PLEASE NOTE: *This study has been imported from ClinicalTrials.gov without additional data checks.*

Trial Description

Title

Deep braIn Stimulation for Tremor TractographIC Versus Traditional

Trial Acronym

DISTINCT

URL of the trial

[---]*

Brief Summary in Lay Language

**This is a monocentric, randomized, controlled, 2 arms, interventional, observer-blinded
feasibility trial.**

**Patients suffering from essential tremor (ET) will be treated with Deep Brain Stimulation
(DBS). For the implantation of the DBS electrodes and the DBS system (Activa INS, Medtronic)
patients will randomized either to conventional stereotactic surgery of thalamic/subthalamic
region with short anesthesia or to MR-tractography guided stereotactic surgery with target
point of the dentato-rubro-thalamic bundle (DRT) in general anesthesia.**

**Patients will visit the study center at screening, baseline/neurosurgery, six and twelve
months after neurosurgery.**

Brief Summary in Scientific Language

**In this monocentric, randomized, controlled, 2 arms, interventional, observer-blinded
feasibility trial patients suffering from therapy resistant essential tremor (ET) will be
treated with Deep Brain Stimulation (DBS).**

**After screening (e.g. obtaining informed consent, assessment of inclusion/exclusion criteria
etc.) patients will be randomized to one of the following groups:**

Group 1 (conventional):

Conventional AC-PC based DBS implantation in the thalamic/subthalamic region (Vim-cZI)
starting as awake surgery with a brief general anesthesia for stimulator implantation at the
end of surgery.

Group 2 (tractographic):

Magnetic resonance (MR)-tractography guided DBS implantation in the dentato-rubro-thalamic
bundle (DRT) in general anesthesia

At the baseline/neurosurgery visit Quality of Life (QoL) and other parameters will assessed.
Medtronic's Activa INS DBS will be implanted according to randomization. DBS will be
started approximately one month after surgery and will be applied as per routine.

Patients will have their routine visits. For this trial data of the (routine) visits six and
twelve months after neurosurgery will be collected.

Patients receive DBS after the end of the trial according to local standards.

Do you plan to share individual participant data with other researchers?

[---]*

Description IPD sharing plan

[---]*

Organizational Data

- DRKS-ID: **DRKS00008913**
- Date of Registration in DRKS: **2015/07/13**
- Date of Registration in Partner Registry or other Primary Registry: **2015/06/30**
- Investigator Sponsored/Initiated Trial (IST/IIT): **yes**
- Ethics Approval/Approval of the Ethics Committee: **[---]***
- (leading) Ethics Committee Nr.: **[---]***

Secondary IDs

- Primary Registry-ID: **NCT02491554 (ClinicalTrials.gov)**
- Sponsor-ID: **P000847 (University Hospital Freiburg)**

Health condition or Problem studied

- Free text: **Essential Tremor**

Interventions/Observational Groups

- Arm 1: **Device: Conventional AC-PC based implantation of ACTIVA INS DBS system**
- Arm 2: **Device: MR-tractography guided implantation of ACTIVA INS DBS system**

Characteristics

- Study Type: **Interventional**
- Study Type Non-Interventional: **[---]***
- Allocation: **Randomized controlled trial**
- Blinding: **[---]***
- Who is blinded: **investigator/therapist, assessor**
- Control: **Active control**
- Purpose: **Treatment**
- Assignment: **Parallel**
- Phase: **N/A**
- Off-label use (Zulassungsüberschreitende Anwendung eines Arzneimittels): **[---]***

Primary Outcome

- Tremor reduction defined by the difference in FTMTRS at 6 months after intervention to baseline; time frame: Baseline, 6 months after neurosurgery; Tremor reduction defined by the difference in Fahn-Tolosa-Marin Tremor Rating Scale (FTMTRS) at 6 months after intervention to baseline

Secondary Outcome

- Effective tremor reduction at 12 months after intervention; time frame: Baseline, 12 months after neurosurgery; Effective tremor reduction (an FTMTRS score reduction by 50% compared to baseline is regarded as "response") at 12 months after intervention
- Tremor reduction measured by tremor analysis at baseline and 6 and 12 months after intervention; time frame: Baseline, 6 and 12 months after neurosurgery; Tremor reduction will be measured by tremor analysis (an accelerometric examination); Unit: Hertz (Hz)
- Tremor reduction measured by calculation of total power at baseline and 6 and 12 months after intervention; time frame: Baseline, 6 and 12 months after neurosurgery; Tremor reduction will be assessed during Electromyography (EMG) by the calculation of total power; Unit: mg^2, with g=9,81 m/s^2

- Quality of Life: QUEST, SF-36; time frame: Baseline, 6 and 12 months after neurosurgery; Qualitiy of Life assessed by Quality of Life Essential Tremor Questionnaire (QUEST) and Short Form (36) Health Survey
- Size of VAT; time frame: Day 0 (Day of neurosurgery); Size of Volume of activated tissue (VAT)
- Effective contact position with respect to DRT and AC-PC coordinates; time frame: Day 0 (Day of neurosurgery); Effective contact position of stimulation electrodes (with respect to the Dentato-rubro-thalamic bundle (DRT) and anterior commissure (AC) - posterior commissure (PC) line (ACPC) coordinaties)
- Duration of neurosurgery; time frame: Day 0 (Day of neurosurgery); Duration of neurosurgery (time points of mounting frame, start surgery, stop surgery (= dismounting frame)
- Changes in BDI; time frame: Baseline, 6 and 12 months after neurosurgery; Psychiatric assessment: changes in Beck's Depression Inventory (BDI)
- Assessment of (Serious) Adverse Events related to intervention; time frame: Up to 12 months after neurosurgery

Countries of recruitment

- DE **Germany**

Locations of Recruitment

- **University of Freiburg - Medical Center - Dept. of Stereotactic and Functional Neurosurgery, Freiburg**

Recruitment

- Planned/Actual: **[---]***
- (Anticipated or Actual) Date of First Enrollment: **2015/07/31**
- Target Sample Size: **24**
- Monocenter/Multicenter trial: **[---]***
- National/International: **[---]***

Inclusion Criteria

- Gender: **Both, male and female**
- Minimum Age: **25 Years**
- Maximum Age: **80 Years**

Additional Inclusion Criteria

1. Male or female patients aged ≥ 25 and ≤ 80 years

2. Patients with Essential Tremor according to the criteria of the consensus statement

of the movement disorders society (Deuschl et al. 1998) are included with a medical treatment resistant and disabling postural and/or intentional tremor.

3. FTMTRS to be completed within 42 days prior surgery

4. Stable tremor medication for at least 3 months prior inclusion

5. Written informed consent

Exclusion criteria

1. Major Depression with suicidal thoughts or suicidal thoughts in history

2. Dementia (Mattis Dementia Rating Score ≤ 130)

3. Acute psychosis

4. Patient incapability

5. Nursing care at home

6. Surgical contraindications

7. Medications that are likely to cause interactions in the opinion of the investigator

8. Known or persistent abuse of medication, drugs or alcohol

9. Persons who are in a relationship of dependence/employment with the sponsor or the investigator

10. Fertile women not using adequate contraceptive methods: female condoms, diaphragm or coil, each used in combination with spermicides; intra-uterine device; hormonal contraception in combination with a mechanical method of contraception;

11. Current or planned pregnancy, nursing period

Addresses

■ **Primary Sponsor**

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Primary Sponsor

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- **Collaborator, Other Address**

Medtronic Neuromodulation Europe

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URL: **[---]***

Sources of Monetary or Material Support

- **[---]***

Bitte wenden Sie sich an den Sponsor / Please refer to primary sponsor

Telephone: **[---]***
Fax: **[---]***
E-mail: **[---]***
URL: **[---]***

Status

- Recruitment Status: **Recruiting planned**

- Study Closing (LPLV): **[---]***

Trial Publications, Results and other documents

- Further trial documents **Zappia M, Albanese A, Bruno E, Colosimo C, Filippini G, Martinelli P, Nicoletti A, Quattrocchi G, Abbruzzese G, Berardelli A, Allegra R, Aniello MS, Elia AE, Martino D, Murgia D, Picillo M, Squintani G. Treatment of essential tremor: a systematic review of evidence and recommendations from the Italian Movement Disorders Association. J Neurol. 2013 Mar;260(3):714-40. doi: 10.1007/s00415-012-6628-x. Epub 2012 Aug 11. Review. Erratum in: J Neurol. 2013 Mar;260(3):741. Abbruzzese, Giovanni [added]; Berardelli, Alfredo [added]; Allegra, Roberta [added]; Aniello, Maria Stella [added]; Elia, Antonio E [added]; Martino, Davide [added]; Murgia, Daniela [added]; Picillo, Marina [added]; Squintani, Giovanna [added].; 22886006**
- Further trial documents **Koller W, Biary N, Cone S. Disability in essential tremor: effect of treatment. Neurology. 1986 Jul;36(7):1001-4.; 2940473**
- Further trial documents **Chopra A, Klassen BT, Stead M. Current clinical application of deep-brain stimulation for essential tremor. Neuropsychiatr Dis Treat. 2013;9:1859-65. doi: 10.2147/NDT.S32342. Epub 2013 Dec 2. Review.; 24324335**
- Further trial documents **Benabid AL, Pollak P, Gao D, Hoffmann D, Limousin P, Gay E, Payen I, Benazzouz A. Chronic electrical stimulation of the ventralis intermedius nucleus of the thalamus as a treatment of movement disorders. J Neurosurg. 1996 Feb;84(2):203-14.; 8592222**
- Further trial documents **Deistung A, Schäfer A, Schweser F, Biedermann U, Turner R, Reichenbach JR. Toward in vivo histology: a comparison of quantitative susceptibility mapping (QSM) with magnitude-, phase-, and R2*-imaging at ultra-high magnetic field strength. Neuroimage. 2013 Jan 15;65:299-314. doi: 10.1016/j.neuroimage.2012.09.055. Epub 2012 Oct 2.; 23036448**
- Further trial documents **Lemaire JJ, Sakka L, Ouchchane L, Caire F, Gabrillargues J, Bonny JM. Anatomy of the human thalamus based on spontaneous contrast and microscopic voxels in high-field magnetic resonance imaging. Neurosurgery. 2010 Mar;66(3 Suppl Operative):161-72. doi: 10.1227/01.NEU.0000365617.41061.A3.; 20173566**
- Further trial documents **Coenen VA, Allert N, Mädler B. A role of diffusion tensor imaging fiber tracking in deep brain stimulation surgery: DBS of the dentato-rubro-thalamic tract (drt) for the treatment of therapy-refractory tremor. Acta Neurochir (Wien). 2011 Aug;153(8):1579-85; discussion 1585. doi: 10.1007/s00701-011-1036-z. Epub 2011 May 8.; 21553318**
- Further trial documents **Coenen VA, Allert N, Paus S, Kronenbürger M, Urbach H, Mädler B. Modulation of the cerebello-thalamo-cortical network in thalamic deep brain stimulation for tremor: a diffusion tensor imaging study. Neurosurgery. 2014 Dec;75(6):657-69; discussion 669-70. doi: 10.1227/NEU.0000000000000540.; 25161000**
- Further trial documents **Coenen VA, Mädler B, Schiffbauer H, Urbach H, Allert N. Individual fiber anatomy of the subthalamic region revealed with diffusion tensor imaging: a concept to identify the deep brain stimulation target for tremor suppression. Neurosurgery. 2011 Apr;68(4):1069-75; discussion 1075-6. doi: 10.1227/NEU.0b013e31820a1a20. Erratum in: Neurosurgery. 2011 Jun;68(6):E1780-1.; 21242831**
- Further trial documents **Torres CV, Manzanares R, Sola RG. Integrating diffusion tensor imaging-based tractography into deep brain stimulation surgery: a review of the literature. Stereotact Funct Neurosurg. 2014;92(5):282-90. doi: 10.1159/000362937. Epub 2014 Sep 18. Review.; 25248076**
- Further trial documents **Klein JC, Barbe MT, Seifried C, Baudrexel S, Runge M, Maarouf M, Gasser T, Hattingen E, Liebig T, Deichmann R, Timmermann L, Weise L, Hilker R. The tremor network targeted by successful VIM deep brain**

stimulation in humans. Neurology. 2012 Mar 13;78(11):787-95. doi: 10.1212/WNL.0b013e318249f702. Epub 2012 Feb 29.; 22377809