Histological factors contributing to the viscoelasticity of intracranial meningiomas analyzed by Atomic Force Microscopy

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Introduction

Meningiomas are the most frequent primary intracranial tumor[1]. They cause symptoms that can lead to a surgery.

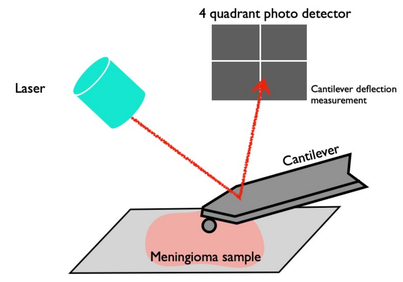
The viscoelasticity of a meningioma is a determining factor in the ease of resection, particularly in relation to critical structures such as vessels and cranial nerves.

Atomic Force Microscope (AFM) is increasingly being used to analyze human tissues, such as tumors. It is a recent tool to find the most precise tumor's consistency.

Histopathological factors impacting meningiomas' viscoelasticity have not been studied.

A better understanding of the histopathological factors influencing meningiomas' viscoelasticity can lead to the prediction of its consistency according to neuroimaging.

Figure 1: Schematic representation of AFM tissue viscoelasticity measurements



Objectives

1) Establish histopathological factors influencing meningiomas' viscoelasticity
2) Determine if the meningiomas' consistency influenced the patients' prognosis

Methods

This is a prospective study using meningioma specimens from a tumor bank (-80°C). All adults' intracranial meningiomas that have not undergone embolization or radiation were included. The median viscoelasticity obtained by Atomic Force Microscopy (3 to 13 measures for each meningioma) was correlated to the collagen percentage, with Masson's trichrome stain; the vascularity percentage, with CD31 as a marker for endothelial cells; the elastin percentage, with Verhoeff stain; the reticulin percentage with Laidlaw stain, and the mean cellularity, assessed by counting cells in a 400X field. The viscoelasticity was calculated using the Hertz modulus:

$$F = \frac{4}{3}\left(\frac{E}{1-\mu^2}\right)\sqrt{R}\delta^{3/2}$$

where F is the force, E is the Young modulus, μ is the Poisson's ratio (0.5), R is the cantilever's radius, and δ the indentation depth. Meningiomas' viscoelasticity obtained with Atomic Force Microscopy was correlated with clinical data, including intraoperative complications, extent of surgical resection and progression-free-survival. Statistical analysis was conducted using student-t test, chi square, linear regression, logistic regression and Kaplan-Meier.

Figure 2: Example of a slide prepared for the analysis of the meningioma with AFM

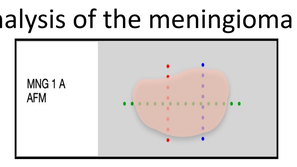


Figure 3: Photo of the AFM used in our study

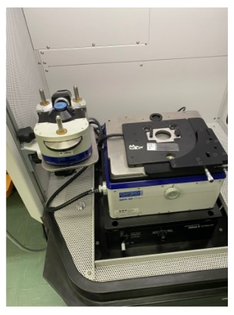
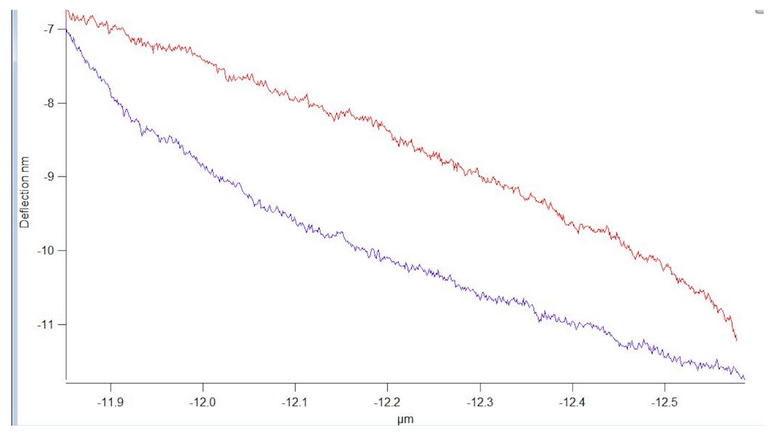


Figure 4: Example of a graph with curves obtained by AFM



Results

Atomic Force Microscope Data

Thirty-six meningiomas were analyzed.

The mean viscoelasticity for all the tumors was 5.336 kPa (0.483 kPa to 23.881 kPa). Two groups were formed according to this mean viscoelasticity. All meningiomas having a lower viscoelasticity than 5.336 kPa were selected in the «soft» group, while all meningiomas with a higher viscoelasticity than 5.336 kPa composed the «hard» group of tumors.

Demographic Data

The mean age at surgery for the soft meningiomas was 60.38 years old, while the mean age for the hard group was 62.81 years old (p = 0.607). There were 35.1% of men and 64.9 % of women in the study. The mean elasticity of men's meningiomas was 4.871 kPa versus 5.568 kPa for women's meningiomas (p = 0.692).

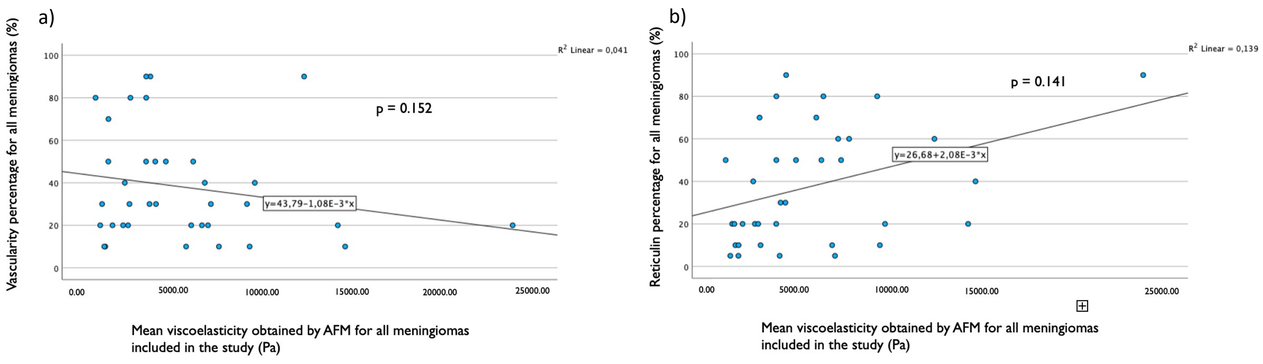
Histology Data

Table 1: Comparison of Histological Data for Both Soft and Hard Tumors' Groups

	Surface area (mm²)	Mean cellularity (cells/mm²)	Mean vascularity (%)	Mean collagen (%)	Mean elastin (%)	Mean reticulin (%)
Soft	25.43	4096	45.24	37.14	9.29	31.19
Hard	17.47	3865	28.00	40.00	8.00	47.00
p value	0.058	0.538	0.023	0.374	0.356	0.043

The mean elasticity of meningiomas was lower in WHO grade 2 than in WHO grade 1 (3004.46 vs 5898.27, p=0.028).

Figure 5: Linear Regression of Mean Meningiomas' Viscoelasticity Depending on a) Vascularity and b) Reticulin



Survival Data

The surgical time was shorter for meningiomas in the hard group, but no statistical significance was found (326 minutes in the hard group vs 431 minutes in the soft group, p= 0.331). Hospitalization time was similar between both groups (7,05 days in soft group vs 5.71 days in hard group, p=0.533). The blood loss was increased in the soft group, with no statistical significance (581 mL in the soft group vs 363 mL in the hard group, p=0.226). Forty percent of patients in the hard group had surgical complications, while 19% of patients in the soft group had complications (p=0.26). The mean follow-up period for both groups was 39 months (36.4 months in the soft group vs 42.4 months in the hard group, p=0.469). Only one patient in the hard group had a recurrence, none in the soft group.

Conclusion

The mean viscoelasticity of 5.336 kPa for all tumors was expected, as Cieśluk M and al.[2] have found in their study. The soft group having a higher vascularity percentage was predictable, as Rutland and al.[3] discovered in their study. In our study, reticulin had a greater association with meningiomas' viscoelasticity, which is a new discovery. We expected collagen to have a strong correlation with our tumors' consistency, as Li J and al.[4] proposed in their study, which was not the case in ours. AFM being a very precise tool to analyse tumors' viscoelasticity, the other histological factors might have not been correlated in our study since the meningiomas have a large intrinsic variability.

We found a strong correlation between WHO grade 2 meningiomas and softer viscoelasticity, which is a new discovery.

Since our study included only 36 tumors and the mean follow-up period was short (39 months), we expected the survival data to not be statistically significant between the soft and the hard group. More meningiomas need to be included in a further study. A longer follow-up time would be better to objectify a statistically significant difference between the two groups.

References
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