

Introduction

Meningiomas comprise 1/3 of brain tumors. Though they are often considered benign, even benign meningiomas can behave aggressively.

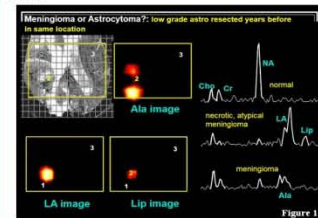
Treatment differs based on grade and behavior:
Grade I: no treatment or surgery alone and MRI follow up

Grade II/III or aggressive behavior: surgery + adjuvant therapy

Currently, grade is dependent on histology after surgery. Knowledge of grade prior to surgery would allow an advantage in resection and treatment of the tumors.

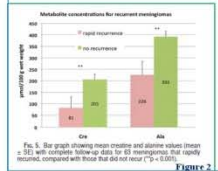
¹H-MR Spectroscopy (¹H-MRS) evaluates metabolite levels and can differentiate tumor types as well as quantify tumor metabolism.

High alanine (Ala) concentration in meningiomas can differentiate it from other CNS tumors using ¹H-MRS.



Ex vivo tissue analysis in NMR evaluation showed a correlation between decreased alanine levels within meningiomas and more aggressive meningiomas

Pfisterer, et al., 2007



Hypotheses

- In vivo* multi-voxel 3D ¹H-MRS data can be used intraoperatively with coregistration on STEALTH neuronavigation system
- In vivo* multi-voxel 3D ¹H-MRS can detect regional biochemical alterations unique to clinically aggressive meningiomas and can correlate *ex vivo* results
- In vivo* multi-voxel 3D ¹H-MRS integrated with IGS can provide a meningioma resection advantage, or allow metabolically-guided selection of tissue sampling for study

Methods

PATIENTS SCANNED	
18	primary meningiomas with tissue collected
1	recurrent meningiomas with tissue collected
3	not meningiomas
1	moved head during MRS acquisition
2	severely claustrophobic
2	no operation
3-D ¹ H-MRS data sets examined with SAGE/LCModel	
15	sets with quantifiable metabolites, areas of interest identified within tumor and selected for resection
4	sets discarded – inadequate water suppression or voxel placement prevented analysis

3D ¹H-MR Spectroscopy Integrated into a Standard Neurosurgical Image Guidance System: Providing a Resection Advantage and Determining Biochemical Markers of Clinically Aggressive Meningiomas *In Vivo*

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Methods

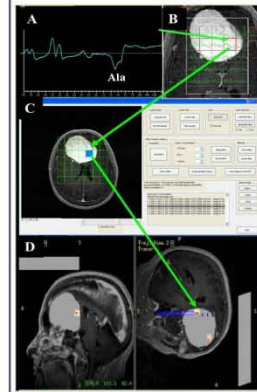


Figure 3

- Newly diagnosed and recurrent meningioma patients are scanned preoperatively with a 3T GE Signa scanner
- 3D CSI ¹H-MRS is performed immediately after the pre-operative MRI STEALTH intraoperative navigation "wand" scan sequence, avoiding placement of the excitation voxel over the skull base, bone and scalp
- The 3D MRS spectral data is quantified using GE's Sage software and LCModel (Provencher) (Figure A)
- Voxels of interest are selected based on presence or absence of alanine, lactate, choline and creatinine (Figure B highlighted in red)
- Selected voxels are entered into our MATLAB software GUI to create a STEALTH overlay (Figure C)
- Neurosurgeons resect the voxels of interest using image guidance system (Figure D: blue arrow showing intra-operative identification of the voxel of interest)
- Histology and MIB-1 indexing of tumor samples was performed
- NMR High Resolution Magic Angle Spinning (HRMAS) was performed on resected tissue to compare *ex vivo* spectra to the corresponding *in vivo* ¹H-MRS spectra and evaluate the STEALTH integrated overlay technique

Results

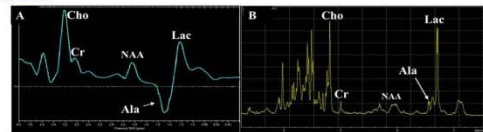


Figure 4 LCMModel Spectra from Patient Voxel A HR-NMR Spectra for Patient Voxel A

Figure 4: Image Guidance System overlay greatly enhances the accuracy of resecting the voxels of interest. ¹HR-MAS NMR spectra showed qualitatively reliable correlation with the *in vivo* ¹H-MRS spectra with 23 of 28 spectra matching.

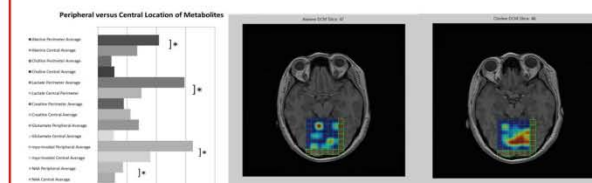


Figure 5

Figure 6

Figures 5 and 6: 14 grade I tumor periphery showed increased Alanine concentrations ($p < .05$). Tumor centers showed increased Cho concentrations and decreased Alanine concentrations

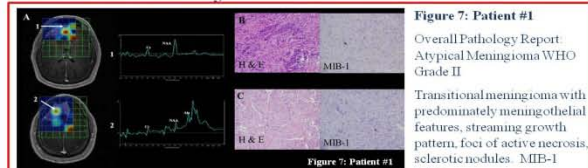


Figure 7: Patient #1

Overall Pathology Report: Atypical Meningioma WHO Grade II

Transitional meningioma with predominantly meningeothelial features, streaming growth pattern, foci of active necrosis, sclerotic nodules. MIB-1 6.1%

Histology for Sample 1 showed a MIB-1 of 2.4% but appeared to be a higher grade than the Sample 2 on H & E; therefore, a more aggressive part of the meningioma that correlated with low alanine concentration.

Histology for Sample 2 showed a MIB-1 of 1.8% and was considered benign sample of meningioma that correlated with elevated alanine concentration.

Figure 8: Patient #2

Overall Pathology Report: Meningothelial Meningioma WHO Grade I

Sheet like growth pattern and focal necrosis. MIB-1 value of 2.8%

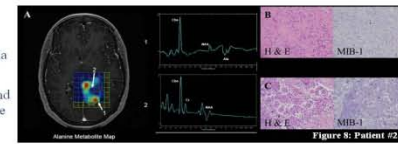


Figure 8: Patient #2

Histology for Sample 1 showed a MIB-1 concentration of 2.6% demonstrating a more benign sample of meningioma that correlated with elevated alanine concentration

Histology for Sample 2 showed a MIB-1 of 4.0% showing a more aggressive part of the meningioma that correlated with low alanine concentration.

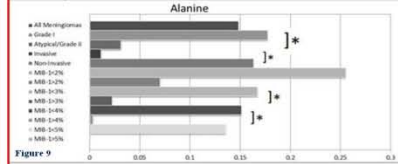


Figure 9: Alanine concentration is decreased in areas of higher MIB-1% meningioma for both grade I and grade II ($p < .05$)

Conclusions

- In vivo* multi-voxel 3D ¹H-MRS detects regional biochemical alterations showing that meningiomas have regionally heterogeneous metabolite distribution.
- In vivo* multi-voxel 3D ¹H-MRS data can be overlaid on the STEALTH neuronavigation system to accurately biopsy and resect areas of interest.
- 3D ¹H-MRS spectra correlate with *ex vivo* ¹HR-MAS NMR spectra
- ¹H-MRS alanine MIB-1 concentration may predict tumor recurrence.

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