Multi-photon Microscopy for Characterization of Renal Cell Carcinoma Pseudocapsule: Implications for Tumour Enucleation

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INTRODUCTION
RCC Tumour Enucleation depends on dissection along its fibrous Pseudocapsule (PC), an Extracellular Matrix (ECM) structure. Collagen, being an abundant ECM component, is the strongest and hardest to penetrate by tumour cells. During tumour expansion, collagen remodeling and reorientation occurs, with increased collagen deposition and density for mechanical strength to resist tumour growth. Degradation of collagen has been shown necessary for tumour invasion.¹ The presence and integrity of PCs have been associated with improved overall survival in RCC.²,³ Multi-Photon Microscopy (MPM) has been successfully employed as a stain-free imaging technique for collagen quantification in other biological tissues.⁴

OBJECTIVES
To use Multi-Photon Microscopy to quantify the collagen content and structure of the PC. The study hypothesised that the PC is not a homogenous layer and has quantifiable intra-tumoral variation.

METHODS

RESULTS
Table 1 shows the baseline patient characteristics. The mean variation difference in PC thickness between the thickest and thinnest PC areas (ROI 2) was 5.9 +/- 1.21mm. In the thickest areas of the PC, collagen content was higher compared to the thinnest areas. Mean Collagen Area Ratio was higher in the thickest (29.9%, 95% CI: 19.9-39.9%) compared to the thinnest areas (19.5%, 95% CI: 17.2-21.8%) of the PC (p=0.12). Mean Collagen Fibre Density was also higher in the thickest (34.0%, 95% CI: 25.2-42.8%) compared to the thinnest areas (24.8%, 95% CI: 21.1-28.6%) of the PC (p=0.09). Compared to the thickest PC areas, the thinnest PC areas showed greater degrees of collagen cross-linking and collagen network complexity. Mean Collagen Reticulation Index was higher in the thickest PC areas (3.54, 95% CI: 2.79-4.29) compared to the thinnest (2.88, 95% CI: 2.15-3.60) PC areas (p=0.13). However, these differences did not reach statistical significance.

CONCLUSIONS
For oncological safety, it is important for surgeons to be aware that Pseudocapsules at the tumour-parenchyma interface are not homogenous during Tumour Enucleation. With MPM, we can quantify PC collagen content and structure objectively, as an indicator of mechanical strength. As a proof-of-concept study, these findings will lead to larger studies using MPM to compare PCs between tumours of different subtypes and nuclear grade, with the long-term goal of correlating with survival outcomes.

REFERENCES