ELUCIDATING THE MECHANICAL SIGNATURE OF DIFFERENT BRAIN LESIONS USING DYNAMIC NANOINDENTATION

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Introduction

The mechanism of human brain lesions, their growth, heterogeneity, and resistance to medications is driven by the dynamic interaction of mechanical cues between the diseased tissues and their surroundings. Elucidating the impact of these mechanical parameters on different brain lesions could lead to developing novel diagnostic techniques [1,2]. This study investigates the viscoelastic properties of healthy and diseased brain tissues, including epilepsy, glioma (malignant tumour) and meningioma (benign tumour), using dynamic nanoindentation in terms of storage and loss modulus.

Methods

The brain samples were obtained from two subjects diagnosed with glioma (5M and 48M) and two diagnosed with meningioma (27F and 52M). Two samples (healthy and diseased) were collected from the surgical excision of an epilepsy patient (19M). The Institute Ethics Committee (Ref. no. IEC-842/07.08.2020) approved this study; written consent was obtained from all subjects. We used iNano (KLA Inc. USA) nanoindenter equipped with a 100 µm diameter flat end indenter, 50 mN actuator and a temperature-specific liquid bath chamber. It utilises the continuous stiffness measurement method to calculate the viscoelastic parameters [3]. All the samples were tested within 3 hours post-operative surgery at physiological body temperature (37°C) submerged in normal saline solution. The Oliver-Pharr method was used to calculate the storage G' and loss modulus G".

$$K_s = \left[\frac{F_0}{x_0}\cos\phi\right]_{\text{in-contact}} - \left[\frac{F_0}{x_0}\cos\phi\right]_{\text{out-of-contact}}$$

$$D_s\omega = \left[\frac{F_0}{x_0}\sin\phi\right]_{\text{in-contact}} - \left[\frac{F_0}{x_0}\sin\phi\right]_{\text{out-of-contact}}$$

$$G' = \frac{K_s(1-\nu)}{2d};\ G'' = \frac{D_s\omega(1-\nu)}{2d}$$

where K_s is contact stiffness, $D_s\omega$ is contact damping, F_0 is applied oscillating force amplitude, x_0 is the recorded oscillating displacement amplitude, φ is the phase lag between force and displacement, ν is Poisson's ratio (considered 0.5), and d is the indenter diameter.

Results

We conducted dynamic nanoindentation on human brain samples, including those from patients with epilepsy, glioma, and meningioma. Our measure reported the diseased tissues to be stiffer than healthy tissue. The storage moduli of epilepsy, glioma and meningioma tissue were 300%, 64%, and 18% higher, whereas loss moduli were 354%, 46%, and 10% higher than healthy tissue, respectively.

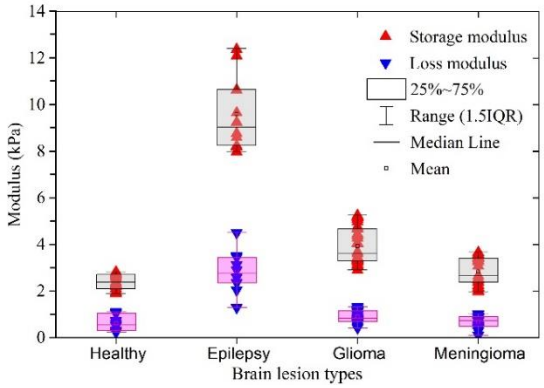

Figure 1: Viscoelastic parameters of healthy and diseased brain tissues.

Discussion

This study evaluates the viscoelastic properties of healthy and diseased brain tissue and found significant differences in their stiffness. The primary cause of these differences is the microstructure alteration of diseased tissue. Overexpression of high molecular polysaccharide (hyaluronic acid) in glioma cells, procollagen molecules secreted to produce the fibrous structure in me, and abnormal arrangement of neurons in epilepsy make them stiffer than healthy brain tissues [1,4]. These findings will provide a deeper understanding of the mechanical behaviour of brain tumours and have the potential for developing improved diagnostic and treatment strategies based on mechanical signatures. However, further research with larger sample sizes is required to generalise these findings. Additionally, the use of in-vitro mechanical markers, combined with machine learning-based approaches, could potentially classify brain tumours with greater accuracy.

References

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