

Development of 'Ready to Use Kits' for the simultaneous qualification and quantification of drugs in different matrices using Mass Spectrometry, expanded with the application of multimodal imaging techniques

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Chapter 7

Valorization



7 Valorization

This thesis sets out to explore and improve different aspects and applications of mass spectrometry as a device 'able to distinguish' (diagnostic tool) and characterize compounds in biological matrices in order to improve current methodologies.

This work pushes the boundaries of mass spectrometry and mass spectrometry imaging in terms of quantification, identification, analysis speed and coupling together of different techniques. These parameters are crucial for the applicability of mass spectrometry in clinical and non-clinical settings.

Constant improvement in methodology is crucial in all scientific fields, including MS and MSI. In this thesis, several protocols are improved in both the qualitative and quantitative aspects of MS/MSI.

Special care concerning the development of robust sample preparation and analytical procedures is required for mass spectrometry. This thesis firstly describes fast, robust and sensitive analytical procedures able to monitor the abuse of steroidal compounds in animal matrices (**Chapter 2**). These analytical methodologies were developed aiming to establish easy, robust and fast procedures for a market not yet fully regulated. These methodologies were not developed as a means to an end, but aimed to start a collaboration with a company which develops and produces *ready-to-use* diagnostic kits for the analysis of compounds in biological matrices. The procedures created have already been applied to several samples for doping control and will be developed into *ready-to-use* diagnostic kits by Eureka Lab division.

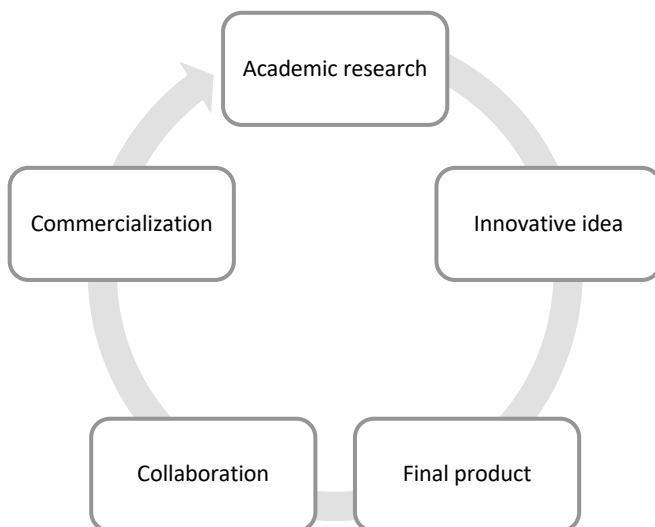


Figure 42 - Valorization circle

Liquid chromatography tandem mass spectrometry is a formidable technique able to precisely quantify and qualify substances in liquid matrices. However, it lacks spatial resolution. **Chapter 3** is the perfect example of why combining two different mass spectrometric analyses is crucial for gaining a broader understanding of biological processes. In this chapter, the analysis of feces and plasma via UHPLC-MS/MS provided an insight on how a lentil extract is able to lower the total cholesterol in rats. MALDI-MSI allows the precisely localization and qualification of lipids, bile acids and cholesterol within tissues. The MALDI analysis of organs harvested from the same animal sacrificed for the previous study not only confirmed the earlier findings but allowed for the understanding of the activation of a more complex biological pathway. After this joint research between M4I (NL) and the Unicam (IT), scientists from different fields in Unicam started seeking possible collaborations with M4I to expand their research.

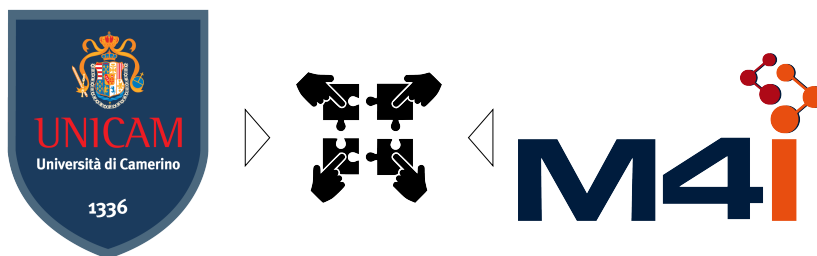


Figure 43 – Collaboration between M4I and Unicam.

Chapter 4 addressed a well-known problem for MALDI-MSI. The extensive sample preparation for FFPE tissues analyzed with MALDI-MSI can lead to artifacts in the results. Uncontrollable conditions such as humidity and temperature in the laboratory can influence the extraction or digestion of compounds from tissues. This chapter compares two innovative quality control QC methodologies able to monitor tissue digestion and peptide extraction of tissues. After the comparison, the QC was used to improve the classification of breast cancer tissues in order to prevent unnecessary surgery. The implementation of the QC led to a great improvement in the statistical analysis applied to these samples. Specifically, after filtering the samples using the QC, it was possible to use a prediction model to identify responders and non-responders before treatment. This chapter acts as a pioneer in innovatively improving MALDI-MSI analysis.

Lastly, **Chapter 5** describes mass spectrometry as a versatile tool for quasi-instantaneous tissue classification during surgery. Surgeons routinely use electrosurgery or laser scalpels in the operating room. These instruments generate smokes which can be aspirated and driven into a mass spectrometer thanks to the REIMS ionization source. The smoke is aspirated through a venturi pump after which it is thermally ionized and analyzed. Chapter 5 compares a CO₂ surgical laser and a diathermic knife as handpieces coupled to a REIMS-

TOF-MS. This shows the possibility to build a unique classification model for instantaneous tissue recognition (<3 seconds). Additionally, the field of REIMS applications is expanded to hard tissue for in vivo surgical applications.

The work presented in this thesis is of interest to researchers working in biomedical and chemistry related fields. Mass spectrometry can complement and improve analytical methodologies routinely employed in clinical and non-clinical setups. Furthermore, the work reported includes collaborative studies involving research groups specialized in different scientific fields. By the combination of a broad range of expertise, this thesis presents novel MS approaches for the improvement of current diagnostic practices.