



Simultaneous Dual-Target Magnetic Resonance-Guided Focused Ultrasound Treatment for Patients with Tremor-Dominant Parkinson's Disease

Rezida M. Galimova^{1,2}, Sergey N. Illarioshkin³, Gulnara N. Akhmadeeva^{1,2}, Dinara I. Nabiullina², Felix F. Kashapov², Shamil M. Safin¹, Igor V. Buzaev^{1,2}, Dinara R. Teregulova², Yulia A. Sidorova², Olga V. Kachemaeva^{1,2}

¹Bashkir State Medical University, Ufa, Russia;

²Intellectual Neurosurgery Clinic, V.S. Buzaev International Medical Center, Ufa, Russia;

³Research Center of Neurology, Moscow, Russia

Abstract

Introduction. Non-invasive magnetic resonance-guided focused ultrasound (MRgFUS) is a new neurosurgical treatment option for tremor-dominant Parkinson's disease (TDPD). Outcomes of ablation with dual targeting of two subcortical nuclei to improve functional treatment results are yet to be explored.

Aim. This study aimed to evaluate the safety and efficacy of MRgFUS with simultaneous unilateral ablation of two cerebral targets in patients with TDPD.

Materials and methods. A total of 82 TDPD patients (20 women, 62 men; median age 65.0 [52.5; 70.0] years) received unilateral MRgFUS, i.e. ventrointermedial (VIM) nucleus thalamotomy and/or pallidothalamotomectomy (PTT). Motor symptoms, including tremor, were assessed using MDS-Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS-III). VIM, PTT, and VIM + PTT ablation was received by 34, 12, and 36 patients, respectively.

Results. After surgery, MDS-UPDRS-III score improved by 40.1% (30.2; 51.7) without early or late-onset serious complications. Tremor returned in 18 patients (all after VIM thalamotomy); 9 of them successfully underwent re-treatment 9–12 months after the first procedure. Simultaneous dual-target (VIM + PPT) intervention was successfully received by 36 patients without any serious complications. A total of 89.3% and 69.7% of patients remained relapse-free in the dual-target and single-target groups, respectively ($p = 0.039$).

Conclusion. Simultaneous dual-target (VIM and PTT) MRgFUS showed favorable safety and efficacy profiles and can be considered a symptomatic treatment option for TDPD patients.

Keywords: magnetic resonance-guided focused ultrasound; Parkinson's disease, VIM-thalamotomy; pallidothalamotomectomy; tremor

Ethics approval. All patients provided their voluntary informed consent to participate in the study. The study protocol was approved by the Local Ethics Committee of Bashkir State Medical University, Ufa, Russia (protocol No. 8, October 21, 2021).

Source of funding. The study was not supported by any external sources of funding.

Conflict of interest. The authors declare no apparent or potential conflicts of interest related to the publication of this article.

For correspondence: 3, Lenina Str., Ufa, Russia. Bashkir State Medical University. E-mail: rezida@galimova.com. Galimova R.M.

For citation: Galimova R.M., Illarioshkin S.N., Akhmadeeva G.N., Nabiullina D.I., Kashapov F.F., Safin Sh.M., Buzaev I.V., Teregulova D.R., Sidorova Yu.A., Kachemaeva O.V. Simultaneous dual-target magnetic resonance-guided focused ultrasound treatment for patients with tremor-dominant Parkinson's disease. *Annals of Clinical and Experimental Neurology*. 2024;18(2):5–12.

DOI: <https://doi.org/10.17816/ACEN.1085>

Received 30.01.2024 / Accepted 13.03.2024 / Published 25.06.2024

Одновременное воздействие на две мишени методом фокусированного ультразвука под контролем МРТ при лечении пациентов с дрожательными фенотипами болезни Паркинсона

Р.М. Галимова^{1,2}, С.Н. Иллариошкин³, Г.Н. Ахмадеева^{1,2}, Д.И. Набиуллина², Ф.Ф. Кашапов²,
Ш.М. Сафин¹, И.В. Бузаев^{1,2}, Д.Р. Терегулова², Ю.А. Сидорова², О.В. Качемаева^{1,2}

¹Башкирский государственный медицинский университет, Уфа, Россия;

²Клиника интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия;

³Научный центр неврологии, Москва, Россия

Аннотация

Введение. Неинвазивная технология воздействия фокусированным ультразвуком под контролем магнитно-резонансной томографии (МР-ФУЗ) является одним из новых методов нейрохирургического лечения преимущественно дрожательных фенотипов болезни Паркинсона (Д-БП). Возможность абляционного воздействия одновременно на две мишени в области подкорковых ядер с целью улучшения функциональных результатов лечения нуждается в изучении.

Цель работы – оценить безопасность и эффективность лечения пациентов с Д-БП методом МР-ФУЗ при одновременном одностороннем воздействии на две церебральные мишени.

Материалы и методы. Методом МР-ФУЗ 82 пациентам (20 женщин, 62 мужчин; медиана возраста – 65,0 [52,5; 70,0] лет) с Д-БП проведено одностороннее лечение – таламотомия вентроинтермедиального ядра (VIM) и/или паллидотрактомия (РТТ). Выраженность двигательных проявлений, включая тремор, оценивали по III части шкалы MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS-III). Воздействие на VIM осуществлено в 34 случаях, на РТТ – в 12, комбинированное воздействие VIM и РТТ – в 36.

Результаты. После операции у пациентов выявлено улучшение симптомов по шкале MDS-UPDRS-III на 40,1% (30,2; 51,7) без развития ранних и отдалённых серьёзных осложнений. У 18 пациентов наблюдался рецидив тремора (все случаи после VIM-таламотомии), 9 из них успешно выполнены повторные воздействия через 9–12 мес после первого лечения. Одновременное воздействие на 2 мишени (VIM и РТТ) успешно проведено у 36 пациентов, без серьёзных осложнений. В результате комбинации 2 мишеней безрецидивное течение Д-БП на протяжении года имело место у 89,3% больных, в то время как в подгруппе с абляцией 1 мишени – у 69,7% ($p = 0,039$).

Заключение. Одновременное воздействие на две мишени (VIM и РТТ) методом МР-ФУЗ может рассматриваться как один из вариантов лечения симптомов у пациентов с Д-БП при благоприятном профиле безопасности таких вмешательств.

Ключевые слова: фокусированный ультразвук под контролем МРТ; болезнь Паркинсона; VIM-таламотомия; паллидотрактомия; тремор

Этическое утверждение. Исследование проводилось при добровольном информированном согласии пациентов. Протокол исследования одобрен локальным этическим комитетом Башкирского государственного медицинского университета (протокол № 8 от 21.10.2021).

Источник финансирования. Авторы заявляют об отсутствии внешних источников финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Адрес для корреспонденции: Россия, Уфа, ул. Ленина, д. 3. Башкирский государственный медицинский университет. E-mail: rezida@galimova.com. Галимова Р.М.

Для цитирования: Галимова Р.М., Иллариошкин С.Н., Ахмадеева Г.Н., Набиуллина Д.И., Кашапов Ф.Ф., Сафин Ш.М., Бузаев И.В., Терегулова Д.Р., Сидорова Ю.А., Качемаева О.В. Одновременное воздействие на две мишени методом фокусированного ультразвука под контролем МРТ при лечении пациентов с дрожательными фенотипами болезни Паркинсона. *Анналы клинической и экспериментальной неврологии.* 2024;18(2):5–12.

DOI: <https://doi.org/10.17816/ACEN.1085>

Поступила 30.01.2024 / Принята в печать 13.03.2024 / Опубликовано 25.06.2024

Introduction

Parkinson's disease (PD) is one of the most common progressive neurodegenerative disorders. The incidence of PD is 5 to 35 per 100,000 person-years [1–4]. In the next 20 years, the prevalence of PD is expected to double [5], and, without any new effective treatment options, this might lead to a significant increase in social and economic disease burden [6].

Medication therapy to manage symptoms of neurotransmitter imbalance in the brain is indicated to patients with tremor-dominant Parkinson disease (TDPD). If there are no alternative medication treatment options, patients are usually administered functional neurosurgery with deep brain stimulation (DBS) or stereotactic ablation: radiofrequency ablation, gamma knife, or magnetic resonance guided focused ultrasound surgery (MRgFUS) [7–14]. Before widespread introduction of DBS, destructive surgery with an efficacy of 50–80% was the leading treatment option for PD symptoms [11, 15]. Since the end of the 20th century, DBS has become the leading neurosurgery option for PD [16–18]. Recently, ablative treatment methods have become popular again due to the introduction of MRgFUS, which allows managing movement disorders with high accuracy and avoiding any surgical incisions, anesthesia, long hospitalization, and pain [11, 19–21].

MRgFUS involves a combination of two procedures: high-intensity focused ultrasound and MRI, which are used to plan the target point and conduct thermometry in real time. Bond et al. in 2017 were one of the first to describe successful treatment of PD-associated tremor by MRgFUS in the ventral intermediate thalamic nucleus in 27 patients [22]. Among the authors who evaluated long-term results of MRgFUS in patients with PD, A. Sinai et al. reported the longest follow-up in 26 TDPD patients after VIM-ablation (median follow-up 36 months, range 12–60 months) [23]. Treatment resulted in 100% improvement in tremor in 23 patients and 90% improvement in 3 patients. In 2 patients tremor returned completely and in 8 patients there was partial return of tremor. This study demonstrated that unilateral MRgFUS VIM-thalamotomy in TDPD patients was effective and safe and provided long-term response. Heading to the premotor cortex, several important tracts (pallidothalamic, cerebellothalamic, and vestibulothalamic) converge in the VIM nucleus, and this makes it an optimal candidate for managing tremor and justifies intervention in this area [15, 24].

Attempts to perform MRgFUS ablation of the subthalamic nucleus (STN) were described by R. Martínez-Fernández et al. However, analysis of their results showed that this intervention, compared with other targets, was associated with a higher incidence of adverse effects (such as ballism, chorea, paresis, speech disturbances, and gait disturbances) with a similar efficacy [25]. With such adverse effects developing after subthalamotomy (with some of them persisting for up to one year or more), many medical centers prefer to target

the VIM nucleus, which has become the key target for the treatment of essential tremor and the most common target for tremor in PD.

No effect on hypobradycinesia and muscle rigidity is a disadvantage of targeting the VIM nucleus [26]. Meanwhile, targeting the pallidothalamic tract (PTT) at the level where the Forel's fields H1 and H2 converge was shown to reduce tremor, rigidity, and hypobradycinesia by an average of 70–93% while leaving the thalamus intact [20]. M.N. Gallay et al. assessed MRgFUS pallidothalamic tractotomy results in 51 patients with late-stage TDPD and complications of levodopa treatment (dyskinesia and fluctuations) [27]. They found percentage reductions of 84% for tremor, 70% for rigidity, and 73% for hypokinesia with almost complete suppression of levodopa-induced dyskinesia. This study showed that pallidothalamic tractotomy is very promising for the treatment of TDPD and complications of levodopa treatment.

Numerous studies have been conducted to evaluate MRgFUS with ablation of one target, while the feasibility, safety, and efficacy of simultaneous dual targeting are barely represented in available literature. A single study published in 2023 described 3 TDPD patients who received stepwise dual-target MRgFUS with VIM and PTT ablation [28]. All patients tolerated the two treatment steps adequately without any complications.

Aim. Our study aimed to evaluate the safety and efficacy of simultaneous unilateral dual-target MRgFUS in TDPD patients.

Materials and methods

Treatment with a MRgFUS system (ExAblate 4000, Insightec) was received by 82 patients (20 women and 62 men) with TDPD. Median patients' age was 65.0 [52.5; 70] years. Mean age was 64.5 (55; 70.5) for men and 63.0 (61.0; 72.0) for women with no statistically significant gender differences ($p = 0.95$, Wilcoxon's test). This prospective study included patients who received MRgFUS treatment at V.S. Buzaev International Medical Center from May 05, 2020 to July 29, 2023.

PD was diagnosed based on the PD diagnostic criteria of the International Parkinson and Movement Disorder Society [29]; the stage was determined using the Hoehn–Yahr functional scale [30]; and disease severity was assessed using the Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Part III (MDS-UPDRS-III) [31, 32]. A total of 37 and 28 patients had Hoehn and Yahr Rating Scale stage 2 and 3, respectively. Median MDS-UPDRS-III score before treatment was 54 (43; 65).

Eligibility criteria for the neurosurgical intervention:

- 1) idiopathic PD lasting for 2 years or more;
- 2) age over 30 years;

- 3) persistence of tremor when using standard levodopa agents (at least 500 mg) or side effects with required doses of standard levodopa agents;
- 4) on-medication fluctuations (on-off phenomenon) or dyskinesia;
- 5) tremor intensity score at rest and/or hypokinesia score of ≥ 3 –4;
- 6) no significant cognitive impairment (i.e. total Montreal Cognitive Function Assessment Scale score of at least 20) and no psychotic disorders;
- 7) bone ultrasound permeability factor of ≥ 0.35 ;
- 8) no current treatment with anticoagulants and/or antiplatelet agents, no brain tumors or vascular malformations;
- 9) no contraindications to MRI, such as claustrophobia or incompatible implants.

All patients were informed about DBS but did not consider it for several reasons (fear of a device in the brain; difficulties with access to medical centers that adjust DBS parameters due to remoteness of patients' place of residence, etc.). During the screening period for MRgFUS, all patients also underwent brain MRI with the SWI/SWAN sequence, which has a certain diagnostic value in PD [33, 34].

We described MRgFUS in detail before [12]. In all cases, unilateral intervention was performed; the side of intervention was chosen as a joint decision with the patient and their relatives, considering severity of their symptoms or dominant limb. Median bone ultrasound permeability factor was 0.48 (0.41; 0.58); median treatment duration was 97.2 (73.6; 126.4) min; median number of sonications was 11 (9.5; 13.0).

We chose two targets for MRgFUS: VIM and PTT. The VIM nucleus was used in first patients because this target was approved earlier (in 2018) [12]. After PTT tractotomy was approved in November 2021, targets were selected for each patient in accordance with their clinical status (presence of severe muscle rigidity, hypokinesia, or disabling tremor) [35]. Of 82 treated patients, 34 received VIM, 12 PTT, and 36 VIM + PTT thalamotomy. A total of 51 and 31 patients received left-sided and right-sided interventions, respectively.

After treatment, all patients were followed up according to the approved protocol with clinical neurological examination and brain MRI at Months 1, 3, 6, and 12.

Statistical analysis was performed in x86_64-apple-darwin17.0 platform under macOS Monterey v. 12.0.1 in R v. 4.2.1 software package distributed under open license. Continuous numerical variables were tested for normal distribution using the Shapiro–Wilk test. Non-parametric methods were used in case of a relatively small number of observations and no normal distribution. Dependent groups were compared using the paired Wilcoxon test, and independent groups were compared using the Wilcoxon test. If there were more than two

groups, the Kruskal–Wallis comparison method was used. Spearman correlation analysis was performed. Data were evaluated visually using graphs plotted using functions built into R. Time to return of symptoms was analyzed by Kaplan–Meier survival methods using survival v. 0.4.9 and survminer v. 0.4.9 packages.

Results

Positive MDS-UPDRS-III response to MRgFUS was achieved in all TDPD patients. Median score before and after surgery was 54 (43; 65) and 31 (24; 39), respectively, $p < 0.00001$ (Fig. 1). No statistically significant differences were found in treatment results between men and women ($p = 0.68$).

Evaluation of MRgFUS results by target (Fig. 2) showed greater improvement with PTT or VIM + PTT targets ($p < 0.001$, Kruskal–Wallis method). Improvement was 32.0% (24.5; 40.2) in the VIM group, 50.0% (40.3; 57.5) in the VIM + PTT group, and 40.1% (37.2; 58.7) in the PTT group; differences were statistically significant ($p < 0.001$, Kruskal–Wallis test). If tremor persisted after a sufficient PTT lesion, the patient received a second ablation intervention in another target. Fig. 3 shows a TDPD patient's MRI scan after MRgFUS treatment in both PTT and VIM.

Statistically significant differences were found in percentage improvement (vs. baseline MDS-UPDRS-III score) between patients with isolated PTT and VIM ablation ($p = 0.000024$, Wilcoxon's test). However, no statistically significant differences were found between PTT + VIM and PTT ablation groups ($p = 0.9245$). Median improvement in MDS-UPDRS-III score was 47.9% (38.8; 57.6) and 32% (24.2; 40.2) in patients with and without PTT thalamotomy, respectively. Median absolute improvement in MDS-UPDRS-III was 29 (21; 34) and

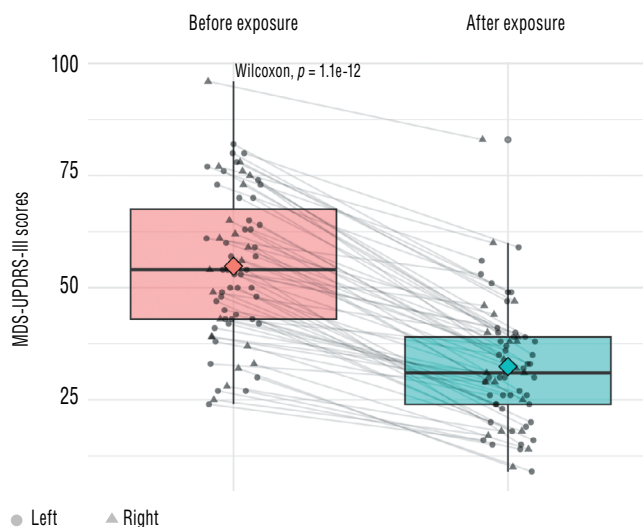


Fig. 1. MRgFUS treatment response (score, before and after) in TDPD patients.

* $p < 0.00001$, Wilcoxon's test.

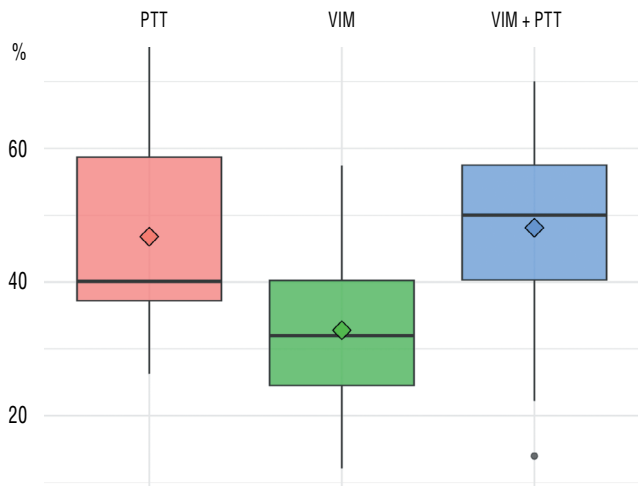


Fig. 2. Percentage improvement achieved in TDPD patients after MRgFUS (MDS-UPDRS, part III) vs. baseline by different targets. * $p < 0.001$, Kruskal–Wallis method.

13.5 (10.2; 21) in patients with and without PTT ablation, respectively ($p < 0.0001$, Wilcoxon's test).

A total of 73 patients received MRgFUS without any adverse effects. During the procedure, few patients developed complications related to the procedure itself: headache ($n = 4$), which resulted in procedure discontinuation in 1 case; increased blood pressure ($n = 5$); transitory obtundation ($n = 1$); arterial hypotension in response to medication

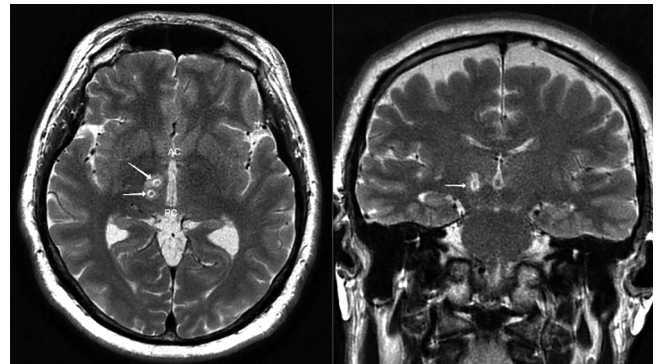


Fig. 3. Patient's MRI scan 2 h after simultaneous right-sided PTT + VIM ablation (axial and coronary planes). Ablation lesions are shown with arrows.

administration during installation of the stereotactic frame ($n = 2$). No complications were observed after the end of treatment.

Several complications were observed in the early period after MRgFUS due to edema in the treatment target: apraxia within month 1 occurred in 6 out of 48 patients in the group with PTT ablation and 2 out of 34 in the group without PTT ablation ($p = 0.32$, χ^2 method): 2 patients had dysarthria, 1 had decreased flow of speech, and 1 had numbness of the tip of the tongue. Most of these symptoms improved by follow-up month 6. One year after surgery, apraxia persisted in 2 and 2 patients with and without PTT ablation, respectively.

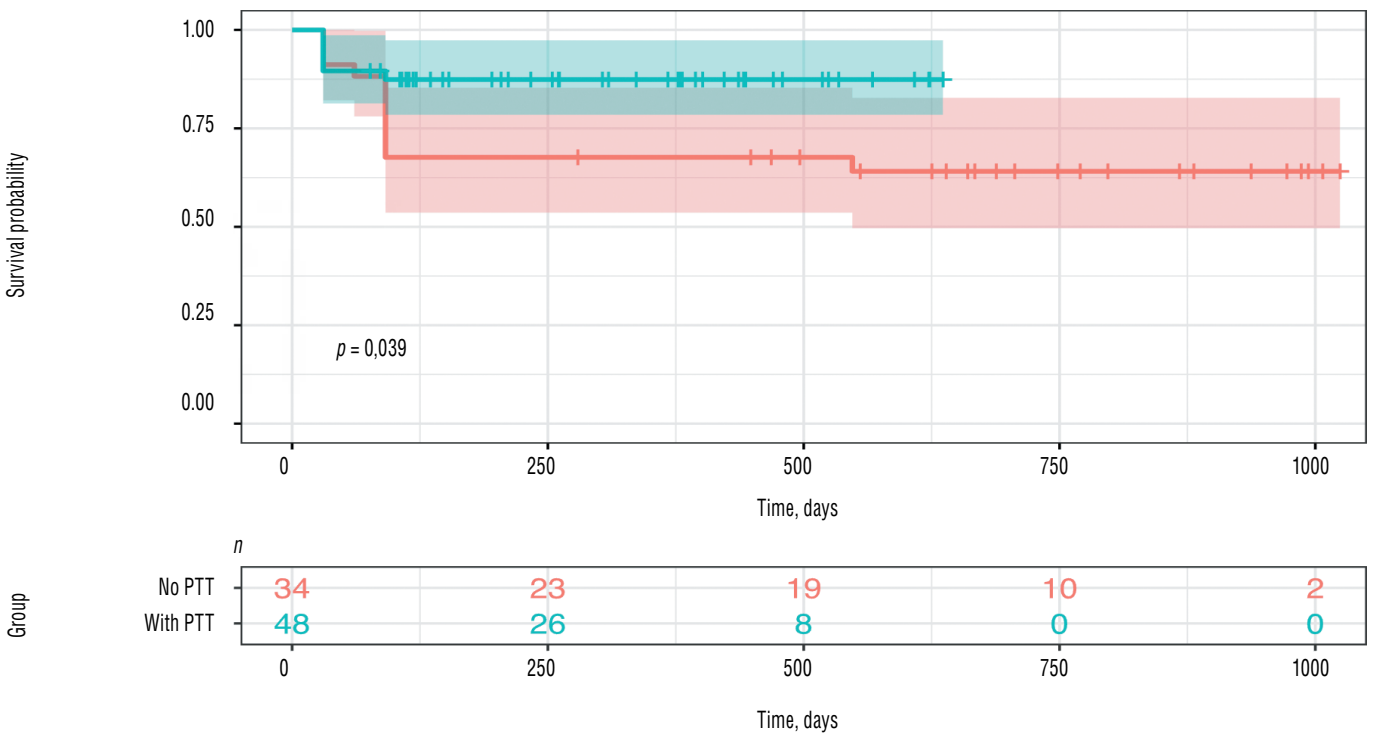


Fig. 4. Kaplan–Meier curve for symptom return depending on PTT targeting.

Median follow-up in TDPD patients after MRgFUS was 376 days (107.5; 612). Return of tremor (less pronounced compared with hyperkinesia before surgery) was recorded in 18 patients, including 5 and 13 patients with and without PTT ablation, respectively. Nine patients (2 women and 7 men; median age 63 (41; 69) years) of 18 received repeat treatment. All 9 patients did not receive PTT thalamotomy after specific targeting the VIM nucleus. During re-treatment, 5, 3, and 1 patient received PTT ablation, repeat VIM ablation, and PTT + VIM ablation, respectively. As a result, all patients achieved a satisfactory result without return of tremor throughout the entire follow-up period. In other 9 patients with tremor return, the symptoms were not significant enough to be an indication for re-treatment, and they remained being followed up.

We evaluated long-term treatment results after MRgFUS in men and women; no significant gender differences were found ($p = 0.64$; Kaplan–Meier method). However, when long-term treatment results were compared between single-target and dual-target treatment, long-term results were statistically significantly better in patients who received PTT + VIM ($p = 0.039$, Fig. 4).

Discussion

Treatment of TDPD patients is still a major challenge [1–3, 35]. The efficacy of conventional treatment with various groups of medications decreases over time, which is complicated by the development of persistent adverse effects [2, 8]. To date, DBS has been the best treatment option providing a significant reduction in tremor and other PD symptoms [10, 16–18]. However, DBS limitations include its invasive nature, complexity, implantation of the device into the body, insufficient availability, and the need for constant follow-up in large specialized medical centers in order to monitor the parameters of the generator.

References / Список источников

- Иллариошкин С.Н., Иванова-Смоленская И.А. Дрожательные гиперкинезы. Руководство для врачей. М.; 2011. Illarioshkin S.N., Ivanova-Smolenskaya I.A. Trembling hyperkinesia. Guide for doctors. Moscow; 2011.
- Богданов Р.Р., Богданов А.Р., Котов С.В. Тактика ведения пациентов с начальными проявлениями болезни Паркинсона. *Доктор.Ру*. 2012;(5):15–21. Bogdanov R.R., Bogdanov A.R., Kotov S.V. Early Parkinson's disease: approaches to patient management. *Doctor.ru*. 2012;(5):15–21.
- Левин О.С., Иллариошкин С.Н., Артемьев Д.В. Диагностика болезней Паркинсона. В кн.: Иллариошкин С.Н., Левин О.С. (ред.) Руководство по диагностике и лечению болезней Паркинсона. М.; 2017:34–98. Levin O.S., Illarioshkin S.N., Artemiev D.B. Diagnosis of Parkinson's disease. In: Illarioshkin S.N., Levin O.S. (eds.). Guidelines for the diagnosis and treatment of Parkinson's disease. Moscow; 2017:34–98.
- Simon D.K., Tanner C.M., Brundin P. Parkinson disease epidemiology, pathology, genetics, and pathophysiology. *Clin. Geriatr. Med.* 2020;36(1):1–12. DOI: 10.1016/j.cger.2019.08.002
- Dorsey E.R., Sherer T., Okun M.S., Bloem B.R. The emerging evidence of the Parkinson pandemic. *J. Parkinsons Dis.* 2018;8(s1):3–8. DOI: 10.3233/JPD-181474

In recent years, MRgFUS has been widely used to treat tremor-dominant Parkinson disease [12]. We reported our positive experience with MRgFUS in the treatment of 82 TDPD patients with a mean follow-up duration of 1 year or more, an improvement of MDS-UPDRS-III score of 40.1%, and no serious early or long-term complications. Here, we present a unique experience of dual-target MRgFUS in PTT and VIM. In 18 patients, tremor returned (all cases after VIM nucleus ablation); 9 of them successfully underwent re-treatment 6–9 months after the first procedure.

A thorough analysis of cases when tremor returned after MRgFUS and an assessment of treatment results in other centers allowed us to introduce MRgFUS PTT ablation (after its approval in 2021) in this category of patients in our clinical practice. According to our data, PTT ultrasound ablation in TDPD patients resulted in a greater improvement in early and long-term results compared with conventional VIM nucleus ablation, which is consistent to results of other authors [27]. Simultaneous dual-target (i.e. VIM and PTT) MRgFUS, which is reported in our publication, is a global priority since we have not found any previous studies on this topic, except for 3 cases of stepwise treatment [28].

Overall, an analysis of the early and long-term treatment results with MRgFUS showed that our data were comparable with efficacy and safety data in other studies [19–23, 27, 28]. In our opinion, simultaneous unilateral MRgFUS treatment can be considered an effective treatment option for patients with medication-resistant TDPD. To make a final decision on whether to include this method in the list of recommended treatment options for PD, determine precise criteria for patient selection, understand outcome variability, and assess the possibility of conducting bilateral interventions, multicenter studies in large cohorts of patients are needed.

- Kaltenboeck A., Johnson S.J., Davis M.R. Direct costs and survival of medicare beneficiaries with early and advanced Parkinson's disease. *Parkinsonism Relat. Disord.* 2012;18(4):321–326. DOI: 10.1016/j.parkreldis.2011.11.015
- Иванов П.И., Зубаткина И.С., Бутовская Д.А., Кожокар Т.И. Радиохирургическое лечение резистентного к медикаментозной терапии тремора при болезни Паркинсона. *Нейрохирургия*. 2021;23(1):16–25. Ivanov P.I., Zubatkina I.S., Butovskaya D.A., Kozhokar T.I. Radiosurgical treatment of medically refractory Parkinson's tremor. *Russian journal of neurosurgery*. 2021;23(1):16–25. DOI: 10.17650/1683-3295-2021-23-1-16-25
- Иллариошкин С.Н. Современные подходы к лечению болезни Паркинсона. *Нервные болезни*. 2004;(4):14–21. Illarioshkin S.N. Modern approaches to the treatment of Parkinson's disease. *Nervous diseases*. 2004;(4):14–21.
- Kostiuk K., Lomadze V., Vasylyv N. Stereotactic thalamotomy and contralateral subthalamotomy in treatment of Parkinson's disease. *Georgian Med. News*. 2017;(272):12–17.
- Гуца А.О., Тюрников В.М., Кащеев А.А. Современные возможности хирургической нейромодуляции. *Анналы клинической и экспериментальной неврологии*. 2018;12(5S):32–37.

- Gushcha A.O., Tyurnikov V.M., Kashcheev A.A. Modern aspects of surgical neuromodulation. *Annals of Clinical and Experimental Neurology*. 2018;12(5S):32–37. (In Russ.). DOI: 10.25692/ACEN.2018.5.4
11. Холявин А.И., Аничков А.Д., Шамрей В.К. Функциональная нейрохирургия в лечении нервных и психических заболеваний. СПб.; 2018.
- Kholyavin A.I., Anichkov A.D., Shamrey V.K. *Functional neurosurgery in the treatment of nervous and mental diseases*. St. Petersburg; 2018.
12. Галимова Р.М., Набиуллина Д.И., Иллариошкин С.Н. и др. Первый в России опыт лечения пациентов с эссенциальным тремором методом фокусированного ультразвука под контролем МРТ. *Анналы клинической и экспериментальной неврологии*. 2022;16(2):5–14.
- Galimova R.M., Nabiullina D.I., Illarioshkin S.N. et al. First use of MRI-guided focused ultrasound to treat patients with essential tremor in Russia. *Annals of Clinical and Experimental Neurology*. 2022;16(2):5–14. DOI: <https://doi.org/10.54101/ACEN.2022.2.1>
13. Christian E., Yu C., Apuzzo M.L. Focused ultrasound: relevant history and prospects for the addition of mechanical energy to the neurosurgical armamentarium. *World Neurosurg*. 2014;82(3-4):354–365.
14. Dobrakowski P.P., Machowska-Majchrzak A.K., Labuz-Rozzak B. MR-guided focused ultrasound: a new generation treatment of Parkinson's disease, essential tremor and neuropathic pain. *Interv. Neuroradiol*. 2014;20(3):275–282.
15. Ohye C., Hirai T., Miyazaki M. Vim thalamotomy for the treatment of various kinds of tremor. *Appl. Neurophysiol*. 1982;45(3):275–280.
16. Гамалея А.А., Томский А.А., Поддубская А.А. и др. Эффективность двусторонней электростимуляции внутреннего сегмента бледного шара в лечении сегментарной и генерализованной форм дистонии. *Медицинский алфавит*. 2017;1(2):47–55.
- Gamaleya A.A., Tomsky A.A., Poddubskaya A.A. et al. Efficacy of bilateral pallidal deep brain stimulation in treatment of patients with segmental and generalized dystonia. *Medical alphabet*. 2017;1(2):47–55.
17. Хабарова Е.А., Пилипенко П.И., Денисова Н.П., Ефремов Ф.А. Сравнительная эффективность нейростимуляции субталамического ядра и стереотаксических деструктивных вмешательств на подкорковых структурах головного мозга у пациентов с болезнью Паркинсона. *Нервные болезни*. 2023;(2):12–18.
- Khabarova E.A., Pilipenko P.I., Denisova N.P., Efremov F.A. Comparative efficacy of deep brain stimulation of subthalamic nucleus and stereotactic destruction of subcortical brain structures in patients with Parkinson's disease. *Nervous diseases*. 2023;(2):12–18.
18. Томский А.А., Бриль Е.В., Гамалея А.А. и др. Функциональная нейрохирургия при болезни Паркинсона в России. *Анналы клинической и экспериментальной неврологии*. 2019;13(4):10–15.
- Tomskiy A.A., Bril' E.V., Gamaleya A.A., Fedorova N.V., Levin O.S. Functional neurosurgery in Parkinson's disease in Russia. *Annals of clinical and experimental neurology*. 2019;13(4):10–15. DOI: <https://doi.org/10.25692/ACEN.2019.4.2>
19. Fasano A., De Vloot P., Linas M. et al. Magnetic resonance imaging-guided focused ultrasound thalamotomy in Parkinson tremor: reoperation after benefit decay. *Mov. Disord*. 2018;33(5):848–849. DOI: 10.1002/mds.27348
20. Gallay M.N., Moser D., Magara A.E. et al. Bilateral MR-guided focused ultrasound pallidothalamic tractotomy for Parkinson's disease with 1-year follow up. *Front. Neurol*. 2021;12:601153. DOI: 10.3389/fneur.2021.601153
21. Sperling S.A., Shah B.B., Barrett M.J. Focused ultrasound thalamotomy in Parkinson disease: nonmotor outcomes and quality of life. *Neurology*. 2018;91(14):e1275–e1284. DOI: 10.1212/WNL.00000000000006279
22. Bond A.E., Shah B.B., Huss D.S. Safety and efficacy of focused ultrasound thalamotomy for patients with medication-refractory, tremor-dominant Parkinson disease: a randomized clinical trial. *JAMA Neurol*. 2017;74(12):1412–1418.
23. Sinai A., Nassar M., Sprecher E. Focused ultrasound thalamotomy in tremor dominant Parkinson's disease: long-term results. *J. Parkinsons Dis*. 2022;12(1):199–206. DOI: 10.3233/JPD-212810
24. Milosevic L., Kalia S.K., Hodaie M. et al. Physiological mechanisms of thalamic ventral intermediate nucleus stimulation for tremor suppression. *Brain*. 2018;141(7):2142–2155. DOI: 10.1093/brain/awy139
25. Martínez-Fernández R., Mániz-Miró J.U., Rodríguez-Rojas R. et al. Randomized trial of focused ultrasound subthalamotomy for Parkinson's disease. *N. Engl. J. Med*. 2020;383(26):2501–2513. DOI: 10.1056/NEJMoa2016311
26. Speelman J.D., Schuurman R., de Bie R.M. et al. Stereotactic neurosurgery for tremor. *Mov. Disord*. 2002;17(Suppl. 3):84–88. DOI: 10.1002/mds.10147
27. Gallay M.N., Moser D., Rossi F. et al. MRgFUS pallidothalamic tractotomy for chronic therapy-resistant Parkinson's disease in 51 consecutive patients: single center experience. *Front. Surg*. 2020;6:76. DOI: 10.3389/fsurg.2019.00076
28. Jui-Cheng C., Ming-Kuei L., Chun-Ming C., Chon-Haw T. Stepwise dual-target magnetic resonance-guided focused ultrasound in tremor-dominant Parkinson disease: a feasibility study. *World Neurosurg*. 2023;171:e464–e470. DOI: 10.1016/j.wneu.2022.12.049
29. Berardelli A., Wenning G.K., Antonini A. et al. EFNS/MDS-ES/ENS [corrected] recommendations for the diagnosis of Parkinson's disease. *Eur. J. Neurol*. 2013;20(1):16–34.
30. Bhidayasiri R. Parkinson's disease: Hoehn and Yahr scale. In: Bhidayasiri R., Tarsy D. *Movement disorders: a Video Atlas*. Springer; 2012.
31. The Unified Parkinson's Disease Rating Scale (UPDRS): status and recommendations. *Mov. Disord*. 2003;18(7):738–750. DOI: 10.1002/mds.10473
32. Смоленцева И.Г., Амосова Н.А. Применение международной классификации функционирования в реабилитации при болезни Паркинсона. *Кремлевская медицина*. 2018;(3):49–54.
- Smolentseva I.G., Amosova N.A. The application of the International Classification of Functioning, Disability and Health in the rehabilitation of Parkinson's disease. *Kremlin medicine*. 2018;(3):49–54.
33. Иллариошкин С.Н., Коновалов Р.Н., Федотова Е.Ю., Москаленко А.Н. Новые МРТ-методики в диагностике болезни Паркинсона: оценка нигральной дегенерации. *Анналы клинической и экспериментальной неврологии*; 2019;13(4):77–84.
- Illarioshkin S.N., Kononov R.N., Fedotova E.Yu., Moskalenko A.N. New MRI diagnostic methods in Parkinson's disease: evaluating nigral degeneration. *Annals of clinical and experimental neurology*. 2019;13(4):77–84. DOI: <https://doi.org/10.25692/ACEN.2019.4.10>
34. Богданов Р.Р., Мананикова Е.И., Абраменко А.С. и др. Визуализация дофаминергических структур среднего мозга при болезни Паркинсона. *Анналы клинической и экспериментальной неврологии*. 2013;7(3):31–36.
- Bogdanov R.R., Manannikova E.I., Abramenko A.S. et al. Visualization of dopaminergic midbrain structures in Parkinson's disease. *Annals of clinical and experimental neurology*. 2013;7(3):31–36. DOI: <https://doi.org/10.17816/psaic229>
35. Tzu-Hsiang K., Yu-Hsuan L., Lung C. et al. Magnetic resonance-guided focused ultrasound surgery for Parkinson's disease: a mini-review and comparison between deep brain stimulation. *Parkinsonism Relat. Disord*. 2023;111:105431.

Information about the authors

Rezida M. Galimova – Cand. Sci. (Med.), Department of neurosurgery, Bashkir State Medical University, Ufa, Russia; chief, neurosurgeon, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0003-2758-0351>

Sergey N. Illarionov – D. Sci. (Med.), Prof., RAS Full Member, Director, Brain Institute, Deputy director, Research Center of Neurology, Moscow, Russia,
<https://orcid.org/0000-0002-2704-6282>

Gulnara N. Akhmadeeva – Cand. Sci. (Med.), Department of neurology, Bashkir State Medical University, Ufa, Russia; neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0001-5516-0587>

Felix F. Kashapov – neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0003-3355-4096>

Dinara I. Nabiullina – neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0003-2570-3709>

Shamil M. Safin – D. Sci. (Med.), Prof., Head, Department of neurosurgery, Bashkir State Medical University, Ufa, Russia,
<https://orcid.org/0000-0002-0100-6100>

Igor V. Buzaev – D. Sci. (Med.), Prof., Surgery department, Bashkir State Medical University, Ufa, Russia; cardiovascular surgeon, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0003-0511-9345>

Dinara R. Teregulova – Cand. Sci. (Med.), neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0001-6283-3735>

Yulia A. Sidorova – neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0002-0992-0239>

Olga V. Kachemaeva – Cand. Sci. (Med.), Associate Professor, Department of neurology, Bashkir State Medical University, Ufa, Russia; neurologist, Intelligent Neurosurgery Clinic, International Medical Center V.S. Buzaev Memorial, Ufa, Russia,
<https://orcid.org/0000-0001-9949-9582>

Author contribution: *Galimova R.M.* – the concept and design of the study, data curation, project administration, writing the text of the article; *Illarionov S.N.* – the concept and design of the study, discussion of results of the study, edition of the article; *Akhmadeeva G.N.* – data and evidence base acquisition, participation in the development of concept and design of the study; *Nabiullina D.I.* – participation in development of concept and design of the study, data and evidence base acquisition; *Kashapov F.F.* – data analysis; *Safin Sh.M.* – discussion of results of the study, project administration, edition of the article; *Buzaev I.V.* – data analysis, statistical analysis of data, edition of the article; *Teregulova D.R.* – data analysis; *Sidorova Yu.A.* – primary processing the base of the study; *Kachemaeva O.V.* – data analysis. All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published.

Информация об авторах

Галимова Резида Маратовна – к.м.н., ассистент каф. нейрохирургии и медицинской реабилитации с курсом ИДПО Башкирского государственного медицинского университета, Уфа, Россия; генеральный директор Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия,
<https://orcid.org/0000-0003-2758-0351>

Илларионов Сергей Николаевич – д.м.н., профессор, акад. РАН, зам. директора по научной работе, директор Института мозга Научного центра неврологии, Москва, Россия, <https://orcid.org/0000-0002-2704-6282>
Ахмадеева Гульнара Наилевна – к.м.н., ассистент каф. неврологии Башкирского государственного медицинского университета, Уфа, Россия; врач-невролог, паркинсонолог Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0001-5516-0587>

Кашапов Феликс Фаритович – врач-невролог Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0003-3355-4096>

Набиуллина Динара Ильгизовна – врач-невролог Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0003-2570-3709>

Сафин Шамиль Махматович – д.м.н., доцент, зав. каф. нейрохирургии и медицинской реабилитации с курсом ИДПО Башкирского государственного медицинского университета, Уфа, Россия; зав. отд. нейрохирургии Республиканской клинической больницы им. Г.Г. Куватова, Уфа, Россия, <https://orcid.org/0000-0002-0100-6100>

Бузаев Игорь Вячеславович – д.м.н., профессор каф. госпитальной хирургии Башкирского государственного медицинского университета, Уфа, Россия; директор по развитию Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0003-0511-9345>

Терегулова Динара Равильевна – к.м.н., врач-невролог Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0001-6283-3735>

Сидорова Юлия Александровна – врач-невролог Клиники интеллектуальной нейрохирургии Международного медицинского центра им. В.С. Бузаева, Уфа, Россия, <https://orcid.org/0000-0002-0992-0239>

Качемаева Ольга Валерьевна – к.м.н., доцент каф. неврологии Башкирского государственного медицинского университета, Уфа, Россия; врач-невролог Клиники интеллектуальной нейрохирургии, Международного медицинского центра им. В.С. Бузаева, Уфа, Россия,
<https://orcid.org/0000-0001-9949-9582>

Вклад авторов: *Галимова Р.М.* – создание концепции и дизайна исследования, курирование данных, руководство научно-исследовательской группой, написание текста статьи; *Илларионов С.Н.* – участие в разработке концепции и дизайна исследования, обсуждение результатов исследования, редактирование текста рукописи; *Ахмадеева Г.Н.* – сбор данных и доказательной базы исследования, участие в разработке концепции и дизайна исследования; *Набиуллина Д.И.* – участие в разработке концепции и дизайна исследования, сбор данных и доказательной базы исследования; *Кашапов Ф.Ф.* – анализ данных исследования; *Сафин Ш.М.* – обсуждение результатов исследования, руководство научно-исследовательской группой, редактирование текста рукописи; *Бузаев И.В.* – анализ данных исследования, проведение статистической обработки, редактирование текста рукописи; *Терегулова Д.Р.* – анализ данных исследования; *Сидорова Ю.А.* – первичная обработка доказательной базы исследования; *Качемаева О.В.* – анализ данных исследования. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией.