Nye metoder: Innspill til metoder (forslag/metodevarsler/oppdrag)

Alle har anledning til å komme med tilleggsopplysninger til en metode som er foreslått for nasjonal metodevurdering. Det er ønskelig at innspill kommer inn så tidlig som mulig i prosessen, fortrinnsvis før behandling i Bestillerforum RHF.

Bruk dette skjemaet for å gi innspill til forslag, metodevarsler og oppdrag. På nyemetoder.no vil nye forslag/metodevarsler ha statusen «Forslag mottatt/åpent for innspill» før behandling i Bestillerforum RHF. Utfylt skjema sendes nyemetoder@helse-sorost.no.

NB: **Punkt 1-3 og 11 fylles ut av alle.** Punkt 4-9 fylles ut avhengig av rolle og kjennskap til metoden.

Jeg er klar over at skjemaet vil bli publisert i sin helhet på nyemetoder.no (kryss av): ☒
Har du informasjon du mener ikke kan offentliggjøres, ta kontakt med sekretariatet før innsending.

Jeg har fylt ut punkt 11 nedenfor «Interesser og eventuelle interessekonflikter» (kryss av): ☒

1.Hvilken metode gjelder innspillet?	
Metodens ID nummer*:	ID2016_007
Metodens tittel:	MR-guided high-intensity focused ultrasound (ExAblate Neuro) in the treatment of 1) essential tremor, 2) Parkinson's disease

*ID-nummer finner du på metodesiden på nyemetoder.no og har formen ID2020_XXX

2. Opplysninger om den som gir innspill	
Navn	Klaus Lundby Kristiansen
Eventuell organisasjon/arbeidsplass	Vingmed AS
Kontaktinformasjon (e-post / telefon)	Klaus.lundby@vingmed-as.no

3. Oppsummert innspill til metoden (besvares av alle)
Magnetic resonance (MR) guided high-intensity focused ultrasound (abbreviated MR guided HIFU; often abbreviated MRgFUS in English), is claimed to be a highly accurate and effective method for reducing disabling symptoms in patients with essential tremor (ET) that does not respond satisfactorily to drug treatment. Recent studies have further demonstrated that the therapy could prove a promising therapeutic option for patients with medically refractory Parkinson's Disease when not eligible for DBS. The MRgFUS transcranial system combines the proven techniques of FUS with MRI guidance. It includes a helmet-like device that is placed over the patient's head and directs ultrasound beams via focused transmitters to a well-defined area of the brain. For the treatment of patients with

Essential Tremor, the ultrasound waves create a permanent thermal ablation of the Vim in the thalamus.

Specific clinical data supporting efficacy and safety of ExAblate Neuro for ET indication are currently available (see point 7. below for details):

- 1 RCT with follow-up data up to 5 years
- 11 Retrospective and Prospective cohort studies
- 4 recent meta-analysis

Moreover, a total of five medical guidelines and numerous opinions by HTA bodies in Europe and accross the globe support the use of MRgFUS for the treatment of ET (see point 6. below)

Regarding Parkinson's disease (PD) indication, there are currently 3 RCTs and 1 observational cohort study available providing results between 1 and 5-years follow-up.

These data provides a strong basis for a method assessment of MR-guided HIFU for ET, and if desired also for Parkinson's disease in Norway.

Nærmere informasjon om metoden og innspill til PICO*

*PICO er et verktøy for å formulere presise problemstillinger i metodevurderingsarbeid. PICO er en forkortelse for Population/Problem – Intervention – Comparison – Outcome. PICO brukes til å presisere hvilken populasjon/problem som skal studeres, hvilke(t) tiltak (metode/behandling) som skal vurderes, hvilket tiltak det er naturlig å sammenligne med, og hvilke utfall/endepunkter det å er relevant å måle/vurdere. PICO er viktig for planlegging og gjennomføring av en metodevurdering.

4. Kjenner du til om metoden er i bruk i Norge i dag?

Er metoden i bruk utenom kliniske studier i dag:
NO
Fra hvilket tidspunkt har den vært i bruk:
Not applicable
Hvor er eventuelt metoden i bruk:
Not applicable

5. Hvilken pasientgruppe i den norske spesialisthelsetjenesten er metoden aktuell for? (PICO)

Beskriv kortfattet:

The target population comprises all patients over 18 years of age with moderate to severe medically refractory Essential Tremor. This target population can be divided into two subgroups:

- Patients with medically refractory ET that are not eligible for DBS. For these patients, MRgFUS covers an unmet need since there is no alternative therapy available;
- Patients with medically refractory ET that are eligible for DBS but refuse it while being also considered eligible for MRgFUS by the medical team: For this 2nd subgroup, clinical studies tend to indicate that Unilateral MRgFUS has a similar safety profile as DBS (Altinel et al. 2019, Huss et al 2015, Kim et al. 2017) but can be considered economically dominant compared to unilateral DBS (Jameel et al. 2022).

Tremor is one of the most common movement disorders and the most common cause of abnormal tremor in humans. In 2021, a meta-analysis published by the Global Health Epidemiology Reference Group (GHERG) estimates the prevalence of ET at 0.32% of the world population (Song et al. 2021), an estimate in line with the findings of Louis et al. (2021). Applied to Norway, the GHERG's data tends to indicate that 26,881 people may have essential tremor in the country (0.50% of the entire Norwegian population).

One can extrapolate the number of patients that will be treated each year by applying the patient algorithm below on the prevalence presented above and to one year incidence, it is expected that ca. 143 to 201 procedures could take place each year in Norway:

Prevalence – Of all 26.881 people with ET:

- Only 20,3% seeks medical care[1]
- 30% of them will be diagnosed with moderate to severe ET[2],
- 50% of ET patients will not experience any therapeutic effect[3,4] or will suffer from side effects[5]
- 85% of patients being refractory to pharmacological treatment, could be eligible to MRgFUS or DBS[6]
- Using Balachandar et al. (2022), one can assume that 10 to 15% of this pool of patients could be treated each year with MRgFUS[7]

Altogether, 70 to 104 MRgFUS procedures could take place each year in the country, based only on prevalence.

Incidence:

- Antonazzo et al, 2022 tend to indicate that 952 new patients with essential tremor could seek medical care each year in Norway.[8]
- It is estimated that 30% of them will be diagnosed with moderate to severe ET and 50% been refractory to drugs
- 85% of patients being refractory to pharmacological treatment, could be eligible to MRgFUS or DBS, which represents 121 new patients per year, a number that is slightly higher than extrapolations from Rajput et al, 1984, but lower than Benito-Leon et al, 2005.

Altogether, assuming that 60% to 80% of these patients will be treated with MRgFUS, 73 to 97 MRgFUS procedures could take place each year in the country, based on incidence.

[1] Romero JP, Benito-Leon J, Bermejo-Pareja F. The NEDICES study: recent advances in the understanding of the epidemiology of essential tremor. Tremor Other Hyperkinet Mov 2012;2: http://tremorjournal.org/article/view/70

[2] Health Quality Ontario. Magnetic Resonance-Guided Focused Ultrasound Neurosurgery for Essential Tremor: A Health Technology Assessment. Ont Health Technol Assess Ser. 2018;18(4):1-141.

[3] Zesiewicz TA, Elbe R, Louis ED, et al. Evidence-based guideline update: Treatment of essential tremor: Report of the Quality Standards Subcommittee of the American Academy of neurology, Neurology. 2011

[4] Koller WC, Vetere-Overfield B. Acute and chronic effects of propranolol and primidone in essential tremor. Neurology 1989;39(12):1587-8. [published Online First: 1989/12/01]

[5] Louis ED. Treatment of Essential Tremor: Are there Issues We are Overlooking? Frontiers in neurology 2012;2:91. doi: 10.3389/fneur.2011.00091

[6] Health Quality Ontario. Magnetic Resonance-Guided Focused Ultrasound Neurosurgery for Essential Tremor: A Health Technology Assessment. Ont Health Technol Assess Ser. 2018;18(4):1-141. Published 2018 May 3.

[7] Balachandar, A. et al. 2022 Effect of Public Interest in Magnetic Resonance Imaging–Guided Focused Ultrasound on Enrolment for Deep Brain Stimulation. Movement Disord (2022) doi:10.1002/mds.28963.

[8] Antonazzo IC et al. (2022) Time trends in the incidence of essential tremor: Evidences from UK and France primary care data. Front. Neurol. 13:987618. doi: 10.3389/fneur.2022.987618 Antonazzo et al 2022.

6. Er du kjent med behandlingsalternativer til denne metoden og hvordan disse fungerer for pasientgruppen i dag? (PICO)

Beskriv kortfattet:

Currently, the standard of care for the treatment of ET in patients with drug-resistant tremor is deep brain stimulation (DBS). It's an invasive procedure that consists of surgically implanting one or two electrodes in the brain connected to a program and a battery placed under the skin that delivers high-frequency electrical stimulation with the goal of reducing tremors. This procedure has been shown to reduce tremors by approximately 60% (M. Giordano et al., 2020), but is associated with numerous complications due to its invasive nature. The risks and adverse events associated with DBS have been reported in numerous studies. The invasive implantation procedure is associated with serious intra- and post-operative adverse events, including intracranial hemorrhage, seizures, and wound infections.[9,10,11,12 13]
DBS can't be considered for all patients due to its invasive nature and safety profile. For the same reasons, a significant proportion of patients refuse this procedure and remain without alternative treatment: in Norway, it is estimated only 24 DBS procedures were performed on patients with essential tremor last year.

As previously described, the target population is mostly composed of patients who are contraindicated to DBS or have refused it. That's why actually there are no comparative treatments recommended by the medical societies for these patients. The absence of therapeutical alternatives (or treatments as usual for lack of better options) can be therefore considered be a comparator, which is in line with the RCT that took place in the last 5 years.

There are currently five medical recommendations, consensus papers, and position papers from medical societies in Europe and across the globe supporting the use of MRgFUS in the treatment of essential tremor:

- Guidelines by the **German Neurological Society (DGN)** published in September 2022 stating that unilateral MRgFUS can be offered to all patients with medication refractory ET if the treatment is considered promising and/or when the improvement in their quality-of-life is considered satisfactory[14]**;**
- In Switzerland, 18 experienced neurosurgeons and neurologists representing 15 departments from 12 Swiss clinical centers and 5 medical societies published a consensus statement on high-intensity focused ultrasound for functional neurosurgery in September 2021. This statement indicates that MRgFUS works well for the treatment of

[9] Voges J, Hilker R, Botzel K, et al. Thirty days complication rate following surgery performed for deep-brain-stimulation. Mov Disord 2007;22(10):1486-1489.
[10] Engel K, Huckhagel T, Gulberti A, et al. Towards unambiguous reporting of complications related to deep brain stimulation surgery: A retrospective single-center analysis and systematic review of the literature. PLoS One 2018;13(8):e0198529.
[11] Kim MS, Jeong JS, Ryu HS, Choi SH, Chung SJ. Infection related to deep brain stimulation in patients with Parkinson disease: Clinical characteristics and risk factors. J Neurol Sci 2017;383:135-141.
[12] Montgomery EB. Deep brain stimulation programming: principles, techniques and side effects 2014.
[13] Pepper J, Zrinzo L, Mirza B, Foltynie T, Limousin P, Hariz M. The risk of hardware infection in deep brain stimulation surgery is greater at impulse generator replacement than at the primary procedure. Stereotact Funct Neurosurg 2013;91(1):56-65.
[14] Neurologie DGf. Leitlinien für Diagnostik und Therapie in der Neurologie. 2022

essential tremor. The document also states that MRgFUS may move from being a second-line treatment option for patients with a contraindication to DBS to a preferred option for a very specific subset of patients (Stieglitz LH et al., 2021).[15]

- In 2020, the American Society of Sterotactic and Functional Neurosurgery (ASSFN) published a position statement on MRgFUS for the management of essential tremor (N. Pouratian et al., 2020). The Society concluded that "MRgFUS is an effective and safe treatment option for essential tremor refractory to drug therapy. The indications and preferences for this treatment modality are distinct from those for deep brain stimulation." [16]
- The International Parkinson and Movement Disorder Society (IPMDS) developed recommendations on the treatment of essential tremor in 2019 in which it concluded that MRI-guided focused ultrasound thalamotomy (MRgFUS) could potentially be useful for patients with essential tremor (JJ. Ferreira et al. 2019).[17]

7. Har du innspill til hva som vil være viktig for pasienter som er aktuelle for behandling med metoden? (PICO)

Hva kan oppfattes som en fordel for pasienter og brukere med denne metoden sammenlignet med aktuelle alternativer? Hvilke endepunkter/resultater av behandlingen er det aktuelt å måle? Beskriv kortfattet:

The expected clinical benefits of MRgFUS treatment are:

- The instant and lasting decrease in the severity and intensity of tremor.
- Instant and lasting improvement in the patient's quality of life.

The minimally invasive nature of the procedure significantly reduces the length of hospital stay compared to deep brain stimulation.
It allows a relatively simple management of the surgical treatment. The procedure does not require general anesthesia, only sedation, as the procedure is performed in a single session in an awake patient.
The complication rate is low, reducing the need for re-hospitalization and aftercare.
The minimally invasive, incisionless nature of the procedure not only significantly reduces hospitalization time but also simplifies patient follow-up. Indeed, treatment with MRgFUS requires only standard neurological follow-up, considerably reducing the need for specialized consultations.

Endpoints/outcomes relevant to measure for essential tremor indication:

- Effectiveness: clinical rating scale for tremor (CRST), Hand tremor
- Safety: Adverse events occurrence rate
- Quality of life: Quality of Life Questionnaire for Essential Tremor (QUEST)

[15] Stieglitz LH, Oertel MF, Accolla EA, et al. Consensus Statement on High-Intensity Focused Ultrasound for Functional Neurosurgery in Switzerland. Frontiers in neurology 2021;12:722762. doi: 10.3389/fneur.2021.722762 [published Online First: 2021/10/12]
[16] Pouratian N, Baltuch G, Elias WJ, Gross R. American Society for Stereotactic and Functional Neurosurgery Position Statement on Magnetic Resonance-Guided Focused Ultrasound for the Management of Essential Tremor. Neurosurgery. 2020 Aug 1;87(2):E126-E129. doi: 10.1093/neuros/nyz510. PMID: 31832649.
[17] Stieglitz LH, Oertel MF, Accolla EA, et al. Consensus Statement on High-Intensity Focused Ultrasound for Functional Neurosurgery in Switzerland. Frontiers in neurology 2021;12:722762. doi: 10.3389/fneur.2021.722762 [published Online First: 2021/10/12]

Available clinical data supporting MRgFUS for ET indication:

- 1 RCT with follow-up data up to 5 years described by:
  - Elias et al., *A Randomized Trial of Focused Ultrasound Thalamotomy for Essential Tremor. N Engl J Med. 2016 Aug 25;375(8):730-9.*
  - Chang et al., *A prospective trial of magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: Results at the 2-year follow-up. Ann Neurol. 2018 Jan;83(1):107-114*
  - Halpern et al., *Three-year follow-up of prospective trial of focused ultrasound thalamotomy for essential tremor. Neurology. 2019 Dec 10;93(24):e2284-e2293.*
  - Cosgrove et al., *Magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: 5-year follow-up results. J Neurosurg. 2022 Aug 5:1-6.*

- 4 recent meta-analysis (earlier publications not considered):
  - Miller et al., *Magnetic resonance-guided focused ultrasound treatment for essential tremor shows sustained efficacy: a meta-analysis. Neurosurg Rev. 2022 Feb;45(1):533-544. doi: 10.1007/s10143-021-01562-w. Epub 2021 May 12. PMID: 33978922.*
  - Agrawal et al., *Outcome and Complications of MR Guided Focused Ultrasound for Essential Tremor: A Systematic Review and Meta-Analysis. Front. Neurol. 12:654711. doi: 10.3389/fneur.2021.654711*
  - Altinel et al., *Outcomes in Lesion Surgery versus Deep Brain Stimulation in Patients with Tremor: A Systematic Review and Meta-Analysis. World Neurosurg. 2019 Mar;123:443-452.e8. doi: 10.1016/j.wneu.2018.11.175. Epub 2018 Nov 27. PMID: 30500587.*
  - Mohammed et al., *A meta-analysis of outcomes and complications of magnetic resonance-guided focused ultrasound in the treatment of essential tremor. Neurosurgical focus 2018;44(2):E4. doi: 10.3171/2017.11.focus17628 [published Online First: 2018/02/02]*

- 11 Retrospective and Prospective cohort studies:
  - Abe et al., *Focused Ultrasound Thalamotomy for Refractory Essential Tremor: A Japanese Multicenter Single-Arm Study. Neurosurgery. 2021 Mar 15;88(4):751-757. doi: 10.1093/neuros/nyaa536. PMID: 33469648*
  - Gasca-Salas et al., *Cognitive safety after unilateral magnetic resonance-guided focused ultrasound thalamotomy for essential tremor. J Neurol Neurosurg Psychiatry. 2019 Jul;90(7):830-831.*
  - Sinai et al., *Magnetic resonance-guided focused ultrasound thalamotomy for essential tremor: a 5-year single-center experience. J Neurosurg . 2019 Jul 5;1-8. doi: 10.3171/2019.3.JNS19466*
  - Meng et al., *Magnetic resonance-guided focused ultrasound thalamotomy for treatment of essential tremor: A 2-year outcome study. Mov Disord. 2018 Oct;33(10):1647-1650.*

- Lak et al., *Magnetic Resonance Image Guided Focused Ultrasound Thalamotomy. A Single Center Experience With 160 Procedures. Front Neurol. 2022 Feb 18;13:743649*
- Segar et al., *Lesion location and lesion creation affect outcomes after focused ultrasound thalamotomy. Brain. 2021 Nov 29;144(10):3089-3100. doi: 10.1093/brain/awab176. PMID: 34750621.*
- Kim et al., *Technical and operative factors affecting magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor: experience from 250 treatments. J Neurosurg. 2021 May 21:1-9. doi: 10.3171/2020.11.JNS202580. Epub ahead of print. PMID: 34020416*
- Kim et al., *Comparative Evaluation of Magnetic Resonance-Guided Focused Ultrasound Surgery for Essential Tremor. Stereotact Funct Neurosurg. 2017;95(4):279-286. doi: 10.1159/000478866. Epub 2017 Aug 16. PMID: 28810261.*
- Wu et al*., Focused Ultrasound Thalamotomy for the Treatment of Essential Tremor: A 2-Year Outcome Study of Chinese People. Front. Aging Neurosci. 13:697029. doi: 10.3389/fnagi.2021.697029*
- Krishna et al*., Predictors of Outcomes After Focused Ultrasound Thalamotomy. Neurosurgery. 2020 Aug 1;87(2):229-237. doi: 10.1093/neuros/nyz417. Erratum in: Neurosurgery. 2020 Apr 1;86(4):604. PMID: 31690945.*
- Fishman et al*., Neurological adverse event profile of magnetic resonance imaging-guided focused ultrasound thalamotomy for essential tremor. Mov Disord. 2018 May;33(5):843-847. doi: 10.1002/mds.27401. Epub 2018 Apr 27. PMID: 29701263.*

8. Spesielt for medisinsk utstyr (besvares av leverandør): CE-merking

Foreligger det CE-merking for bruksområdet som beskrives i metoden? I så fall angi type og tidspunkt:

MR-guided high-intensity focused ultrasound procedure is performed with the Exablate Neuro medical device which is a class IIb medical device CE marked according to the 93/42/CE directive since November 29th 2012 for ET indication.
In 2022, Exablate Neuro obtained the CE mark for PD indication.

9. Spesielt for legemidler (besvares av leverandør): Markedsføringstillatelse (MT)

Har legemiddelet MT for indikasjonen som omfattes av metoden? Angi i så fall tidspunkt eller ventet tidspunkt for MT:

Not applicable

10. Andre kommentarer

In addition to the clinical data listed above, the following publications have demonstrated that MRgFUS is cost-dominant versus DBS and cost-effective versus no treatment:

- **Finland**: Roberto Blanco Sequeiros, Mini-HTA of Neuro-HIFU or High Intensity Focused Ultrasound (HIFU), on behalf of FINCCHTA, HUS, KYS, OYS, Tays, and TYKS Turku mini HTA in March 2021, publication available on demand
- **United Kingdom**: Jameel et al., 2022, The Cost-Effectiveness of Unilateral Magnetic Resonance-Guided Focused Ultrasound in comparison to Unilateral Deep Brain Stimulation for the treatment of medically refractory Essential Tremor in England. *British Journal of Radiology* 2022
- **Japan**: Igarashi et al., 2019, Cost-minimisation model of magnetic resonance-guided focussed ultrasound therapy compared to unilateral deep brain stimulation for essential tremor treatment in Japan. PLoS One. 2019 Jul 17;14(7):e0219929. doi: 10.1371/journal.pone.0219929. PMID: 31314791; PMCID: PMC6636755.
- **Canada**: Li et al, 2018, Li C, Gajic-Veljanoski O, Schaink AK, et al. Cost-Effectiveness of Magnetic Resonance-Guided Focused Ultrasound for Essential Tremor. *Movement Disorders* 2018 doi: http://dx.doi.org/10.1002/mds.27587
- **US**: Ravikumar et al. 2017, Cost-effectiveness of focused ultrasound, radiosurgery, and DBS for essential tremor. Mov Disord. 2017 Aug;32(8):1165-1173. doi: 10.1002/mds.26997. Epub 2017 Apr 3. PMID: 28370272.

Based on the clinical results and professional guidelines available to date, the use of MRgFUS in the treatment of essential tremor for drug resistant patients is no longer debated.

Moreover, many HTA bodies have published opinion in favor of MRgFUS in this indication:

- **Australia** – Recommendation of MSAC in July 2022 1614.1 - Final PSD_Mar-Apr2022_Redacted.pdf (msac.gov.au). The Australian Ministry of Health indicated in May 2023 that the reimbursement of the therapy would start with the next budget cycle (in March 2024).
- **Spain** – in December 2022, the Catalan authority AQuAS published a report recommending the use of MRgFUS for the treatment of patients with medically-refractory essential tremor or tremor-dominant Parkinson's Disease when they are not candidates for DBS: https://aquas.gencat.cat/web/.content/minisite/aquas/publicacions/2022/opcions_cirurgia_parkinson_tremolor_aquas2022.pdf
- **Germany** – The German Federal Joint Committee (G-BA) published a decision in May 2021 in the 137h - SGB V procedure. This decision concludes that the existing clinical evidence is sufficient to demonstrate the clinical benefits of MRgFUS therapy and to justify its reimbursement for the treatment of patients with essential tremor refractory to drug treatment and unsuitable for deep brain stimulation. In its April 2022 decision, the G-BA extended its previous decision to patients eligible for deep brain stimulation.
  - Beschluss des GBA im May 2021 (§137h-Verfahren): https://www.g-ba.de/bewertungsverfahren/verfahren-137h/40
  - Beschluss des G-BA im April 2022 (§137e-Verfahren): https://www.g-ba.de/beschluesse/5398/
- **Denmark** – report of the National Board of Health and Welfare (Socialstyrelsen): https://www.sst.dk/-/media/Udgivelser/2021/Essentiel-Tremor/2021-Visitationsretningslinje-for-behandling-af-essentiel-tremor-med-

neuromodulation.ashx?la=da&hash=B03519BF457816E9CA655F50DCB84ACF1EFDC3FD. The therapy obtained a national DRG in January 2023.

- **Finland** – Roberto Blanco Sequeiros, Mini-HTA of Neuro-HIFU or High Intensity Focused Ultrasound (HIFU), on behalf of FINCCHTA, HUS, KYS, OYS, Tays, and TYKS Turku mini HTA in March 2021, publication available on demand.
- **Japan** – In December 2016, the Japanese Ministry of Health, Labour, and Welfare (MHLW) approved MRgFUS to treat medication-refractory essential tremor. National reimbursement was approved in 2019.[18]
- **UK** – NICE (National Institute for Health and Care Excellence) in England assessed and validated this procedure in June 2018. https://www.nice.org.uk/guidance/ipg617/resources/unilateral-mriguided-focused-ultrasound-thalamotomy-for-treatmentresistant-essential-tremor-pdf-1899873927215557 accessed 25 April 2019.
- **Canada** – The HQO (Health Quality Ontario), a Canadian-based HTA body, assessed and validated this procedure in May 2018. https://pubmed.ncbi.nlm.nih.gov/29805721/
- **United States** – Premarket Approval (PMA) in July 2016. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150038

For information, MRgFUS procedure is currently under HTA in the following countries: Sweden, France, Austria, Estonia.

Regarding the Parkinson's Disease (PD) indication, Exabalte Neuro obtained the CE mark in 2022 and is the first FDA-approved MRgFUS device for the treatment of PD, indicated for use in pallidotomy (GPi-MRgFUS) of patients with advanced, idiopathic PD with medication-refractory moderate to severe motor complications.

PD is characterized by the loss of dopamine-producing neurons and the presence of Lewy bodies in the substantia nigra of the midbrain. The neuropathology of PD shows a considerable degree of heterogeneity, which suggests that there may be several pathophysiological pathways that lead to a loss of dopamine signalling (Lill et al., 2016). Structures within, or associated with, the basal ganglia and the thalamus are impacted by the impaired dopaminergic function, and therefore contribute to motor dysfunction in PD (Magrinelli et al., 2016). These regions include, but are not limited to:

- Subthalamic nucleus (STN) – part of the basal ganglia, which is involved in critical motor and cognitive processes, including voluntary movement(Guillaumin et al., 2021)
- Globus pallidus internus (GPi) – central to the basal ganglia and relays signals from the STN to control motor and cognitive functions(Weintraub et al., 2013)
- Ventral intermediate nucleus (Vim) – within the thalamus, adjacent to the basal ganglia, and is a key relay centre for motor functions believed to contribute to tremor symptoms exclusively(Bohnen et al., 2011)
- Pallidothalamic tracts (PTT) – facilitate signalling between the thalamus and GPi (Gallay et al., 2008)

PD is the second most common degenerative disorder of the central nervous system (Tysnes et al. 2017). By 2040, it is estimated that neurodegenerative diseases will overtake cancers and become the second leading cause of death worldwide, after cardiovascular disease (Gammon K. 2014).

[18] Insightec. INSIGHTEC MR-Guided Focused Ultrasound Receives Reimbursement from Japanese Ministry of Health, Labour and Welfare for the Treatment of Essential Tremor, 2019.

The global incidence of PD was estimated to be 13 per 100,000 in 2019; an increase of 160% since 1990 (Ou et al., 2021). In 2019, the global prevalence of PD was estimated to be 106 per 100,000 people and prevalence increased by 156% between 1990 and 2019 (Ou et al., 2021).

MRgFUS has been considered for a number of brain targets for the treatment of PD, including unilateral ablation of the GPi, PTT and STN. Despite the fact symptoms of PD normally affect patients bilaterally, unilateral treatment significantly improves patient HRQoL. Staged bilateral ablation of these brain targets is also in early stages of investigation. Targeting these brain regions can treat the various motor symptoms associated with PD, including: tremor, bradykinesia, rigidity and dyskinesia

Available clinical data supporting MRgFUS for PD indication:

- 1 RCT (Bond et al., 2017) on 27 patients (20 MRgFUS and 7 sham procedure) reporting results on changes in CRST Score, changes in the MDS-UPDRS motor score, adverse events and quality of life at 12 months.
- 1 RCT (Krishna et al., 2023) on 94 patients (69 MRgFUS and 25 sham procedure) reporting results on efficacy and safety of unilateral pallidotomy with MRgFUS for treatment of medication-refractory PD at 12 months.
- 1 RCT (Martinez-Fernandez et al., 2020) on 40 patients (27 MRgFUS and 13 sham procedure)reporting results on changes in the MDS-UPDRS motor score and procedure-related complications at 4 months.
- 1 observational cohort study (Sinai et al., 2022) on 26 patients treated by MRgFUS reporting changes in CRST and in MDS-UPDRS scores and adverse events up to 5 years.

11. Interesser og eventuelle interessekonflikter

Beskriv dine relasjoner eller aktiviteter som kan påvirke, påvirkes av eller oppfattes av andre å ha betydning for den videre håndteringen av metoden som det gis innspill på (for eksempel: økonomiske interesser i saken, oppdrag eller andre bindinger).

Beskriv kortfattet:
Vi, Vingmed AS, er en distributør av medisinsk utstyr, og vi samarbeider med Insightec (produsent av MRgFUS) for å få fokusert ultralyd til norske sykehus. Vi tenker at mer kunnskap om MRgFUS vil være gunstig i prosessen med metodevurdering i Norge. Vi har en kommersiell interesse av å gi et helhetlig bilde av MRgFUS som metode før bestillerforummøtet, derfor vårt innspill.