Multimodal imaging of the vagal cardiac innervation to visualize the vago-cardial anatomy and topography

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Introduction

To date, heart transplant patients suffer from negative side-effects of cardiac denervation after heart transplantation, such as autonomic imbalance at rest and insufficient chronotropic exercise response[1]. Within this project, we are addressing this clinical problem by mapping the anatomy of the cardiac Vagus Nerve to provide structural and functional in-detail information for selective vagal-cardiac neuromodulation.

Materials and Methods

The Cervical Vagus Nerve (CVN) including the upper cardiac branches (CB) were carefully isolated from the cadavers of New-Zeeland female rabbits (n=4; 2.6-3.3kg) and male domestic pigs (n=4; 60-92kg) as presented in Fig. 1.

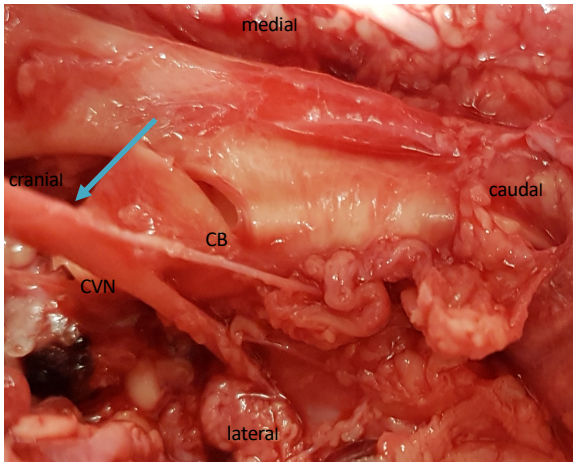

Figure 1: Dissection of the cervical Vagus Nerve with its upper cardiac branch in a pig. The intended stimulation site for selective cardiac vagal stimulation at the base of the cardiac branch is highlighted by the blue arrow

One group of the VN samples were topographically mapped to visualize the vagal course from the cervical to the cardiac level as well as the tissue structure using contrast- enhanced micro-computed tomography (µCT)[2] and High Resolution Episcopic Microscopy (HREM)[3](Fig. 2).

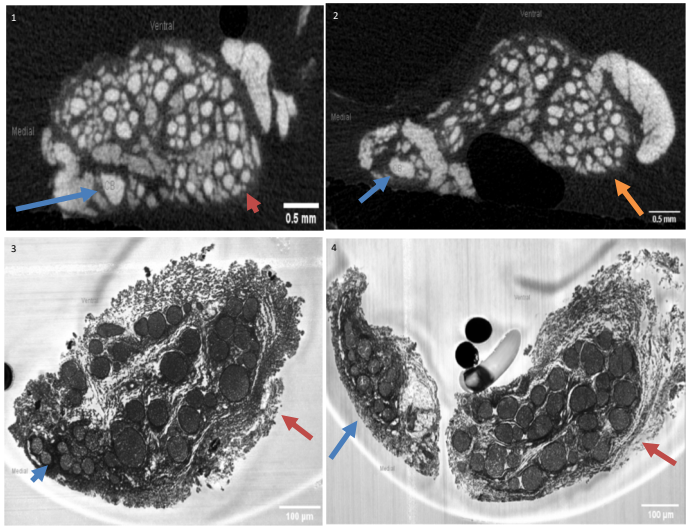

Figure 2: Topographical mapping of the pig cardiac vagal branch (blue arrow) within the cervical Vagus Nerve (orange arrow; Images 1 and 3) and after branching (Images 2 and 4) using µCT (upper row) and High Resolution Episcopic Microscopy (bottom row).

The other group of nerves was scanned using Optical coherence tomography (OCT)[4],providing access to detailed information about tissue structure and molecular composition in a fast, label-free manner and Immunohistochemistry[5] with antibodies labeling Neurofilament (NF), Myelin Basic Protein (MBP), choline Acetyltransferase (ChAT) and Tyrosine Hydroxylase (TH) (Fig.3).

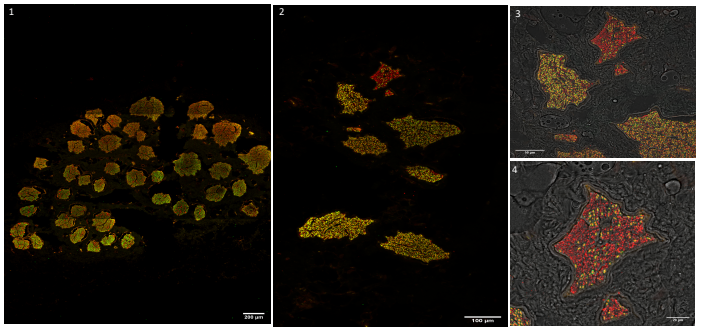

Figure 3: Immunohistochemistry of the pig cervical (Image 1) and cardiac Vagus Nerve (Images 2-4). Images 1 and 2 provide an overview on the fascicular structure of the nerves. Images 3 and 4 provide magnified insights into the axonal anatomy of the cardiac vagal branch. The red markers labels Neurofilament, the green marker labels Myelin Basis Protein.

Results

Our data provide morphological information on the cardiac vagal innervation with respect to selective cardiac neuromodulation. Among species, the pig model is anatomically the most comparable one to the humans. In the pig, the average number of fascicles in the CVN was 28.44 ± 6 fascicles. The perimeter of the cervical and cardiac VNs was 6.63 ±1.91 µm and 1.37± 0.34µm, respectively. The cross-sectional area of the CVN was 2.73µm² ± 1.0µm² and for CB 0.12µm²± 0.06µm². Our study approach was the first one that generated an anatomical model for selective stimulation of the cardiac VN. Species-related anatomical differences, such as nerve sizes and branching patterns, should be considered, especially regarding translational research for human medicine.

Conclusion

Multimodal imaging provides novel anatomical and structural information for selective cardiac Vagus Nerve Stimulation and thus, support the design, development and test of a novel, smart cardiac Neuroprosthesis.

Acknowledgement

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