lower than the corresponding lethal (LCt50) value and minimal effect doses, and, except for V-agents, even lower than the eight hour worker exposure limit. Furthermore, the direct detection of HD was possible using a dry atmosphere, suggesting the possibility of gaseous HD detection under ambient conditions using sample gas preconditioning (heating and drying). A combination of the active capillary plasma source with a portable mass spectrometer has already been reported.17 This is also part of an ongoing study on the detection limits that can be reached with portable instrumentation, as well as on matrix influences, which may in the end lead to a portable device for on-site CWA detection and quantification. Finally, the active capillary plasma ionization source has proved to be a very robust and sensitive soft ionization source, which can be mounted in a “plug and play” fashion to different API mass spectrometers giving them “ambient” detection capabilities as well as an enhanced sensitivity (femtogram range) not only for CWAs but for a broad range of other analytes as well

DOI: https://doi.org/10.1255/ejms.1347

Real-time breath analysis with active capillary plasma ionization-ambient mass spectrometry

Lukas Bregy, Pablo Martinez-Lozano Sinues, Maryia M Nudnova, Renato Zenobi



A B S T R A C T

On-line analysis of exhaled human breath is a growing area in analytical science, for applications such as fast and non-invasive medical diagnosis and monitoring. In this work, we present a novel approach based on ambient ionization of compounds in breath and subsequent real-time mass spectrometric analysis. We introduce a plasma ionization source for this purpose, which has no need for additional gases, is very small, and is easily interfaced with virtually any commercial atmospheric pressure ionization mass spectrometer (API-MS) without major modifications. If an API-MS instrument exists in a laboratory, the cost to implement this technology is only around €500, far less than the investment for a specialized mass spectrometric system designed for volatile organic compounds (VOCs) analysis. In this proof-of-principle study we were able to measure mass spectra of exhaled human breath and found these to be comparable to spectra obtained with other electrospray based methods. We detected over 100 VOCs, including relevant metabolites like fatty acids, with molecular weights extending up to 340 Da. In addition, we were able to monitor the time-dependent evolution of the peaks and show the enhancement of the metabolism after a meal. We conclude that this approach may complement current methods to analyze breath or other types of vapors, offering an affordable option to upgrade any pre-existing API-MS to a real-time breath analyzer.

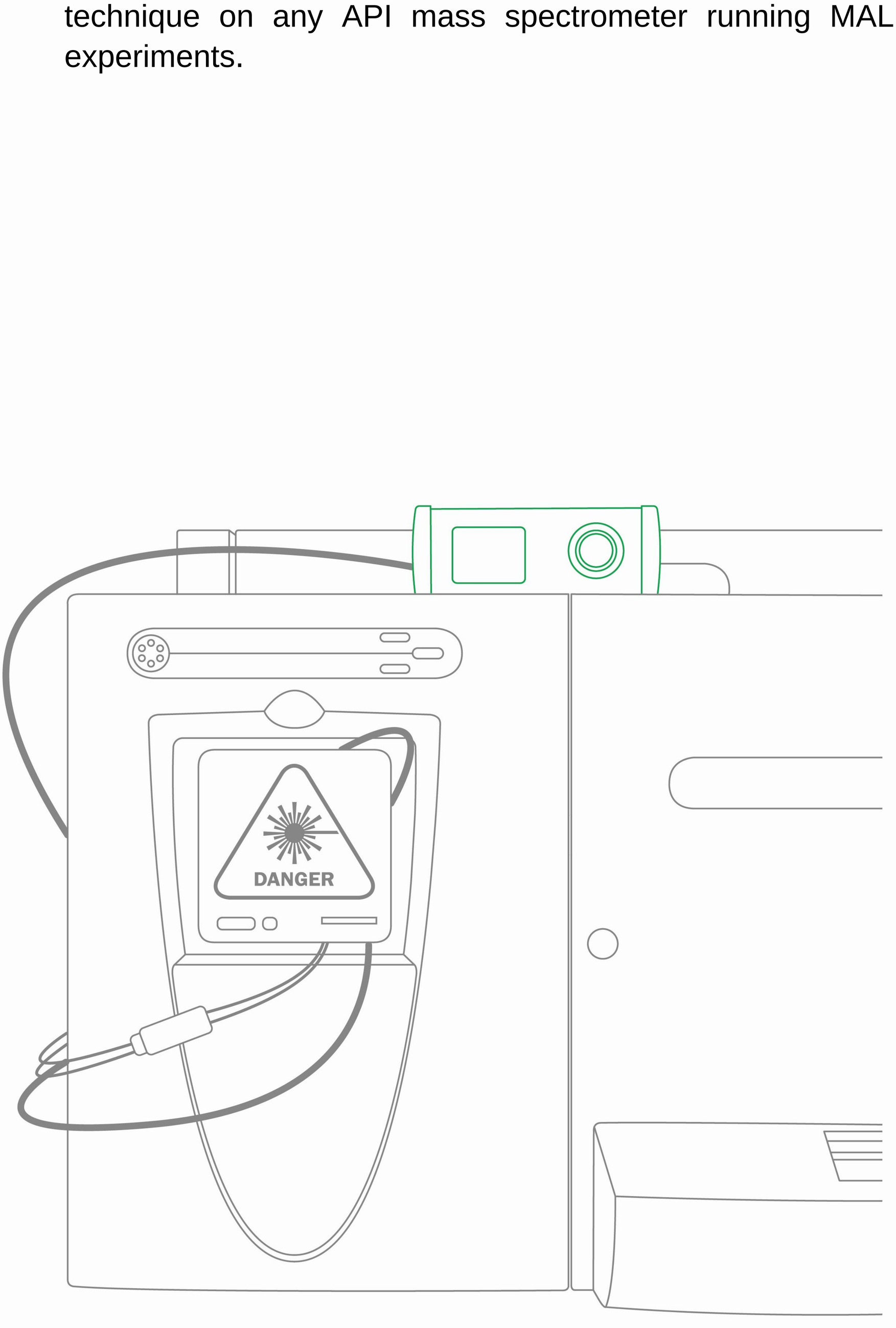
C O N C L U S I O N S

We coupled a home-built soft plasma ionization source to a mass spectrometer without major modifications of the interface. We showed that the active capillary plasma ionization is suitable for real-time analysis of exhaled breath with ambient mass spectrometry. The technique is sensitive enough to detect relevant VOCs like fatty acids in the mass range up to m/z 340. In addition, we were able to detect the metabolic pattern differences between three individuals and monitor the time-dependent evolution of these patterns. We showed that several metabolites are enhanced or decreased after food intake. It was observable that the intensity changes are mostly similar for both subjects as far as the sign of the change. In contrast, it was shown that the magnitude of the intensity changes is different from one subject to the other. Summarizing all measurements and data analysis, the analytical results have similarities to SESI-MS and add to other real-time techniques like PTR-MS and SIFT-MS.

DOI: http://dx.doi.org/10.1088/1752-7155/8/2/027102

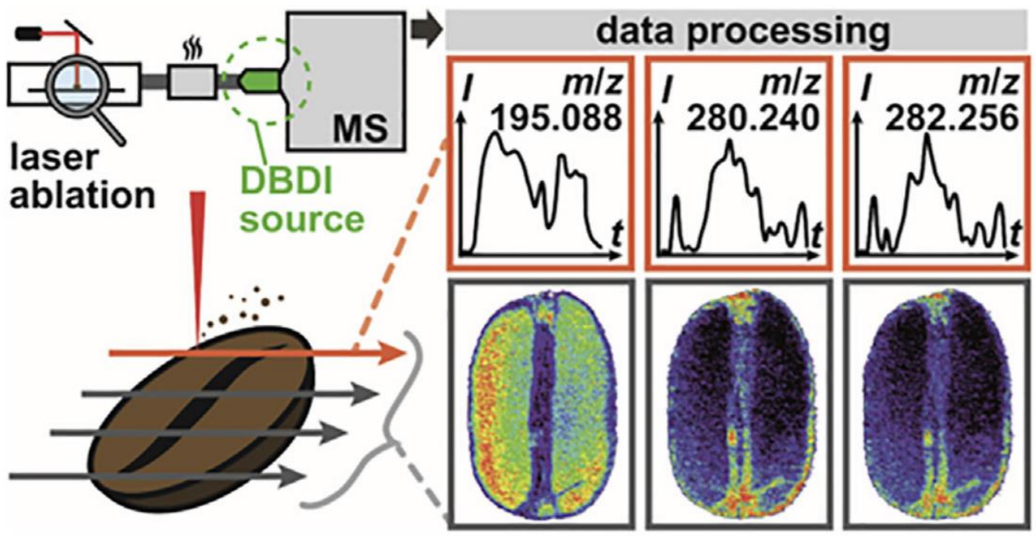
MS Imaging

Applying minimum effort SICRIT® is able to enhance your existing mass spectrometry imaging method by increasing spatial resolution. There is nearly no optimization needed before one can simply employ SICRIT® as post-ionization technique on any API mass spectrometer running MALDI or laser ablation experiments.



Plug-and-play laser ablation-mass spectrometry for molecular imaging by means of dielectric barrier discharge ionization

Sabrina K.I. Funke, Valerie A. Brückel, Markus Weber, Elias Lützen, Jan-Christoph Wolf, Christoph Haisch, Uwe Karst



A B S T R A C T

The plug-and-play hyphenation of UV-laser ablation (LA) and mass spectrometry is presented, using dielectric barrier discharge ionization (DBDI). The DBDI source employed here is characterized by its unique geometry, being directly mounted onto the inlet capillary of a mass spectrometer. In the literature, this particular kind of DBDI source is also referred to as active capillary plasma ionization. It has been commercialized as soft ionization by chemical reaction in transfer (SICRIT) and will be addressed as DBDI in this study. LA-DBDI-MS was used for the direct, molecule-specific and spatially resolved analysis of various solid samples, such as coffee beans and pain killer tablets without extensive sample preparation. The combination of fast washout UV-laser ablation and the principle of the DBDI source used here allowed for highly efficient soft ionization as well as high spatial resolution down to 10 mm for molecular imaging.

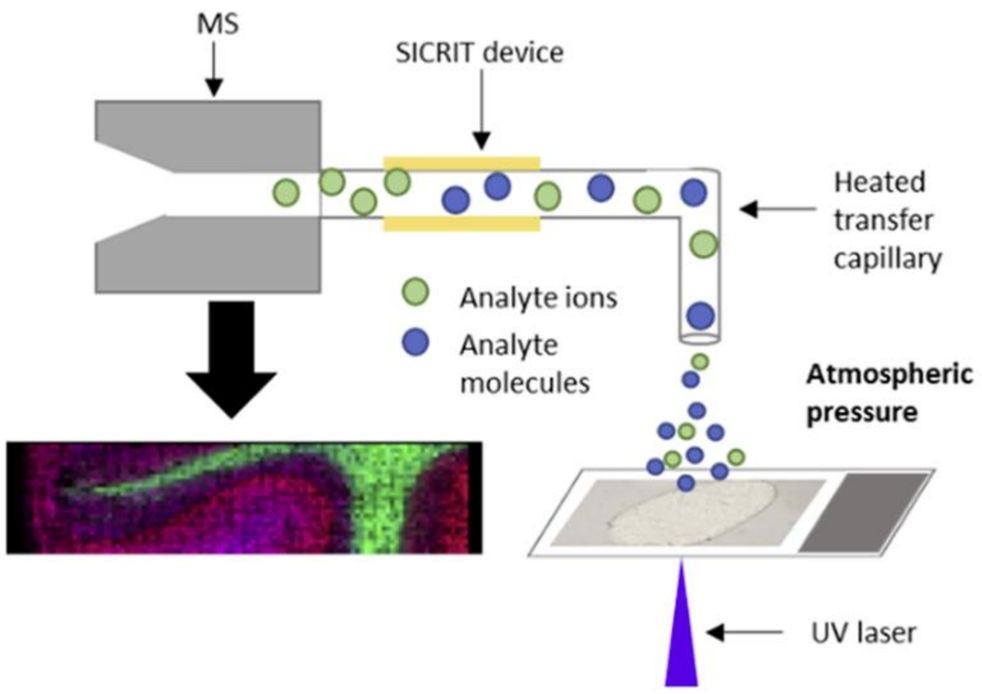
C O N C L U S I O N S

In this proof-of-principle study, molecular imaging was performed by LA-DBDI-MS on the example of pain killer tablets and coffee beans. Spot sizes down to 10 mm were tested, yielding satisfactory sensitivity. A two-fold scan speed was applicable without any image distortion or blurring effects. The low internal volume of the DBDI source provides a washout time of approximately 1 s, allowing for such high scan speeds, as well as a high sensitivity, sufficient to enable chemical imaging with laser spots as small as 10 mm. Therefore, the combination of these advantages allows high-resolution molecular imaging under ambient conditions with scan rates that are shown to be significantly faster than in previously presented studies based on common, openly constructed API sources. Furthermore, the DBDI source can be hyphenated to any commercial laser ablation system and nearly any mass spectrometer that is commercially provided with an API source. This makes this technique easy to adapt to individual needs regarding the sample type and analytical question. Especially in combination with high resolution mass spectrometry, as it was used in this study, this technique offers a promising alternative to common approaches for non-target analysis, such as MALDI-MS. Moreover, the simplicity due to the potential use of room air as plasma gas makes this an interesting tool for fast and easy analyses of various sample types without any extensive sample preparation.

DOI: https://doi.org/10.1016/j.aca.2021.338770

Atmospheric Pressure MALDI Mass Spectrometry Imaging Using In Line Plasma Induced Postionization

Efstathios A. Elia, Marcel Niehaus, Rory T. Steven, Jan-Christoph Wolf, Josephine Bunchi



A B S T R A C T

Atmospheric pressure ionization methods confer a number of advantages over more traditional vacuum based techniques, in particular ease of hyphenation to a range of mass spectrometers. For atmospheric pressure matrix assisted desorption/ionization (AP-MALDI), several ion sources, operating in a range of geometries have been reported. Most of these platforms have, to date, generally demonstrated relatively low ion yields and/or poor ion transmission compared to vacuum sources. To improve the detection of certain ions, we have developed a second-generation transmission mode (TM) AP-MALDI imaging platform with in-line plasma postionization using the commercially available SICRIT device, replacing the previously used low temperature plasma probe from our developmental AP-TM-MALDI stage. Both plasma devices produce a significant ionization enhancement for a range of compounds, but the overall higher enhancement obtained by the SICRIT device in addition to the ease of installation and the minimal need for optimization presents this commercially available tool as an attractive method for simple postionization in AP-MALDI MSI.

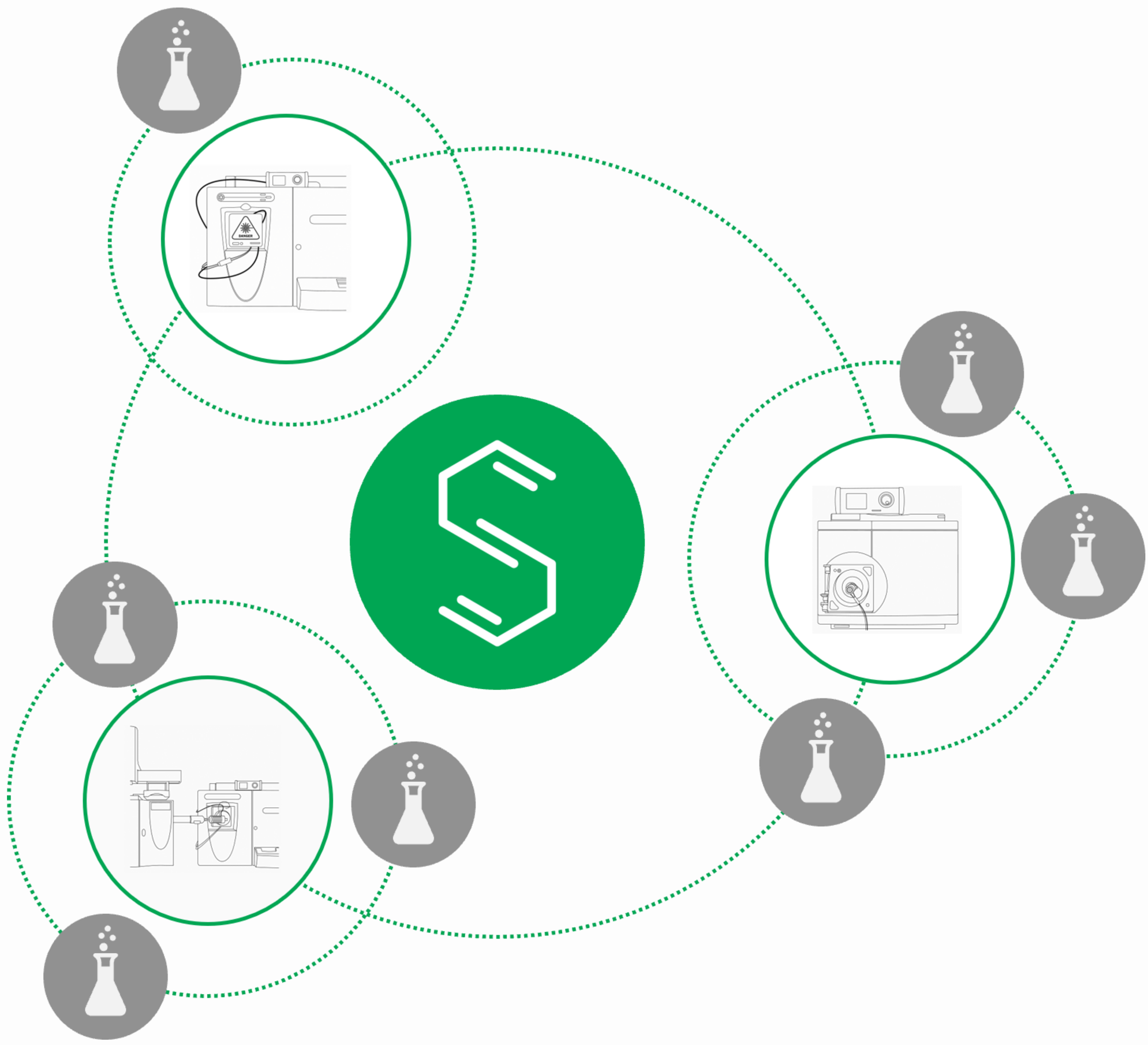
C O N C L U S I O N S

In this proof-of-principle study, molecular imaging was performed by LA-DBDI-MS on the example of pain killer tablets and coffee beans. Spot sizes down to 10 mm were tested, yielding satisfactory sensitivity. A two-fold scan speed was applicable without any image distortion or blurring effects. The low internal volume of the DBDI source provides a washout time of approximately 1 s, allowing for such high scan speeds, as well as a high sensitivity, sufficient to enable chemical imaging with laser spots as small as 10 mm. Therefore, the combination of these advantages allows high-resolution molecular imaging under ambient conditions with scan rates that are shown to be significantly faster than in previously presented studies based on common, openly constructed API sources. Furthermore, the DBDI source can be hyphenated to any commercial laser ablation system and nearly any mass spectrometer that is commercially provided with an API source. This makes this technique easy to adapt to individual needs regarding the sample type and analytical question. Especially in combination with high resolution mass spectrometry, as it was used in this study, this technique offers a promising alternative to common approaches for non-target analysis, such as MALDI-MS. Moreover, the simplicity due to the potential use of room air as plasma gas makes this an interesting tool for fast and easy analyses of various sample types without any extensive sample preparation.

DOI: https://dx.doi.org/10.1021/acs.analchem.0c03524

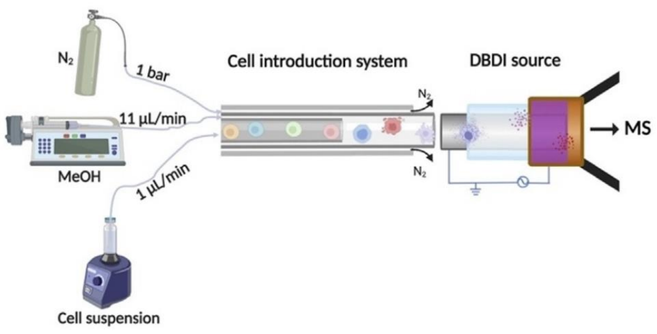
Special applications

Enormous modularity and versatility of SICRIT® technology allows its usage with nearly no limits. Any of previously mentioned setups can be easily modified to accept major scientific challenges. All by strictly plug-and-play technology with a high level of user- friendliness.



High-Throughput Single-Cell Mass Spectrometry Reveals Abnormal Lipid Metabolism in Pancreatic Ductal Adenocarcinoma

Qinlei Liu, Wenjie Ge, Tongtong Wang, Jiayi Lan, Sandra Martínez-Jarquín, Christian Wolfrum, Markus Stoffel, Renato Zenobi



A B S T R A C T

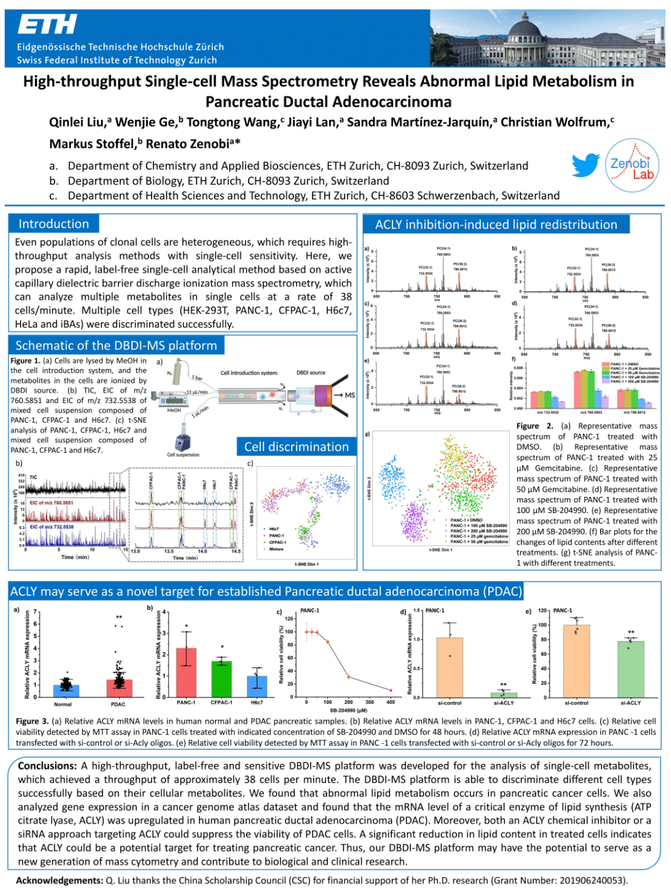
Even populations of clonal cells are heterogeneous, which requires high-throughput analysis methods with singlecell sensitivity. Here, we propose a rapid, label-free single-cell analytical method based on active capillary dielectric barrier discharge ionization mass spectrometry, which can analyze multiple metabolites in single cells at a rate of 38 cells/minute. Multiple cell types (HEK-293T, PANC-1, CFPAC-1, H6c7, HeLa and iBAs) were discriminated successfully. We found evidence for abnormal lipid metabolism in pancreatic cancer cells. We also analyzed gene expression in a cancer genome atlas dataset and found that the mRNA level of a critical enzyme of lipid synthesis (ATP citrate lyase, ACLY) was upregulated in human pancreatic ductal adenocarcinoma (PDAC). Moreover, both an ACLY chemical inhibitor and a siRNA approach targeting ACLY could suppress the viability of PDAC cells. A significant reduction in lipid content in treated cells indicates that ACLY could be a potential target for treating pancreatic cancer.

C O N C L U S I O N S

In conclusion, a high-throughput, label-free and sensitive DBDI-MS platform was developed for the analysis of singlecell metabolites, which achieved a throughput of approximately 38 cells per minute. The DBDI-MS platform is able to discriminate different cell types successfully based on their cellular metabolites. Compared with bulk cell analysis, our single-cell DBDI-MS platform can separate different cells from mixed cell suspensions according to its characteristic single-cell metabolite profile, and classify each type of cell into a specific group, which may help detect lipid metabolism in clinical cancer tissues. Since the DBDI-MS platform found that abnormal lipid metabolism occurs in pancreatic cancer cells, a series of biological methods were used to analyze the expression levels of ACLY and the activation of related biological pathways in the TCGA dataset and PDAC cells. We indeed found the deregulated ACLY, acetyl-CoA synthesis and lipid homeostasis pathways in PDAC. We further identified deregulated PI3K/AKT and mTORC1 pathways may promote the ACLY expression in PDAC. By treating PDAC cells with different dosages of specific ACLY inhibitor, the redistribution of lipids in PDAC cells was observed by the DBDI-MS platform. Further biological experiments also demonstrated that both ACLY inhibitor or genetic approach that targeting ACLY could repress cell viability of PDAC cells. These results prove the high sensitivity of our DBDI-MS platform and also confirmed that ACLY indeed contributes to the lipid metabolism in PDAC cells, indicating ACLY may serve as a novel therapeutic target in PDAC. Thus, our DBDI-MS platform may have the potential to serve as a new generation of mass cytometry and contribute to biological and clinical research

DOI: doi.org/10.1002/anie.202107223

Download related ASMS21 poster here



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