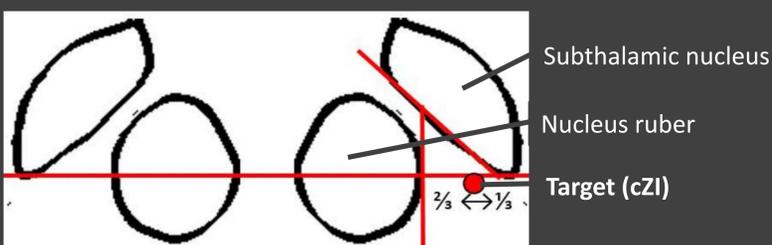


## Introduction

Orthostatic tremor (OT) is a rare hyperkinetic movement disorder characterized by a high-frequency tremor affecting weight-bearing limbs. Patients typically complain of a sensation of unsteadiness and imbalance while standing relieved by sitting, walking or leaning on an object. On routine clinical examination this tremor is not visible, what makes the diagnosis challenging. Auscultation of the gastrocnemius sometimes reveals the helicopter sign (the sound of the rotor of a helicopter). The diagnosis is confirmed by an electromyography, which shows typical high-frequency discharges between 13 and 18 Hz. The first-line therapy are oral medications like clonazepam. In medically refractory cases, bilateral deep brain stimulation of the ventral intermediate nucleus (VIM) of the thalamus has shown to be effective and safe. However recent years Zona incerta (ZI) stimulation has become more and more popular in treatment of movement disorders, more specifically in the caudal area, which is believed to be associated with motor functions. This has also brought promising results in OT cases.

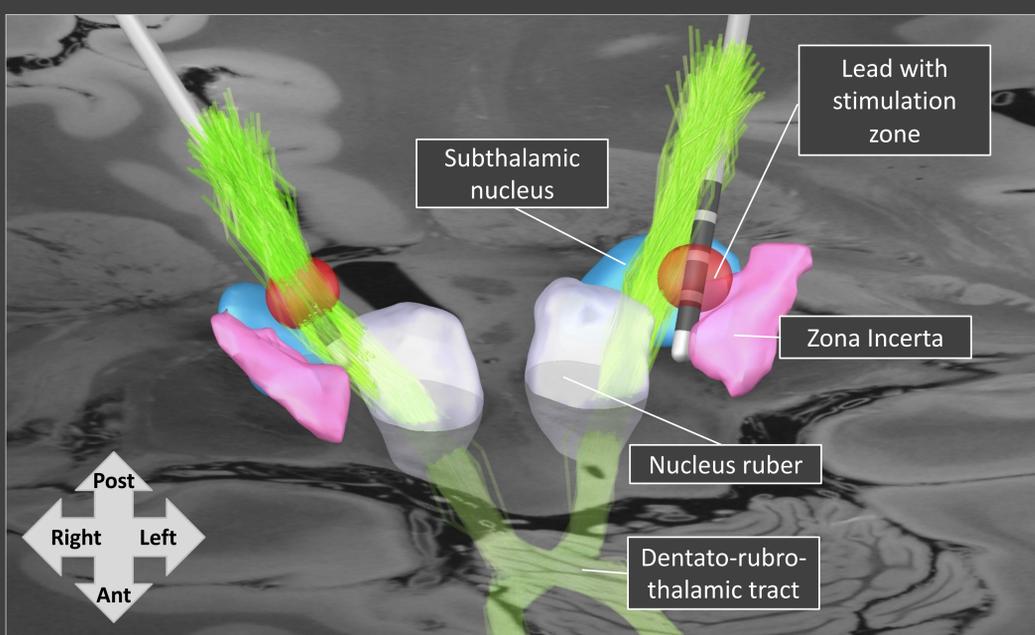
## Case presentation

A 70-year old woman suffered from progressive unsteadiness and imbalance while standing since more than 10 year. EMG confirmed OT. There was no effect of multiple oral medications such as Propranolol, Mysoline, Gabapentine, Topiramaat, Rivotril,... Because of significant impact on her quality of life we decided to perform caudal zona incerta (cZI) deep brain stimulation. The target was calculated on a preoperative T2 MRI as shown on the figure below.



We used intra-operative micro-electrode-recordings and lower limb EMG during isometric contraction to check the location during the surgery. Directional DBS electrodes (St Jude medical) were implanted bilaterally. Intra-operative CT scan with the O-arm was fused with the MRI planning and showed a good location of the leads.

**Lead reconstructions with lead DBS software:** Many thanks to PD Dr. med. Christian Moll



The patient experienced a dystonic cramp in the lower limbs the first week after surgery. This is described by Blomstedt as a possible side-effect of zona incerta stimulation. Because lead verification showed a good location we only changed the pulse width to 40  $\mu$ s which resulted in vanishing of the cramp. Frequent changes in deep brain stimulation settings were required in the first 3 months after surgery. Patient is now, 8 months after the surgery, in a steady state with good improvement of the unsteadiness and quality of life. Since it is often observed that the effect of the stimulation decreases over the years, the patient turns the stimulation off at night to delay habituation.

## References

- Merola A, Fasano A, Hassan A et al. Thalamic deep brain stimulation for orthostatic tremor: A multicenter international registry. *Mov Disord*. 2017 Aug;32(8):1240-1244.
- Athauda D, Georgiev D, Aviles-Olmos I et al. Thalamic-Caudal Zona Incerta Deep Brain Stimulation for Refractory Orthostatic Tremor: A Report of 3 Cases. *Mov Disord Clin Pract*. 2016 Mar 11;4(1):105-110.
- Benito-León J, Domingo-Santos Á. Orthostatic Tremor: An Update on a Rare Entity. *Tremor Other Hyperkinet Mov (N Y)*. 2016 Sep 22;6:411.
- Gilmore G, Murgai A, Nazer A et al. Zona incerta deep-brain stimulation in orthostatic tremor: efficacy and mechanism of improvement. *J Neurol*. 2019 Nov;266(11):2829-2837.
- Contarino MF, Bour LJ, Schuurman PR et al. Thalamic deep brain stimulation for orthostatic tremor: Clinical and neurophysiological correlates. *Parkinsonism Relat Disord*. 2015 Aug;21(8):1005-7.
- Stereotactic Academy – Lectures about caudal zona incerta – Patrick Blomstedt

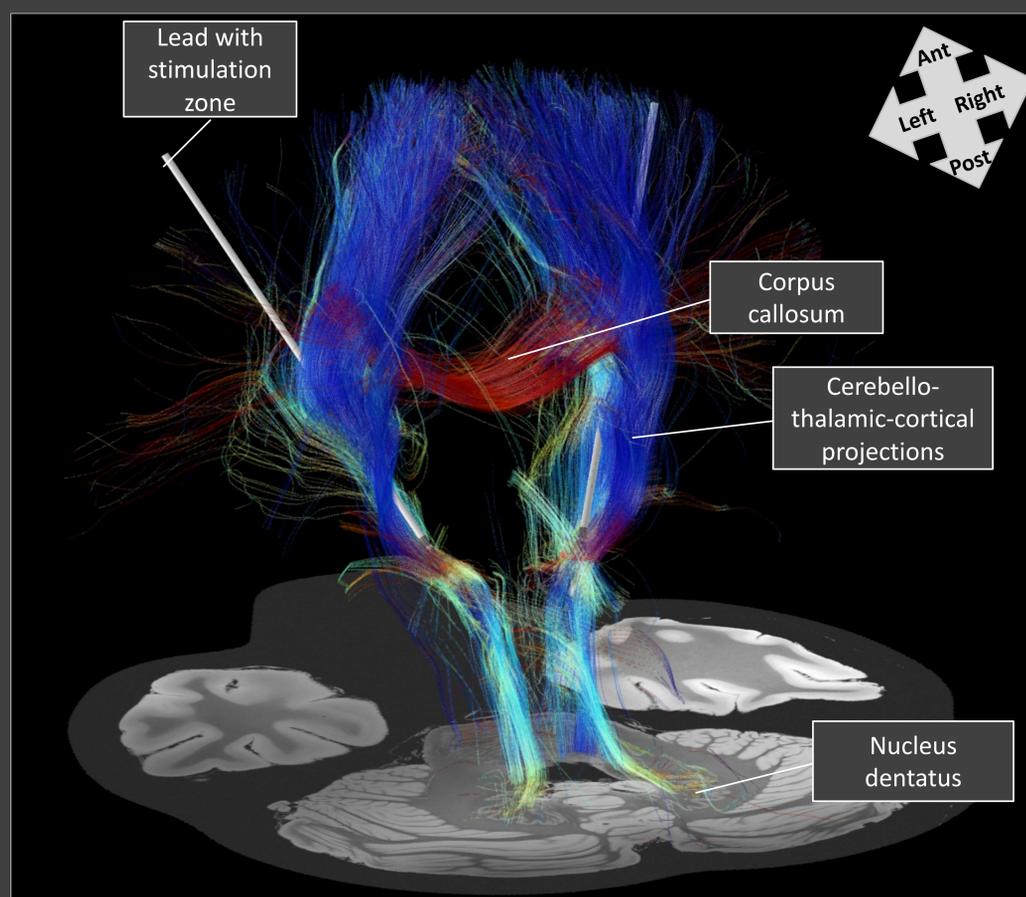
## Discussion

This case report shows the efficacy of stimulating the caudal Zona Incerta in medically refractory cases of orthostatic tremor. There are two main arguments for preferring cZI to VIM as a target.

First, recent research suggests that orthostatic tremor occurs at the level of a central oscillator that would be located either in the brainstem or cerebellum and mediated by cerebello-thalamic-cortical projections. Hence the importance of the zona incerta. This is a strip of grey matter that is located ventro-caudal to the VIM and exchanges information with the basal ganglia, deep cerebellar nuclei, thalamus and cortex. It is also very dense with cerebello-thalamic axons, who are projecting into the VIM. It is even plausible that stimulation of axons, rather than nuclei, affects more neurons by antidromic and orthodromic propagation and also alters tremor oscillations more efficiently.

Second, targeting of VIM is based on atlas targeting and identification of ventricular landmarks. It cannot be visualized on MRI. As we all know, electrode misplacement is a frequent problem and is a major cause of poor results in DBS stimulation. Since the cZI is easy to visualize on MRI, there is a growing interest in targeting the cZI or combined targeting of VIM & cZI.

**Lead reconstructions and DTI with lead DBS software:** Many thanks to PD Dr. med. Christian Moll



## Conclusion

Although literature is still scarce, we think deep brain stimulation is a good option for medically refractory OT. We also suggest that, as seen for essential tremor, the posterior subthalamic region might be a better target than VIM.