ABSTRACT

The three-dimensional microarchitecture of the mammalian kidney is of keen interest in the fields of cell biology and biomedical engineering as it plays a crucial role in renal function. This study presents a novel approach to the automatic tracking of individual nephrons through three-dimensional histological image sets of mouse and rat kidneys. The image database forms part of a previous study carried out at the University of Aarhus, Denmark. The previous study involved manually tracking a few hundred nephrons through the image sets in order to explore the renal microarchitecture, the results of which forms the gold standard for this study. The purpose of the current research is to develop methods which contribute towards creating an automated, intelligent system as a standard tool for such image sets. This would reduce the excessive time and human effort previously required for the tracking task, enabling a larger sample of nephrons to be tracked. It would also be desirable, in future, to explore the renal microstructure of various species and diseased specimens.

The developed algorithm is robust, able to isolate closely packed nephrons and track their convoluted paths despite a number of non-ideal conditions such as local image distortions, artefacts and connective tissue interference. The system consists of initial image pre-processing steps such as background removal, adaptive histogram equalisation and image segmentation. A feature extraction stage achieves data abstraction and information concentration by extracting shape descriptors, radial shape profiles and key coordinates for each nephron cross-section. A custom graph-based tracking algorithm is implemented to track the nephrons using the extracted coordinates. A rule-base and machine learning algorithms including an Artificial Neural Network and Support Vector Machine are used to evaluate the shape features and other information to validate the algorithm's results through each of its iterations.

The validation steps prove to be highly effective in rejecting incorrect tracking moves, with the rule-base having greater than 90% accuracy and the Artificial Neural Network and Support Vector Machine both producing 93% classification accuracies. Comparison of a selection of automatically and manually tracked nephrons yielded results of 95% accuracy and 98% tracking extent for the proximal convoluted tubule, proximal straight tubule and ascending thick limb of the loop of Henle. The ascending and descending thin limbs of the loop of Henle pose a challenge, having low accuracy and low tracking extent due to the low resolution, narrow diameter and high density of cross-sections in the inner medulla. Limited manual intervention is proposed as a solution to these limitations, enabling full nephron paths to be obtained with an average of 17 manual corrections per mouse nephron and 58 manual corrections per rat nephron.

The developed semi-automatic system saves a considerable amount of time and effort in comparison with the manual task. Furthermore, the developed methodology forms a foundation for future development towards a fully automated tracking system for nephrons.