Discrimination of Human Astrocytoma Subtypes by Lipid Analysis Using Desorption Electrospray Ionization Imaging Mass Spectrometry

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INTRODUCTION

- Imaging technique is very important for accurate characterization of tissue to optimize resection specially for brain tumors
- Microscopy, fluoroscopy, magnetic resonance imaging and computed tomography are the common used tools
- Limited chemical information, low sensitivity and systematic administration of contrast agents are not possible
- DESI-MS imaging: No sample preparation, very little time, high quality analytical data and chemical information
- Work has been done on lipid distributions in mouse brain, images of antifungals in algae, distinguishment of cancerous and non-cancerous canine bladder tissue samples using multiple marker lipids
- Little work with human tissue: Observation of distinctive lipid markers associated with tumor and non-tumor regions in human liver adenocarcinoma tissue sections

- World Health Organization (WHO) recognizes over 125 types of brain tumors according to histopathological evaluation
  - Classified them according to cellular characteristics
  - Grades malignancy according to proliferation, cellular and nuclear morphology, vascularization, and a few biomarkers
- Gliomas are the most common human primary brain tumors with astrocytomas comprising the most common subtype ranging in grade from WHO grade II to WHO grade IV
- Current diagnosis is based on neuropathological examination of a biopsy sample and characteristic cytogenetic aberrations which needs an expert neuropathologist and longer time
- MS imaging rapidly provides extensive chemical information from biopsy samples, which could differentiate brain tumors from healthy and functional brain

IN THIS PAPER

- 7 glioma specimens from seven human subjects were examined using DESI-MS. Those 7 were categorised by an expert neuropathologist as
  1. Diffuse astrocytoma (WHO grade II) :1
  2. Anaplastic astrocytoma (WHO grade III) :2
  3. Glioblastoma (GBM) (WHO grade IV) :4

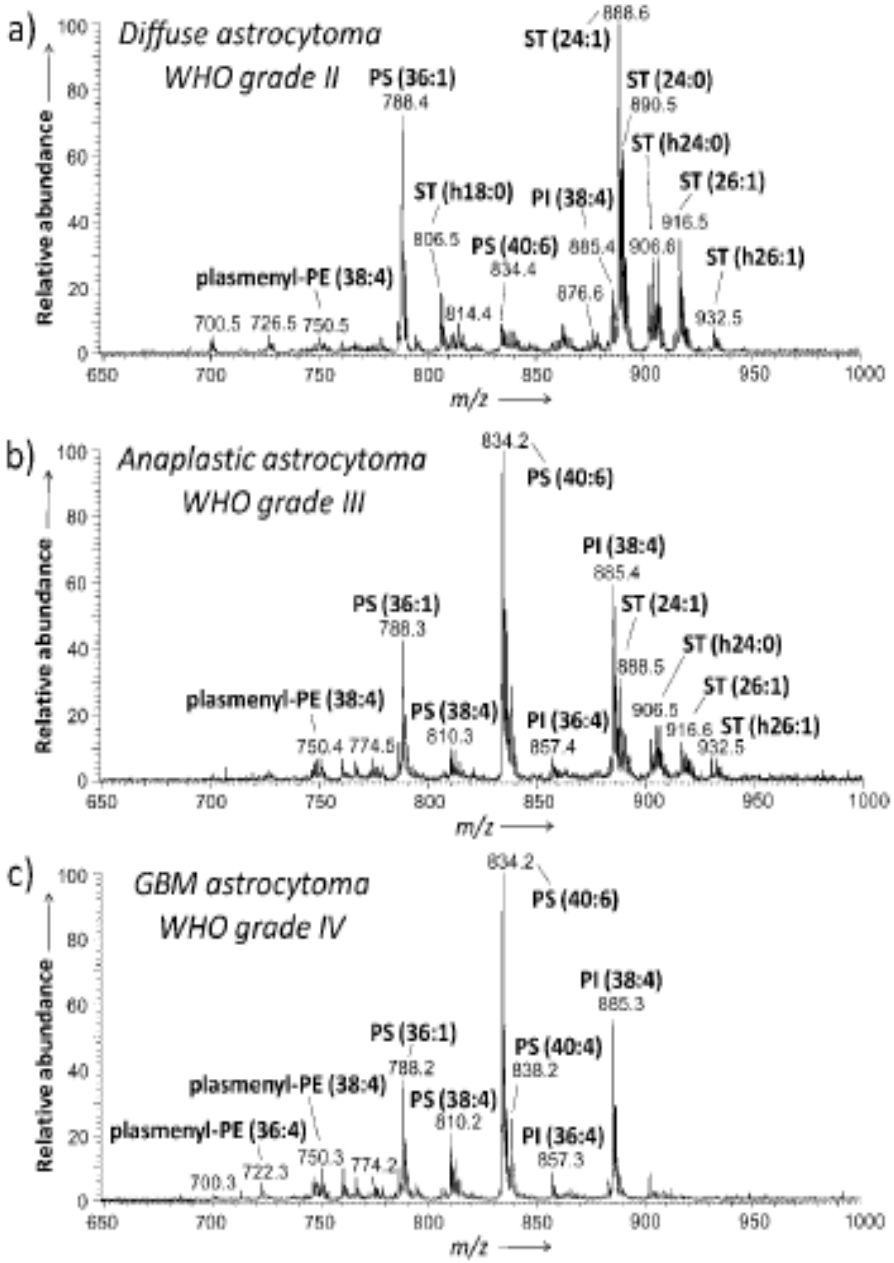
- Tissue specimens were analyzed for obtaining lipid profile using DESI-MS in both positive and negative ion mode and confirmed by tandem MS

  Positive mode: Glycerophosphocholines (PC), Sphingomyelins (SM) and Galactoceramides (GalCer)

  Negative mode: Glycerophosphoinositols (PI), Glycerophosphoserines (PS), Plasmenyl glycerophosphoethanolamines (plasmenyl-PE) and Sulfatides (ST)

LIPID: The major component of brain tissue and alteration of composition associated with several diseases

NEGATIVE ION MODE DESI SPECTRA



Major lipids
ST, PS, PI

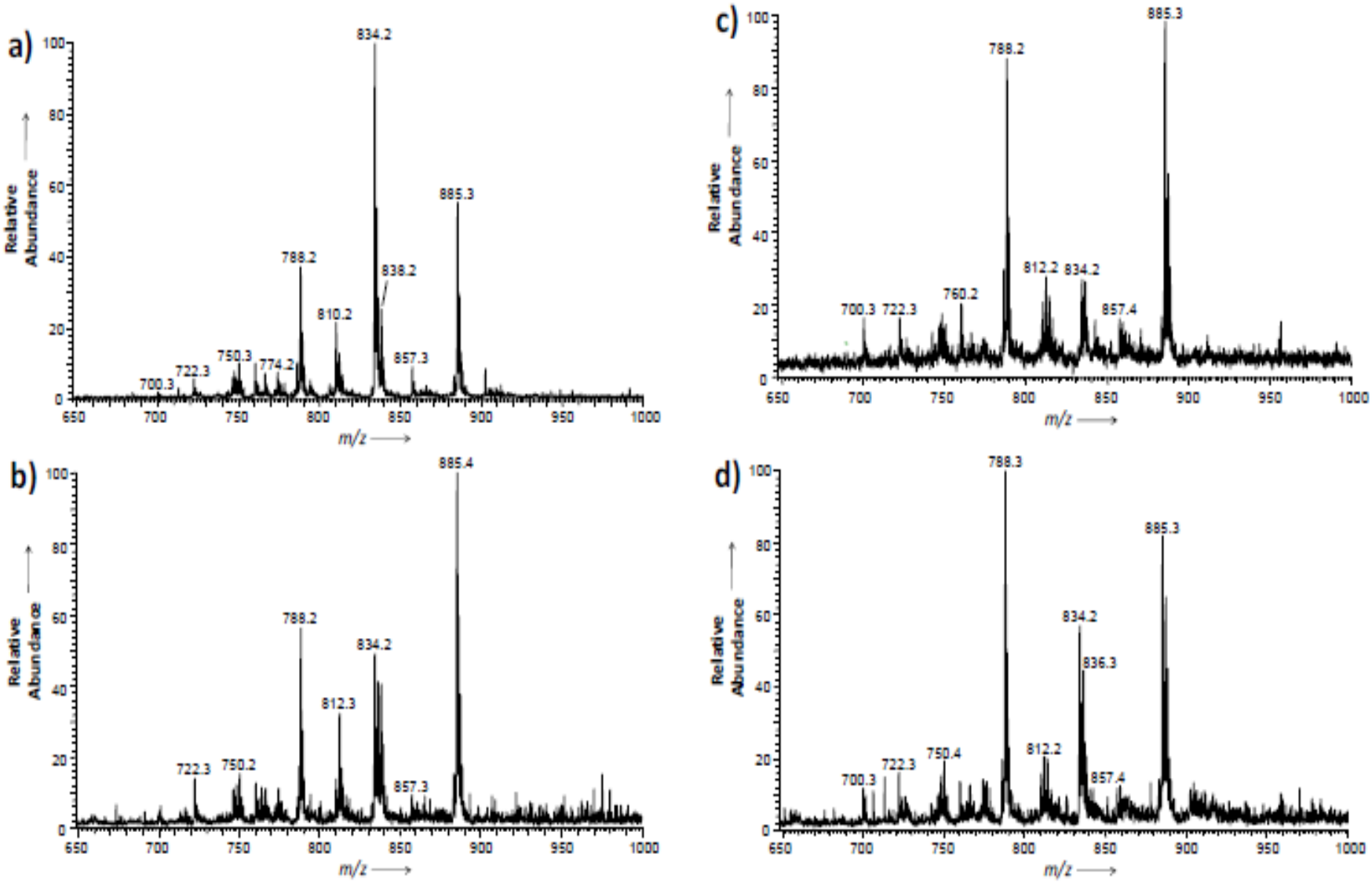
Major lipids
PS, PI,
plasmenyl-PE

ST decreases

PS increases

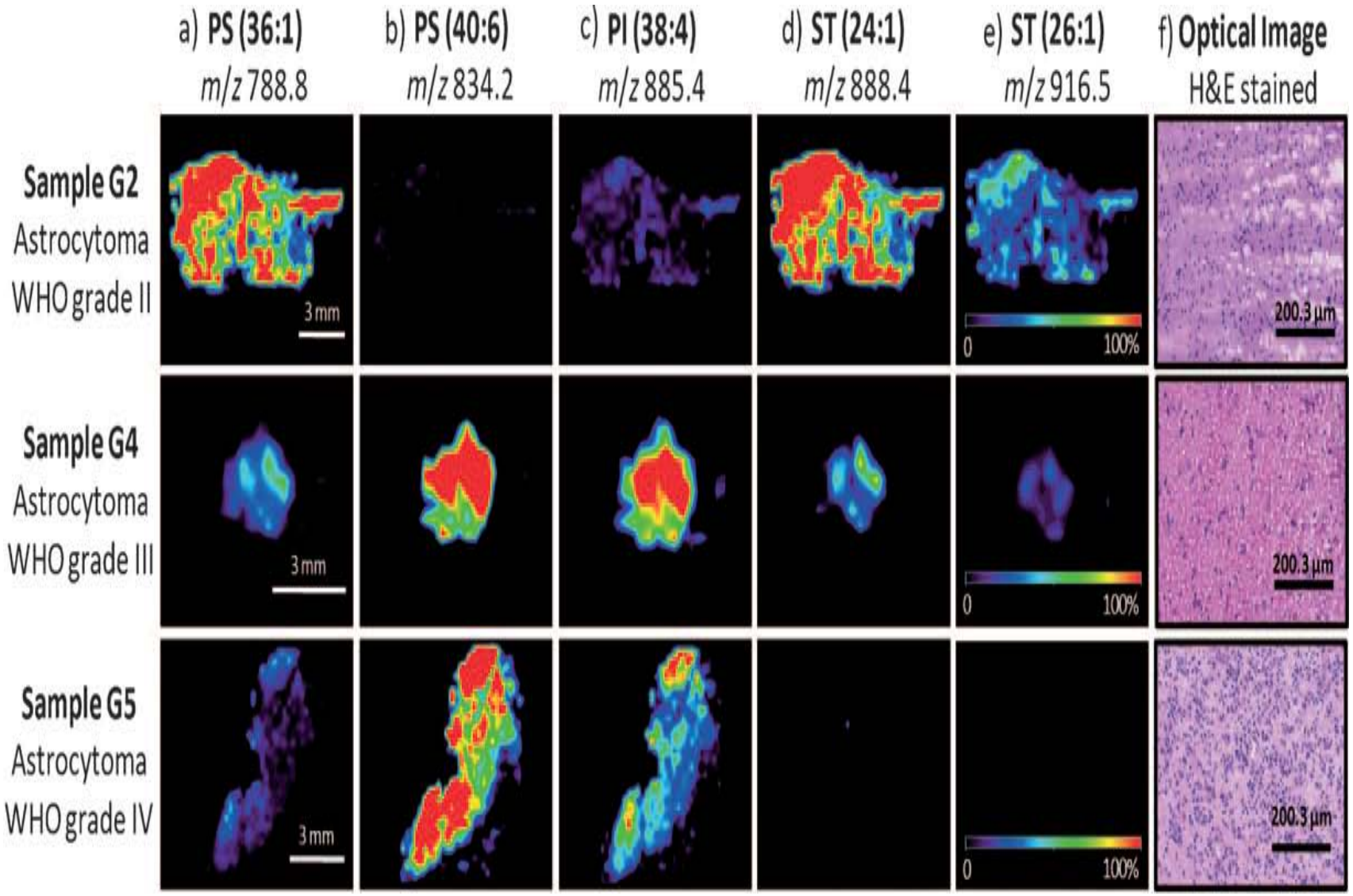
PI increases

NEGATIVE ION MODE DESI SPECTRA OF 4 GBM SAMPLES

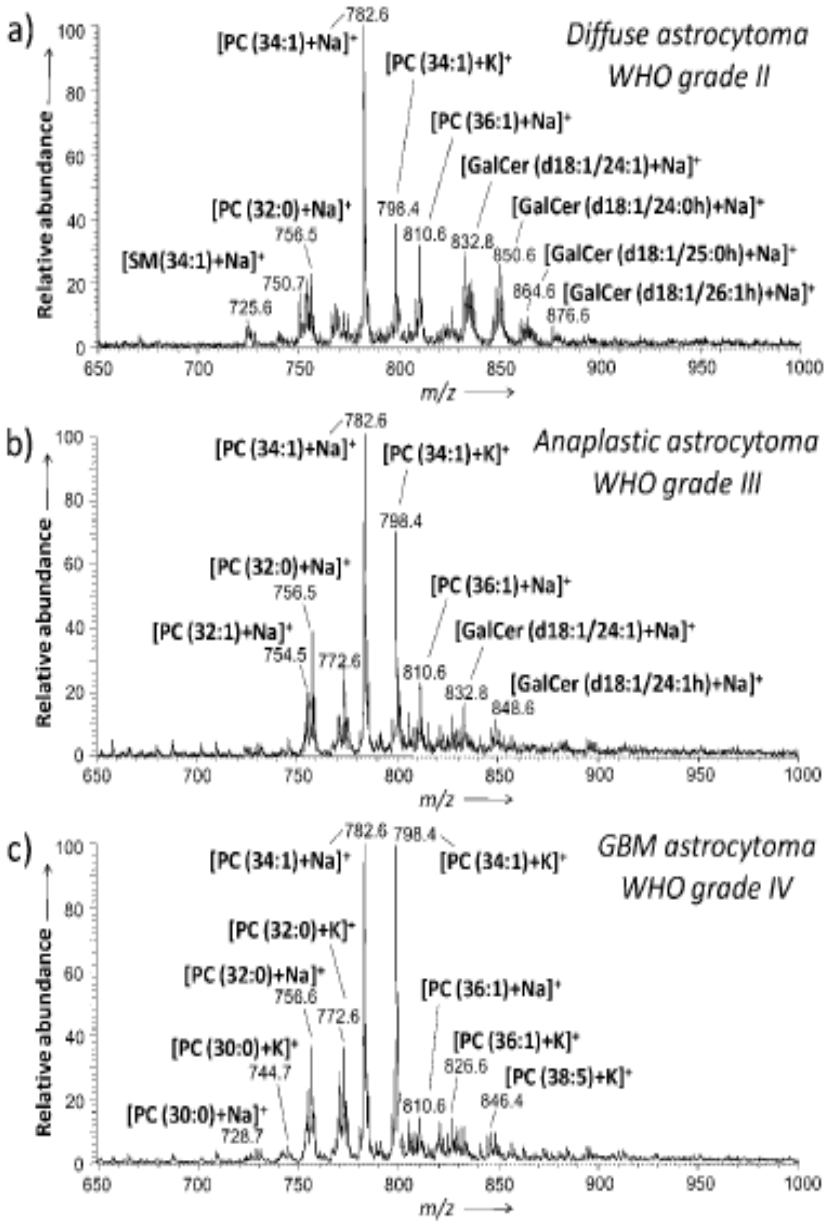


Most abundant peaks are from the lipids PS(40:6), PI(38:4), and PS(36:1)

DESI-MS IMAGES FOR THE MAIN IONS IN THE NEGATIVE ION MODE



POSITIVE ION MODE DESI SPECTRA



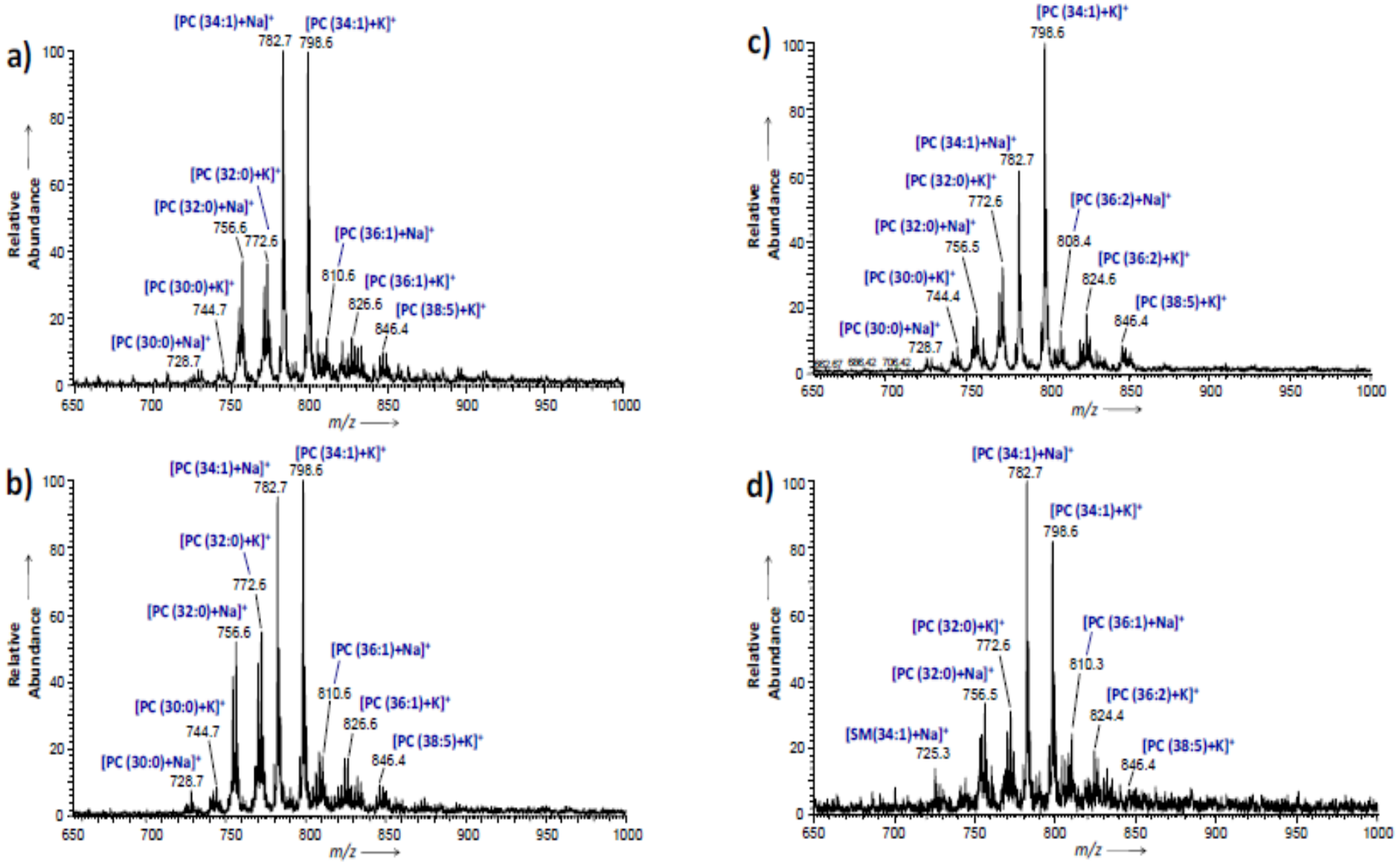
Major peaks
PC(34:1)+Na^+
PC(34:1)+K^+
PC(32:0)+Na^+

PC(34:1)+K^+ increases

PC(32:0)+Na^+ increases

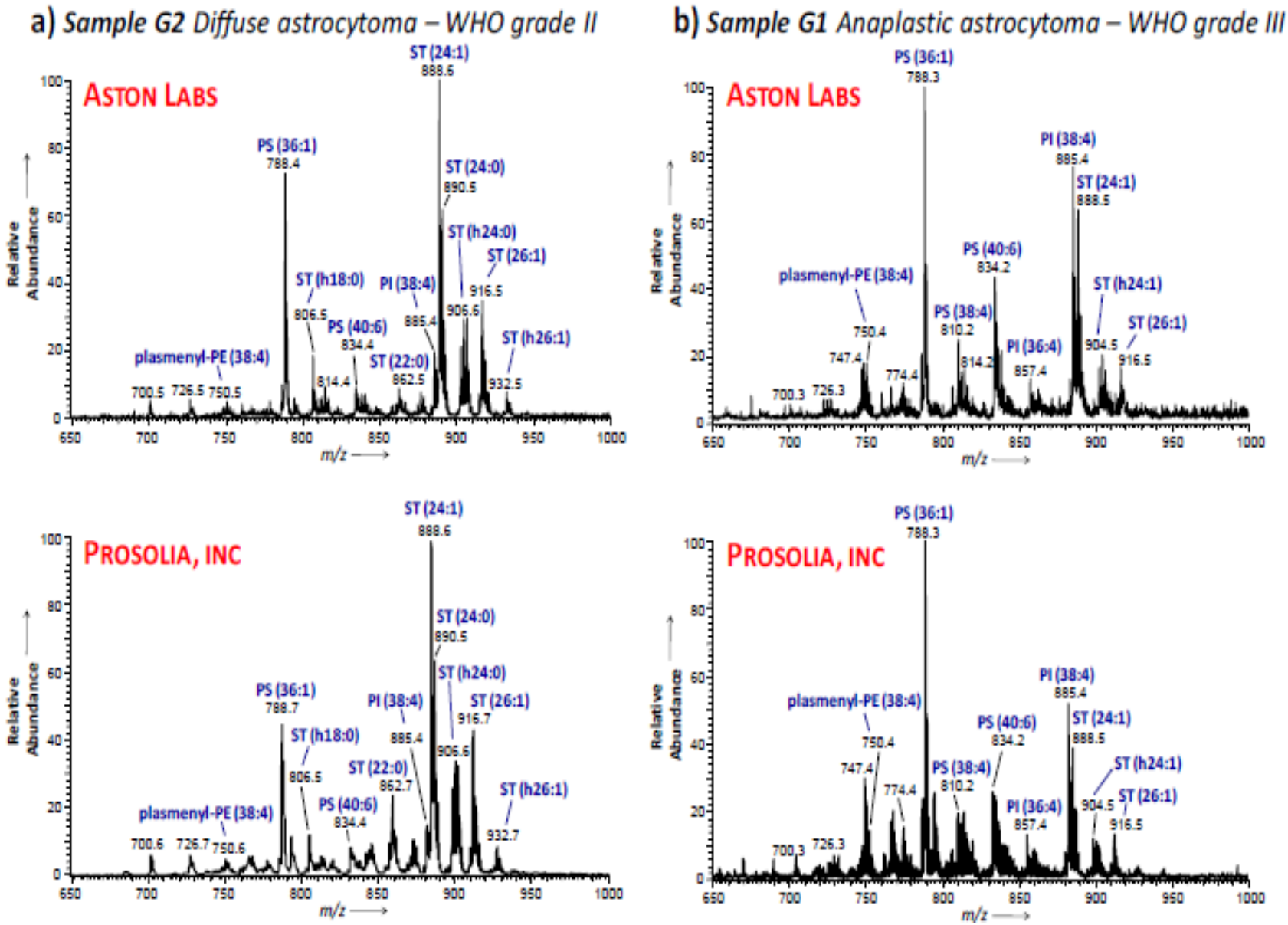
GalCer decreases

POSITIVE ION MODE DESI SPECTRA OF 4 GBM SAMPLES



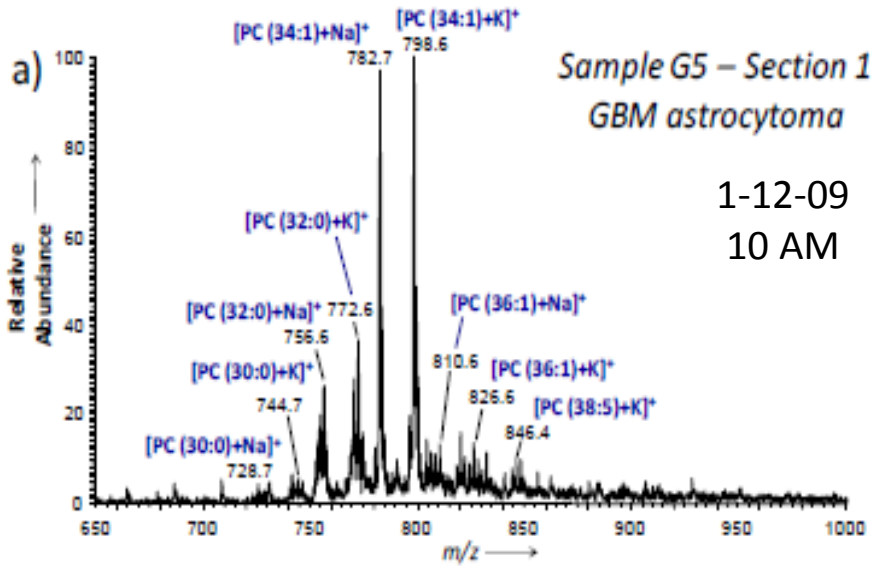
Most abundant peaks are from the lipids PC

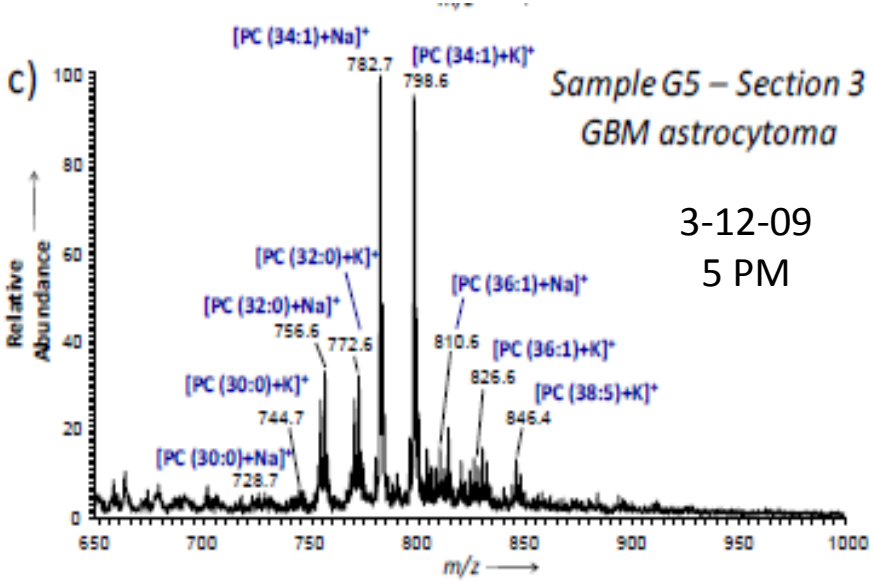
REPRODUCIBILITY OF DATA

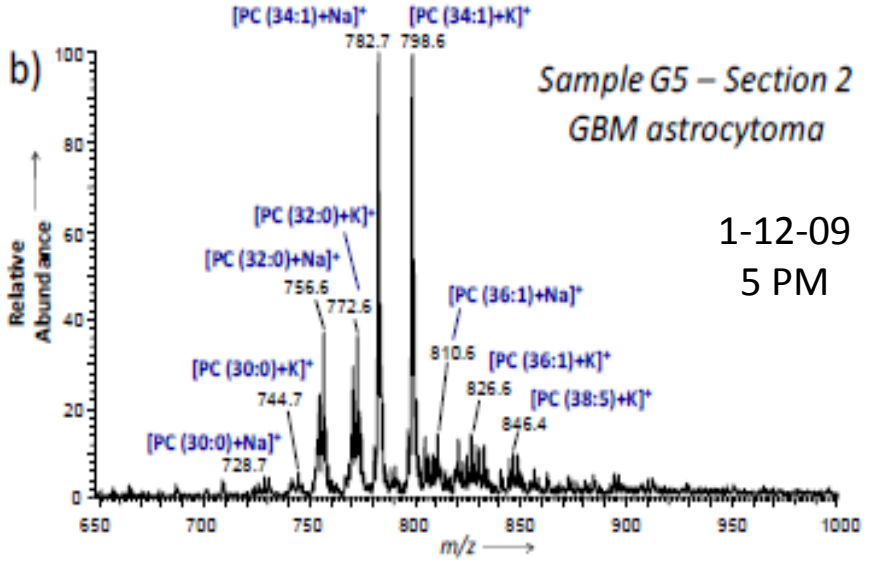


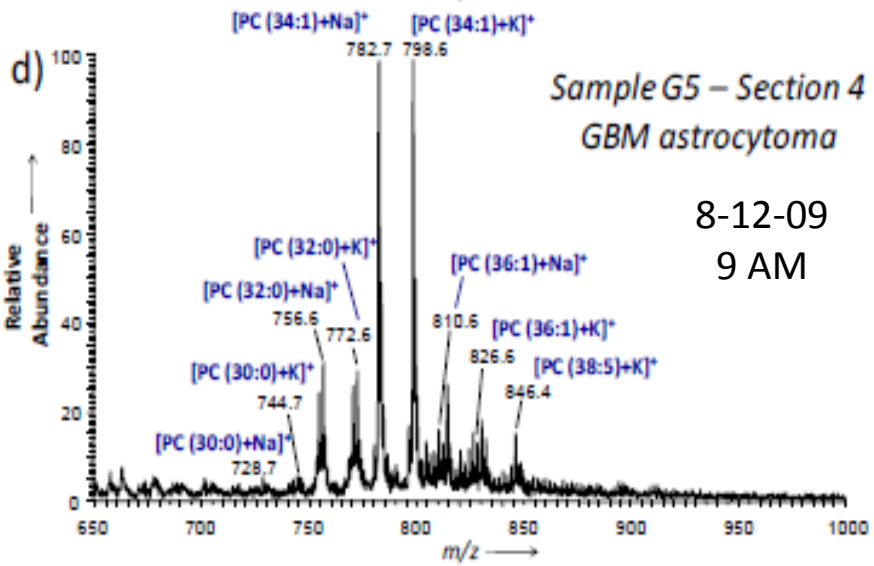
Negative ion mode DESI-MS in different labs

POSITIVE ION MODE DESI SPECTRA IN DIFFERENT TIME









SUMMARY

- DESI imaging of lipid profile is an important tool to differentiate various degrees of malignancy in astrocytic tumors in both positive and negative ion mode
- With increased malignancy of astrocytomas abundance of STs decreases in negative ion mode and GalCers also decreases in positive ion mode
- These reports also corroborates previous reports based on classical lipid extraction methodologies
- Sample size has to be increased to establish this as a proper diagnostic tool for various astrocytomas
- Same m/z lipids has to be differentiated by using high resolution MS

CONCLUSIONS

- DESI-MS can be used to diagnosis of various diseases
- If we can find bio-markers for different diseases then we can easily monitor it accurately in very short time and without any expert histopathologist
- The fast analysis can help in taking decision during critical surgeries

THANK YOU