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Predicting Meningioma Consistency on Preoperative Neuroimaging Studies

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Synopsis

This article provides an overview of the neuroimaging literature focused on pre-operative prediction of meningioma consistency. A validated, non-invasive neuroimaging method to predict tumor consistency can provide valuable information regarding neurosurgical planning and patient counseling. Most of the neuroimaging literature indicates conventional MRI using T2-weighted imaging (T2WI) may be helpful to predict meningioma consistency, however, further rigorous validation is necessary. Much less is known about advanced MRI techniques such as diffusion MRI, MR elastography (MRE) and MR spectroscopy (MRS). Of these methods, MRE and DTI appear particularly promising.

Keywords

meningioma; consistency; firmness; texture; MRI; prediction; neurosurgical planning; minimally invasive neurosurgery

Introduction

Meningioma is the most common primary brain tumor¹. With surgery being a primary mode of therapy, minimally invasive alternatives to conventional open approaches to the resection of intracranial meningiomas, such as key-hole or endoscopic transnasal approaches, have recently become more commonplace in tumors of the skull base²⁻⁵. However, proper patient selection is critical to determine which neurosurgical operation is most appropriate for a given patient. Multiple factors such as tumor location, invasiveness, encasement of vital structures and vascularity must be taken into consideration^{3,6-8}. Tumor consistency, also referred to as firmness or texture, is another factor that has been increasingly recognized as an important criterion to consider prior to a meningioma operation. Multiple reports have described the significance of a meningioma's consistency to determine surgical planning and expectations regarding the extent of resection^{3,9-13}. Furthermore, this information can be very helpful when patients are counseled regarding potential risks and length of operating time¹⁴. This is particular true for tumors which demonstrate extremes of consistency (i.e. extremely soft vs extremely firm). While it appears that water and collagen content are important determinants of meningioma consistency, no definite association with histopathological subtype has been established^{2,5-7,15-17}. This review will summarize the current neuroimaging literature as it relates to the pre-operative evaluation of meningioma consistency.

Reference Standards of Meningioma Consistency

Before delving into the neuroimaging aspects of meningioma consistency determination, it is necessary to consider what reference standards are being used when a neuroimaging method is being evaluated for its discriminative ability. In 2013, Zada and colleagues² proposed a meningioma consistency grading system that would be based on an ordinal scale rather than simply labeling meningiomas as either “soft” or “hard”. The impetus for their approach was due to the common practice in neuroimaging studies of *retrospectively* using this binary approach based on neurosurgical operative reports - a method that also failed to recognize areas of mixed consistency within the tumor. Their 5-point scale was based on the surgeon's ability to internally debulk the meningioma as well as the ease with which the tumor capsule could be folded after debulking. A grade of 1 corresponded to an extremely soft tumor that required only suction for internal debulking and either had no capsule or the capsule was easily folded. At the other extreme, a 5 represented a calcified, extremely firm tumor with a density that was close to that of bone and whose rigid capsule did not allow for collapse or folding. Debulking of these tumors was difficult despite the use of ultrasonic aspiration, cautery loop or sharp/mechanical dissection. Using this scale, 2 neurosurgeons independently evaluated 50 consecutive meningioma patients who underwent surgical resection in a *prospective* fashion. The authors found that this proposed grading system resulted in a high degree of user agreement between the 2 surgeons for overall tumor consistency. The authors of a very recent neuroimaging study of meningioma consistency felt that the Zada classification resulted in less variability and subjectivity compared to a neurosurgeon's qualitative assessment of “hard” vs “soft”⁵. Utilization of grading schemes such as those proposed by Zada et al.² may allow for more objective comparison of studies examining meningioma consistency.

Neuroimaging Studies of Meningioma Consistency

There have been a variety of neuroimaging approaches that have sought to predict meningioma consistency. However, there have been conflicting results and *no* universally accepted method has been established to date. These studies have used imaging approaches ranging from conventional imaging (MRI, CT) to the application of advanced MRI techniques (Table 1).

Conventional MRI

Most of the literature concerned with imaging prediction of meningioma consistency has utilized conventional MRI techniques. Table 2 provides an overview of these studies. To the best of our knowledge, the earliest of these was that by Chen et al. from our institution¹⁶. Their retrospective study of 54 patients found that hyperintensity on T2-weighted imaging (T2WI) relative to gray matter was associated with soft tumor consistency. On the other hand, T1-weighted imaging (T1WI) had no association with consistency. Indeed, multiple other studies have shown that there is an association between signal intensity on T2WI and meningioma consistency^{4,6-9,17-22}. The hyperintensity on T2WI of soft tumors may be related to higher water content while the lower signal on T2WI for hard tumors might be due to less water and more collagen and calcium content^{5,6,8,16,17,21,22}. Increased cellularity is

also thought to play a role in decreasing signal intensity on T2WI. Its interaction with fibrous content and interstitial fluid, which may increase signal intensity on T2WI, can affect signal intensity in a complex manner that could limit diagnostic accuracy of meningioma consistency prediction²³.

Most conventional MRI studies have not found that there is an association between T1WI and meningioma consistency^{4,6-8,16}. However, in one study, Hoover et al. found that meningiomas that were hyperintense on T2WI and hypointense on T1WI were more likely soft while those that were hypointense on T2WI and isointense on T1WI were more likely firm²⁰. However, they reported low sensitivity to detect firm tumors. In another study, Ortega-Porcayo et al.⁵ found that using combined T1WI and T2WI signal intensities relative to cerebral cortex were associated very soft or very hard tumors, however, this technique also suffered from low sensitivity for detecting hard tumors.

It is important to note, however, that not all studies have found an association between conventional MRI and meningioma consistency. Carpeggiani et al. examined 43 meningiomas and found no correlation between MRI signal intensity and consistency²⁴. However, the authors did feel that soft tumors tended to show hyperintensity on T2WI. Similarly, Kashimura et al. found that there was no association between T2WI and consistency²⁵. A more recent larger series from Romani et al. also found no association using T1- or T2WI, as well as FLAIR or proton density weighted imaging (PDWI)²⁶. However, several other studies have found MRI techniques other than T2WI like FLAIR and PDWI were indeed associated with consistency^{4,7,8}.

The obvious appeal of using conventional MRI lies in its practicality as imaging techniques like T2WI are routinely incorporated in standard brain MRI protocols. In its simplest form, signal intensity can be evaluated visually without the need for specialized post-processing techniques or expertise. Figures 1 and 2 demonstrate meningiomas which would be unambiguously categorized as hypo-, iso- and hyperintense on T2WI. However, it must be kept in mind that evaluation in this way is not quantitative. Reconstructed MR image intensity is based on arbitrary units and direct comparison between different acquisitions cannot be performed. Often, enhanced tissue separation via pulse sequence or hardware design is not only vendor propriety information, but also a competitive marketing advantage for the MR manufacturer. Also, because of its subjective nature, visual evaluation of signal intensity can become difficult (Figure 3). This is particularly true when heterogeneous signal intensities can appear in larger tumors^{6,24} (Figure 4). A few studies have incorporated the use of signal intensity ratios comparing the signal intensity of the meningioma relative to the cerebral cortex in order to provide a bit more objectivity to signal intensity assessment^{4,19,22}. Also, most of the studies which have found an association between consistency and conventional MRI have not reported measures of diagnostic accuracy; the results of those few that did do not appear sufficient to support its use in routine clinical practice^{4,5,20,21}.

Other factors that could be determined from conventional MRI images such as contrast enhancement on T1WI, presence of cystic components, peritumoral vasogenic edema, brain-tumor contact interface or bony appearance also have not been associated with tumor

consistency in several studies^{8,20,21,26}. Furthermore, neither angiographic characteristics nor clinical factors such as gender or age have been associated with consistency.

Diffusion MRI

Diffusion-weighted imaging (DWI) is a routinely applied functional MRI technique that depends on the microscopic mobility of water to determine tissue contrast. The apparent diffusion coefficient (ADC) provides a measure of water motion where lower ADC values will be seen in areas of restricted diffusion²⁷⁻²⁹. DWI has found application in a variety of neurologic processes, particularly for the evaluation of cerebral ischemia as well as neoplasms. While a detailed understanding of the biophysical basis of DWI on a microscopic scale remains incomplete, it is thought that DWI can provide information regarding tissue architecture at the millimeter scale by characterizing impedance of water diffusion due to cellular packing, macromolecules, membranes and intracellular elements²⁷. DWI measures water diffusion as an average of all directions while diffusion tensor imaging (DTI) is a more sophisticated 3D Gaussian model-based method that can fit both magnitude and directionality of diffusion to provide insight into the 3D microstructure of the brain parenchyma²⁷.

Although DWI is routinely performed during clinical MRI examinations, there has been relatively little work using this to predict meningioma consistency. Presently, the handful of studies that have been performed have produced contradictory results. Hoover et al. found that a meningioma's appearance on DWI or its apparent diffusion coefficient (ADC) had no association with tumor consistency while T1/T2WI did demonstrate an association²⁰. Similar findings were also seen more recently by Watanabe et al. where ADC showed no association while quantitative assessment of T2WI and FLAIR was helpful⁴. On the other hand, Yogi et al. found that hard meningiomas contained significantly lower minimum ADC values compared to soft tumors²³. Using a minimum ADC cut-off value of 0.64×10^{-3} mm²/s, they reported a sensitivity of 88%, specificity of 81% and receiver operating characteristics (ROC) analysis revealed an area under the curve (AUC) of 0.9. The authors theorized that these results were presumably related to higher cellularity and fibrous content in harder lesions, although they lacked histopathological validation. However, overlap of ADC values was still present, which could limit its use as a determinant of consistency.

In 2007, using the assumption that fibroblastic meningiomas are typically hard in consistency, Tropine et al. examined 30 meningiomas using DTI to attempt to distinguish fibroblastic histologic subtypes from other subtypes of meningioma¹⁵. Fractional anisotropy (FA) as well as geometrical shape of the diffusion tensors appeared to be able to differentiate fibroblastic meningiomas from the other types. However, these results were not compared with an actual assessment of meningioma consistency. The same year, Kashimura et al. showed that FA values for hard meningiomas were significantly higher compared to soft ones²⁵. Using an FA cut-off value of 0.3, they demonstrated sensitivity of 91% and specificity of 67%. Fibrous content has been thought to underlie a given FA value where parallel-oriented cellular membranes result in diffusion preferentially in one direction while being restricted along other axes⁴. A recent large prospective series of 110 meningiomas by Romani et al. also found that the quantitative FA value as well as signal intensity on FA and

mean diffusivity (MD) maps were predictive of meningioma consistency²⁶. Using rigorous statistical methodology with a relatively large sample size, they determined an impressive AUC of 0.9459. Interestingly, these authors also found that conventional MRI sequences such as T1WI, T2WI, FLAIR, PDWI and arterial spin labeling (ASL) perfusion had no association with consistency (see above under Conventional MRI). However, not all studies are in agreement regarding DTI; Ortega-Porcayo et al. found that FA values showed no association with consistency⁵.

MR Elastography (MRE)

MRE is an emerging advanced MRI technique that has promise to determine meningioma consistency. Meant to provide a measure of tissue stiffness akin to manual palpation, MRE has been investigated in other parts of the body³⁰. One such application is in the evaluation of hepatic fibrosis, where its use has taken the place of needle biopsies in some centers³¹. In MRE, stiffness is determined by evaluation of shear wave movement through tissue. This is accomplished by applying an external mechanical shear wave and measuring the viscoelastic properties of the tissue³². Although the use of MRE in the brain is made technically challenging by the by several factors such as the presence of the skull, a few recent publications have examined its utility in determining meningioma consistency.

In 2007, Xu et al. used MRE in a series of 6 patients, 4 patients with meningioma and 1 patient each with schwannoma and hemangiopericytoma³³. Based on intraoperative assessment, 1 meningioma as well as the schwannoma and hemangiopericytoma had hard intraoperative consistency, while 2 meningiomas had intermediate consistency and 1 meningioma had soft consistency. In this pilot study, their qualitative MRE measurements appeared to agree with intraoperative assessment of consistency. In 2013, Murphy et al. performed a prospective study of 13 meningiomas using quantitative MRE stiffness measurements where MRE measurements were significantly correlated with intraoperative qualitative assessment of tumor consistency³². The authors put forth that a major advantage of MRE is its ability to capture the full spectrum of meningioma consistency (i.e. intermediate hardness). On the other hand, conventional measurements based on T1WI and T2WI may best predict only very soft or hard tumors. A subsequent prospective study by the same group used higher-resolution MRE in an attempt to better capture the intratumoral heterogeneity of consistency³⁴. They found that higher-resolution (3 mm isotropic resolution as opposed to 4 mm performed in Murphy et al.³²), had high specificity and positive predictive value to detect heterogeneity and hard consistency. However, it had low specificity and positive predictive value to rule in homogeneity and soft consistency as well as low sensitivity to rule out hard tumors.

MR spectroscopy (MRS)

MRS is another advanced MRI functional technique that has been used clinically and in research settings for several decades for many applications, particularly brain tumors^{35,36}. Proton (¹H)-MRS is the most commonly used MRS technique and it can provide metabolic data of brain lesions by measuring metabolites such as choline and N-acetyl aspartate, which are involved in membrane synthesis/degradation and neuronal integrity, respectively. Although MRS is not a new technique, there has been very little in the literature regarding

its utility to predict meningioma consistency. In 2011, Chernov et al. evaluated 100 meningiomas using ^1H -MRS, 49 of which had intraoperative consistency data²¹. In this study, no metabolic information from ^1H -MRS had an association with meningioma consistency, while T2WI did show an association (see Table 2).

CT

CT scans are ubiquitous in clinical practice and are frequently utilized in the work-up of patients who may have an intracranial mass. As with diffusion MRI and MRS, very little has been published regarding the use of CT imaging for determining meningioma consistency. In 1979, Kendall and Pullicino reported on a series of 77 meningiomas using both visual and quantitative CT assessment of hard vs soft meningiomas³⁷. There was a significant overlap of the CT features between hard vs soft tumors, making differentiation of tumor consistency difficult^{15,32}. The more recent study by Hoover et al. referred to above also found that CT showed no association with tumor consistency²⁰. Likewise, Sitthinamsuwan et al. found that neither contrast-enhanced CT nor calcified composition on non-contrast enhanced CT was associated with consistency⁸.

Other Imaging Techniques

In addition to the imaging methods mentioned above, a couple of publications have utilized other advanced MRI techniques in the context of meningioma consistency prediction. The work by Yrjänä et al¹⁹ mentioned previously in the Conventional MRI section was one of multiple studies which demonstrated an association of T2WI with meningioma consistency. Their study, which was performed using a low-field 0.23T MRI scanner, also utilized T1-weighted dynamic contrast-enhanced (DCE) MRI. This technique employs rapid T1WI before, during and after gadolinium-based contrast agent administration in order to characterize features associated with microvascular perfusion and permeability of brain lesions such as tumors. The authors found that no DCE-MRI parameters were correlated with meningioma consistency, however, semiquantitative parameters such as time to maximum enhancement was associated with microvessel density.

Work by Yoneoka et al.³⁸ used a variation of conventional MRI called T2 reversed (T2R) imaging, which takes of advantage of high-field MRI with its high signal-to-noise ratio with gray scale reversal to improve contrast resolution³⁹. Using T2R imaging, they showed that differences in T2R heterogeneity were associated with meningioma consistency.

Magnetization transfer (MT) imaging is an advanced MRI technique that can generate unique contrast in tissues not obtainable with standard techniques. MT imaging depends on the use of off-resonance radio-frequency pulses where a magnetization transfer ratio (MTR) can be determined by measuring signal intensity with and without the off-resonance pulse^{40,41}. In 1999, Okumura applied MT imaging in meningiomas as well as a variety of other brain tumors and found that there was a significant difference in MTR between soft and hard tumors⁴².

Conclusions

This review has summarized the neuroimaging literature focused on pre-operative prediction of meningioma consistency. A diagnostically accurate and robust technique would provide critical information that can guide the neurosurgical decision-making as well as inform patients and their families regarding risks and expectations. Thus far, most work has focused on conventional MRI methods, and while there have been multiple articles showing the promise of T2WI to predict consistency, it is still not a validated method. Most studies have small sample sizes, many are retrospective and not all studies are in agreement. The actual diagnostic accuracy is not known in most studies, and in those cases where it has been reported, there is often poor sensitivity and/or specificity³². In addition, other factors such as variations in MRI scanners and acquisition parameters and methodological issues relating to qualitative vs quantitative analysis, variations in reference standards of consistency and other differences in data analysis can potentially limit the internal as well as the external validity of these studies. Future, well-powered, prospective multi-center imaging studies are needed to validate these and other neuroimaging methods. Similar issues are also concerns for more advanced MRI techniques such as diffusion MRI, MRE and MRS, where there is a relative paucity of data compared to conventional MRI methods. Of these methods, MRE and DTI appear particularly promising and deserve further rigorous examination.

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Key Points

1. There are currently no validated neuroimaging techniques to predict pre-operative meningioma consistency.
2. T2WI evaluation is relatively straightforward and may be useful. However, further validation is needed.
3. Little is known about advanced MRI techniques such as diffusion MRI, MR elastography (MRE) and MR spectroscopy (MRS). Of these techniques, MRE and DTI appear particularly promising.

Figure 1.

Multiple meningiomas showing the spectrum of signal intensities on T2WI. Axial contrast-enhanced T1WI (A) demonstrates multiple small contrast-enhancing meningiomas. The corresponding axial T2WI (B) demonstrates that the 2 meningiomas along the anterior falx show hypointensity relative to gray matter (red arrows). The meningioma along the left frontal convexity appears isointense on T2WI (yellow arrow) while a small left parietal convexity parafalcine meningioma adjacent to the superior sagittal sinus appears hyperintense on T2WI (blue arrow).

Figure 2. Hyperintense meningioma on T2WI. Axial contrast-enhanced T1WI (A) demonstrates a homogeneously enhancing left fronto-temporal convexity meningioma. Axial T2WI (B) shows that the mass appears hyperintense compared to cortex.

Figure 3.

Iso- to slightly hyperintense meningioma on T2WI. Axial contrast-enhanced T1WI (A) demonstrates a large homogeneously enhancing anterior skull-base meningioma. Axial T2WI (B) shows this mass appears iso- to slightly hyperintense compared to the cortex. The use of subjective visual criteria to classify signal intensity can be problematic in cases such as this.

Figure 4.

Heterogeneous signal intensity on T2WI in a large meningioma. Axial contrast-enhanced T1WI (A) demonstrates a large heterogeneously enhancing right sphenoid-wing meningioma growing superiorly into the temporoinsular region along with mass effect and midline shift. Axial T2WI (B) demonstrates surrounding vasogenic edema and very heterogeneous signal intensity within the mass. Subjective categorization of signal intensity in the face of marked heterogeneity can be difficult.

Table 1
Various Neuroimaging Techniques That Have Been Examined To Predict Meningioma Consistency

Conventional MRI - mainly T2WI
Diffusion MRI - DWI and DTI
MR spectroscopy
MR elastography
Dynamic contrast-enhanced MRI
Magnetization transfer MRI
Conventional CT

Table 2
Conventional MRI Studies That Have Sought To Predict Meningioma Consistency

Author	Year	No. of Cases	Association Between Conventional MRI and Consistency?	Method of MRI Signal Intensity Determination	Reference Standard for Consistency
Chen et al. ¹⁶	1992	54	Yes, T2WI	Visual	Operative report, described as “soft” or firm”
Carpegiani et al. ²⁴	1993	43	No	Visual	Operative and pathological report, described as “soft”, “hard” or “mixed”
Suzuki et al. ⁶	1994	73	Yes, T2WI	Visual	Operative report and video recordings taking into consideration surgical instruments, described as “soft”, “moderate” or “hard”
Yamaguchi et al. ⁷	1997	50	Yes, T2WI and PDWI	Visual	Intraoperative based on surgical instruments used, described as “soft”, “mixed” or “hard”
Maituri et al. ¹⁷	1997	35	Yes, T2WI	Visual	Pathological report examining histological subtype
Yrjänä et al. ¹⁹	2006	21	Yes, T2WI	Relative signal intensities were created by dividing tumor signal intensity by cortical gray matter	Intraoperative based on visual analog scale
Kashimura et al. ²⁵	2007	29	No	Visual	Intraoperative based on surgical instruments used, described as “soft” or “hard”
Kim et al. ⁹	2008	27	Yes, T2WI	Visual	Intraoperative findings, described as “friable soft” or “hard”
Hoover et al. ²⁰	2011	101	Yes, T1WI and T2WI	Visual	Operative report, described as “soft and/or suckable” or “firm and/or fibrous”
Chernov et al. ²¹	2011	49	Yes, T2WI	Visual	Intraoperative based on instruments used, described as “soft”, “mixed” or “hard”
Sithinamsuwan et al. ⁸	2012	243	Yes, T2WI and FLAIR	Visual	Intraoperative based on instruments used and video recordings, described as “soft”, “intermediate” or “hard”
Romani et al. ²⁶	2014	110	No	Visual	Intraoperative assessment based on surgical instruments used and tactile sense, described as “soft”, “medium” or “hard”
Ortega-Porcayo et al. ⁵	2015	16	Yes, T1WI and T2WI	Visual	Intraoperative assessment using Zada et al. [] grading system and dichotomous “soft” or “hard” grading
Smith et al. ²²	2015	20	Yes, T2WI	Used T2WI to create tumor to Middle cerebellar peduncle ratios	Intraoperative assessment based on Cavitron Ultrasonic Surgical Aspirator (CUSA) intensity to designate tumors as “soft”, “intermediate” or “firm”
Watanabe et al. ⁴	2015	43	Yes, T2WI, FLAIR, contrast-enhanced FIESTA	Created signal intensity ratio by comparing tumor to cerebral cortex	Intraoperative based on visual analog scale

T1WI: T1-weighted imaging

T2WI: T2-weighted imaging

FLAIR: Fluid attenuation inversion recovery imaging

PDWI: Proton density-weighted imaging

FIESTA: fast imaging employing steady-state acquisition

Data from Refs 4-9, 16, 17, 19, 20-22, 24-26.