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Sustained acoustic medicine treatment of discogenic chronic low back pain: A randomized, multisite, double-blind, placebo-controlled trial

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Abstract.
BACKGROUND: Sustained acoustic medicine (SAM) is a noninvasive long-term treatment that provides essential mechanical and thermal stimulus to accelerate soft tissue healing, alleviate pain, and improve physical activity. SAM increases localized deep tissue temperature, blood flow, cellular proliferation, migration, and nutrition exchange, resulting in reduced inflammation and an increased rate of tissue regeneration.
OBJECTIVE: To assess the efficacy of SAM treatment of discogenic back pain in the lower spinal column to reduce pain, improve quality of life, and lower pharmacotherapy use.
METHODS: Sixty-five subjects with chronic low back pain were randomly assigned to SAM ($N = 33$) or placebo ($N = 32$) groups. Subjects self-applied SAM device bilaterality on the lower lumbar region for 4 hours daily for 8 weeks and completed daily pain diaries before, during, and after treatment. Subjects recorded pain reduction using a numeric rating scale (NRS), medication use, and physical activity using the Global Rating of Change (GROC) and Oswestry Disability Index (ODI).
RESULTS: SAM treatment significantly reduced chronic lower back pain from baseline relative to placebo treatment ($p < 0.0001$). SAM treated subjects reported significantly lower back pain at 4 weeks, with the highest pain reduction (-2.58 points NRS, $p < 0.0001$) reported at 8 weeks. Similar trends were observed in improved physical activity (3.48 GROC, $p < 0.0001$, 69–88% ODI, $p < 0.0001$) and 22.5% (15.2 morphine milligram equivalent) reduction in the use of opioid medication from baseline to 8 weeks.
CONCLUSION: Daily, home-use SAM treatment significantly improves the clinical symptoms of chronic lower back pain, improves physical mobility, and reduces daily medication use. SAM treatment is well-tolerated by patients and may be considered a safe, non-invasive treatment option for chronic discogenic, lower back pain.

Keywords: Low back pain, low-intensity continuous ultrasound, ultrasound therapy, sustained acoustic medicine, mechanotransduction, herniated discs, chronic pain, durable medical equipment

1. Introduction

Lower back pain is a prevalent health problem and affects people of all ages, from children to the elderly. Sixty to 85% of the population experiences lower back

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pain at least once in their lifetime, with the highest prevalence in people between 40 and 69 years old. Chronic lower back pain (e.g., back pain greater than 3 months) impacts 10% to 23.3% of the adult population in the United States [1,2]. The highest prevalence of lower back pain is in women between 40 to 80 years old [3]. The annual cost of lower back pain management in the United States exceeds $100 billion [4,5]. While only 1.2% of patients receive surgery within the first year of diagnosis, they account for approximately $784 million in annual healthcare cost [6]. The largest portion of the cost is associated with indirect economic costs such as lost workdays and reduced overall productivity. Besides economic effects, lower back pain significantly affects the quality of life and daily activities, leading to depression and anxiety for many patients [7,8,9].

Back pain is a complex pathology. It can be due to trauma or degeneration involving spine structure, including muscles, fascia, ligaments, tendons, facet joints, neurovascular elements, vertebrae, and intervertebral discs. In trauma or degeneration, physical damage and improper healing can lead to chronic localized inflammation and pain [10,11]. The intervertebral disc degradation (herniated disks) reduces the intervertebral space, thus changing the local biochemical and biomechanical function, leading to localized chronic inflammation, degeneration of nucleus pulposus cells, and pain [11,12]. Accelerated spinal degeneration has been shown to reduce the space between two vertebrae as the intervertebral disc and associated elements break down, resulting in lower back pain spreading out to the lower limbs. Studies have reported that the level of disc herniation does not correlate with the severity of pain and physical mobility. The physical damage is typically confirmed using MRI and CT imaging [13]. Clinically, 54% of back pain patients have recurrent pain at 6 months, and 47% of patients reported recurrent pain at 24 months with physical damage to spinal structures [14].

Considering the complication of lower back pain, multiple modes of treatment are used concurrently, including behavioral management and nonpharmacological, pharmacological, and surgical treatments. The first line of treatment for lower back pain includes strength and stabilization exercises, physical therapy, cognitive therapy, nonpharmacological therapies, and pharmacological approaches [15,16,17,18]. Physical therapy, cognitive therapy, and other nonpharmacological therapies may be effective but take a long time and persistence. Pharmacological therapies are effective but have multi-organ adverse effects and are not recommended for long-term use [17,19]. Finally, surgical treatment is considered in trauma or after the failure of other therapies, which may include implantable devices [20, 21].

The intervertebral structure is highly mechanosensitive and requires mechanical stimulus to recover and regenerate [22]. Ultrasound is an acoustic wave providing alternating mechanical force [23,24,25]. Studies have shown that ultrasound increases cellular migration, proliferation, and localized vascularization, reducing inflammation and accelerating soft tissue healing [23, 24,26,27,28,29,30]. The Food and Drug Administration (FDA) has approved ultrasound treatment systems for non-union fracture healing, musculoskeletal pain, and soft tissue injuries as a standalone or combination therapy [31,32,33,34,35].

Sustained acoustic medicine (SAM) is an FDA-approved, non-invasive, long-term source of high-dose, high-frequency, continuous ultrasound that provides 18,720 joules of energy over 4 hours of treatment [36, 37]. Clinical studies have shown that SAM application has limited adverse effects, reduces chronic musculoskeletal pain (e.g., soft-tissue injuries including tendinopathy, osteoarthritis, and myofascial pain), accelerates soft tissue healing, improves patients' quality of life [37,38,39,40,41,42]. SAM increases localized temperature deep into skeletal muscle (greater than 5 cm deep and 8°C), blood flow, cellular proliferation, migration, and nutrition exchange, resulting in reduced inflammation and an increased rate of tissue regeneration, providing significant pain reduction and functional gains [35,38,40,43]. Clinical studies on SAM have established the clinical effectiveness of treatment in upper and lower limbs and joints, but there is limited data specifically evaluating the efficacy of SAM on chronic discogenic lower back pain. Chronic lower back pain significantly affects mobility and quality of life. We aim to evaluate SAM as an alternative deep-penetrating treatment option for chronic lower back pain.

This study aims to determine the efficacy and safety of SAM treatment in alleviating chronic lower back pain over an 8-week treatment. We hypothesized that 8 weeks of SAM would result in more significant pain reduction, improved quality of life, reduced medication use, and improved physical activity limitation compared to placebo treatment.

2. Methods

A prospective, randomized, double-blinded, multisite, placebo-controlled study in the outpatient commu-

nity hospital pain management clinics of Ithaca, NY, and Chapel Hill, NC, United States, was conducted from November 2015 to April 2016. This study was approved by the Medical Ethical Committee at the institutional review board of Schuman (#2015/20140901), and the trial was registered with the United States National Institutes of Health Clinical Trails registry (NCT02609854). Written informed consent was obtained from all subjects prior to participation. The study was conducted in accordance with relevant guidelines, regulations, and the World Medical Association Declaration of Helsinki. Funding for the study was provided by the National Space Biomedical Research Institute, a subsidiary of The National Aeronautics and Space Administration of the United States of America, to evaluate emerging medical technologies for space-relevant human health concerns.

Recruitment strategies involved posters, flyers, and clinic/hospital pull-up displays to inform potential subjects of the chronic lower back pain research study. The recruiters had a bachelor's degree or higher with a minimum experience of 10 years in health care sciences. Potential subjects were initially screened over the phone for general eligibility by the study site research assistants. Phone screening covered symptomology, study intervention ability to apply treatment to the lower lumbar region, and length of study involvement. Any subject passing the initial screening was advised to consult with their primary healthcare or pain management provider to confirm clearance prior to study participation.

2.1. Inclusion criteria

All potential subjects were evaluated by physical examination conducted by board-certified physicians, blood tests, and radiographs to identify any exclusion factors. Board-certificated radiologists interpreted the radiographs. Ambulatory male and female patients 20 to 60 years of age with lower back pain for more than 3 months presenting with or without associated leg pain, MRI confirmation of lower lumbar spine herniated disc ($L_1 - L_5$), mean Numeric Rating Scale (NRS) pain of four or more out of ten the week preceding enrollment and 2-weeks of baseline pain measures, and capable of self-applying SAM treatment to the lower lumbar region ($L_1 - L_5$) were included in this study.

2.2. Exclusion criteria

The subjects were excluded if they had arthritis, bone spur, stenosis, fusion, or implants near the herniated disc. Patients with active infections, open sores or wounds, undergoing chemotherapy or having known neuropathy, hereditary disposition to excessive bleeding, and peripheral artery disease were also excluded. Patients with malignancy or metastasis on the vertebra, acute compression fracture, and collagen disease, such as ankylosing spondylitis, were excluded. Evidence of nerve root, spinal cord, or cauda equina compression; severe spinal stenosis indicated by signs of neurogenic claudication; grade 3 to 4 spondylolisthesis; fibromyalgia or systemic/inflammatory disorder; as well as any other current lower extremity musculoskeletal injuries were excluded. The latter included any medical condition limiting mobility or pregnancy. In addition, patients who had a prior diagnosis of dementia were excluded. All potential subjects underwent the Mini Mental State Examination, and those with a score of less than 24 were excluded. Finally, subjects who did not show the ability to use the SAM device properly failed to follow the instructions, were unable to walk, or participated in other clinical trials within the last 30 days were excluded from the study.

2.3. Study procedures

Eligible and willing subjects provided written informed consent, underwent basic demographic and vital measures, and completed a 2-week (minimum of 14 days) daily pain diary prior to randomization in the placebo-controlled study. Study arms were randomized with a Microsoft® Excel RAND function computer-generated random number allocation list of active and non-active ultrasound transducer emitters provided by the manufacturer. Subjects were sequentially enrolled into either the active group (active SAM device) or the placebo group (SAM device with deactivated ultrasound emitting transducers). Treatment allocation was blinded from the clinical sites and research staff enrolling patients and performing data entry, and all study devices and materials appeared and operated equivalently. Study participants were also blinded to treatment group allocation and were informed that they may or may not receive active intervention. The study biostatistician held the device status key for analysis and unblinding.

All subjects were provided with a power controller, 2 applicators, ultrasound coupling bandages, an ultrasound gel bottle, a Y-adapter, a charger, and the user manual. All patients were trained on how to use the SAM device properly to ensure it would not interfere with their daily life routine and provide the essential

Fig. 1. Sustained Acoustic Medicine (SAM) application to lower back. The ultrasound delivery system spreads ultrasound diathermy to the size of the star-shaped ultrasound coupling patch.

treatment to the spinal column. The ultrasound applicator(s) were placed bilaterally on either side of the herniation approximately 3 to 5 cm from the centerline, ensuring ultrasonic coverage of the injury site, as shown in Fig. 1. The ultrasound gel coupling patch secured each applicator in place on the back and filled the space between the ultrasound transducer and the skin to provide little or no loss of acoustic intensity propagation into deep tissue. The SAM treatment was to be administered during normal daily activities, including deskwork, light chores, and exercise. The device was to be removed prior to any bathing or aquatic activity.

The active SAM device was programmed to deliver continuous high-frequency 3MHz, an intensity of 132 mW/cm^2, and a total power of 1.3W, providing deep (5 cm) ultrasound stimulation for a total of 18,720 joules of energy over 4 hours of treatment. The non-active device functioned identically to the active device with a timer, power, and all user indications. However, power to the ultrasound transducer crystal was internally disconnected to prevent ultrasound energy delivery by the manufacturer. The active and placebo treatment was administered for 4 hours daily during day-to-day activities at the site of pain ($L_1 - L_5$), excluding water-related activities (potentially immersing in the device). In addition, the subjects were provided with a daily diary to record changes in the time of treatment, effects on pain, and day-to-day activities. Weekly patient video phone calls and bi-weekly in-person reviews were conducted to ensure subjects were completing reporting and addressing any study-related questions with the research staff.

2.4. Primary outcome measure

The NRS pain score was the primary outcome measure. NRS pain is an 11-point scale, with 0 being no pain and 10 being the most pain. NRS score was assessed at baseline and reassessed every two weeks for 8-weeks (bi-weekly) in-person follow-up. A minimally clinically important reduction in pain was defined as 2 points on the NRS scale.

Patients were also instructed to record the incremental change in back pain in a daily diary during treatment over the 8-week period. Pain scores were recorded immediately before treatment, 30 minutes into the treatment, 2 hours into treatment, and immediately after treatment.

2.5. Secondary outcome measures

The Global Rating of Change GROC score was measured at the end of week 8. The GROC assesses a patient's level of back pain well-being on a 15-point scale ranging from (-7, a great deal worse) to ($+7$, a great deal better) from the SAM intervention. The GROC is a well-established tool that is easy to administer and interpret.

The use of prescription opioid pain medication, morphine milligram equivalent (MME) dosage, and over-the-counter NSAIDS were tracked on study enrollment and study completion. This included physician medication reports and patient diary documentation of medication usage. Patients were required not to increase pain medication usage during the study period. Patients were allowed to reduce their medication usage if it did not increase their pain, which was evaluated by daily diary tracking (both by the patient and staff during on-site meetings).

A functional back pain treatment survey regarding walking, gardening, and lifestyle activities based on the modified Oswestry disability index (ODI) questionnaire was also completed at the end of the intervention. Subject satisfaction with treatment was evaluated with a yes/no questionnaire at the completion of the study in regard to ease of use, continued use, and effectiveness of treatment.

2.6. Statistics

All data were analyzed using The R Project for Statistical Computing using an intention-to-treat analysis.

The Kolmogorov-Smirnov test was used to determine if data were normally distributed. No evidence of non-normality was found to merit the use of non-parametric tests on the primary or secondary outcome measures. A repeated measure ANOVA and t-test were used to determine the main and interaction effects of time and intervention for the primary outcome measure. Analysis was grouped into weeks of two, including baseline, 2-, 4-, 6-, and 8-weeks intervention periods. Daily starting and ending pain scores, changes in pain scores from baseline, and changes in pain scores within weekly treatment days were analyzed within and between treatment groups. All pain measurement data was utilized in the analysis, and missing data from incomplete diary reporting was excluded. Additionally, a secondary analysis of the primary outcome included subjects who completed the entire intervention period as well as subjects who dropped out of the study. For the secondary outcome measures, including GROC, medication use, treatment satisfaction, and functional activity, the active and placebo study groups were compared using t-tests at the end of the study period (8 weeks). The Chi^2-test was used for categorical data.

A sample calculation for the primary outcome measure of NRS pain was conducted based on previous therapeutic ultrasound clinical trials on chronic low back pain with an average pain reduction of 2 points after intervention. To detect this difference with 90% power and $p < 0.05$, approximately 40 participants were required (20 per group). Allowing for a 30% dropout, we intended to recruit 60 subjects for the study. The statistical difference of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Patient distribution

Seventy-two subjects were screened for eligibility and 65 subjects were eligible for randomization (Fig. 2). The active group had 33 subjects (14 males, 19 females, average age 50.2 $\pm$ 10.2 years and BMI of 29.8 $\pm$ 6.4). The placebo group had 32 subjects (12 males, 20 females, average age 47.0 $\pm$ 13.9 years and BMI of 29.6 $\pm$ 9.6) (Table 1). There were no significant differences in age ($p = 0.2931$) or BMI ($p = 0.8911$) between the groups. Forty-one subjects completed all visits through the 8-week study visit (Fig. 2). The majority of study dropouts were related to protocol burden ($n = 19$) from travel to the study site and daily administration/reporting required of the protocol. Additionally, 3 subjects reported the device was too hot on the back, and 1 subject reported a skin rash from the intervention after the first 2 weeks of use. Overall, 25 (76%) participants in the active SAM group and 16 (50%) participants in the placebo group completed all outcome measures at 8 weeks. The significant majority of dropouts occurred in the placebo arm (16 of 24, $p < 0.0001$). No adverse events were reported for either active or placebo intervention.

3.2. Primary outcomes

Table 2 shows a gradual decrease in the active group's pain score relative to the placebo group, with a statically significant change in pain recorded after 6-weeks (mean NRS difference -1.10, 95% CI: -2.00 to -0.19, $p = 0.0184$) and 8-weeks (mean NRS difference 1.48, 95% CI: -2.57 to -0.41, $p = 0.0079$) of the active SAM treatment (Table 2).

The longitudinal analysis shows a significant and clinically relevant decrease in pain from the baseline after 2-weeks of treatment (Fig. 3). A 35% decrease in pain (2.40-point NRS pain reduction) was seen during the first 2-weeks of treatment from the baseline in the active SAM group and up to a 45% decrease (3.15-point NRS pain reduction) in pain at the week 8 study completion ($p < 0.0001$). The mean change in pain reduction was statistically significant compared with placebo at 2, 4, 6, and 8 weeks, with the greatest difference at 8 weeks (mean NRS change from baseline difference -2.58, 95% CI: -3.46 to -1.69, $p < 0.0001$).

A subgroup pain reduction analysis was completed on participants who completed the full 8 weeks of the study in both the active ($n = 25$) and placebo groups ($n = 16$). Table 3 shows completers with a gradual decrease in the active group's pain score relative to the placebo group, with a statistically significant change in pain recorded after 6 weeks ($p = 0.0293$) and 8 weeks ($p = 0.0079$). The mean change in pain reduction for study completers was statistically significant compared with placebo at 2, 4, 6, and 8 weeks, with the greatest difference at 8 weeks (mean NRS change from baseline difference -2.25, 95% CI: -2.88 to -1.63, $p = 0.0001$).

A secondary subgroup analysis of non-completers ($n = 8$ active and $n = 16$ placebo) was conducted on participants who dropped out of the study and completed at least one biweekly data point after baseline measures for comparison. Most dropouts occurred prior to the first 2-week measurement point limiting sample

Table 1
Patient demographic information for enrolled subjects

Patient demographic data			
Variable	Active ultrasound	Placebo ultrasound	P-value
n	33	32	NA
Sex (M/F)	14/19	12/20	NA
Age, years	50.2 ± 10.2	47.0 ± 13.9	0.2931
BMI	29.8 ± 6.4	29.6 ± 9.6	0.8911

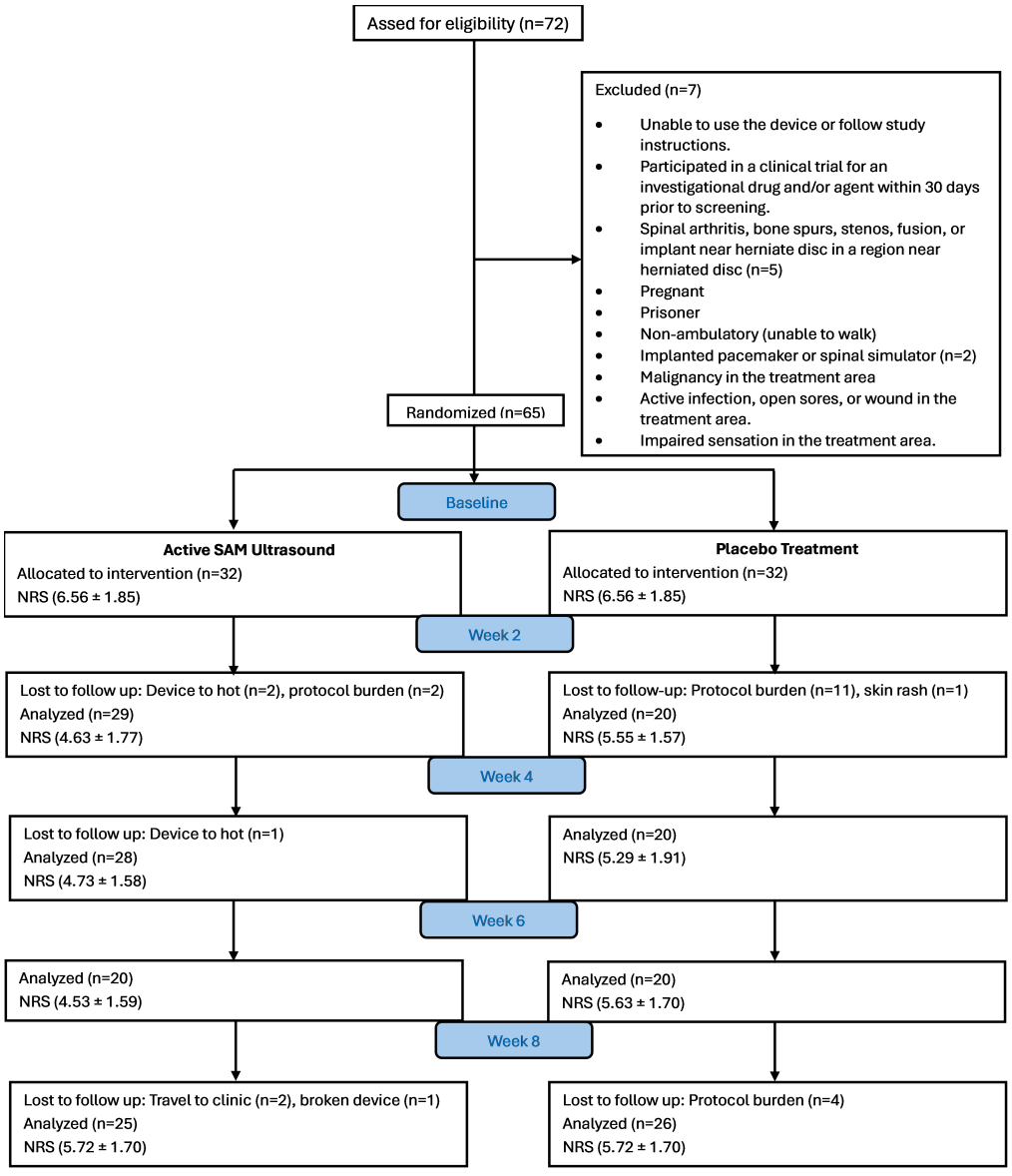

Fig. 2. CONSORT flow diagram of study inclusion, randomization and follow-up.

analysis to four ($n = 4$) active participants and twelve ($n = 12$) placebo participants. There were no baseline differences in pain scores for non-completers between active and placebo groups (mean NRS difference -0.03, 95% CI: -2.63 to 2.56, $p = 0.9779$). The non-completer active group showed a trend in mean pain reduction change from baseline at 2 weeks ($p = 0.0607$) and 8 weeks ($p = 0.0838$). However, there

Table 2
Back pain reduction from baseline (NRS) and mean change from baseline (NRS) for all study participants

Week	Active	Placebo	Mean difference 95% CI	P value
Primary outcome NRS data				
Baseline	7.04 ± 1.42	6.56 ± 1.85	0.48 (−0.40 to 1.35)	0.4767
	$n = 33$	$n = 32$		
2 weeks	4.63 ± 1.77	5.55 ± 1.57	−0.92 (−1.87 to 0.05)	0.0635
	$n = 29$	$n = 22$		
4 weeks	4.73 ± 1.58	5.29 ± 1.91	−0.56 (−1.57 to 0.44)	0.2655
	$n = 29$	$n = 20$		
6 weeks	4.53 ± 1.59	5.63 ± 1.45	−1.10 (−2.00 to −0.19)	0.0184
	$n = 28$	$n = 20$		
8 weeks	4.24 ± 1.64	5.72 ± 1.70	−1.48 (−2.57 to −0.41)	0.0079
	$n = 25$	$n = 16$		
NRS mean change from baseline 95% CI				
2 weeks	-2.40 ± 1.53	-0.68 ± 0.92	−1.72 (−2.47 to −0.98)	0.0001
	$n = 33$	$n = 32$		
4 weeks	-2.31 ± 1.22	-0.91 ± 0.95	−1.40 (−2.05 to −0.74)	0.0001
	$n = 29$	$n = 22$		
6 weeks	-2.51 ± 1.05	-0.58 ± 0.87	−1.93 (−2.51 to −1.35)	0.0001
	$n = 28$	$n = 20$		
8 weeks	-3.15 ± 1.66	-0.57 ± 0.71	−2.58 (−3.46 to −1.69)	0.0001
	$n = 25$	$n = 16$		

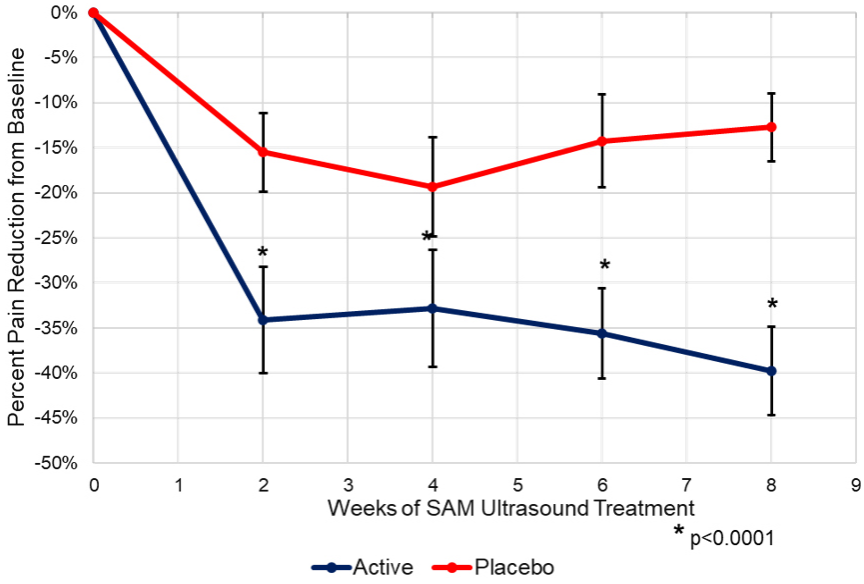

Fig. 3. Back pain percent reduction from baseline.

were no significant differences between non-completers in the study primary outcome measure. Additionally, no differences were found between completers or non-completers in terms of baseline pain characteristics.

The within-day-treatment change in the pain during intervention was recorded in daily diaries and analyzed biweekly (Fig. 4). A significant decrease in pain scores was recorded during treatment in the active SAM group across all eight weeks. A significant difference in pain scores between active and placebo SAM groups was also observed at 6 weeks ($p = 0.0185$) and 8 weeks ($p = 0.0079$) of treatment. The placebo group did not show any change in pain score during the treatment administration except for week 6 ($p = 0.0426$).

3.3. *Secondary outcome measures*

The active SAM group reported significant improvement in lower back well-being as measured by the GROC compared to the placebo group at the end of the

Table 3
Back pain reduction from baseline (NRS) and mean change from baseline (NRS) for the participants who completed the full 8-week intervention

Week	Active ($n = 25$)	Placebo ($n = 16$)	Mean	P value
Primary outcome NRS data (Completers)				
Baseline	7.07 ± 1.40	6.31 ± 1.59	0.76 (−0.19 to 1.72)	0.1138
2 Weeks	4.59 ± 1.82	5.41 ± 1.68	−0.83 (−2.00 to 0.35)	0.1613
4 Weeks	4.60 ± 1.48	5.39 ± 1.68	−0.79 (−1.86 to 0.27)	0.1410
6 Weeks	4.51 ± 1.52	5.63 ± 1.57	−1.12 (−2.11 to −0.12)	0.0293
8 Weeks	4.24 ± 1.64	5.72 ± 1.70	−1.48 (−2.57 to −0.41)	0.0079
NRS mean change from baseline 95% CI				
2 Weeks	-2.48 ± 1.51	-0.92 ± 0.81	−1.56 (−2.42 to −0.70)	0.0007
4 Weeks	-2.47 ± 1.17	-0.92 ± 0.80	−1.55 (−2.23 to −0.88)	0.0001
6 Weeks	-2.56 ± 1.10	-0.68 ± 0.70	−1.88 (−2.51 to −1.26)	0.0001
8 Weeks	-2.82 ± 1.09	-0.57 ± 0.71	−2.25 (−2.88 to −1.63)	0.0001

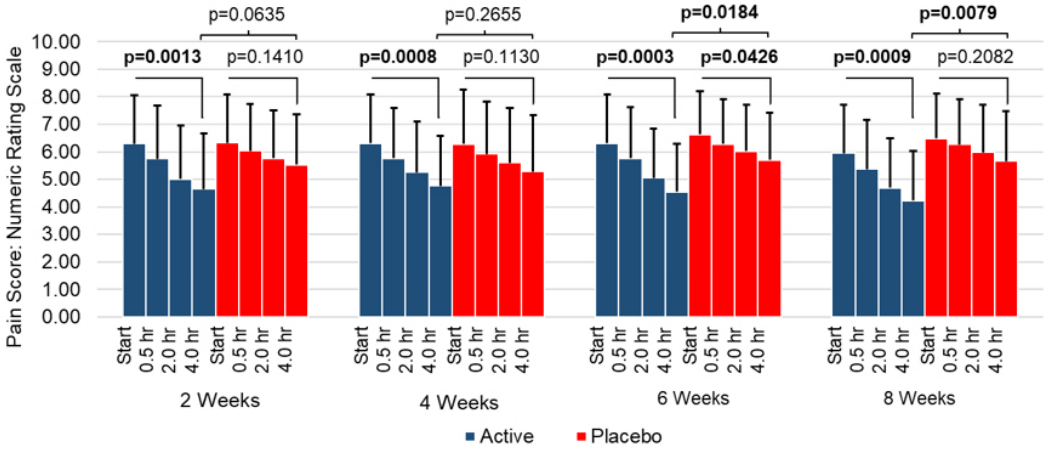

Fig. 4. Back pain reduction (NRS) by week during treatment administration.

intervention. Mean GROC for the active SAM group was 3.67 ± 1.28 relative to 0.19 ± 0.91 in the placebo group (mean difference 3.48, 95% CI: 2.71 to 4.24, $p < 0.0001$) (Table 4).

The active SAM group reported a 22.5% reduction in pain medication with no change reported in the placebo group (mean difference 22.52%, 95% CI: 10.94% to 34.11%, $p = 0.0004$). On average, this represented a 720mg per day reduction of acetaminophen and ibuprofen and a 15.2 morphine milligram equivalent (MME) dosage reduction of oxycodone, hydromorphone, and tramadol documented in the subjects' medical records and medication use diary.

At the 8-week exit survey, the majority of active SAM treatment group subjects reported a reduction in back pain (100%, $p < 0.0001$), improved quality of life (100%, $p = 0.0004$), and improved daily functional activity (95%, $p < 0.0001$) based on the Oswestry disability questionnaire that were all significantly greater than the placebo group (Table 4). Additionally, active treatment group subjects reported the intervention as effective and would continue to use it for their back pain ($p < 0.0001$). Both active and placebo group subjects found the treatment easy to use as recommended. However, there was a modestly significant difference between ease of use favoring active SAM treatment ($p = 0.0327$).

4. Discussion

Lower back pain is a clinical challenge with complex epidemiology and pathogenesis [10,11]. Acute pain can be treated with physical exercise and therapy, but chronic low back pain causes significant socioeconomic effects and requires lifelong treatment, including analgesics and NSAIDs [10,15,19,44]. The long-term use of these drugs leads to an opioid epidemic and adverse effects on multiple organs [17,44,45,46,47,48,49,50,51,52]. The lower back plays an essential role in day-to-day activity, and chronic pain significantly limits day-to-day activities and impairs mobility to the

Table 4
Secondary outcome measures including GROC, medication, function, and patient receptivity

Secondary outcomes GROC, medication, life activity, compliance				
Outcome	Active	Placebo	Mean difference 95% CI	P value
Health improvement score (GROC)	3.67 ($\pm$ 1.28) $n = 25$	0.19 ($\pm$ 0.91) $n = 16$	3.48 (2.71 to 4.24)	0.0001
Reduction in medication use	22.5% ($\pm$ 22.75%) $n = 25$	00.0% ($\pm$ 0.00) $n = 16$	22.5% (10.9% to 34.1%)	0.0004
Did treatment reduce your back pain?	100% ($\pm$ 00%) $n = 25$	25% ($\pm$ 45%) $n = 16$	75% (55% to 95%)	0.0001
Did treatment improve your quality of life?	100% ($\pm$ 00%) $n = 25$	31% ($\pm$ 48%) $n = 16$	69% (48% to 90%)	0.0001
Did your functional activity, such as walking, playing, gardening, etc., improve?	95% ($\pm$ 22%) $n = 25$	19% ($\pm$ 40%) $n = 16$	76% (56% to 97%)	0.0001
Was treatment an effective solution for your back pain?	100% ($\pm$ 00%) $n = 25$	13% ($\pm$ 34%) $n = 16$	88% (72% to 103%)	0.0001
Would you like to continue to use treatment after the study?	100% ($\pm$ 00%) $n = 25$	19% ($\pm$ 40%) $n = 16$	81% (63% to 99%)	0.0001
Do you have a daily use requirement for treatment?	100% ($\pm$ 00%) $n = 25$	31% ($\pm$ 48%) $n = 16$	69% (48% to 90%)	0.0001
Was treatment easy to use as recommended?	100% ($\pm$ 00%) $n = 25$	80% ($\pm$ 41%) $n = 16$	20% (2% to 38%)	0.0327

extent of causing physical disability and depression [53, 54]. Recent advancements have explored nonpharmacological therapies [18,55]. This study shows the effectiveness of the non-invasive, self-administered, in-home use of SAM for the treatment of chronic, discogenic low back pain. SAM delivers continuous ultrasound at the high-frequency 3 MHz, an intensity of 132 mW/cm^2, and a total power of 1.3 W, providing deep (> 5 cm) heat to the damaged herniated disc. SAM increases blood flow and tissue regeneration, leading to an incremental decrease in pain during the 4-hour treatment. The long-term effects of the treatment were observed after 8 weeks in the active group. Further, the effect of treatment led to a significant decrease in NSAIDs and opioids throughout the treatment, showing the efficacy of the treatment and its potential to reduce the application of analgesics and other pharmacological agents to treat lower back pain.

Multiple studies have shown the effectiveness of SAM in increasing musculoskeletal tissue regeneration, pain management, and mobility. This includes a recent systematic review and meta-analysis on SAM treatment for musculoskeletal pain and soft tissue healing by Winkler et al. 2021 and a 135 subject clinical study by Jarit et al. 2023 demonstrating both pain and health improvements for soft-tissue injuries, including the back. To our knowledge, this is the first RCT to evaluate SAM's clinical effectiveness and safety on discogenic, chronic, and low back pain. The encouraging data from this study confirms previous findings and shows that SAM can be used to treat lower back pain as a standalone therapy. In addition, the cross-sectional analysis of data with active and placebo groups shows that the active group significantly improves pain after 8 weeks of treatment (8 weeks $\times$ 7 days $= 56$ unique treatment sessions).

Interestingly, a comparison from baseline shows the highest, approximately 35%, decrease in pain occurs during the first 2-weeks of treatment in the active group (14 treatment sessions). However, only a 5% decrease in pain was recorded in the following 6 weeks, and another 5% decrease occurred after 8 weeks of treatment (56 treatment sessions). Over the course of 8 weeks, the difference between active and placebo pain reduction also increased. These findings suggest that patients and prescribing physicians may be able to modulate treatment use to reduce daily application burden while still achieving clinically meaningful pain reduction and quality life improvement.

The use of therapeutic ultrasound administered in the clinical setting for the management of chronic low back pain has been investigated in prior RCTs. Haile et al. 2021 recently conducted a systematic review of ultrasound therapy RCTs and found that five studies demonstrated ultrasound therapy significantly reduced lower back pain scores when sequentially administered over a regular treatment period (typically 10 to 12 treatment sessions over 3 to 6 weeks) [56]. The authors concluded that based on the literature, ultrasound therapy may be considered a non-drug and non-invasive alternative treatment for lower back pain. The SAM long-duration ultrasound device used in this study enabled patients to receive multi-hour ultrasound treatment daily in the home setting for 8 weeks (56 treatment sessions). The data from the study shows that regular home treatment

with SAM has a significant clinical benefit for patients, including greater pain reduction, health improvement, and reduction of lost time from clinic visits and associated costs. The minimal clinically important difference (MCID) for chronic low back pain treatment ranges in the literature from 11% to greater than 50% change on the Oswestry disability index depending on intervention type [57]. After 8 weeks of daily sustained acoustic medicine treatment, the active SAM group significantly exceed MCID change, with subjects reporting a mean improvement ranging from 69% to 88% over placebo intervention ($p < 0.0001$). The effectiveness of an at-home ultrasound therapy regimen with new wearable technology should be considered for patients with chronic low back pain.

Ebadi et al. have previously shown continuous ultrasound efficacy (1 MHz and 1.5 W/cm^2) for 4 weeks, with 10 treatments showing significant lumbar improvement in mobility and global visual analog scale (VAS) pain [58]. Durmus et al. treated lower back pain in the lumbar spine with 10 treatments of continuous ultrasound at 1 MHz and 1 W/cm^2 over 3 weeks, demonstrating significant improvement relative to placebo treatments [59]. Tantawy et al. treated 15 chronic lumbar pain patients with 1 MHz continuous ultrasound at 1 W/cm^2 intensity for 10 mins for 2 days /week over 8 weeks and reported a significant reduction in VAS pain scores and an increase in ROM in a comparative study [60]. These studies use short-duration continuous ultrasound in conjunction with exercise compared to standalone SAM therapy, which uses long-duration continuous ultrasound in the comfort of home during daily activities. In addition, the SAM allows daily treatment over 8 weeks compared to limited weekly sessions delivered by a healthcare provider. This study also reports on daily changes in pain and quality of life and conducts longitudinal bi-weekly analysis over 8 weeks, further confirming the cumulative effects of SAM therapy on chronic discogenic back pain.

The study is not without some limitations. A significantly larger number of dropouts occurred in the placebo arm due to the protocol burden on the subjects, which could potentially affect the study results. Since the clinical benefit of ultrasound therapy and home-use SAM intervention has been evaluated with placebo control, future studies should consider utilizing intervention arms with alternative treatments, such as corticosteroids or oral/topical medication, and recruit a higher sample size to reduce patient attrition. Expanded and comparative study arms will be helpful for clinical decision-making in the use of SAM treatment in the care continuum. Additionally, a longer-term intervention and follow-up period could help determine the lasting clinical benefit for patients.

5. Conclusion

This double-blind, placebo-controlled, randomized clinical trial in patients with discogenic chronic low back pain demonstrated that 18,720 joules of daily 3 MHz SAM treatment had a significant beneficial effect on pain, health, function, and reduction of medication use, including NSAIDs and opioids compared to the control group. SAM treatment has a role in managing chronic low back pain symptoms with limited side effects so that patients can improve their quality of life.

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None to report.

Author contributions

Study conception and design: RO and TM. Data collection and analysis: all authors. Drafting of the manuscript: all authors. Critical revision of the manuscript: all authors. All authors read and approved the final manuscript.

Conflict of interest

The authors declare that they have no conflict of interest.

Datat availibilty

Data is available from the corresponding author upon reasonable request.

Ethical approval

The study has been performed in accordance with the Declaration of Helsinki and later amendments and was approved by the Medical Ethical Committee at the institutional review board of Schuman (# 2015/20140901).

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Informed consent

All participants provided written informed consent.

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