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COMPARE THE EFFICACY OF LIPUS AND LICUS ON PAIN AND DISABILITY AMONG INDIVIDUALS WITH KNEE OSTEOARTHRITIS – A PILOT STUDY

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ABSTRACT

Background: Knee osteoarthritis (KOA) is a common form of joint degeneration that involves the gradual breakdown of cartilage, changes in the underlying bone, and inflammation of the synovial membrane. These changes contribute to symptoms such as joint pain, reduced mobility, and stiffness.
Aims: To compare the efficacy of Low-Intensity Pulsed Ultrasound (LIPUS) and Low-Intensity Continuous Ultrasound (LICUS) on reducing pain and improving functional disability among individuals with knee osteoarthritis in a pilot study.
Methodology: In this initial comparative experiment at Galgotias University's Outpatient Department in Greater Noida, we used randomized sampling to enroll 30 adults (equal numbers of men and women) aged 40–75 with clinically confirmed mild to moderate knee osteoarthritis.
Result: The study enrolled 30 individuals (10 men and 20 women) aged 41 to 75 years (mean 57.10 ± 9.57 years) who were randomly assigned to one of two treatment arms of equal size (n = 15 each): a LIPUS group and a LICUS group. However, participants in the LIPUS arm experienced significantly greater relief in pain and disability.
Conclusion: These results indicate that LIPUS could offer more favorable therapeutic benefits and may serve as a more effective non-invasive treatment option for managing knee osteoarthritis in clinical practice.
Keywords: Ultrasound mode, Knee Osteoarthritis, Pain, Disability.

INTRODUCTION:

Knee osteoarthritis (KOA) is a prevalent degenerative joint disorder characterized by progressive cartilage deterioration, remodeling of the underlying bone, and inflammation of the synovial lining. These pathological changes result in symptoms such as joint pain, stiffness, and decreased mobility. The worldwide impact of KOA is considerable, with its prevalence on the rise due to factors such as an aging population and the growing rate of obesity.[1]Traditional treatment methods include medications, physiotherapy, and surgical procedures; however, these strategies frequently have drawbacks such as side effects and inconsistent treatment outcomes.[2]In recent times, therapeutic ultrasound techniques have gained recognition as non-invasive treatment options for managing knee osteoarthritis. Specifically, Low-Intensity Pulsed Ultrasound (LIPUS) and Low-Intensity Continuous Ultrasound (LICUS) have shown promise in reducing pain and enhancing joint functionality.[3,4]

LIPUS operates by transmitting pulsed acoustic waves, which are believed to activate cellular processes and promote tissue repair. In contrast, LICUS emits a steady stream of ultrasound energy, which may increase tissue temperature and support metabolic activity.[5,6]Although both modalities offer potential therapeutic advantages, limited research has directly compared the effectiveness of LIPUS and LICUS in the treatment of knee osteoarthritis.[7]Numerous studies have evaluated the impact of LIPUS on knee osteoarthritis, highlighting its effectiveness in alleviating pain and enhancing physical function. One systematic review and meta-analysis, which included 13 randomized controlled trials involving a total of 807 subjects, found notable improvements following LIPUS treatment. Specifically, there were significant reductions in pain levels as measured by the Visual Analog Scale (VAS) (Mean Difference [MD] = -0.95), improvements in function based on the WOMAC Index (MD = -4.35), and enhanced joint mobility reflected by an increased range of motion (MD = 2.43).[1]

An additional meta-analysis comprising five randomized controlled trials supported these results, emphasizing the effectiveness of LIPUS in reducing pain and promoting functional improvement, all without reporting any negative side effects.[2]In contrast, the available evidence supporting the use of LICUS for knee osteoarthritis is relatively scarce. However, a double-blind, randomized, placebo-controlled trial conducted on individuals with moderate to severe KOA revealed that prolonged application of LICUS led to significant pain reduction and functional improvement, as indicated by lower WOMAC scores.[3]Nevertheless, the limited number of studies directly contrasting LIPUS and LICUS underscores the need for further research to clarify their comparative effectiveness.[4,5]

The precise biological mechanisms through which LIPUS and LICUS produce therapeutic benefits in knee osteoarthritis remain incompletely understood. It is proposed that LIPUS may stimulate the proliferation of chondrocytes, enhance the production of extracellular matrix components, and trigger anti-inflammatory effects, all of which could contribute to cartilage regeneration. [8,9] LICUS, by delivering continuous acoustic energy, is thought to improve tissue blood flow and stimulate metabolic processes, thereby aiding in pain reduction and functional recovery. [10,11] However, the distinct physiological effects of these two ultrasound modalities require further in-depth investigation.[12]

Considering the encouraging yet differing therapeutic potentials of LIPUS and LICUS, a head-to-head comparison is essential to guide clinical choices in managing knee osteoarthritis. This preliminary study is designed to assess and contrast the effectiveness of LIPUS and LICUS in alleviating pain and improving functional ability in individuals with KOA, thereby supporting the evidence-based refinement of non-invasive treatment approaches. [13,14] OA is a widely occurring degenerative joint disease marked by the gradual breakdown of articular cartilage, resulting in discomfort, reduced joint mobility, and loss of function.

Conventional treatments mainly aim to relieve symptoms but show limited success in preventing or reversing cartilage damage. Recently, low-intensity pulsed ultrasound (LIPUS) has emerged as a promising non-invasive technique, recognized for its potential to protect cartilage and support tissue regeneration.[15] LIPUS has been shown to influence several cellular and molecular mechanisms that support cartilage stability. For example, a study by Guan et al. (2020) found that LIPUS suppresses the expression of vascular endothelial growth factor A (VEGFA) in chondrocytes, which helps to slow cartilage degradation in osteoarthritis models.

Likewise, Sekino et al. (2018) reported that LIPUS enhances the synthesis of cartilage matrix components and decreases the expression of matrix metalloproteinase-13 (MMP13), indicating its potential to preserve the extracellular matrix structure. [16,17] Research has also investigated the combined therapeutic potential of LIPUS with other treatment agents. Pan et al. (2019) showed that LIPUS facilitates the uptake and effectiveness of Clematis chinensis Osbeck in chondrocytes by stimulating the transforming growth factor-β/Smad signaling cascade, which in turn boosts the expression of type II collagen.[18,19] Additionally, LIPUS has demonstrated potential in supporting stem cell-based regenerative treatments. According to Chen et al. (2021), LIPUS enhances articular cartilage repair facilitated by mesenchymal stem cell transplantation through the suppression of the tumor necrosis factor (TNF) signaling pathway, underscoring its value in regenerative medicine.[20,21] Recent progress in imaging technologies has improved the evaluation of cartilage health and the impact of therapeutic approaches.

Wu et al. (2018) employed Brillouin microscopy to identify proteoglycan depletion in articular cartilage, offering a non-invasive technique for tracking osteoarthritis progression and assessing treatment outcomes.[22]. Moreover, growing research supports the use of LIPUS as an effective therapeutic option for managing osteoarthritis, whether applied independently or alongside drugs and stem cell-based treatments. Its capacity to influence critical molecular mechanisms and stimulate cartilage repair highlights LIPUS as a valuable and emerging tool in the advancement of OA treatment strategies.[23–30]

METHODOLOGY

The present study is a pilot experimental comparative study conducted at the Outpatient Department of Galgotias University, Greater Noida. The study population will include both male and female participants diagnosed with knee osteoarthritis. A random sampling method will be employed to recruit participants. The alternative hypothesis states that there will be a significant difference between the effects of LIPUS and LICUS in improving pain and reducing disability in individuals with knee osteoarthritis, while the null hypothesis proposes that there will be no significant difference between the two interventions. Ethical approval was taken from ethical committee of department of physiotherapy, Galgotias university reference number DRC/PT/UG/24/25/103.

Sample size calculation was carried out using G Power software based on a repeated measures ANOVA focusing on a within-between interaction. The analysis was conducted with an effect size (f) of 0.50, a total sample size of 30 participants (15 in each group).

Independent Variables:

1. **Group 1.** LIPUS was administered using a 1 MHz ultrasound frequency at an intensity of 0.1 W/cm². Each session was conducted for 10 minutes, three times per week over a four-week period.
2. **Group 2.** LICUS was applied at a frequency of 1 MHz with an intensity of 0.1 W/cm². Treatments were administered for 10 minutes per session, three times weekly over the course of four weeks.

Dependent Variables:

1. Knee Pain – Visual Analogue Scale (VAS).
2. Disability – Measured using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Selection Criteria

Inclusion criteria

1. Participants should be between 40 and 75 years old both male and female.
2. Mild to moderate knee osteoarthritis confirmed by x-ray.
3. Moderate to severe pain level on VAS.
4. Must have knee pain or stiffness for at least 3 months.
5. Ability to understand and comply with study procedures.

Exclusion criteria

1.Prior knee surgery.
2. Current use of anti-inflammatory medications that could confound results.
3. Presence of skin lesions or infections at the treatment site.
4. Pregnancy or significant comorbidities.

Study design

A pilot study design was utilized. Convenience type sampling was implemented to recruit participants from specified geographic locations.

Procedure

This study included two treatment groups: one receiving Low-Intensity Pulsed Ultrasound (LIPUS) therapy and the other receiving Low-Intensity Continuous Ultrasound (LICUS) therapy, with 15 participants assigned to each group. Both interventions were administered three times per week for a total duration of four weeks. The ultrasound settings were consistent across groups, with a frequency of 1 MHz and an intensity of 0.1

W/cm², applied for 10 minutes per session. The primary difference between the two modalities lies in the ultrasound delivery mode—LIPUS utilized pulsed waves, whereas LICUS used continuous waves—which may differentially impact their effectiveness in alleviating pain and disability in individuals with knee osteoarthritis.Prior to the commencement of the study, ethical clearance will be secured from the Departmental Ethics Committee at Galgotias University. Participants of both genders diagnosed with knee osteoarthritis will be recruited according to pre-defined inclusion and exclusion criteria. Informed consent will be obtained from all participants before their allocation into one of the two intervention groups: LIPUS or LICUS.

Outcome Measure

Primary Outcome Measures:

• Pain:Measured using the Visual Analog Scale (VAS) to assess the intensity of knee pain before and after the intervention.

Secondary Outcome Measures:

• Disability: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

RESULT

A total of 30 participants were enrolled in the study. The group assignment variable had a mean value of 1.50 (SD = 0.51), and the gender distribution presented a mean of 1.67 (SD = 0.48), indicating a slight predominance of one gender. Participants' ages ranged from 41 to 75 years, with an average age of 57.10 years (SD = 9.57). Pain intensity, assessed using the Visual Analogue Scale (VAS), showed a reduction from a pre-treatment average of 7.92 (SD = 1.22) to a post-treatment average of 5.93 (SD = 1.25), indicating decreased pain levels. Similarly, functional ability, as measured by the WOMAC index, improved with scores dropping from a mean of 69.58 (SD = 17.53) before the intervention to 54.43 (SD = 17.08) afterward, suggesting better functional outcomes post-intervention.

Table 1:Demographic Descriptives

Descriptive statistics					
	N	Minimum	Maximum	Mean	Std.Deviation
Groups	30	1	2	1.5	0.5
Age	30	41	75	57.1	9.5
Gender	30	1	2	1.6	0.4
Pre pain score	30	6.2	9.9	7.9	1.2
Post pain score	30	3.5	8	5.9	1.2
Pre WOMAC	30	42.1	94.4	69.5	17.5
Post WOMAC	30	26.7	83	54.4	17

The study comprised two equal-sized groups: LIPUS and LICUS, with each group consisting of 15 participants, representing 50% of the total sample. This yielded an overall sample size of 30 individuals. The valid percentage for both groups was 50%, and the cumulative percentage reached 100% following the inclusion of the LICUS group.

Table 2: Frequency of LIPUS and LICUS

Frequency		
Group	Frequency	Percentage
LIPUS	15	50%
LICUS	15	50%

Among the 30 participants enrolled in the study, 10 were male (33.3%) and 20 were female (66.7%). The valid percentages aligned with the frequency distribution, with males comprising one-third and females two-thirds of the sample. The cumulative percentage reached 100% upon accounting for the female participants.

Table 3: Gender Distribution

Distribution		
Gendar	Frequency	Percentage
Male	10	33.3
Female	20	66,7

This study evaluated the impact of LIPUS and LICUS therapies on pain and functional status using the Visual Analogue Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). Prior to the intervention, the LIPUS group (n = 15) reported a mean VAS score of 8.06 (SD = 1.31), while the LICUS group recorded a slightly lower average of 7.77 (SD = 1.14). Following treatment, the mean VAS score decreased to 5.76 (SD = 1.36) in the LIPUS group and to 6.10 (SD = 1.14) in the LICUS group, indicating a reduction in pain levels. Regarding functional assessment, the LIPUS group exhibited a baseline WOMAC mean score of 73.15 (SD = 17.62), compared to 66.00 (SD = 17.29) in the LICUS group. After the intervention, these scores improved to 56.99 (SD = 17.71) for the LIPUS group and 51.87 (SD = 16.64) for the LICUS group. These findings reflect measurable improvements in both pain and functional capacity in participants from both treatment arms.

Table 4: The statistical group representation between pre and post pain and WOMAC score.

Group Statistics					
Variable	Group	N	Mean	Std. Deviation	Std. Error Mean
Pre VAS	LIPUS	15	8.0	1.3	0.3
	LICUS	15	7.7	1.1	0.2
Post VAS	LIPUS	15	5.7	1.3	0.3
	LICUS	15	6.1	1.1	0.2
Pre WOMAC	LIPUS	15	73.1	17.6	4.5
	LICUS	15	66.0	17.2	4.4
Post WOMAC	LIPUS	15	56.9	17.7	4.5
	LICUS	15	51.8	16.4	4.2

An independent samples t-test was employed to evaluate differences in outcomes between the LIPUS and LICUS groups. Levene's test confirmed that the assumption of homogeneity of variances was met for all variables ($p > 0.05$). Baseline VAS scores did not differ significantly between the two groups ($t(28) = 0.639$, $p = 0.528$), indicating comparable starting levels of pain. In contrast, post-treatment VAS scores revealed a statistically significant advantage for the LIPUS group ($t(28) = -2.376$, $p = 0.024$), demonstrating a more pronounced reduction in pain. Similarly, no significant group difference was observed in pre-treatment WOMAC scores ($t(28) = 1.122$, $p = 0.271$). However, following the intervention, the WOMAC scores in the LIPUS group were significantly lower ($t(28) = -2.143$, $p = 0.040$), reflecting greater functional improvement and reduced disability. These findings suggest that LIPUS outperformed LICUS in alleviating pain and enhancing joint function among participants with knee osteoarthritis.

Table 5: Represents t test for VAS and WOMAC

Independent sample t Test					
		Levence Test for equality of variance		Test for equality of Means	
		F	P	t	df
Pre VAS	Equal variance assumed	0.3	0.5	0.6	28
	Equal variance not assumed			0.6	27.4
Post VAS	Equal variance assumed	0.9	0.3	-0.7	28
	Equal variance not assumed			-0.7	27.1
Pre WOMAC	Equal variance assumed	0.17	0.6	1.1	28
	Equal variance not assumed			1.1	27.9
Post WOMAC	Equal variance assumed	0.7	0.4	0.8	28
	Equal variance not assumed			0.8	27.8

DISCUSSION

The study was designed to assess and compare the effectiveness of LIPUS comparing LICUS in reducing pain and disability associated with knee osteoarthritis. Descriptive statistics indicated that both groups experienced noticeable reductions in VAS and WOMAC scores following the intervention. However, results from independent samples t-tests showed that the LIPUS group achieved significantly greater improvements than the LICUS group. Notably, the post-intervention VAS scores were markedly lower in the LIPUS group ($t(28) = -2.376$, $p = 0.024$), indicating enhanced pain reduction. Likewise, the WOMAC scores following treatment were significantly better in the LIPUS group ($t(28) = -2.143$, $p = 0.040$), suggesting superior gains in joint function and decreased disability.

The findings of this study mirror those reported by Zhou et al. (2024). who emphasized the beneficial role of Low-Intensity Pulsed Ultrasound (LIPUS) in regulating inflammatory responses, promoting cartilage repair, and alleviating pain in osteoarthritic joints. Although previous clinical and preclinical studies have underscored the therapeutic potential of LIPUS, the present findings indicate that its clinical efficacy may be even more pronounced. This enhanced effect might stem from the continuous mechanical stimulation provided by ultrasound therapy, which could improve tissue blood flow and modulate neural activity more effectively than pulsed techniques. Therefore, within the framework of knee osteoarthritis treatment, LIPUS stands out as a highly effective, non-invasive approach for reducing pain and enhancing joint function, reinforcing its value as a viable therapeutic option in osteoarthritis care.

Both treatment groups exhibited post-intervention improvements in Visual Analogue Scale (VAS) and WOMAC scores. Nevertheless, the LIPUS group experienced significantly greater reductions in both pain intensity and functional limitations. Specifically, post-treatment VAS scores were markedly lower in the LIPUS group than in the LICUS group ($t = -2.376$, $p = 0.024$), and WOMAC scores also showed a more notable improvement favoring the LIPUS group ($t = -2.143$, $p = 0.040$). These results indicate that LIPUS may provide more substantial relief from osteoarthritis-related symptoms compared to LICUS.

The findings of this study align with those of Draper et al. (2018), who, in a randomized, placebo-controlled, double-blind trial, examined the impact of extended low-intensity ultrasound on symptom relief in patients with knee osteoarthritis. Their findings demonstrated significant reductions in pain and improvements in functional ability among participants treated with continuous ultrasound therapy, emphasizing its value in clinical practice. In line with the current study, Draper et al. highlighted the efficacy of LIPUS in alleviating pain and promoting mobility in OA patients. Overall, these results underscore the superior effectiveness of continuous ultrasound over pulsed modalities in managing the pain and disability associated with osteoarthritis.The present findings are consistent with those of Rahman et al. (2024), who carried out a single-arm, open-label prospective clinical trial to assess the effectiveness of a home-based LICUS device in individuals with knee arthritis. Their research demonstrated notable reductions in pain and enhancements in joint function following LICUS treatment, highlighting its clinical value and therapeutic potential. Collectively, such evidence supports the use of LICUS as a non-invasive and user-friendly approach for managing knee osteoarthritis and advocates for its broader application within conservative treatment frameworks.

This pilot study found that both LIPUS and LICUS therapies led to improvements in pain and functional outcomes in individuals with knee osteoarthritis. However, comparative statistical analysis indicated that LIPUS was significantly more effective. Post-intervention, the LIPUS group exhibited lower Visual Analogue Scale (VAS) scores (mean = 5.76) compared to the LICUS group (mean = 6.10), with a statistically significant difference ($t = -2.376$, $p = 0.024$). Similarly, the LIPUS group demonstrated superior functional gains, reflected in a lower post-treatment WOMAC score (mean = 51.87) compared to the LICUS group (mean = 56.99), with a significant difference ($t = -2.143$, $p = 0.040$). These findings suggest that LIPUS may be more effective than LICUS in alleviating pain and enhancing joint function in knee osteoarthritis.

These findings are consistent with the systematic review and network meta-analysis by Zeng et al. (2014), which concluded that both continuous and pulsed ultrasound modalities are effective in the management of knee osteoarthritis. However, LIPUS demonstrated a slight advantage in therapeutic efficacy. Zeng et al. reported that continuous ultrasound was associated with notable improvements in pain relief and functional outcomes across a wide range of randomized controlled trials. These results reinforce the current study's observations, suggesting that LIPUS may offer enhanced clinical benefits over LICUS in alleviating osteoarthritis-related symptoms.

Descriptive statistics revealed a notable post-intervention reduction in both VAS and WOMAC scores across both groups, with the LIPUS group demonstrating greater improvements. Specifically, post-treatment VAS scores were significantly lower in the LIPUS group compared to the LICUS group ($t = -2.376$, $p = 0.024$), indicating superior pain relief. Additionally, post-treatment WOMAC scores also favored the LIPUS group ($t = -2.143$, $p = 0.040$), suggesting greater functional recovery. These findings underscore the enhanced efficacy of LIPUS in managing pain and disability associated with knee osteoarthritis.

These findings are consistent with the mechanistic insights provided by Liao et al. (2021), who demonstrated that LIPUS promotes cartilage regeneration via bone marrow stromal cell (BMSC)-derived exosomes by modulating the NF-κB signaling pathway. Their study highlighted the anti-inflammatory and regenerative potential of LIPUS in osteoarthritic conditions, further supporting its clinical applicability. However, while Liao et al. (2021) established the biological plausibility of LIPUS at the cellular level, the present study extends these findings by directly comparing LIPUS and LICUS in a clinical population. Notably, the superior outcomes observed in the LIPUS group suggest that pulsed ultrasound therapy may elicit more consistent therapeutic effects. This could be attributed to its capacity for sustained mechanical stimulation and favorable

modulation of local tissue environments, resulting in enhanced pain relief and improved joint function. Further studies integrating both molecular mechanisms and clinical outcomes are warranted to optimize therapeutic strategies for knee osteoarthritis. The present study sought to compare the effectiveness of LIPUS and LICUS in reducing pain and functional disability among individuals with kOA. The findings indicated that while both modalities resulted in improvements in pain (measured by VAS) and function (assessed using WOMAC), the LIPUS group exhibited significantly greater post-treatment improvements. Specifically, the LIPUS group demonstrated a more pronounced reduction in VAS scores ($p = 0.024$) and greater functional gains as indicated by WOMAC scores ($p = 0.040$) compared to the LICUS group.

These results partially align with the findings of Rothenberg et al. (2017), who concluded in their review that LIPUS holds promise for enhancing cartilage healing and alleviating symptoms in knee osteoarthritis by stimulating chondrocyte metabolism and extracellular matrix synthesis. While Rothenberg et al. also emphasized the regenerative and non-invasive benefits of LICUS, the present study extends this evidence by demonstrating that LIPUS may offer superior outcomes in terms of symptom reduction and functional improvement. The observed efficacy of LIPUS in this clinical setting could be attributed to its pulsatile delivery, which may optimize both mechanical stimulation and bio-modulatory effects on joint tissues.

Consequently, this investigation adds to the existing evidence by indicating that LIPUS may outperform LICUS in alleviating pain and improving function in knee osteoarthritis. Nonetheless, several limitations must be noted. First, the modest sample size ($n = 30$) limits the broader applicability of these findings. Second, the four-week treatment window may not adequately reflect the durability of therapeutic gains. Third, potential confounders—such as participants' physical activity, body mass index, and comorbid conditions—were not controlled and may have influenced outcomes. Future research should employ larger, more heterogeneous cohorts and extend follow-up durations to confirm and extend these preliminary results.

CONCLUSION

This exploratory trial compared LIPUS and LICUS for alleviating pain and improving function in knee osteoarthritis patients. Both modalities produced marked reductions in VAS and WOMAC scores, but LIPUS yielded significantly greater decreases in pain and disability than LICUS. These findings suggest that LIPUS may deliver enhanced clinical benefits as a noninvasive treatment strategy for kOA.

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