Prediction of Mechanical Properties and Subjective Consistency of Meningiomas Using $T_1$-$T_2$ Assessment Versus Fractional Anisotropy

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- **OBJECTIVE:** This study aims to evaluate quantitatively the mechanical properties of meningiomas and their correlation with the qualitative surgeon’s assessment of consistency, as well as comparing the capability to predict tumor consistency of fractional anisotropy values calculated from the diffusion tensor imaging and $T_1/T_2$ signal intensities.

- **METHODS:** Sixteen patients with the diagnosis of intracranial meningioma were included. Fractional anisotropy values were calculated and $T_1/T_2$ assessment was performed. The qualitative assessment of the tumor consistency intraoperatively was determined by a neurosurgeon and quantitative assessment was obtained with the Warner-Bratzler mechanical test.

- **RESULTS:** Surgeon’s qualitative assessment was concordant with the cutting force obtained from the mechanical tests ($P = 0.046$). There was a high correlation between tumor consistency reported by the surgeon and $T_1/T_2$ assessment (0.622/$P = 0.01$) and a moderate correlation with cutting force (0.532/$P = 0.034$) and elasticity (0.49/$P = 0.05$). Fractional anisotropy values for hard tumors were not significantly higher than for soft tumors ($P = 0.115$). There was no significant correlation between the fractional anisotropy and mechanical measurements (0.192/$P = 0.3$). Predictions of hard consistency in meningiomas were obtained with a sensitivity of 25% and a specificity of 100% when using the $T_1/T_2$ assessment and a sensitivity of 87.5% and a specificity of 50% when using the fractional anisotropy value.

- **CONCLUSIONS:** Qualitative surgeon’s assessment was in accordance with measured mechanical properties. Fractional anisotropy value was not an independent predictor for tumor consistency and was not correlated with the mechanical tests results. $T_1/T_2$ assessment was correlated with mechanical properties and it can be used to discriminate very hard or soft tumors.

**INTRODUCTION**

Meningiomas account for approximately 20% of all intracranial tumors in men and 38% in women (5). The incidence varies between 1.85 (24), 2.3 (20), and 13.27 (6) per 100,000 individuals. In Mexico, meningiomas represent 13%–26% of the intracranial tumors (18). In the developing world, neurosurgical procedures sometimes may imply the rent of the necessary equipment at a high cost (e.g., ultrasonic aspirator). Knowing the consistency of a tumor using presurgical imaging not only may facilitate surgical planning but also may allow optimizing equipment availability. The relationship between magnetic resonance imaging (MRI) findings with tumor consistency (2, 3, 12, 26, 28) and histopathology (2-4, 8, 9, 23, 26, 28) had been contradictory in several studies. There is no actual consensus that defines the relationship among MRI, histopathology, and tumor consistency.

During the past years, minimally invasive techniques have been developed for the resection of skull base tumors. Tumor characteristics including cleavage plane, vascularity, and tumor...
consistency are crucial for the selection of minimally invasive approaches. Therefore, measuring the actual mechanical properties of meningiomas is essential to understand the correlation between imaging and tumor consistency.

The hyperintensity on T2-weighted images has been associated in some series (12, 16, 26, 28) with soft consistency in meningiomas, apparently because of the higher water content compared with hard tumors that may contain more collagen (3). New imaging modalities, like MRI elastography (19) and fractional anisotropy (FA) (15), showed promising results for tumor stiffness prediction. However, the main limitation of previous studies is the qualitative tumor consistency intraoperative assessment. Consequently, a quantitative method to evaluate consistency is necessary to validate an image method for consistency prediction.

The present study was conducted to show the correlation between the mechanical quantitative properties with the qualitative surgeon assessment of tumor consistency. Subsequently, we compared the tumor consistency prediction accuracy between the FA values calculated from the diffusion tensor imaging against T1/T2 meningioma signals relative to cerebral cortex.

METHODS

The study was designed according to the Health Law of the United States of Mexico and the Ethics Committee approval of the National Institute of Neurology and Neurosurgery “Manuel Velasco Suárez”. An analytical, longitudinal, and prospective study was conducted. We first included 20 patients with the diagnoses of meningioma but only 16 patient samples were able to complete the mechanical measurements in the first 72 hours and were confirmed as meningiomas.

All 16 patients underwent MRI using a Signa HDxt 3T system (General Electric, Medical Systems, Milwaukee, Wisconsin, USA). We obtained from each patient 43 images from the diffusion tensor imaging (spin echo planar imaging; repetition time, 10,150 milliseconds; echo time, 84.1 milliseconds; matrix, 128 × 28; gap, 2.6 mm). Diffusion gradients were obtained in 35 parallel directions (B = 800 s/mm²). FA values were acquired using the Functool Image Analysis Software (General Electric version 9.4.05a) from the computer workstation (Advantage Workstation General Electric version AW4.5.02.113.CTT: 5.X). Using this software, 3 localization techniques for the regions of interest (ROI) were chosen (Figure 1). In the first technique, 2 perpendicular vectors were drawn over the maximal diameter of the tumor. One central ROI and 2 ROIs in each positive and negative direction were placed. The average of the intensity values from the 9 ROIs was obtained (Figure 1A). In the second technique, 2 ROIs were placed at the zone of major homogeneity and hyperintensity in the FA map, excluding cystic areas, blood, or necrosis (Figure 1B). In the third technique, 1 ROI was placed at the maximal diameter of the tumor including the complete area of the tumor (Figure 1C). Image analysis of the tumor was performed from T1, T2, diffusion sequences, apparent diffusion coefficient, and gadolinium-enhancement. T1/T2 assessment was classified according to Hoover et al. (12): 1, high probability soft (hypo/hyper); 2, probably soft (iso/hyper, hypo/iso); 3, probably hard (iso/iso); and 4, high probability hard (iso/hypo). An independent observer blinded to the surgeon qualitative analysis and the mechanical properties performed the measurements and analysis of the images.

After tumor resection was performed, the surgeon was asked about tumor consistency and Simpson resection (21). The surgeon qualitative assessment of the tumor consistency was evaluated using the Zada et al. (27) meningioma consistency grading system and a dichotomous soft/hard surgeon’s qualitative scale. The Zada et al. (27) grading system considers tumor consistency and mechanical debulking required during the surgical

Figure 1. Location of diffusion tensor imaging regions of interest (ROIs) for 3 fractional anisotropy evaluation techniques. (A) 9 ROIs. (B) 2 ROIs. (C) 1 ROI of the maximal diameter of the tumor.
procedure and ranges from grade 1 (extremely soft tumors) to grade 5 (extremely firm tumors). Demographic and relevant clinical patient data, such as Karnofsky performance status scale, age, and sex, were also collected.

After the tumor was extracted, 3 cube-like samples with a square cross section of 2.5 cm and 5 mm width were carefully cut using a scalpel for further mechanical measurements. The remaining tumor was sent to the neuropathology department for histopathology diagnosis. The meningioma cut samples were immediately placed in a cooler with ice, kept at 0°C, and transferred to the mechanical tests laboratory.

The mechanical response of the meningioma specimens was analyzed using a testing machine (MTS, model Sintech 1/S, Eden Prairie, Minnesota, USA). A Warner-Bratzler cell was used, 1.016-mm thick, with a V-shaped blade, a beveled rim, and a flat plate with a 2.032-mm gap for blade passage. The blade speed was 240 mm/min. Cutting force, elastic modulus (force/velocity × time of rupture), mechanical impulse (force × time), fracturability (loss of tumor cohesiveness before or after the maximum cutting force), and mechanical strength (tumors with a cutting force >35 N were considered hard and <35 N were considered soft) were determined. An independent observer blinded to the surgeon qualitative analysis and the MRI results performed mechanical tests.

Statistical analysis was performed using IBM SPSS Statistics V20 (Armonk, New York, USA). Descriptive statistics were expressed as means ± standard deviations. Variables were analyzed using the Pearson correlation coefficients for normal samples or Spearman correlation coefficients otherwise. Nonparametric independent samples were analyzed using Kruskal-Wallis test and χ² test to analyze the relationship between T1/T2, histopathology, and Karnofsky performance status scale. The FA values were compared according to tumor consistency and the mechanical properties using the Mann-Whitney U test. Statistical significance was set at a probability value less than 0.05.

RESULTS

Imagenologic, surgical, mechanical, and histopathologic properties of 16 meningiomas were studied. Demographic data are shown in Table 1. All the patients were Hispanic, with a slightly higher percentage of women (62.5%) and a ratio of male-to-female of 1.4:1. Histopathologically, 81% of meningiomas were grade 1 and 19% were grade II. Forty-four percent of meningiomas were localized in the skull base and 56% in the cranial vault. Surgical technique was debulking and resection in 14 patients and en bloc resection in 2 patients. Values for consistency, histopathology, T1/T2, relationship, anisotropy factor, and cutting force are shown in Table 2.

### Table 1. Location, Demographic Data, and Histopathology

<table>
<thead>
<tr>
<th>Tumor Location</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Histopathology</th>
<th>Simpson Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sphenoid wing clinoidal</td>
<td>F</td>
<td>26</td>
<td>Meningothelial</td>
<td>2</td>
</tr>
<tr>
<td>Sphenoid wing clinoidal</td>
<td>M</td>
<td>37</td>
<td>Meningothelial</td>
<td>4</td>
</tr>
<tr>
<td>Sphenoid wing clinoidal</td>
<td>M</td>
<td>64</td>
<td>Transitional</td>
<td>3</td>
</tr>
<tr>
<td>Frontal convexity</td>
<td>M</td>
<td>61</td>
<td>Fibroblastic</td>
<td>1</td>
</tr>
<tr>
<td>Parietal convexity</td>
<td>M</td>
<td>66</td>
<td>Atypical</td>
<td>2</td>
</tr>
<tr>
<td>Falciile middle third.</td>
<td>F</td>
<td>40</td>
<td>Transitional</td>
<td>2</td>
</tr>
<tr>
<td>Falciile middle third.</td>
<td>F</td>
<td>59</td>
<td>Transitional</td>
<td>1</td>
</tr>
<tr>
<td>Intraventricular</td>
<td>F</td>
<td>62</td>
<td>Fibroblastic</td>
<td>2</td>
</tr>
<tr>
<td>Parasagittal middle third.</td>
<td>F</td>
<td>16</td>
<td>Meningothelial</td>
<td>1</td>
</tr>
<tr>
<td>Parasagittal middle third.</td>
<td>F</td>
<td>51</td>
<td>Fibroblastic</td>
<td>2</td>
</tr>
<tr>
<td>Parasagittal posterior third.</td>
<td>F</td>
<td>52</td>
<td>Atypical</td>
<td>2</td>
</tr>
<tr>
<td>Petrous</td>
<td>F</td>
<td>66</td>
<td>Atypical</td>
<td>2</td>
</tr>
<tr>
<td>Planum sphenoidale</td>
<td>M</td>
<td>22</td>
<td>Transitional</td>
<td>2</td>
</tr>
<tr>
<td>Sphenoid wing pterional</td>
<td>F</td>
<td>76</td>
<td>Meningothelial</td>
<td>1</td>
</tr>
<tr>
<td>Tentorial</td>
<td>F</td>
<td>52</td>
<td>Transitional</td>
<td>2</td>
</tr>
<tr>
<td>Tentorial</td>
<td>M</td>
<td>28</td>
<td>Meningothelial</td>
<td>3</td>
</tr>
</tbody>
</table>

### Mechanical Tests

The cutting force showed a high correlation coefficient (CC) (0.653/P = 0.034) with the consistency grades assigned by the surgeon according to the Zada et al. (27) scale. Differences in cutting force were statistically significant between groups 3 (average consistency) and 5 (extremely firm consistency) (P = 0.04) and also between soft and hard tumors (P = 0.046) (Figure 2). Meningiomas with a mechanical cutting force >35 N had less fracturability (P = 0.01). Most of the soft tumors (cutting force, <35 N) lost cohesiveness before or after tumor rupture with the Warner-Bratzler cell. Mechanical impulse had a higher CC with tumor consistency evaluated by the surgeon.
Impulse and elastic modulus were statistically higher for the hardest tumors reported by the surgeon ($P = 0.04$). Tumor Consistency Prediction Using MRI ($T_1/T_2$ vs. Fractional Anisotropy)

There was a high correlation between tumor consistency reported by the surgeon and $T_1/T_2$ assessment ($0.623/P = 0.01$; Figure 3) and a moderate correlation with cutting force ($0.532/P = 0.034$) and elastic modulus ($0.49/P = 0.05$). When we used the hard/soft grading system, the $T_1/T_2$ assessment had a sensitivity of 25% and a specificity of 100% for a hard tumor, with a positive predictive value (PPV) of 100% and a negative predictive value (NPV) of 100%.

### Table 2. Relationship Between Consistency, Histopathology, $T_1/T_2$ Assessment, Fractional Anisotropy Value, and Cutting Force

<table>
<thead>
<tr>
<th>Surgeon Evaluation of Tumor Consistency</th>
<th>Histopathology</th>
<th>$T_1/T_2$ Assessment</th>
<th>Fractional Anisotropy Value</th>
<th>Cutting Force (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 (soft)</td>
<td>Meningothelial</td>
<td>1/High probability soft Hypo/Hyper</td>
<td>0.46</td>
<td>0.21</td>
</tr>
<tr>
<td>Grade 2 (soft)</td>
<td>Transitional</td>
<td>1/High probability soft Hypo/Hyper</td>
<td>0.174</td>
<td>3.82</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Fibroblastic</td>
<td>3/Probably hard Iso/Iso</td>
<td>0.205</td>
<td>6.54</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Transitional</td>
<td>2/Probably soft Iso/Hyper</td>
<td>0.362</td>
<td>9.15</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Atypical</td>
<td>1/High probability soft Hypo/Hyper</td>
<td>0.205</td>
<td>17.43</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Atypical</td>
<td>2/Probably soft Hypo/Iso</td>
<td>0.55</td>
<td>18.48</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Transitional</td>
<td>3/Probably hard Iso/Iso</td>
<td>0.268</td>
<td>25.54</td>
</tr>
<tr>
<td>Grade 3 (average)</td>
<td>Meningothelial</td>
<td>2/Probably soft Hypo/Iso</td>
<td>0.333</td>
<td>33.24</td>
</tr>
<tr>
<td>Grade 4 (firm)</td>
<td>Fibroblastic</td>
<td>2/Probably soft Iso/Hyper</td>
<td>0.346</td>
<td>4.96</td>
</tr>
<tr>
<td>Grade 4 (firm)</td>
<td>Fibroblastic</td>
<td>2/Probably soft Hypo/Iso</td>
<td>0.392</td>
<td>10.32</td>
</tr>
<tr>
<td>Grade 4 (firm)</td>
<td>Meningothelial</td>
<td>3/Probably hard Iso/Iso</td>
<td>0.186</td>
<td>13.46</td>
</tr>
<tr>
<td>Grade 4 (firm)</td>
<td>Transitional</td>
<td>3/Probably hard Iso/Iso</td>
<td>0.354</td>
<td>37.16</td>
</tr>
<tr>
<td>Grade 4 (firm)</td>
<td>Atypical</td>
<td>1/High probability soft Hypo/Hyper</td>
<td>0.318</td>
<td>70.56</td>
</tr>
<tr>
<td>Grade 5 (extremely firm)</td>
<td>Meningothelial</td>
<td>4/High probability hard Iso/Hypo</td>
<td>0.453</td>
<td>54.25</td>
</tr>
<tr>
<td>Grade 5 (extremely firm)</td>
<td>Meningothelial</td>
<td>4/High probability hard Iso/Hypo</td>
<td>0.464</td>
<td>76.041</td>
</tr>
</tbody>
</table>

The cutting force is directly proportional to the tumor consistency reported by the surgeon. (0.549/P = 0.028).

![Figure 2](image1.png)

**Figure 2.** Graph showing the relation between the subjective surgeon’s assessment and the objective quantitative assessment ($P = 0.04$). The cutting force is directly proportional to the tumor consistency reported by the surgeon.

![Figure 3](image2.png)

**Figure 3.** Plot showing tumor consistency prediction using $T_1/T_2$ assessment. Notice that tumors grade 5 (extremely hard) had a specificity of 100% using the $T_1/T_2$ assessment. Scatter along the x-axis is random and for display purposes.
sensitivity and specificity of FA value above 0.3 for predicting a hard tumor were 88% and 43% with a positive predictive value and negative predictive value of 64% and 75%, respectively. FA values for hard meningiomas were not significantly higher than for soft meningiomas (P = 0.115).

Histopathology, Surgical Time, and Prognosis
There was no significant correlation between histopathology and tumor consistency. FA and T1/T2 assessment could not predict the tumor histopathology. The hardest tumors were meningothelial.

The surgical time was correlated with localization (0.477/P = 0.062). Skull base tumors required longer average surgical times (343 vs. 235 minutes). Extension of the surgical resection measured with the Simpson scale and the Karnofsky prognosis scale did not have a significant correlation with tumor consistency.

DISCUSSION
Meningioma consistency is a key characteristic for preoperative planning and a valuable tool in skull base meningiomas in which cranial nerves and arteries are encased (26). Safe patient selection for minimally invasive approaches could be guided based on cleavage plane, vascularity, and tumor consistency. At present, there are no reliable imaging modalities to predict consistency and no quantitative method to measure it.

To our knowledge, this is the first study in which mechanical properties of the meningiomas are studied. We applied a mechanical shear method, used in other areas like biomechanics (17) and food engineering (1, 7, 13), to measure cutting force, mechanical impulse, elastic modulus, and fracturability of meningiomas. The formula used for the elastic modulus in the present study does not represent the complete shear elasticity modulus, as it was impossible to measure the complete deformability because the shear test is destructive. However, the hardest tumors had a higher elastic modulus (P = 0.04), which may represent a major difficulty for aspiration and a greater resistance to rupture. The measured mechanical properties of the meningiomas gave objectivity to the consistency reported by the surgeon. We found a statistically significant correlation between the measured cutting force and the tumor consistency evaluated using qualitative classifications (hard/soft, P = 0.046; Zada et al. (27) 5 grades, P = 0.04). However, the hard/soft classification has a variability and subjectivity that is well improved with the Zada et al. (27) consistency grading system, which includes the meningioma general description, capsule characteristics, and instrumentation used for internal debulking.

Some investigators (3, 16, 25, 26, 28) reported that hyperintensity in T2 was associated with a soft consistency and an invasive behavior. We found that 2 of the 3 atypical tumors reported in the present case series were hyperintense in T2, but we did not find a clear correlation with tumor consistency and meningioma histopathology using only T2. In addition, the correlation between signal intensity on MRI and meningioma consistency is controversial (2, 3, 16, 25, 26, 28). T1/T2 assessment had been proposed by Hoover et al. (12) as an accurate method to predict consistency in selected patients. The probability of a soft meningioma is high when the tumor is hypointense in T1 and hyperintense in T2, and a hard meningioma is expected if it is isointense in T1 and hypointense in T2. Accordingly, in our results

(higher than for soft tumors (P = 0.115). There was no significant correlation between the FA and mechanical properties of the meningiomas: cutting force (0.192/P = 0.3), mechanical impulse (0.087/P = 0.749), elastic modulus (0.110/P = 0.684), and fracturability (0.397/P = 0.69) (Figure 5).

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we found a sensitivity of 25% and a specificity of 100% for predicting a hard tumor with a PPV of 100%. T1/T2 assessment also correlated with both grading tumor consistency systems and with the mechanical properties. However, most meningiomas do not have “high probability” signal intensities (iso-hypo/hard—hypo-hyper/soft), which explains the low sensitivity of the test.

Kashimura et al. (15) were the first to report that the FA was statistically higher in tumors evaluated as hard by a surgeon. Therefore, the FA value was considered as a significant independent predictor factor for tumor consistency. After investigators set cutoff points for hard meningiomas (FA = 0.3), sensitivity and specificity of FA values for detecting a hard tumor were 91% and 67%, respectively. However, in our study the FA values reach a sensitivity of 87.5%, more than the T1/T2 assessment, but with a lower specificity of only 50%, which increases to 87.5% when we used the cutoff point of 0.42, but not as high as the 100% of specificity and PPV previously reported (15). The main limitations of the Kashimura et al. (15) study were the qualitative intraoperative assessment of tumor consistency (hard/soft) and the placement of only 1 ROI in the central area of the tumor. We approach these limitations by using a more objective 5 grades consistency scale scoring system, 3 techniques for the ROI placement and quantitative mechanical measurements. In our analyses, FA values for hard meningiomas were not significantly higher than for soft meningiomas (P = 0.115). Although there was a tendency of hard tumors to show higher FA values, we did not find the FA value to be an independent predictor for tumor consistency. The problem with FA is the variability of this value inside a tumor because of the heterogeneity of meningiomas. We used 3 techniques (Figure 1) for its measurement, whether we used 9 ROIs or 1 ROI we got heterogeneous results without correlation with tumor consistency. We found the best results when we used the 2 ROI technique, in which 2 ROIs were placed at the zone of major homogeneity and hyperintensity in the FA map. However, this technique was to our interpretation, the more subjective and less reliable of the 3 measurement techniques.

FA and T1/T2 assessment can only accurately differentiate very hard from extremely soft meningiomas. Intermediate consistency grades 3 and 4 meningiomas were not accurately predicted (Figure 3). Magnetic resonance elastography is a promising technique to study viscoelastic brain properties (11) and stiffness (19) of hard, intermediate, and soft meningiomas. Using this technique Murphy et al. (19) demonstrated that meningioma stiffness and the ratio of tumor stiffness to surrounding brain tissue stiffness significantly correlates with surgeon’s qualitative assessment (5 grades), with a promising sensitivity and specificity of 85.7% and 89%, respectively. However, no quantitative assessment of tumor stiffness was performed.

Carpeggiani et al. (2) reported that the prevalence of hard tumors is statistically significant within the fibroblastic subtypes; however, the studies to predict histopathology with MRI have been contradictory (2, 4, 10, 14, 16, 22, 29). In our series the hardest tumors were meningothelial and not fibroblastic. There was no
REFERENCES


ACKNOWLEDGMENTS

Authors are in debt of the surgical, nursing, and anaesthesiology staff of the National Institute of Neurology and Neurosurgery “Manuel Velasco Suárez.” Thanks to Karla Ortega for proofreading this article.


Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.