Title: The effect of solid stresses in tumour growth

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Project Background

Novel research is highlighting the important role that biomechanics play in tumour development, complementing the latter's well documented biochemical underpinnings. Biophysical cues such as tissue rigidity have already been established as regulators of tumour cell behaviour. However, mechanical stress has recently been found to elicit far-reaching effects on tumour progression that are distinct from other cues. This project contributes to efforts to elucidate the underlying mechanisms by which mechanical stress evolution influences tumour progression.

Project Aims

Due to a lack of suitable techniques, studies investigating the effect of mechanical stresses on tumour behaviour have not been capable of accurately characterising the tumour-induced stress field in vivo. Apart from a consequent lack of an accurate experimental basis, this also precludes the correlation of stress evolution with specific tumourigenic events such as the onset of metastasis. As such, the aim of this project is to develop a novel technique that enables the accurate and dynamic measurement of mechanical stresses originating in both the fluid and solid domain of a tumour. Techniques may range from mechanical to optics based, or others.

Research Plan

The applicant is to develop an in-depth knowledge of the origins of elevated mechanical stresses observed in tumours. Subsequently, current methods of quantifying tumour-induced stresses are to be reviewed so as to identify limitations in the state of the art. Based on these findings, the applicant is to design and develop a novel technique which addresses these shortcomings. As part of the design process, the stress measurement technique is also to be validated and ultimately demonstrate its ability to map intratumoural stresses with unprecedented accuracy.

Skills - skills that the student will develop during the project (

Design of measurement tools and experimental protocols are the basis of this project. The applicant is offered the opportunity to work within a highly interdisciplinary field in which engineering skills are applied to cancer research. As such, the project will involve communication of complex ideas to starkly different target audiences. In addition to developing the ability to quickly assimilate new concepts, the applicant is also expected to demonstrate strong problem solving and critical thinking skills in a laboratory environment.

References

Tumour-induced stress background:

- Jain et al (2014) Annual review of biomedical engineering. The Role of Mechanical Forces in Tumor Growth and Therapy

  http://www.annualreviews.org/doi/abs/10.1146/annurev-bioeng-071813-105259

Current stress measurement techniques:

- Stylianopoulos et al (2012) PNAS. Causes, consequences, and remedies for growth-induced solid stress in murine and human tumors http://www.pnas.org/content/109/38/15101.full
- Nia et al (2016) Nature Biomedical Engineering. Solid stress and elastic energy as measures of tumour mechanopathology https://www.nature.com/articles/s41551-016-0004
- Nieskoski et al (2017) ASME. Separation of Solid Stress From Interstitial Fluid Pressure in Pancreas Cancer Correlates With Collagen Area Fraction http://biomechanical.asmedigitalcollection.asme.org/article.aspx?articleid=2618331

Prakash et al 2016 Convergent Science Physical Oncology. Physicochemical modeling of tumorigenic homeorhesis: a system-dynamics interpretation of computer simulations. http://iopscience.iop.org/article/10.1088/2057-1739/2/3/035001?fromSearchPage=true

Lowengrub et al 2010. NonLinearity Nonlinear modelling of cancer: bridging the gap between cells and tumours

http://iopscience.iop.org/article/10.1088/0951-7715/23/1/R01/pdf