The structure of the human glomerulus.

We recently discovered striking differences between the microvascular structure of the kidneys of large animals (including humans) compared with small animals. As the size of the glomerulus increases with kidney size in larger species (e.g. human, pig), the blood vessels within the glomerulus form specialised structures that allow distribution of flow. We hypothesise that these enable pressure to distribute allowing control of blood distribution to microvessels in the many lobes of these large glomeruli. Mathematical modelling of these vascular chambers and the blood flow and pressure will allow us to determine whether these manifolds regulate the distribution of blood flow in large glomeruli. These structures are not present in rat and mouse kidneys but glomerular physiology is based on these animals, differences in the regulation of glomerular flow and pressure between large animals and small animals has major implications for understanding the physiology of glomerular filtration and glomerular function and dysfunction. The project will make use of normal human donor kidneys that do not get used for transplantation, and the kidneys of pig, horse and sheep. Serial section, focussed ion beam, and scanning block face electron microscopy of perfusion fixed kidney segments will be used to describe the macrovasculature of these kidneys by defining vessel diameter and connectivity. The microvasculatures will be further investigated using Confocal and two photon microscopy. The micromechanics of the vessel walls will be modelled from image analysis of the structural data and fluid movements through these macro and microvasculatures will be modelled using computational fluid dynamics.

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Band: Low Cost research

Theme: Mathematical modelling of Biological Systems.

Keywords. Fluid dynamics, mathematical modelling, electron microscopy