

Where imaging mass spectrometry stands: here are the numbers

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Abstract

Introduction Imaging Mass Spectrometry (imaging MS) is a technology for spatial analytics that has experienced a significant uptake in recent years. A diverse set of applications and analytical platforms have been reported across the field of imaging MS for imaging molecules from many different chemical classes; but there is little quantified information about the overall composition of the field. Many questions exist, such as: is it used mainly for proteins or metabolites? How widespread is MALDI as compared to other types of ionisation sources (e.g., SIMS, DESI etc.)? What volume of data is generated worldwide? What are the leading application areas?

Methods In order to obtain quantitative data to answer these and other questions, we have organized an online survey. Imaging MS practitioners were recruited and questioned about their backgrounds, application areas, which imaging MS technologies they use as well as providing information on what their current experimental throughput is.

Results We found that imaging MS is more often used for metabolites/lipids/small molecules rather than for proteins/peptides. Moreover, the use of high-resolution mass spectrometry technologies constitutes a significant proportion of the data generated. We estimate that worldwide data generation currently exceeds 1 TB per day so, as a

field, imaging MS has entered the big-data era. Our survey respondents report a continued need for computational tools which are required to aid in translating the spectral data produced into molecular knowledge.

Conclusion With the results of this survey (<http://metaspace2020.eu/survey2015>), for the first time we can draw a picture of the diverse imaging MS community, identify areas of concentrated application and estimate the volume of data generated worldwide. This provides an insight into where cross-disciplinary developments need to be focussed in order to support this field through the coming years where there is an expectation of continued growth. The survey quantifies, for the first time, the breadth of technologies and applications that is spanned by imaging MS.

Keywords Imaging mass spectrometry · Survey · Applications · Technology · Metabolomics · Proteomics

Seven years ago the question was asked, is imaging mass spectrometry hype or hope (Heeren et al., 2009)? Since then, there has been an increasing feeling within the imaging mass spectrometry (MS) community that we are moving past being an ‘emerging field’ and imaging MS became an established technique in multiple application areas (e.g. Aichler and Walch 2015; Boughton et al. 2015; Gessel et al. 2014; Goodwin et al. 2016; Palmer and Alexandrov 2015; Spengler 2015). Whilst a literature survey reveals the extent of areas to which imaging MS has been applied, there is little documentation and quantitative understanding on the overall composition of the field, the trends in techniques used, core technology application areas and the computational challenges that remain. From informal conversations it seemed that computational tools for the molecular annotation of imaging MS data were still

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required to bridge the gap between the technological highlights and routine applications. As part of the European Horizon2020 project METASPACE on Bioinformatics for Spatial Metabolomics (<http://metaspace2020.eu>) we invited imaging MS practitioners to take part in a survey to help steer the development of our spatial metabolomics annotation engine and provide, for the first time, a quantified snapshot of the global community.

The invitation to participate in the online survey was distributed to a broad mailing list which included all attendees at the OurCon III (Pisa, Italy, October 2015) conference on imaging mass spectrometry and the internal mailing list of SCiLS GmbH (a METASPACE project member), and on the LinkedIn Mass Spectrometry Imaging group. The survey was active throughout November 2015, during which time we received responses from 111 individuals, of which 77 completed all questions and were included in the analysis. We asked about which applications imaging MS is being used for, what instrumentation is employed and where there are still challenges for translating analytical data into applicable knowledge. Complete survey data is available via <http://metaspace2020.eu/survey2015>, our analysis and the resulting figures are available at http://metaspace2020.eu/survey2015/metaspace_survey.ipynb, a summary is provided in Fig. 1.

This survey revealed a highly active community which utilises many combinations of ionisation sources and mass spectrometers. The leading area of application is the analysis of low molecular weight molecules with 80 % of respondents applying imaging MS for the analysis of either small molecules, lipidomics, metabolomics or for pharmaceutical studies, whereas 60 % use it for detection of proteins or peptides. Over half of labs conduct imaging studies of both small and large molecules. Although there was no equivalent survey for comparison, it is our understanding that in the recent years a rapid diversification of the field that originated in protein and peptide analysis has occurred, and imaging of both large and small molecules is now commonplace. This has been largely possible due to the wider availability of high-resolving power instruments which provide sufficient mass resolution to make accurate mass measurements in the low m/z range (van Hove et al. 2010; Trim and Snel 2016). Practitioners were found to come overwhelmingly from biological and chemistry backgrounds. This may indicate that barriers still exist for the uptake of imaging MS within the medical and pharmaceutical fields, highlighting the importance of computational tools for translating raw mass spectrometry data into information that can be interpreted and applied by biomedical practitioners.

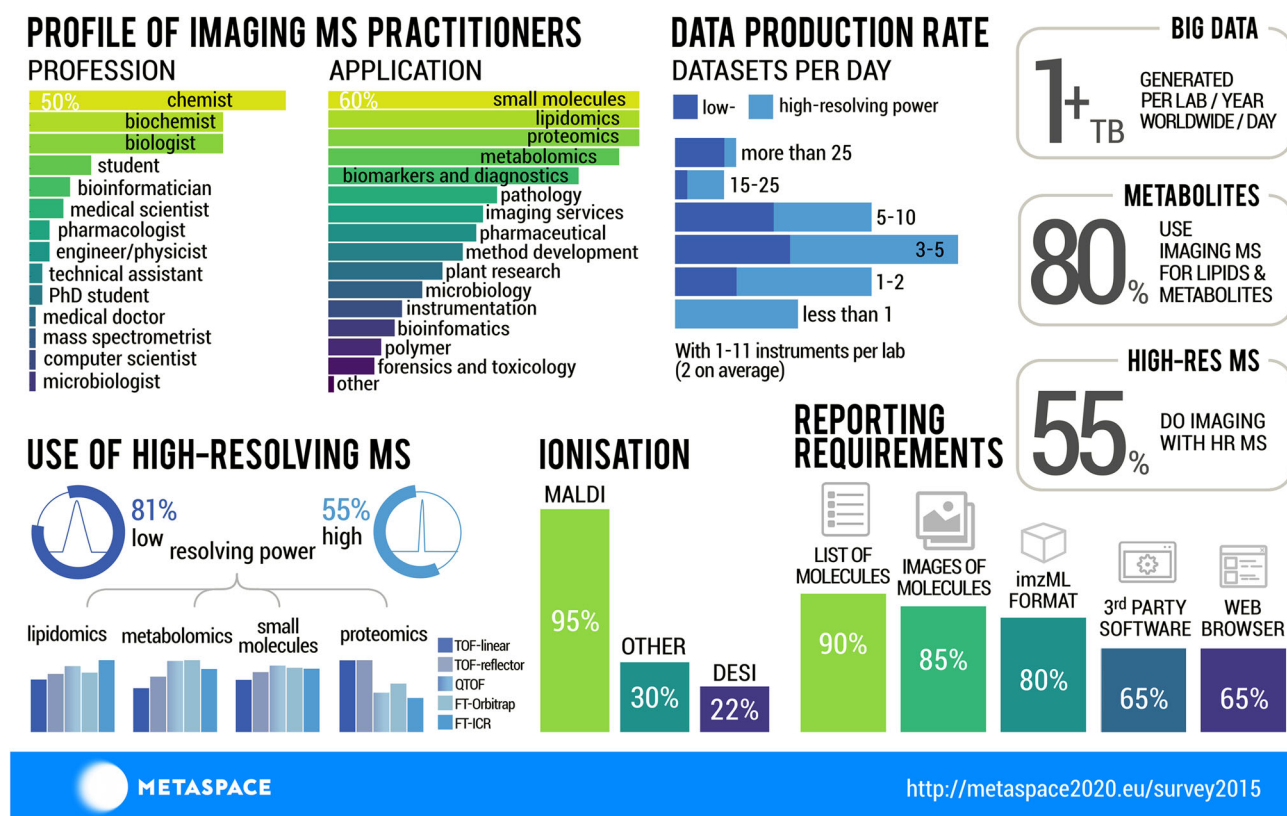


Fig. 1 An overview of the survey results

According to the survey, Matrix Assisted Laser Desorption Ionisation (MALDI) is still the most popular ionisation technique, with 95 % of labs utilising this technology. Desorption ElectroSpray Ionisation (DESI) is the second most popular with almost a quarter of labs making use of this technology, just under 10 % of respondents utilise secondary ionisation mass spectrometry (SIMS). Liquid surface sampling is rapidly emerging as a new imaging technique with 5 % of labs reported using this kind of technology (either Liquid Extraction Surface Analysis or FlowProbe). An ‘average imaging MS lab’ possesses multiple instruments and produces between three and five imaging MS datasets per day, of which more than half are high-mass-resolution. High-resolving power instruments are found in all application areas, but are more frequently applied for small molecule & metabolomics analysis. Labs with multiple instruments typically source them from several vendors, highlighting the need for open data formats such as imzML for the exchange of data (Schramm et al. 2012).

From the survey results, one can see that a large number of imaging MS datasets is being collected. On average 280 high-resolution and 230 low-resolution datasets are collected per year, on the order of 1 TB of data per lab per year. So across just the participants in the survey, a combined estimate is a total collection of 750 datasets and 4 TB per week. It is unsurprising then to find that there is a large appetite within the community for automated computational tools for the analysis of imaging MS data, with 55 % of respondents reporting that the availability of a high-throughput annotation tool for imaging MS as being developed in METASPACE would have high or very high impact on the work they were able to perform.

The survey was promoted to a wide cross-section of the imaging MS field, however the majority of METASPACE consortium partners are based in Europe and the survey was promoted as relating to an ‘European project on automated molecular annotation of imaging MS data’ so it is possible that some bias towards the European community exists. Collecting geographic data would be a useful addition to future surveys. The survey was promoted in part through the mailing list of SCiLS GmbH which may create a bias towards the over-representation of users of Bruker Daltonics instrumentation. However, the breadth of instrument and ionisation types reported leads us to believe that we still achieved good coverage of the whole field.

The survey described a vibrant field which apply multiple imaging MS platforms to a diverse range of applications. We think it would be valuable to repeat a survey of this kind

regularly to quantify the dynamics of the field and how it is changing and to highlight where new opportunities exist.

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Compliance with ethical standards

Conflict of interest DT is the Managing Director and TA is the Scientific Director of SCiLS GmbH, a company providing software for imaging MS. However, no data was concealed for proprietary purposes with all the survey data and results openly available at <http://metaspace2020.eu/survey2015>.

Ethical approval All applicable international, national, and/or institutional guidelines for the care and use of animals were followed. Survey participation was voluntary and confidential. To ensure informed consent of all participants, the scope and purpose of questions was explained beforehand and participants could withdraw at any point during the survey.

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