Stereotact Funct Neurosurg 2012;90:63–65
DOI: [10.1159/000335168](https://doi.org/10.1159/000335168)

¹H-MRS-Guided Stereotactic Brain Biopsy

Mikhail Chernov, Yoshihiro Muragaki, Takaomi Taira, Hiroshi Iseki

Faculty of Advanced Techno-Surgery and Department of
Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan

The recently published article by Frati et al. [1] regarding frameless stereotactic brain biopsy was read with great interest. One of the objectives of that study was the evaluation of the usefulness of proton magnetic resonance spectroscopy (¹H-MRS) for guidance of tissue sampling in 296 brain lesions, including 211 gliomas. In 37 cases, contrast enhancement of the mass was absent. Before the stereotactic procedure, a multivoxel spectroscopic examination was performed, metabolic data were incorporated into the neuro-navigation system and fused with the structural MR images, and a target was selected in the area of the lesion corresponding to the highest value of the choline-containing compounds to N-acetylaspartate (Cho/NAA) ratio, which was identified on the visualized grid of the spectroscopic voxels showing automatically calculated numerical values. Three targets were used in each case, and the number of obtained tissue specimens varied from 4 to 12 (average, 6). Overall, a diagnosis was established in all but one case (diagnostic yield 99.7%). It was found that histopathological grades within the tissue samples taken from the same tumor are well associated with the values of Cho/NAA ratios ($p < 0.01$). Regrettably, no results are presented on the correlation of the metabolic data with the MIB-1 index, while immunostaining for Ki-67 was regularly done. However, the authors concluded that spectroscopic guidance may be very useful for appropriate targeting of the stereotactic brain biopsy, particularly in cases of nonenhancing lesions.

Certainly, the use of metabolic and functional data for target selection during both frame-based and frameless stereotactic tissue sampling seems very promising. The application of chemical shift imaging is especially attractive, because it can be easily attained at the time of routine MRI, is fully noninvasive and highly sensitive to the presence of pathology. Indeed, the reported diagnostic yield of ¹H-MRS-guided brain biopsy typically attains 100% [2–5]. Moreover, according to our own experience, spectroscopic support may facilitate histopathological diagnosis both on frozen and permanent tissue sections [5]. However, we were not able to demonstrate a greater diagnostic yield of ¹H-MRS-guided procedures (100% in 30 patients) compared to MRI-based ones (90% in 39 patients), seemingly due to a relatively small sample size of our series [5]. In fact, a subsequent analysis revealed that with the same parameters of the study, it would be necessary to have 85 and 111 patients in the case and control groups, respectively, to prove the presence of a difference in the diagnostic yield

with a power of 0.8 and type I error probability of 0.05. Anyway, in our opinion, metabolic guidance may be rather useful during stereotactic biopsy of parenchymal brain tumors, and may be especially recommended for recurrent, particularly previously irradiated, neoplasms, or for sampling of the highly vascular lesions since in the latter cases, detection of the spectroscopic abnormalities outside the contrast-enhanced area may permit a surgeon to obtain a representative tissue specimen with reduced risk of hemorrhagic complications [6].

On the other hand, it is clear that just a confirmation of the presence of glioma with stereotactic biopsy is not sufficient enough for modern treatment objectives. These neoplasms are well known for their heterogeneity; therefore, the main requirement for tissue sampling in such cases is detailed characterization of the tumor type and histopathological grade. However, in the series of the MD Anderson Cancer Center, 63% of gliomas designated after stereotactic biopsy as being of low or intermediate grade and 60% of anaplastic astrocytomas were found to be more malignant after open surgery [7]. In our analysis, just 36% of the patients diagnosed as having low-grade glioma after stereotactic biopsy had complete diagnostic agreement in tumor typing and grading compared to subsequent resection [8]. Certainly, the diagnostic accuracy of the stereotactic procedure may be improved by multiple tissue sampling; however, it is not clear, whether or not metabolic guidance may also be helpful. Unfortunately, the referenced study by Frati et al. [1] does not provide reliable information on this issue. From our experience, addition of spectroscopic support with targeting the area of the lesion characterized by the lowest NAA/Cho ratio did not result in improved diagnostic accuracy of the stereotactic procedures [5]. Major diagnostic disagreement between biopsy and subsequent surgical resection was observed in 6 out of 18 cases and was most frequently related to initial undergrading of the nonenhancing WHO grade III gliomas [5]. Others demonstrated that the direction of tissue sampling on the area with the lowest NAA/Cho ratio may lead to erroneous diagnosis of anaplastic astrocytoma in cases of glioblastoma [9].

The NAA/Cho ratio is widely recognized as a marker of glioma presence, proliferative activity, and growth characteristics, but it seems that stereotactic targeting of the tumor area with its lowest value does not necessarily result in the precise determination of the histopathological grade. Further studies are needed to identify the optimal metabolic target during spectroscopy-guided stereotactic procedures. Presence and distribution of other metabolites, particularly lactate and mobile lipids [9], should also be taken into consideration (fig. 1). ¹H-MRS is intrinsically a multi-parameter investigation and limitation of its evaluation to only one metabolite content or single ratio does not seem reasonable. Therefore, at present, during the evaluation of the spectroscopic data in addition to calculation of the various metabolite contents and ratios, we are constantly performing pattern analysis of the whole pathological ¹H-MR spectrum as well (fig. 2).

Fig. 1. Slightly different ^1H -MR spectra in the various parts of glioblastoma. The area of the tumor corresponding to the spectrum with the moderate elevation of mobile lipids (Lip) seems most suitable for biopsy targeting (lower left). Cr = Creatine; Lac = lactate. Automatically calculated values of the NAA/Cho ratio are presented. Figures on the horizontal axes correspond to resonance frequency.

Fig. 2. Classification of the pathological ^1H -MR spectra based on determination of the main metabolites, namely NAA, Cho, lactate (Lac), and mobile lipids (Lip). Types I C and II C are further subdivided in cases with mild and moderate elevation of Lip. From Chernov et al. [10].

References

- 1 Frati A, Pichierri A, Bastianello S, Raco A, Santoro A, Esposito V, Giangaspero F, Salvati M: Frameless stereotactic cerebral biopsy: our experience in 296 cases. *Stereotact Funct Neurosurg* 2011;89:234–245.
- 2 Son BC, Kim MC, Choi BG, Kim EN, Baik HM, Choe BY, Naruse S, Kang JK: Proton magnetic resonance chemical shift imaging (¹H CSI)-directed stereotactic biopsy. *Acta Neurochir (Wien)* 2001;143:45–50.
- 3 Hall WA, Truwit CL: 1.5 T: spectroscopy-supported brain biopsy. *Neurosurg Clin N Am* 2005;16:165–172.
- 4 Hermann EJ, Hattingen E, Krauss JK, Marquardt G, Pilatus U, Franz K, Setzer M, Gasser T, Tews DS, Zanella FE, Seifert V, Lanfermann H: Stereotactic biopsy in gliomas guided by 3-tesla ¹H-chemical-shift imaging of choline. *Stereotact Funct Neurosurg* 2008;86:300–307.
- 5 Chernov MF, Muragaki Y, Ochiai T, Taira T, Ono Y, Usukura M, Maruyama T, Nakaya K, Nakamura R, Iseki H, Kubo O, Hori T, Takakura K: Spectroscopy-supported frame-based image-guided stereotactic biopsy of parenchymal brain lesions: comparative evaluation of diagnostic yield and diagnostic accuracy. *Clin Neurol Neurosurg* 2009;111:527–535.
- 6 Burtscher IM, Skagerberg G, Geijer B, Englund E, Stahlberg F, Holtas S: Proton MR spectroscopy and preoperative diagnostic accuracy: an evaluation of intracranial mass lesions characterized by stereotactic biopsy findings. *AJNR Am J Neuroradiol* 2000;21:84–93.
- 7 Jackson RJ, Fuller GN, Abi-Said D, Lang FF, Gokaslan ZL, Shi WM, Wildrick DM, Sawaya R: Limitations of stereotactic biopsy in the initial management of gliomas. *Neuro Oncol* 2001;3:193–200.
- 8 Muragaki Y, Chernov M, Maruyama T, Ochiai T, Taira T, Kubo O, Nakamura R, Iseki H, Hori T, Takakura K: Low-grade glioma on stereotactic biopsy: how often is the diagnosis accurate? *Minim Invasive Neurosurg* 2008;51:275–279.
- 9 Ng WH, Lim T: Targeting regions with highest lipid content on MR spectroscopy may improve diagnostic yield in stereotactic biopsy. *J Clin Neurosci* 2008;15:502–506.
- 10 Chernov M, Hayashi M, Izawa M, Nakaya K, Ono Y, Usukura M, Yoshida S, Kato K, Muragaki Y, Nakamura R, Iseki H, Hori T, Takakura K: Metabolic characteristics of intracranial metastases, detected by single-voxel proton magnetic resonance spectroscopy, are seemingly not predictive for tumor response to gamma knife radiosurgery. *Minim Invasive Neurosurg* 2007;50:233–238.

Mikhail Chernov, MD
 Faculty of Advanced Techno-Surgery and
 Department of Neurosurgery, Tokyo Women's Medical University
 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666 (Japan)
 Tel. +81 3 3353 8111, ext. 66003, E-Mail m_chernov@yahoo.com