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Interpatient differences in neural recruitment patterns during pudendal nerve stimulation – a computational investigation

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Bladder dysfunction impairs the quality of life for millions of individuals around the world. Common causes of bladder dysfunction include aging, trauma, and neurological disorders. Due to inadequacies in conventional treatments, neuromodulation therapies to address bladder dysfunction, such as sacral nerve stimulation, have emerged. However, patient needs still remain unmet. Pudendal nerve stimulation (PNS) has recently gained clinical interest as a promising treatment for bladder dysfunction. While PNS has been extensively investigated in preclinical settings, there is a gap in our understanding of the mechanisms of action and efficacy of PNS as limited studies of PNS have been performed on human subjects. We developed patient-specific computational models for 10 participants receiving PNS as part of their clinical care to improve our understanding of this therapy.

Our modeling approach consisted of segmentation of pre- and post-operative magnetic resonance and computed tomography images to create a volume conductor model of each participant's pelvic anatomy and implanted stimulator. We used the finite element method to approximate the electric fields generated by PNS for each participant. We then simulated each participant's neural recruitment during PNS by coupling the electric field solutions to multicompartment axon models placed within the pudendal nerve.

We used this modeling approach to simulate the neural recruitment order for each participant over a select range of stimulation parameters. Our simulations demonstrated neural recruitment profiles in agreement with the experimental stimulation thresholds measured in each participant. Our results suggest that stimulation waveform parameters, contact selection, and electrode array placement all have a significant impact on the efficacy of PNS.

PNS is an emerging neuromodulation therapy which may help address bladder dysfunction that is refractory to conventional treatments. In this study, we used computational models to account for patient-specific anatomy and electrode array placement to simulate the effects of PNS. Our model results were in line with experimental measurements and underscore the importance of electrode placement relative to the roots, trunk, and branches of the pudendal

nerve. Future models could be enhanced by considering histological studies that describe the somatotopic organization of the pudendal nerve. Including such data could provide further insight into the therapeutic mechanisms of PNS and optimize its use in clinical applications.