AN IMAGE-BASED METHODOLOGY TO QUANTIFY ULTRASONIC CELL DEFORMATION

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Background

Ultrasonic surgical cutting tools are an emerging technology which are becoming increasing popular in the surgical arena and display several benefits over traditional devices. They utilise ultrasonic vibrations to cut biological tissues and have shown to have enhanced precision and improved healing times [1, 2]. The response to these tools at a cellular level, however, is largely unexplored. This is likely due to difficulties in studying the incision site and observing probe-tissue interactions, but also challenges around quantifying the strains cells experience during cutting and applying this to them in a controlled and clinically relevant manner. An insight into cell responses could lead to a deeper understanding of the tool-tissue interactions and help inform device design and implementation. Furthermore, ultrasonic vibrations are known to stimulate therapeutic biological effects via mechanobiological pathways in damaged tissues [3]. With further knowledge and understanding of the effects of ultrasound on cells, its regenerative capabilities could be applied to cutting devices to further facilitate tissue healing post-incision.

Recent Advances

In this work, we utilise an image-based ultrasonic shaking (IBUS) test to examine ultrasonic cell deformation and their resultant biological response [4]. Practically, this involves culturing cells on a PMMA strip attached to a 20 kHz sonotrode. The PMMA substrate was specifically tuned to create a standing wave during ultrasonic excitation resulting an area of large strain in the centre of the specimen. This enables pre-calibration prior to imaging, creating a test with scalable strain values and ensuring relevant stimulation. Cells are illuminated under a microscope with a phase contrast objective using a pulsed laser. They are then imaged using an ultra-high-speed camera whilst being ultrasonically vibrated, enabling real-time visualisation of cells while they are excited. An example of the images obtained can be seen in figure 1.

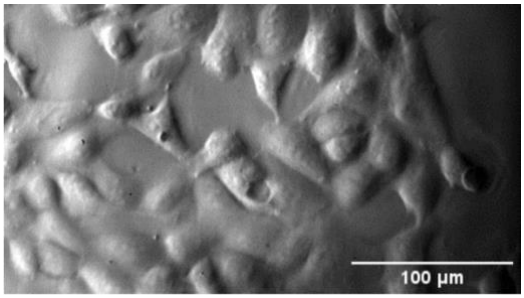

Figure 1: Static image of a group of cells obtained using the IBUS test

Results we have obtained thus far show images of cells deforming with the PMMA substrate with some visible internal cell components. We have shown that digital image correlation (DIC) analysis can be used to quantify the cell displacement and deformation as shown in fig 2.

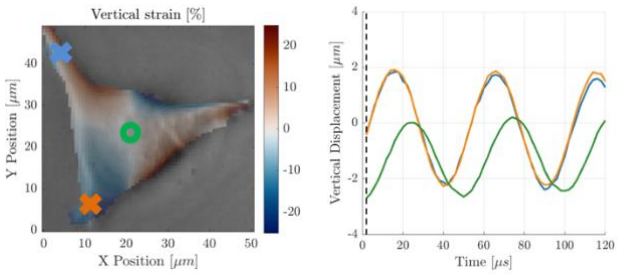

Figure 2: Image of a cell obtained during excitation that has been analysed using DIC. The left plot shows the vertical deformation map and the right plot shows vertical displacement time history of the three marked points.

Future directions

Future work involves imaging with fluorescent staining to highlight internal cell components and understand their role in cell deformation. Extraction of cells post-excitation will also be done to undertake biological assays and understand the biochemical implications of deformation. This will allow us to begin to understand the mechanobiological implications of ultrasound, and specifically ultrasonic surgical cutting tools, on cells. Finally, there is potential for this data to be compiled to inform a mechanical cell model that could be used to study cell mechanics.

References

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Acknowledgements

The authors would like to acknowledge the funding by the Engineering and Physical Sciences Research Council (EPSRC) under the grant number of EP/R045291/1 (Surgery enabled by ultrasonics).