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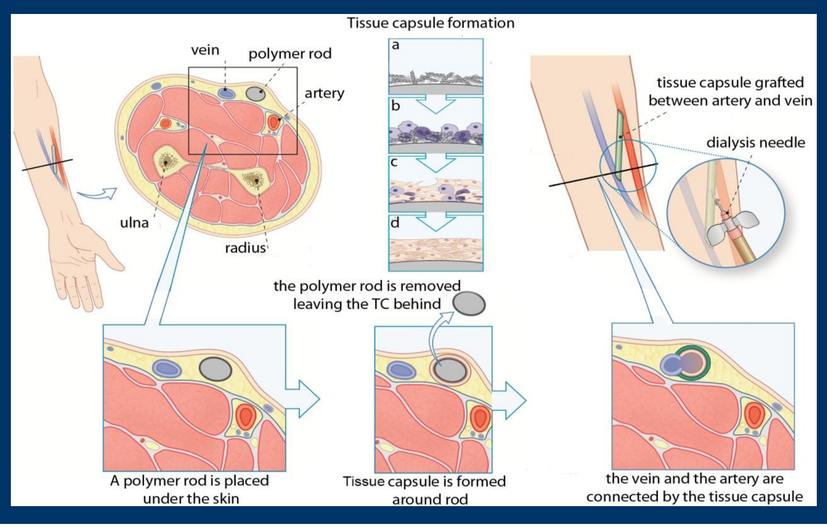
Chronic kidney disease does not impact the morphology and cellular composition of *in vivo* tissue engineered blood vessels in rats.

Introduction

Tissue engineered blood vessels (TEBVs) could offer a suitable alternative for arteriovenous conduits, circumventing the limitations of synthetic grafts and avoiding the need for maturation of fistulas.

Recently, we developed a novel method to generate TEBVs by utilizing the foreign body response directed to a subcutaneously implanted polymeric rod, which culminates in the formation of a fibrocellular tissue capsule (TC). Upon extrusion of the polymer rod, the remaining TC is grafted into the vasculature whereupon it differentiates towards a blood vessel (Fig.1).

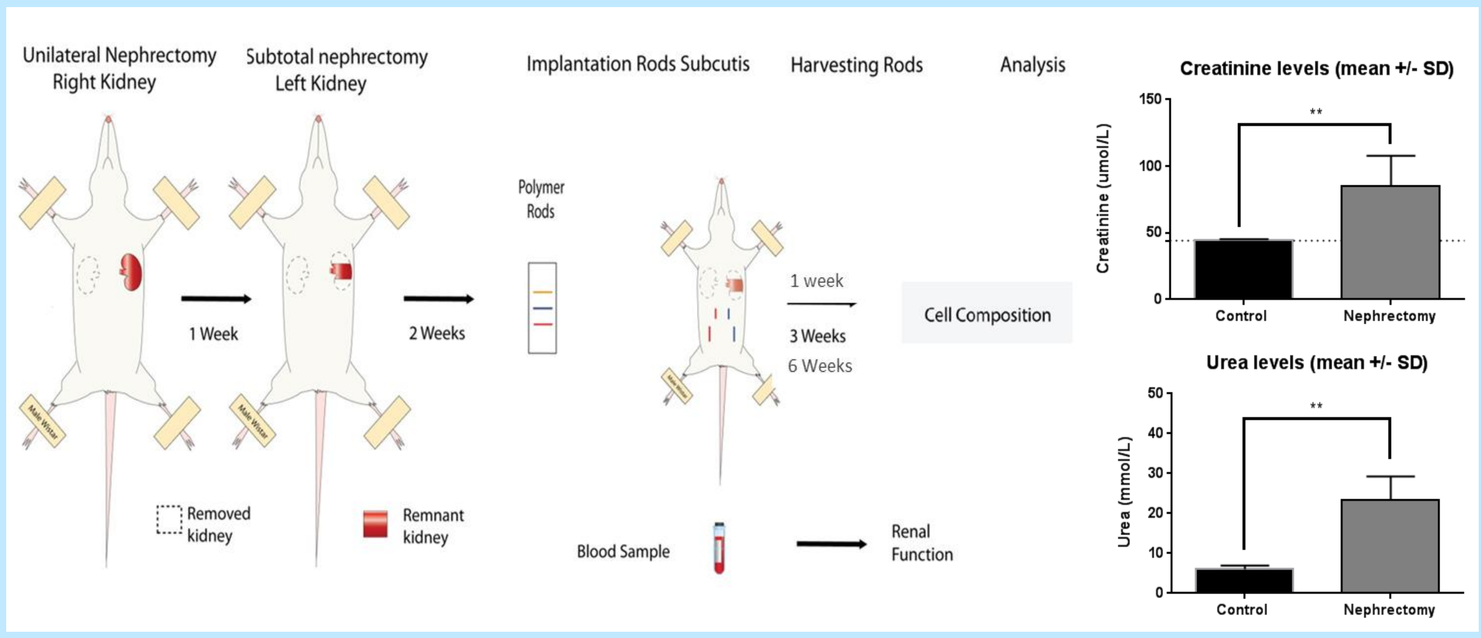
In the present study, the impact of chronic kidney disease (CKD) on TC formation was evaluated in a rat model.



Experimental Setup

Polymeric rods were subcutaneously implanted in CKD rats (n=7) and left in place for 1, 3 or 6 weeks. TCs were harvested and their cellular composition as well as gene expression profile was analyzed and compared with healthy control rats (n=7).

Development of stable CKD is marked by increased levels of creatinine and urea in the blood at the time of TC explanation.

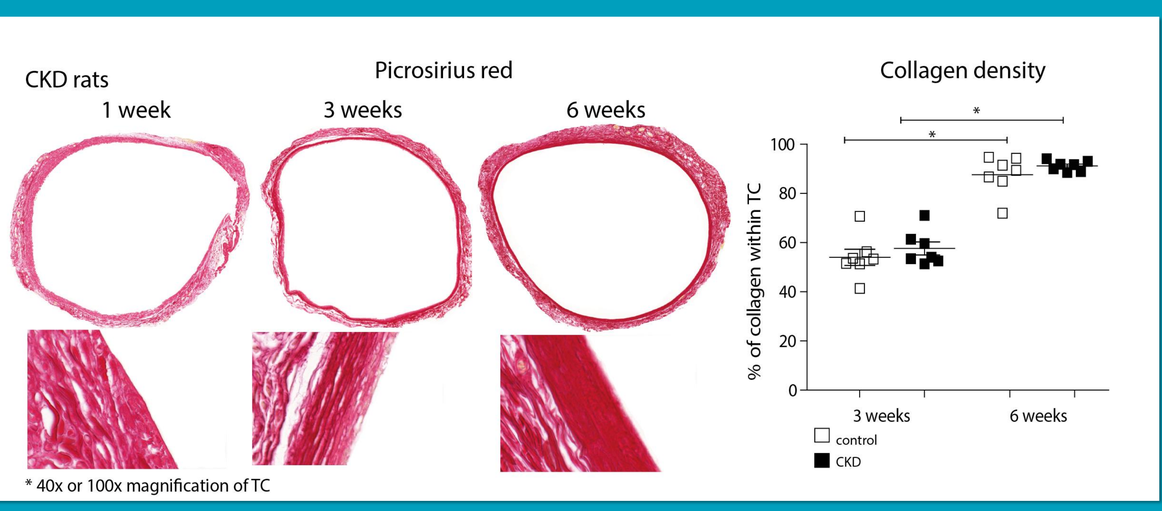


Conclusion

CKD has no impact on TC morphology and composition, making our *in vivo* approach of autologous vascular tissue engineering a relevant strategy for future clinical use in hemodialysis patients.

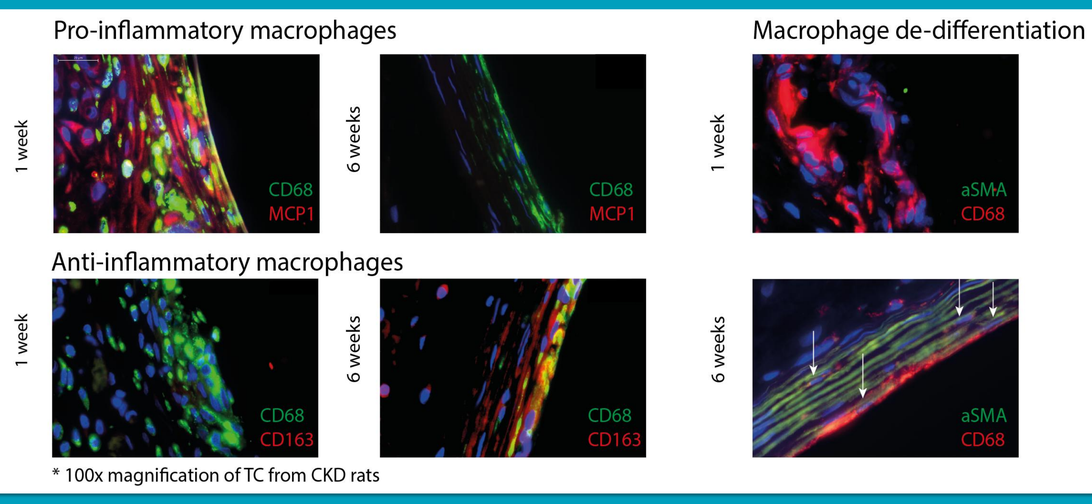
Results

Gradual change in collagen organisation towards circumferentially aligned fibres at 6 weeks. Its density is significantly higher 6 weeks after implantation compared to the 3 week's time point.



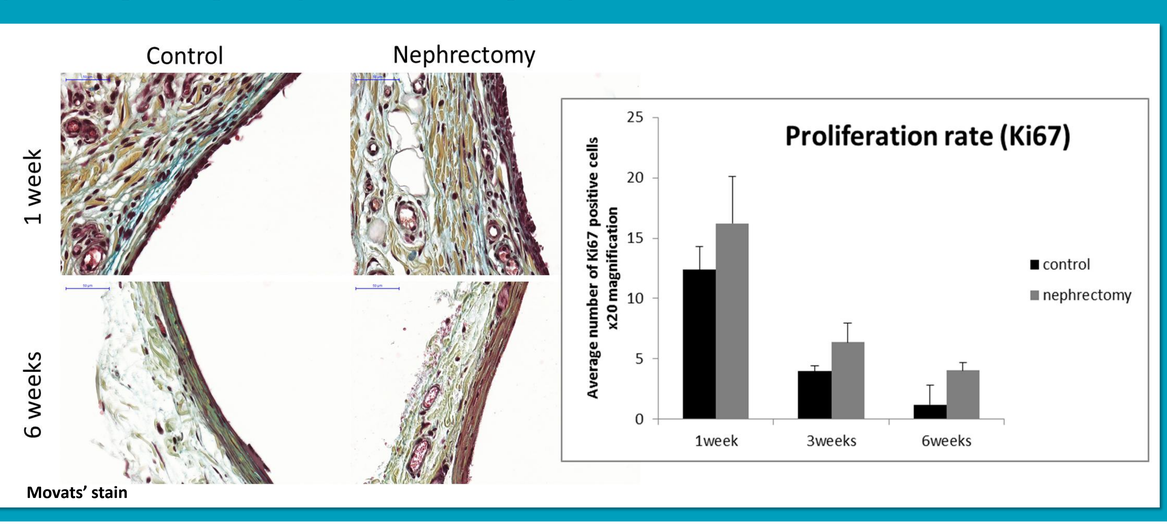
* 40x or 100x magnification of TC

Cellular response changes from pro-inflammatory CD68(+)/MCP1(+)Mϕ towards tissue-repair CD68(+)/CD163(+)Mϕ. The most inner layer of TC at 6 weeks is composed of αSMA(+)/CD68(+) cells, suggesting a crucial role of inflammatory cells as precursors of myofibroblasts in matured TC.



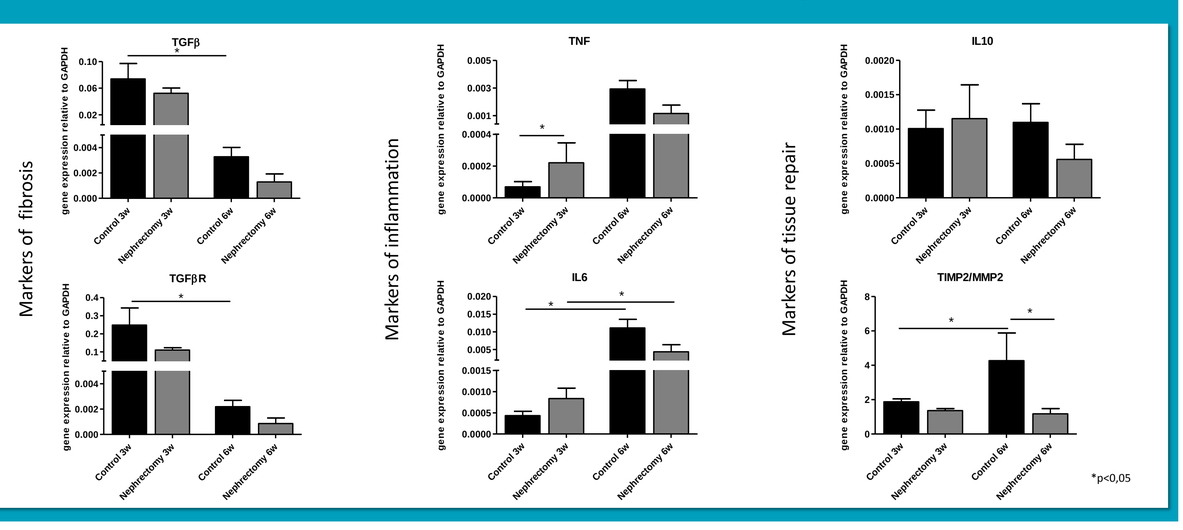
* 100x magnification of TC from CKD rats

Process of TC formation is characterized by initial recruitment of inflammatory/nucleated cells (black color), whereas after 6 weeks TC are mainly composed of collagen/muscle fibers (red/yellow color). Number of proliferating cells is gradually declined, indicating completion of TC formation at 6weeks.



Movats' stain

Comparison of gene expression profile isolated from the whole TC showed trend towards decrease in fibrotic response and increase in inflammatory status (TNF; IL6) of TC at 6 weeks. No difference between control and CKD rats was observed at both 3 and 6 weeks time points.



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