**Magnetic resonance–guided focused ultrasound central lateral thalamotomy against chronic and therapy-resistant neuropathic pain: retrospective long-term follow-up analysis of 63 interventions**

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**OBJECTIVE** Medial thalamotomies were introduced in the late 1940s. Pain relief was shown to be achieved for all body locations. With some exceptions, these early relatively small series showed frequent, more or less complete recurrence of the original pain. The posterior part of the central lateral nucleus in the human medial thalamus was identified in the 1990s using multiarchitectonic studies and intraoperative single-cell recordings and was confirmed as a surgical target. This retrospective patient series extended over 11 years. Its goal was to demonstrate the efficacy and risk profile of the MR-guided focused ultrasound (MRgFUS) central lateral thalamotomy (CLT) against chronic and therapy-resistant neuropathic (i.e., neurogenic) pain.

**METHODS** In this single-center, nonrandomized retrospective cross-sectional analysis of consecutive patients, 63 consecutive MRgFUS CLT interventions were performed in 55 patients.

**RESULTS** The mean follow-up duration was 55 months. A total of 112 CLT targets were performed, and the CLT was applied bilaterally in 48 patients and contralateral to their pain in 7 patients. Repeat MRgFUS interventions were performed in 8 patients. One serious adverse event with numbness of the upper lip was recorded. The mean pain relief rated by patients was 42% ± 32% at 3 months, 43% ± 36% at 1 year, and 42% ± 37% at the last follow-up (n = 63). The proportions of cases with ≥ 30% pain relief were 65% at 3 months, 63% at 1 year, and 61% at the last follow-up. Good outcomes (≥ 50% pain relief) were found in 54% of patients at 3 months, 49% at 1 year, and 51% at the last follow-up. The reduction in mean VAS scores showed similar percentage reductions as those for pain relief (~41% for continuous pain and ~49% for pain attacks) at the 1-year follow-up. The mean frequency of pain attacks was reduced by 92%. Alloodynia was reduced or suppressed in 68% of patients and never appeared de novo after MRgFUS CLT.

**CONCLUSIONS** These results suggest that MRgFUS CLT against neuropathic pain is a safe approach and its results are stable over time. At a mean follow-up duration of 55 months, the mean pain relief was 42% and more than 50% of patients still reported ≥ 50% pain relief. Patients with classical and idiopathic trigeminal neuralgia reported a higher mean pain relief compared with the whole patient group.

https://thejns.org/doi/abs/10.3171/2023.1.JNS222879

**KEYWORDS** neuropathic pain; magnetic resonance–guided focused ultrasound; central lateral thalamotomy; trigeminal neuralgia; functional neurosurgery
of an essential medial thalamic center, localized medial to
a pain-generating lesion in the posterolateral thalamic re-
gion. Later, Sano brought early evidence about the gener-
ation of abnormal impulses in the ventroposterior nucleus
and their amplification in a reverberating circuit between
lateral and medial thalamic nuclei. In an effort starting
in the early 1990s, Jeanmonod and collaborators defined
the posterior part of the central lateral nucleus (CLp) in
the medial thalamus using multiarchitectonic studies and
intraoperative single-cell recordings and showed that it is
an effective surgical target. The central lateral nucleus
(CL) has been considered as part of the anterior group of
the intralaminar nuclei, but in nonhuman primates and
humans, there is a posterior extension of the CL between
the posterior pole of the mediodorsal nucleus and the me-
dial pulvinar nucleus (PuM). The CL has important corti-
cal projections that extend to large cortical domains. As
such, it is in position to transfer nociceptive information,
conveyed through the spinothalamic and spino-recipient-
thalamic tracts, to large cortical domains, including areas
involved in nociception. The CL has known afferents from
the spinothalamic tract. It is distant from primary
somatosensory nuclei and has a combination of "diffuse"
(layer I) and "nondiffuse" (layers III and IV) cortical pro-
jections including areas mediating discriminative (pri-
mary somatosensory cortex, secondary somatosensory
cortex, posterior insula, and posterior parietal), affective-
motivational (anterior cingulate and anterior insula), cog-
nitive (prefrontal), and motor (premotor cortex) aspects of
pain. Advantages of the CLp over other surgical targets in
the medial thalamus (center median/parafascicular [CM/ PF] complex, or PuM) were highlighted previously. Intra-
operative microelectrode recordings in the CLp were
shown to display low threshold calcium spike bursts (aver-
age interburst frequency of 4 Hz) in as much as half of the
recorded neurons, and < 1% of them responded to sensory
or motor stimulations. The rationale of performing a CLp
thalamotomy (CLT) is based on the fact that this area has
lost its normal function over time (< 1% cells with recep-
tive fields and absence of deficits after CLT) and sustains/
amplifies a deleterious low-frequency overproduction (ap-
proximately 4 Hz), which is the source of a thalamocorti-
cal dysfunctional mechanism, that is, thalamocortical dys-
rhythmia. Thalamocortical dysrhythmia is characterized
by the coupled increase of low- and then high-frequency
activities in cortical areas of the pain matrix, which were
demonstrated by quantitative electroencephalography
(EEG) recordings.

Patient series of CLT in chronic and therapy-resistant neuropathic pain were performed first with radiofrequency
lesioning and later with the new technology of the transcranial MR-guided focused ultrasound (MRgFUS) surgery. Gamma Knife technology was and still is
used to perform medial thalamotomies in neuropathic pain
(CM/PF complex or CLp more recently). Deep brain stimulation (DBS) of the CL was first tried very recently in a pilot study.

MRgFUS has been shown to be a safe and accurate lesioning technique removing the risk of infection,
strongly reducing the risk of bleeding, and providing a
targeting accuracy within 1 mm. This is a case series of
patients with chronic and therapy-resistant neuropathic pain syndromes with long-term follow-ups after MRgFUS
CLT performed in a single center over the past 11 years.

Methods

Study Context

This is a single-center, nonrandomized cross-sectional retrospective analysis of consecutive patients with
chronic and therapy-resistant neuropathic pain followed after MRgFUS CLT between 2011 and 2022. The first
11 treatments were part of a study approved by the Eth-
ics Committee of Aargau/Solothurn and Swissmedic and
were sponsored by Insightec Ltd. All patients treated in
this study signed an informed consent form after having
been fully informed about the treatment, its results, and
its risks.

Therapy resistance and thus the indication for MRgFUS
CLT was based on the lack of efficacy and/or side effects
of antiepileptic and antidepressant drugs during at least
1 year. Pain taxonomy followed the updated system of
the International Association for the Study of Pain for
neuropathic pain. Diagnostic criteria for classical and
idiopathic trigeminal neuralgia were as previously pub-
lished. The case report of a patient with cluster headache
included in this analysis was recently published.

Surgical Procedure and Target Determination

All treatments were performed using a 3T MRI system
(Imaging 750, GE Healthcare) using the Exablate Neuro (Insightec). CLT was planned on maps from the
Atlas of the Human Thalamus and Basal Ganglia. Its
3D coordinates in relation to the anterior commissure–
posterior commissure line were transferred onto operative
MR images and were modified according to individual
anatomy as seen on the preoperative high-resolution MR
images cut in the stereotactic planes. Accuracy determina-
tion and target reconstruction were performed according
to the method of Moser et al. based on findings on MRI
performed 2 days after MRgFUS CLT. Determination and
coverage of the CLT target evolved over years of experi-
ence with the MRgFUS system. At first, only one sonica-
tion spot was placed 6 mm dorsal to the intercommissural
plane and 8 mm from the medial thalamic border where
CLP output fibers converge. The present targeting strategy
has as a goal of including the largest part of the CLP
and consists of a set of four target subunits placed at 6
mm (2 subunits) and 8–9 mm (2 subunits) dorsal to the
intercommissural plane. The anteroposterior position of
the target subunits is determined based on visualization
of the junction between the mediodorsal and PuM nuclei
on preoperative axial T2-weighted images. This corresponds
to the anteroposterior position of the CLp, centered in our
experience between 3 mm anterior and 1 mm posterior to
the posterior commissure. In the mediolateral dimension,
two subunits are placed to cover the mediodorsal extent
of the CLp, from the medial thalamic border to 10 mm
laterally (e.g., 5 and 8 mm laterally to the thalamic border
for mediolateral positioning of the target subunits centers)
(Fig. 1). The operative setup and strategy were described
previously. Target coverage was deemed sufficient based
on the achieved thermal dose volume coverage at 240 cumulative equivalent minutes at 43°C, for all target sub-units, as described for other targets. This usually corresponds to temperatures at a focal point between 55°C and 58°C and sonication durations between 8 and 31 seconds.

In most unilateral neuropathic pain syndromes, we perform CLT bilaterally on the basis of the presence of bilateral spinothalamic projections, the recording of bilateral pathological thalamic bursting activity, and the increase of pain relief brought by the addition of an ipsilateral CLT.

Normal coagulation and blood pressure were checked for all patients prior to surgery. A dose of 10 mg domperidone (Motilium lingual) was given before starting the sonications. Since 2017, all patients received 20 mg of intravenous methylprednisolone in the hour after the end of the operation, 20 mg after 12 hours, and 2 mg of dexamethasone three times daily for 3–4 days to control/limit the perifocal edema of the lesion. Anesthesiological support was never needed.

Baseline Assessment and Follow-Up

Pain assessments with a full neurological examination including assessment ofesthesia and algesia and evaluation for any side effects were performed after 2 days, 3 months, and 1 year. Later follow-up assessments were mostly performed through email and telephone conversations. Baseline and follow-up assessments included the items of the McGill Pain Questionnaire. Only 6 different pain qualities were systematically recorded (electricity, stinging, burning, shooting, tearing, and compression). Pain intensity was noted on a visual analog scale (VAS) for the least, the worst, and the mean pain intensities on a scale between 0 and 100 for both continuous pain and pain attacks. If not provided by the patient, the arithmetical mean pain intensity was calculated. A pain attack was defined as a sharp and short-lived (seconds to a few minutes) increase in pain.

Patients were asked for a percentage value of postoperative pain relief compared with their preoperative state (baseline). Good outcome was defined as pain relief ≥ 50%. A recurrence was defined as an initial good outcome (pain relief ≥ 50%) and later a decrease of pain relief to < 50% and/or recurrence of pain attacks.

The Mini–Mental State Examination and later the Montreal Cognitive Assessment (MoCA) were performed preoperatively and after 2 days and 1 year follow-up. All patients were asked to complete the Hospital Anxiety and Depression Scale (HADS) at baseline and each follow-up examination. Three questions of World Health Organization Quality of Life Questionnaire Brief Version (WHOQOL-BREF) were recorded at baseline and at the follow-ups.

Repeat MRgFUS CLT was offered when patients met the criteria of symptom recurrence (defined above) and evidence (radiology and intraoperative thermal doses) for insufficient target coverage.

**Statistical Analysis**

Statistical analysis was performed using Analyse-it for Microsoft Excel version 6.15 (Analyse-it Software Ltd.), as well as with SigmaPlot version 15.0 (Systat Software Inc.). Statistical comparisons of means were obtained by
ANOVA (Kruskal-Wallis ANOVA on ranks when normal distribution and equal variance failed) and Dunn’s method for post hoc pairwise multiple comparison. If not specified otherwise, values given in the text are means ± standard deviation; p ≤ 0.05 indicates statistical significance.

Results

Patient characteristics are summarized in Table 1. Sixty-three consecutive MRgFUS CLT interventions were performed in 55 patients. The ages of the patients ranged between 38 and 80 years (mean 62 ± 11 years). The mean duration of the pain syndrome between onset and MRgFUS CLT was 14 ± 11 years (range 3–47 years). Nine patients were included in earlier publications.20,30

Prior to MRgFUS CLT, 26 patients (47%) had a functional neurosurgical intervention for their neuropathic pain syndrome (discectomies, spine decompression, and fusion were not counted). After MRgFUS CLT, 1 patient underwent pain surgery (1 glycerol rhizotomy). Overall, 112 CLT targets were performed (53 left and 59 right CLTs). One international patient was lost to follow-up (i.e., the patient was examined 2 days after MRgFUS but did not keep contact with our clinic for later assessments, either in person or remotely).

Overall, 30% of patients came from outside of Switzerland. Five patients had died of unrelated causes at the time of this report. The follow-up duration ranged between 3 and 132 months (mean 55 ± 40 months, median 46 months). The Kaplan-Meier estimator of follow-up durations is depicted in Fig. 2.

Surgery

The vast majority of patients received bilateral MRgFUS CLT (48 patients) in one session. In 7 patients, MRgFUS CLT was performed on the side contralateral to their pain syndrome only. Repeat MRgFUS interventions were performed in 8 patients (5 bilaterally and 3 on one side only).

The mean skull density ratio of the patients was 0.56 ± 0.1 (range 0.37–0.77, median 0.56). The mean operation duration from the start of stereotactic frame fixation to its removal was 5.3 ± 1.9 hours (range 3.2–10 hours). For the final 20 treatments, the duration was 4.1 ± 0.6 hours (range 3.2–5.3 hours). The mean lesion volume measured on axial T2-weighted images 2 days after treatment was 160 ± 96 mm³ (range 13–452 mm³). The sonication duration lasted between 8 and 31 seconds. The average power of the final sonications was 1036 ± 190 W. Accuracy of targeting was determined on axial T2-weighted images 2 days after CLT and showed similar values as published previously, with a mean targeting accuracy for each of the three dimensions below 0.5 mm.27,28 All patients were discharged after a 1-night hospital stay.

Morbidity

There was no bleeding or infection. A serious neurological adverse event was recorded in 1 patient (1.6% of interventions or 0.9% of the MRgFUS CLT targets performed). This happened during a repeat MRgFUS CLT in a patient previously treated with radiofrequency ablation. The patient reported numbness on his upper lip laterally, and we found a hypesthesia of moderate intensity in a 1- to 2-cm² area. The numbness was regredient but did not disappear at follow-up 2 years after MRgFUS CLT. Sonications were painful for a few seconds in 35 cases (56%), but a change in the procedure or sedation was never required.

Pain Relief

The mean pain relief rated by patients was 42% ± 32% at 3 months (n = 61), 43% ± 36% at 1 year (n = 57), and 42% ± 37% at the last follow-up (mean 55 months, n = 63). All patients who could not be reached 1 year after MRgFUS CLT were assumed to have 0% pain relief. Figure 3 illustrates the pain relief distribution across the patient series. Pain relief was ≥ 30% in 65% of cases at 3 months (n = 61), in 63% of cases at 1 year (n = 57), and in 61% of cases at the last follow-up (mean 55 months) (n = 63). Good out-

<table>
<thead>
<tr>
<th>TABLE 1. Patient characteristics</th>
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<tbody>
<tr>
<td>Value</td>
</tr>
<tr>
<td>No. of interventions</td>
</tr>
<tr>
<td>No. of pts</td>
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<tr>
<td>Mean age at treatment, yrs (range)</td>
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<tr>
<td>Mean pain duration, yrs (range)</td>
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<tr>
<td>Female sex, %</td>
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<tr>
<td>No. of CLT targets</td>
</tr>
<tr>
<td>Lt</td>
</tr>
<tr>
<td>Rt</td>
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<tr>
<td>No. of pts w/ bilateral CLT</td>
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<tr>
<td>No. of pts w/ contralateral CLT only</td>
</tr>
<tr>
<td>Side effects, % of targets</td>
</tr>
<tr>
<td>No. of repeat MRgFUS CLTs</td>
</tr>
<tr>
<td>No. of pts w/ previous pain ops (%)</td>
</tr>
<tr>
<td>No. of pain ops after MRgFUS CLT</td>
</tr>
<tr>
<td>No. of deaths</td>
</tr>
<tr>
<td>Follow-up, mos</td>
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<tr>
<td>Mean ± SD (range)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>No. of interventions in each neuropathic pain subgroup</td>
</tr>
<tr>
<td>Spinal cord injury</td>
</tr>
<tr>
<td>Secondary trigeminal neuralgia</td>
</tr>
<tr>
<td>Classical &amp; idiopathic trigeminal neuralgia</td>
</tr>
<tr>
<td>Postdiscectomy radiculopathy</td>
</tr>
<tr>
<td>Thalamic infarction</td>
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<tr>
<td>Neuropathy</td>
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<tr>
<td>Cortical &amp; basal ganglia infarctions</td>
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<tr>
<td>Brainstem injury</td>
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<td>Plexus avulsion</td>
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<tr>
<td>Amputation</td>
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<tr>
<td>Postherpetic neuralgia</td>
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<tr>
<td>Cluster headache</td>
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</tbody>
</table>

Pt = patient.
comes (≥ 50% pain relief) were found in 54% of cases at 3 months (n = 61), in 49% of cases at 1 year (n = 57), and in 51% of cases at the last follow-up (n = 63). An absence of pain relief was reported in 28% of cases at 3 months (n = 61), in 28% of cases at 1 year (n = 57), and in 35% of cases at the last follow-up (n = 63).

The number of pain attacks decreased from a mean of 113 ± 231 (n = 39) per day at baseline to 11 ± 29 (n = 35, p < 0.001, 90% reduction) at the 3-month follow-up and 9 ± 30 (n = 30, p < 0.001, 92% reduction) 1 year after MRgFUS CLT. The mean percentage of pain attack reduction was 66% at 3 months and 76% at the 1-year follow-up. At the 1-year follow-up, pain attacks were suppressed in 33% (12/36).

In addition to the analysis of the whole patient group, 4 subgroups with more than 5 interventions were analyzed separately. Subgroup analysis of interventions against classical and idiopathic trigeminal neuralgia (n = 8) revealed a mean pain relief of 76% ± 19% at a mean last follow-up of 80 ± 31 months, and all 8 patients had ≥ 50% pain relief. For secondary trigeminal neuralgia (n = 11), the mean pain relief was 31% ± 42% at the last follow-up (59 ± 35 months),

FIG. 2. Kaplan-Meier estimator of the follow-up durations in this cross-sectional retrospective study.

FIG. 3. Quantile boxes. The median is plotted as a vertical thick line, 1st and 3rd quartiles as a box, mean pain relief as a larger blue square, and all individual results as small squares (light gray). The confidence interval of the box plots is 99%. Figure is available in color online only.
and 4 patients had ≥ 50% pain relief. Interventions for spinal cord injury (n = 14) revealed a mean pain relief of 35% ± 24% at the last follow-up (36 ± 32 months), and 5 patients had ≥ 50% pain relief. For postdiscectomy radiculopathy (n = 6) the mean pain relief was 68% ± 37% at the last follow-up (70 ± 49 months), and 5 patients had ≥ 50% pain relief.

**VAS Results**

At baseline, a continuous pain component was reported in 90% of cases and pain attacks in 71%. The evolution of mean VAS scores from baseline to 3 months and 1 year after CLT is shown in Table 2. At the 1-year follow-up, the mean maximum VAS score for continuous pain was reduced by 34%, and its mean VAS was reduced by 41%. The mean maximum VAS score for pain attacks at 1 year was reduced by 46% and its mean VAS by 49%. Drug intake (opiates, antiepileptics, and antidepressants) at baseline and at follow-up examinations are detailed in Table 2.

**Pain Characteristics**

The pain was localized in 30% of cases on the left, in 37% on the right, and in 33% on both sides of the body. A total of 243 pain qualities were recorded at baseline (mean 3.9 ± 1.3, median 4 per patient). There were 129 pain qualities (mean 2.3 ± 1.3, median 2 per patient) at the 3-month follow-up and 104 at the 1-year follow-up (mean 2.1 ± 1.2, median 2 per patient). Table 3 shows the 6 recorded pain qualities at baseline and their evolution at 3 months and 1 year. At 3 months, 2 patients reported a new burning pain quality and 1 patient a new tearing quality. The 2 new burning qualities were not reported again at 1 year. At 1 year, 4 patients reported a newly developed pain quality (electricity [n = 1], stinging [n = 1], and tearing [n = 2]).

Allodynia was found in 32 of the 63 cases at baseline. At 3 months (n = 61), it was suppressed (16%) or strongly reduced (34%) in 50% of cases. At 1 year (n = 54), allodynia was suppressed in 40% (10/25) or reduced in 28% (7/25) of cases. No patient developed new allodynia after MRgFUS CLT.

Bodily pain distribution as drawn by the patients was compared with the baseline drawings. Its extension was reduced in 51% of cases at 3 months (6% with ≥ 50% pain relief and 45% with < 50%) and in 57% at the 1-year follow-up (24% with ≥ 50% pain reduction and 33% with < 50%). Interestingly, among the 16 cases without any pain relief at 1 year, 6 (38%) drew a clearly smaller painful area. In 3 cases, the reduction of pain extension was > 50%. In 2 cases, the reduction in pain extension preceded a significant pain reduction (70% and 100% at the last follow-up). Figure 4 exemplifies the variability between pain relief and extension of bodily pain distribution, both reported by the patient himself.

**Secondary Outcome Measures**

Answers to questions 1, 2, and 17 of the WHOQOL-BREF showed statistically significant improvement of these 3 items of quality of life (Table 4). HADS scores were reduced (improvement) from baseline 15.0 ± 8.0 (over

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**TABLE 2. Pain intensity according to VAS scores and drug intake at baseline and follow-up**

<table>
<thead>
<tr>
<th>Pain Quality</th>
<th>Baseline</th>
<th>3-mo FU (n = 57)</th>
<th>p Value</th>
<th>1-yr FU (n = 49)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Continuous pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average of mean VAS score</td>
<td>54 ± 16 (n = 57)</td>
<td>43 ± 23 (n = 49)</td>
<td>0.017*</td>
<td>32 ± 25 (n = 42)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Mean minimum VAS score</td>
<td>30 ± 22</td>
<td>22 ± 21</td>
<td>0.15</td>
<td>16 ± 20</td>
<td>0.002**</td>
</tr>
<tr>
<td>Mean maximum VAS score</td>
<td>77 ± 20</td>
<td>62 ± 28</td>
<td>0.009**</td>
<td>51 ± 37</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Suppressed continuous pain</td>
<td>10% (5/49)</td>
<td>29% (12/42)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain attacks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average of mean VAS score</td>
<td>76 ± 16 (n = 45)</td>
<td>47 ± 35 (n = 40)</td>
<td>&lt;0.001***</td>
<td>39 ± 35 (n = 36)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Mean minimum VAS score</td>
<td>62 ± 25</td>
<td>41 ± 35</td>
<td>0.014*</td>
<td>31 ± 30</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Mean maximum VAS score</td>
<td>88 ± 14</td>
<td>52 ± 37</td>
<td>&lt;0.001***</td>
<td>48 ± 40</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Suppressed pain attacks</td>
<td>25% (10/40)</td>
<td>33% (12/36)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean no. of pain attacks per day</td>
<td>113 ± 231 (n = 39)</td>
<td>11.4 ± 29 (n = 35)</td>
<td>&lt;0.001***</td>
<td>9.2 ± 30 (n = 30)</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Drug intake</td>
<td></td>
<td></td>
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<tr>
<td>Opiates</td>
<td>32% (20/63)</td>
<td>13% (8/60)</td>
<td>16% (9/56)</td>
<td></td>
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</tr>
<tr>
<td>Antiepileptics</td>
<td>56% (35/63)</td>
<td>33% (20/60)</td>
<td>46% (26/56)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>49% (31/63)</td>
<td>45% (27/60)</td>
<td>36% (20/56)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Numbers in parentheses indicate the number of interventions.**

**TABLE 3. Presence of pain qualities at baseline and percentage of patients for whom they were suppressed at follow-up**

<table>
<thead>
<tr>
<th>Pain Quality</th>
<th>Baseline</th>
<th>3-mo FU (n = 57)</th>
<th>1-yr FU (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electricity</td>
<td>62%</td>
<td>~49%</td>
<td>~59%</td>
</tr>
<tr>
<td>Stinging</td>
<td>87%</td>
<td>~51%</td>
<td>~47%</td>
</tr>
<tr>
<td>Burning</td>
<td>81%</td>
<td>~29%</td>
<td>~45%</td>
</tr>
<tr>
<td>Shooting</td>
<td>38%</td>
<td>~75%</td>
<td>~79%</td>
</tr>
<tr>
<td>Tearing</td>
<td>57%</td>
<td>~39%</td>
<td>~61%</td>
</tr>
<tr>
<td>Compressive</td>
<td>60%</td>
<td>~53%</td>
<td>~68%</td>
</tr>
</tbody>
</table>
a maximum of 42) to 12.2 ± 8.0 (p = 0.05) at 3 months and
11.7 ± 8.0 (p = 0.02) at the 1-year follow-up. The anxiety
component of the score was 7.5 ± 4.2 at baseline, 6.2 ± 4.5
(p = 0.09) at 3 months, and 6.0 ± 4.3 (p = 0.05) at 1 year.
The depression score was 7.2 ± 4.1 at baseline, 6.0 ± 4.2 (p
= 0.3) at 3 months, and 5.6 ± 5.2 (p = 0.03) at 1 year.

The mean MoCA score was 27.9 ± 2.6 at baseline (n =
50), 28.9 ± 1.8 (p = 0.02) 2 days after MRgFUS CLT (n =
50), and 29.3 ± 1.1 (p = 0.01) at 1 year (n = 37). The MMST
at baseline was 29.4 ± 0.8 (n = 13), 29.5 ± 0.5 (n = 13) at 3
months, and 29.8 ± 0.4 at 1 year (n = 13).

Discussion

This case series of 63 consecutive MRgFUS CLT inter-
ventions, performed in a single center and followed for a
mean of 55 months, confirms the safety profile of the inter-
vention\(^{18,20,27}\) and shows sustained pain relief over time.\(^{13,20}\)
A notion present in the neurosurgical pain literature is that
medial thalamotomies are safe but their efficiency does
not hold over time.\(^{8}\) Mean pain relief as reported by the
patients was shown to remain remarkably stable (42% at 3
months, 43% at 1 year, and 42% at the last follow-up). The
percentage of patients with “good” pain outcomes (≥50%
pain relief) was 54% at 3 months, 49% at 1 year, and 51%
at the last follow-up. Only 1 patient was lost to follow-up.
Thus, contrary to reports in the literature, pain relief did
not decrease over time.

The reduction in mean VAS scores showed similar per-
centage reductions as the pain relief percentage (~41% for

![FIG. 4. Bodily pain distribution as drawn by the patient at baseline (A, C, and E) and 1 year after bilateral MRgFUS CLT (B, D, and
F). A and B: Postherpetic neuralgia (dermatomes T8 and T9 with extension to T10–T12 on the left) 6 years prior to MRgFUS CLT
with 80% pain relief. C and D: Peripheral neuropathic pain after cervical hernia and microdiscectomy (C5–6 and C6–7) 6 years
prior to MRgFUS with 70% pain relief. E and F: Neuropathic pain after spinal cord injury at the thoracic level T4 34 years prior to
MRgFUS CLT with 0% pain relief. Figure is available in color online only.](image-url)
continuous pain and −49% for pain attacks) at the 1-year follow-up. Although the mean intensity of the pain attacks as rated by the VAS was only reduced by 49%, the mean frequency of pain attacks was reduced by 92%. Allodynia was reduced or suppressed in 68% of cases and never appeared de novo after MRgFUS CLT. More than half of the patients taking opiates at baseline had stopped their intake at the 1-year follow-up. Bodily distribution of pain as drawn by the patients globally correlated with the pain relief reported, although some exceptions were observed. In Fig. 4E and F, the patient presented with a substantial reduction of his pain area along with 0% pain relief. The pain relief percentages given by patients provide a global assessment of the obtained relief, which comprises the perception of pain and its psycho-emotional (paralimbic/multimodal) modulation. The relevance of this modulation factor is well recognized and has been addressed, among other studies, in the study by Michels et al. 42 In contrast to their patient subgroup with ≥ 50% pain relief, EEG overactivity was maintained 1 year after radiofrequency ablation in the subgroup with insufficient pain relief (<50%). This happened in parallel with a positive correlation between a frustration scale and an increase in EEG cortical current source density. The latter was located in the bilateral frontopolar, prefrontal interhemispheric and orbitofrontal paralimbic/multimodal cortical areas. The reduction or suppression of a dysrhythmic cortical overactivity at the source of neuropathic pain can thus be hindered by emotions, and, in that case, frustration.

The reduction of pain qualities was higher in general at the 1-year than at the 3-month follow-up assessment. Among the 6 recorded pain qualities mostly associated with neuropathic pain in our experience, shooting, electricity, tearing, and compression were reduced in more than 50%. Stinging (−47%) and burning (−45%) pain qualities were more resistant to MRgFUS CLT.

The MoCA showed a slight but nevertheless statistically significant improvement in the mean score at the 1-year follow-up compared with baseline. Some learning effect of recurrent testing cannot be ruled out. The mean HADS score was significantly improved at the 1-year follow-up. Selected questions of the WHOQOL-BREF (see Table 4) revealed statistically significant improvements.

The analysis of the four subgroups showed similar pain relief for secondary trigeminal neuralgia and spinal cord injury, with long-term mean pain relief of 31% and 35%, respectively. Better results were obtained for the subgroups of postdiscectomy radiculopathy and classical and idiopathic trigeminal neuralgia, where long-term pain relief was 68% and 76%, respectively. Particularly good results of CLT for the treatment of classical and idiopathic trigeminal neuralgia were published in 2020. 20 This observation was also shared by Franzini et al. 24 using the Gamma Knife to perform CLT for trigeminal pain syndromes.

DBS was first explored for the treatment of pain before being dominantly applied against Parkinson’s disease. However, the US FDA withdrew its approval for the treatment of pain in 1989. Two industry-sponsored trials (in 1993 and 1997, reported in 2001 37) showed only an approximately 20% response rate, which led the manufacturer to withdraw its FDA application. 36 In 2006, Hamani et al. 39 reported that 24% of patients maintained long-term benefit of their DBS implantation against pain. At the 1-year follow-up, 76% of patients received no definitive implant or their device was switched off. Later studies showed some benefits, even in the long term but without overcoming the threshold of ≥ 50% pain relief in more than 50% of patients. 40–43 Targets used in DBS were the ventral posterior medial nucleus (VPM) and ventral posterior lateral nucleus (VPL), the periaqueductal gray matter, the CM/Pf complex, and only very recently one trial of 6 patients with the combined targets of CL and VPM and VPL. 26 One major difficulty when analyzing results in the context of medical implants is the number of patients who undergo trials but do not definitively undergo implantation. Rasche et al., 42 for example, applied very strict criteria for successful electrode test trials. Thus, only 57% of patients qualified for definitive internalization of their DBS system.

Results of radiosurgical medial thalamotomies were recently reviewed by Franzini et al. 44 Pooled results of 6 studies (total of 118 patients) reported a “meaningful” pain reduction in 38% of patients at the last follow-up. However, the presence of 51% of cancer pain patients in these series brings uncertainty as to the obtained pain relief for neuropathic pain cases.

**Side Effects**

As expected from an incisionless technique, there was no bleeding and no infection. One patient developed a somatosensory deficit in the trigeminal area most likely due to encroachment of the therapeutic lesion on the VPM nucleus during MRgFUS CLT. This happened in the context of previous radiofrequency lesioning in his medial thalamus, with probable gliotic tissue displacement. The patient had not fully recovered from his deficit at the last follow-up. This remains the only significant side effect recorded

<table>
<thead>
<tr>
<th>Baseline</th>
<th>3-mo FU</th>
<th>p Value</th>
<th>1-yr FU</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>How would you rate your quality of life? (very poor = 1, very good = 5)</td>
<td>2.7 ± 1.0 (n = 52)</td>
<td>3.4 ± 0.9 (n = 43)</td>
<td>0.009**</td>
<td>3.4 ± 0.8 (n = 43)</td>
</tr>
<tr>
<td>How satisfied are you with your health? (very dissatisfied = 1, very satisfied = 5)</td>
<td>2.2 ± 1.0 (n = 52)</td>
<td>2.8 ± 1.1 (n = 44)</td>
<td>0.007**</td>
<td>3.1 ± 1.1 (n = 43)</td>
</tr>
<tr>
<td>How satisfied are you with your ability to perform your daily living activities? (very dissatisfied = 1, very satisfied = 5)</td>
<td>2.6 ± 1.2 (n = 51)</td>
<td>3.3 ± 1.1 (n = 40)</td>
<td>0.024*</td>
<td>3.5 ± 1.1 (n = 40)</td>
</tr>
</tbody>
</table>

*p ≤ 0.05; **p ≤ 0.01; and ***p ≤ 0.001.

Questions 1, 2, and 17 of the WHOQOL-BREF. 35 Numbers in parentheses indicate the number of interventions.
in 112 lesions of the CLT in this series. This compares favorably with the side effects of any implanted devices.35 Pooled Gamma Knife studies on medial thalamotomy reported an adverse event rate of 5% (4% related to radiation).44

**Study Limitations**

This consecutive surgical case series has the limitation of its retrospective nature and not being randomized and sham controlled. In addition, various neuropathic pain conditions were analyzed as a single group. A larger study would allow more subgroup analyses as presented in a recent contribution.20

**Conclusions**

The overall side-effect profile of MRgFUS CLT, retrospectively studied in 63 interventions, speaks for a safe neurosurgical approach. The efficacy in relieving pain in chronic and therapy-resistant neuropathic pain syndromes, although modest as shown by its average pain relief (42%), proved to be remarkably stable over time. At a mean follow-up duration of 55 months, more than 50% of patients reported ≥50% pain relief. Patients with classical and idopathic trigeminal neuralgia reported a higher average pain relief (76%) compared with the whole patient group.

**Acknowledgments**

We thank Dr. Payam Pourtehrani and colleagues at Rodiaq Diagnostic Centers Solothurn for MRI, Dr. Alexander Arnold for internal medicine support, Drs. Maja Strasser and Robert Bühlner for neurological examinations, Tanja Thalmann and Samuel Ryser for nursing care, and Franziska Rossi for administrative support.

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Disclosures
Dr. Jeanmonod reported grants from Insightec Ltd. (the first 11 treatments were sponsored by Insightec Ltd.) during the conduct of the study.

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Conception and design: Gallay. Acquisition of data: Gallay, Magara, Moser, Kowalski, Jeanmonod. Analysis and interpretation of data: Gallay, Magara, Kaeser, Jeanmonod. Drafting the article: Gallay, Jeanmonod. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Gallay. Statistical analysis: Kaeser. Administrative/technical/material support: Moser. Study supervision: Gallay, Jeanmonod.

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