Towards 3-Dimensional MALDI MS Molecular Imaging of the Optic Chiasm

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Overview
- Optic nerve chiasm from a genetically-engineered mouse model of neurofibromatosis type 1-associated optic glioma compared to wild-type mice using MALDI-Imaging MS.
- MALDI-IMS technology was applied on multiple sections utilizing fiducials incorporated in the embedding medium.
- Fiducials provided a high degree of accuracy for transforming and registering images for 3-D reconstruction.
- The resulting 3-D images provided a view into the ion distributions in the chiasm closer to the 3-dimensional reality.

Introduction
- The optic chiasm is the region where the optic nerve tracts coming from the eyes, meet and cross over before entering into the brain. The optic chiasm plays a key part in delivering information from the retina to the visual cortex.
- Individuals with the neurofibromatosis type 1 (NF1) inherited condition have a greater risk for developing optic chiasm anomalies which can result in visual loss.

Materials and methods
- Wild-type optic nerves along with optic nerves from NF1 mice with optic nerve gliomas were excised, and tissues were aligned within a custom mold, ensuring a marker triangle for designated regions of the mold.
- Sections 10 µm thick were thaw mounted onto separate ITO coated glass slides, subject to the same wash protocol and 100% ethanol: chloroform: acetic acid (60:30:10) followed by 100% acetonitrile 0.15% TFA and LC-MS/MS analysis to identify work.
- From a separate section, 10 µm thick were thaw mounted onto separate ITO coated glass slides, washed with 70% , 100% ethanol, and registered images for 3D reconstruction to be prevalent throughout the outer regions of the ITO coated glass slides.

Results and Discussion
- Images displayed in the central panel (2-4) show signals which describe the native structure of the optic nerve chiasm. Figure 1 displays the distribution of myelin basic protein isoform 6 (Identified with LC-IMS ETD) at m/z 14126 which is present throughout the central body of both the tissues with similar abundance. Images in figure 2 show a truncated myelin basic protein (1-43) overlaid with myelin basic protein isoform 8, the truncated version appears to be present in the meninges, which surround the optic nerve and is more abundant in the NF1 model (figure 5).
- Figures 3 displays the distribution of an Acyl CoA binding protein at m/z 1916 overlaid with myelin basic protein isoform 8. Acyl CoA binding protein is present in the dura mater region of the meninges. These distributions become more apparent when all three signals are overlaid in figure 4. Figures 5-8 displays signals which vary between the NF1 optic glioma and wild-type nerve chiasms. The truncated myelin basic protein observed in the meninges can be seen in figure 3 to be more abundant throughout the majority of the NF1 optic glioma and can be seen to proliferate into central regions of the tissue. The 2-D image also shows high abundance in the region of the optic chiasm and the optic nerve treating the chiasm.

Conclusion
- Embedding tissue along with external fiducial markers improved transformation and registration of 2-D IMS into a 3-D volume by making the process more accurate and efficient. Reconstructing the data from 2-D to 3-D provided a view into the ion distributions in the chiasm closer to the 3-dimensional reality.

Due to the very small nature of the starting material, 3-D reconstruction of multiple 2-D mass spectrometry images resulted in a number of proteins with different expression between the wild type and NF1 optic glioma being observed with a higher global expression.

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References
- [List of references related to the study]