Original Review

The Role of Ultrasound Therapy in the Management of Musculoskeletal Soft Tissue Pain

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Abstract

Ultrasound is an invaluable physical modality widely used for diagnosis and therapy in humans and animals. It is noninvasive, atraumatic, and may be used repeatedly. As a therapeutic tool, ultrasound has been in use for some 6 decades. Therapeutic ultrasound (TUS) is used for the treatment of musculoskeletal disorders, including acute soft tissue injuries, overuse syndromes, as well as chronic orthopedic and rheumatologic conditions. The aim of this review was to investigate the clinical effectiveness of TUS in musculoskeletal acute and chronic pain, mainly through the control of inflammation and the promotion of soft tissue injury healing. Based on the evidence presented, TUS is clinically effective in some musculoskeletal soft tissue pain conditions, but due to conflicting results in some studies, no specific positive recommendations can be made, nor does it permit exclusion of TUS from clinical practice. In phonophoresis, TUS plays a significant role, without reported adverse effects. There is scope for improving the evidence base with better designed studies.

Keywords

therapeutic ultrasound, phonophoresis, musculoskeletal injuries, pain, soft tissue healing

Therapeutic ultrasound (TUS) is an electrophysical agent, routinely used in physiotherapy for the treatment of painful musculoskeletal conditions. Ultrasound (US) is an acoustic energy with a frequency of 1.0 to 3.0 MHz and beyond, which is above the upper threshold of human hearing, which ranges from 16 Hz to 15 to20 000 Hz.[1]

The first biological effects of US were noted as early as 1917 by Langevin in fish,[2] followed by Wood and Loomis,[3] who reported erythrocyte lyses and reduced mobility in rats following 300 kHz of US application. Therapeutic application of US was introduced after 1930 in Germany and the United States. TUS was first used to demonstrate in 1947 the treatment of painful muscle spasms in violin players, and this triggered wide clinical applications as well as research into the mechanisms of action.[4] Technical developments in ultrasonic probe design as well in the firmware and software to drive such a probe followed leading to the acceptance of diagnostic US.

TUS has been used by physical therapists for the treatment of injuries including ligament sprains, muscle strains, tendonitis, joint inflammation, plantar fasciitis, metatarsalgia, facet irritation, impingement syndrome, bursitis, rheumatoid arthritis, osteoarthritis (OA), and scar tissue adhesions.[5] The aim of this report is to review the clinical effectiveness of TUS as used in physiotherapy, to treat bone and soft tissue lesions. It is essential to state that US is well established and widely accepted as a diagnostic modality to which no reference is made in this article, but which is the subject of other articles within this issue.

Physiological Effects of Ultrasound

An US beam produces longitudinal waves with areas of compression and rarefaction (Figure 1).[6] US waves pass through materials, creating oscillations of its particles; such oscillations transfer the energy by compression and rarefaction of the media. Similarly, when US passes through the tissues it causes vibrations causing thermal changes in the tissues.[7]

US may induce thermal and nonthermal physical effects in the target tissues, and it is incorrect to assume that only one effect is present at any time and that physical therapy treatment may be classed as either thermal (continuous mode) or nonthermal (pulsed mode, but rather a combination of the 2 phenomena.[7]

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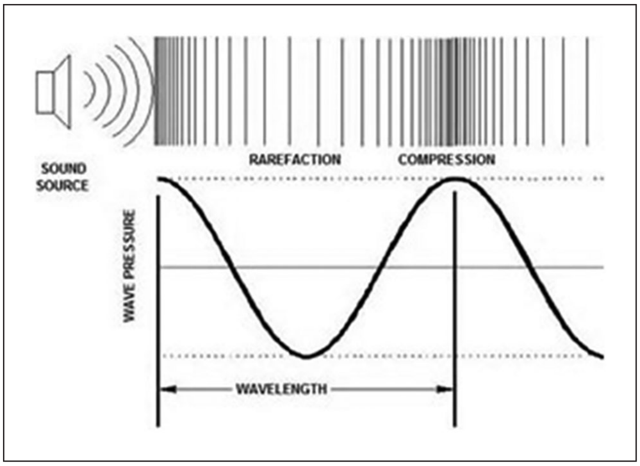

Figure 1. Ultrasound compression and rarefaction. Adapted with permission from Watson (2015).[6]

Thermal TUS effects include the following:

- Increased tissue temperature
- Hyperdynamic tissue metabolism
- Increased local blood flow
- Increased extensibility of collagen fibers
- Reduced viscosity of fluid elements in the tissue[8]

Nonthermal mechanisms include the following:

- Ultrasonic cavitation
- Gas body activation
- Mechanical stress or frequency resonance nonthermalprocesses[8]

The 2 physiological mechanisms of US are interrelated depending on the parameters of application. In the continuous mode, the delivery of US is constant throughout the treatment period, and in the pulsed mode, the delivery of US is intermittently interrupted.[9] The treatment parameters of TUS that can be adjusted according to the patient pathology are frequency, intensity, treatment mode (ie, duty cycle), treatment duration, and treatment area. TUS frequency of 3 MHz is used specifically for the treatment of superficial tissues, whereas frequency of 1 MHz is applied at deeper tissues,[8] since there is an inverse relationship between frequency and US energy penetration depth. It has been reported that destructive effects of US energy, if any, may be due to its mechanical rather than thermal effects.

Ultrasound Impedance

Impedance is a fundamental concept for the transmission/reflection of US, being analogous to friction and movement. The highest impedance (99.998%) is found in the steel/air interface between the probe and the patient, which can be overcome by using gel or water, since both are excellent coupling media.[10] US energy is better transmitted to the tissues with a higher protein content (eg, tendons. ligaments, fascia, capsule, and scar tissue) and to a much lesser extend to tissues with high water, low-protein content (eg, blood, fat, cartilage, and bone).[11,12]

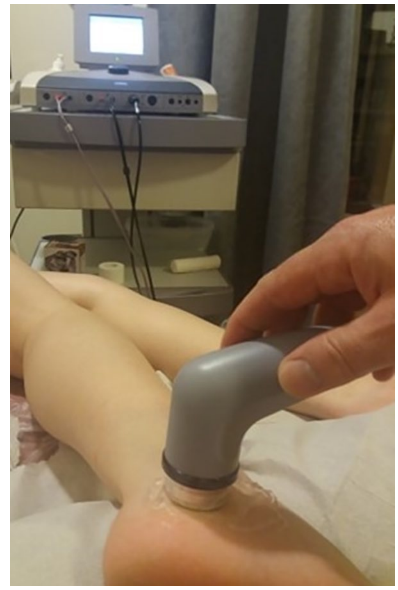

Figure 2. Therapeutic ultrasound application, pulsed mode, frequency: 3 MHz, intensity: 0.5 W/cm^2, in lateral ankle sprain, with a gel medium, and gentle, circular movements in order to avoid local thermal discomfort.

Clinical Applications of TUS

Physiotherapists use TUS for the management of acute and chronic musculoskeletal pain (Figure 2).

Joint Pain

Therapeutic ultrasound is commonly used to treat joint pain, which may be of capsular (arthritic) or noncapsular origin.[11] It was reported that TUS offers statistically significant reduction in chronic pain on the knee, shoulder, or hip when used alone or as part of a regime.[12] In the treatment of rotator cuff tendinopathy, it was argued that TUS combined with low-level laser therapy was a beneficial adjunctive treatment.[13] There is less agreement on the treatment of acute ankle sprains with a systematic review of 6 trials, which showed no significant difference between TUS and placebo. However, insufficient information on risk of bias and intervention details were provided by the studies included.[14] Another systematic review of 47 trials (2388 participants) found clinically important differences favoring TUS over placebo at 6 weeks in terms of overall pain (mean change = −14.9 vs −6.3 on a 52-point scale, mean difference = −8.60, 95% confidence interval = −13.48 to −3.72, 61 participants), and function, in people with calcific tendinitis. However, TUS produced no clinically important additional benefits when combined with other physical therapy interventions.[15] Combining TUS with other modalities benefitted pain and function in a group with adhesive capsulitis (N = 30) though again there were no significant differences between the treatment and control groups[16] and this was broadly in accord with a double-blind randomized clinical trial on N = 50 patients with primary adhesive capsulitis.[17] In another systematic review on the effectiveness of physiotherapeutic interventions in treatment of frozen shoulder/adhesive capsulitis, TUS was not recommended as an effective treatment.[18] In a recent randomized study, however, it was shown that low-intensity US resulted in statistically significant reduction of pain ($P < .001$) in patients with upper trapezius myofascial neck and shoulder pain. The authors suggest that TUS can be used to treat pain related to upper trapezius myofascial trigger points, a common occurrence in patients with acute neck pain.[19]

There would appear to be some weak evidence to support the use of TUS in some joint pain conditions, either singly or combined with a regime.

Plantar Fasciitis

The use of TUS to treat pain in plantar fasciitis is supported by studies. In a recent pivotal study[20] on N = 33 patients, the use of intense TUS, an established US-based therapy, in which sound waves were focused into a well-defined specific area of musculoskeletal tissue,[20] resulted in significant pain reduction at weeks 4, 8, 12, and 26 compared with baseline ($P < .001$) at −39%, −49%, −51%, and −44%, respectively. A concomitant reduction of fluid-filled cysts (from −32% to −44%) was also observed. Foot function index scores, a reliable assessment of tool of pain and function, also improved. There were no reported adverse effects associated with TUS.

Another study, in N = 30 subjects with plantar fasciitis,[21] low-level laser therapy was significantly more effective compared with US in pain numerical rating scale as well as the Foot Ankle Ability Measure. In a systematic review and meta-analysis,[22] TUS led to reduction of plantar fasciitis pain at 0 to 6 weeks but did not reach statistical significance. In another randomized controlled trial (RCT), the addition of 1 MHz continuous US, and stretching, led to significant reduction of plantar fasciitis pain, with no significant difference compared with placebo and stretching.[23] In a RCT, US was found to be significantly more effective than shockwave with regard to pain and disability as determined by the Foot Function Index scale.[24] Last, in another study, TUS led to significant pain relief (Visual Analogue Scale [VAS]), improved function, and decreased plantar fascia thickness as measured from magnetic resonance imaging scans in 60 patients with chronic plantar fasciitis.[25]

These data permit the observation that TUS is effective in pain reduction in plantar fasciitis, either used alone or as part of a therapeutic regime. Details of TUS dose and parameters were provided in most studies but not all according to the guidelines on dose calculation (http://www.electrotherapy.org/modality/ultrasound-dose-calculation).[6]

Low Back and Neck Pain

TUS is often used for the treatment of acute and chronic neck and low back pain of musculoskeletal origin.[8] In a recent systematic review, it was shown that TUS was no more effective than placebo to treat back pain, whereas it resulted in significant neck pain reduction when combined with other modalities.[26] Similarly, in a systematic review, US was shown to have short-term benefit only in improving low-back function.[27] The authors proposed further studies to elucidate their findings. In another study, the combination of laser therapy, TUS, and exercise in N = 45 patients with chronic neck and lower back pain (CNLBP) was effective in reducing pain and functional performance.[28] These studies suggest that TUS has a role to play in the management of low back and neck pain.

Arthritis

The role of low-intensity pulsed US on cartilage healing in knee OA was investigated in a review article of experimental studies, which showed that it can have a promising effect on the cellular elements of the osteoarthritic articular cartilage and specifically on knee chondrocytes.[29] In a critical review, it was demonstrated that TUS was effective in improving pain, function, and cartilage repair in knee OA.[30] Later, in a systematic review and meta-analysis of low-intensity pulsed US on knee OA a significant effect on pain reduction and knee functional recovery was demonstrated.[31] Similarly, in a systematic review in patients with knee OA, it was shown that TUS led to statistically significant improvement of pain ($P < .01$) and physical function ($P < .04$), with the authors suggesting that it is a beneficial and safe treatment for improving pain and function in patients with knee OA.[32] A single-blind controlled trial TUS was equally effective as transcutaneous electrical stimulation (TENS) in improving pain and function in 40 patients with painful knee OA.[33] In another RCT, which investigated the effect of TUS on pain and physical function in N = 62 patients with knee OA, significant short-term improvements were found in both variables.[34] Additionally, in a systematic review and meta-analysis, it was found that both pulsed and continuous US were significantly more effective in improving pain and function, when compared with the control group.[35] The efficacy of TUS on knee OA pain reduction (difference in pain scores between US and control of −1.2 cm on a 10-cm VAS) and function are also supported by previous studies.[36,37] Another systematic review concluded that hand US alone is effective in reducing joint pain and improving grip strength, wrist dorsal flexion, morning stiffness, and joint swelling in patients with rheumatoid arthritis.[38] Overall, it can be concluded that US therapy may significantly improve pain and function in patients with OA and rheumatoid arthritis.

Sports Injuries

TUS is reported to have beneficial effects in sports injuries pain relief, edema control, and range of joint motion,[39] possibly by increasing pain thresholds, collagen extensibility, reducing edema, and therefore inflammation, muscle spasms, and joint stiffness. In a systematic review on acute ankle sprains, it was concluded that TUS was no more effective than placebo in treating pain and edema, with no details of TUS parameters measurement techniques provided. A need for rigorous RCTs to demonstrate efficacy was emphasized.[14] Similar findings on ankle sprains were found in another study described above with no detailed information on treatment parameters.[16]

In a review of the rehabilitation of hamstring injuries, the authors concluded that the efficacy of TUS in this condition was controversial on account of the discord in relevant research.[40]

TUS therapy was reported to be beneficial in treating tendon injuries in an animal model.[41,42] Admittedly these observations were on acute injuries; nonetheless, the observations may have value in understanding TUS use on human trials. Since TUS is clinically applied in the acute and subacute stages of painful conditions, the above-mentioned finding may explain the mechanism of action and the subsequent analgesic effect, which however needs to be established by larger studies.

Lateral Epicondylitis

Several studies have been carried out to investigate the therapeutic efficacy of TUS on lateral epicondylitis. A recent meta-analysis of RCTs, which compared the long-term efficacy of TUS with extracorporeal shockwave therapy in pain relief and function,[42] found that both techniques were effective; however, shockwave therapy was significantly more effective in alleviating pain. Another RCT compared TUS and exercise with corticosteroid injections in N = 49 patients with lateral epicondylitis, and the study found that at 12 weeks, TUS and exercise resulted in statistically significant improvement in VAS, PRTEE (Patient-Rated Tennis Elbow Evaluation) pain score, PRTEE function score, and pain free grip strength, compared with corticosteroid injections group ($P < .001$).[43] Other reviews of TUS use in the same condition showed benefits when used singly or with friction massage[44] or other physiotherapy techniques.[45] These reports lend support to the use of TUS to treat painful, lateral epicondylitis. Positive overall effects of TUS in lateral elbow pain are apparent but need to be further clinically substantiated.

Soft Tissue Healing

According to the evidence presented so far, TUS can significantly contribute to the reduction of musculoskeletal pain, through the reduction of inflammation and the promotion of all stages of soft tissue healing following tissue injury.[46,47] In a recent experimental study, it was shown that low-intensity pulsed US therapy had a biostimulatory effect on fibroblast cells, confirming its therapeutic properties related to the initial phases of tissue healing.[48]

Another experimental study was carried out in N =28 rats following tenotomy and re-suturing of calcaneus tendons, where the experimental group was treated daily, with a 5-minute 1 MHz, 0.1 W/cm^2, TUS, and sham US was applied to the control group. The results showed that the experimental group had significantly higher load and tensile strength, suggesting that TUS can enhance the healing process of acute tendon rupture.[49]

In another experimental study,[50] it was shown that the application of low-intensity pulsed US accelerated patellar bone-tendon junction healing through regulation of vascular endothelial growth factor expression and cartilage formation in rabbits. In a study that combined low-intensity pulsed US with 1.5 MHz frequency and functional electrical stimulation, bone-tendon junction healing was accelerated in a rabbit model.[51] The same conclusion was drawn in a similar study, which investigated the effects of low-intensity TUS on medial collateral ligament acute injury healing in the rabbit model and resulted in increased scar cross-sectional area and type I collagen present at 6 weeks after injury as compared with sham treatment.[52] Finally, in a systematic review that examined the effect of low-intensity TUS on soft tissue healing in animal models, it was shown that it facilitated tendon healing, with increased tensile strength and collagen alignment.[53] It was also shown that US enhanced cell proliferation during muscle regeneration and improved tissue biomechanics in skeletal muscle and ligament injuries (ultimate load, stiffness, and energy absorption). US also promoted tendon-bone junction healing through improved tissue function. According to the authors, these findings provide adequate scientific evidence to explain the mechanism of soft tissue injury healing promotion and pain reduction, through low-intensity US, and

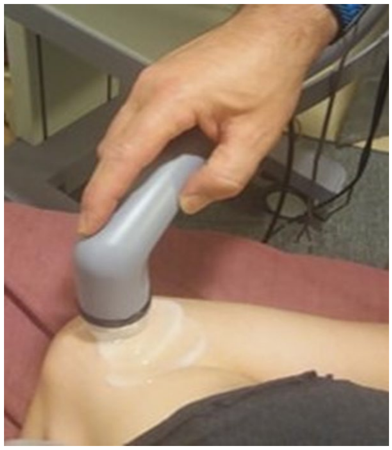

Figure 3. Phonophoresis (diclofenac sodium) in shoulder rotator cuff tendinitis.

improve outcomes for musculoskeletal injuries and postoperative recovery.

Phonophoresis

Phonophoresis is the migration of drug molecules, contained in a contact agent, by US use through the skin, either by structural changes that increase skin permeability, or through convection-related mechanisms that occur only when US is applied (Figure 3).[54] US with 1 to 3 MHz frequency and 0 to 2 W/cm^2 intensity, as indicated, has been shown to be safe and increases percutaneous absorption in animal models.[55]

Phonophoresis, compared with exercise, is reported to be beneficial in reducing neck pain, which, according to the authors, may be of value, in conjunction with other physiotherapy interventions.[56]

Several clinical studies have been carried out investigating the role of phonophoresis in musculoskeletal painful syndromes (Table 1). In an RCT, the application of dexamethasone phonophoresis, TENS, and exercise (study group) was compared with TUS, TENS, and exercise (control group), in N = 46 female patients with knee OA. The experimental group resulted in a greater, statistically significant improvement in pain (VAS: $P < .001$) and function in patients with knee OA than TUS combined with exercise and TENS. The effect size of phonophoresis was clinically significant.[57] A study that compared phonophoresis, dry needling, and myofascial release in N = 60 patients with upper trapezius neck pain showed that phonophoresis and dry needling were significantly more effective ($P <$ s.001) in pain intensity than myofascial release.[58] In a single-blind study, where phonophoresis with TENS was compared with phonophoresis alone, TUS and sham US (control), in N = 100 patients with acute mechanical neck pain and active myofascial trigger points, showed statistically significant improvements in postintervention pressure pain threshold (algometer: an instrument measuring the smallest pressure on the skin that will arouse a sensation of pain) and range of motion values in all treatment groups ($P < .0001$).[59] In an RCT phonophoresis was compared with Mills manipulation and deep transverse frictions in 60 patients with lateral epicondylitis, and it was found that both treatments resulted in significant improvement of pain and grip strength.[60] Last, an RCT compared phonophoresis and iontophoresis using dexamethasone sodium phosphate in the management of 50 patients with knee OA and found that both therapeutic modalities were equally effective and well-tolerated.[61] Similar findings were demonstrated in a systematic review and meta-analysis, examining the effects of TUS and phonophoresis in patients with knee OA,[62] and showed that although both treatments reduced pain and improved function significantly, phonophoresis was significantly more effective in pain elimination, suggesting that it was successful in the transmission of the pharmaceutical agent in the affected tissues. An RCT showed that phonophoresis with diclofenac and thiocolchicoside gel, was superior to US alone in the treatment of low back pain.[63]

Last, in an RCT in 61 patients with chronic neck pain, it was shown that phonophoresis and exercise was significantly more effective than placebo and exercise alone in pain, disability, sleep quality, and depression measurements.[64]

According to the above study findings, it seems that that there is adequate evidence to support the application of Non Steroidal Anti Inflammatory Drugs (NSAIDs) via US since it may lead to clinically significant therapeutic effects in painful musculoskeletal conditions with no reported side effects.[65]

Discussion

The aim of this review was to study the role of TUS in the treatment of soft tissue pain conditions. In painful lateral epicondylitis and arthritis the evidence favors the use of TUS either singly or in combination with another technique. In other common musculoskeletal pain conditions, there are varying levels of evidence of TUS use to benefit pain. The use of phonophoresis clearly benefits pain management in certain soft tissue conditions. It is speculated that the benefits of phonophoresis may be the result of driving molecules of anti-inflammatory agent through the epidermis and this together with the massaging effect of TUS may be causing vasodilatation, and edema reduction. As a technique, TUS is well-accepted and widely available: there is a skill in using it that is transferable.

Clearly there is a role for TUS in managing pain even though the evidence-based needs developing. Does TUS

Table 1. Characteristics of Studies in Phonophoresis Ultrasound Therapy.

Study	Participants	Treatment	N	Outcome measures	Main results
Ahmed et al[57] (2019)	Female patients with knee OA	Study group: Phonophoresis, TENS, and quadriceps strengthening exercises Control group: US, TENS, and exercise	46	Pain (VAS, WOMAC) Function (Timed Up and Go test and total WOMAC)	Significant improvement between experimental and control groups in VAS and WOMAC subscale and function ($P < .001$)
Tabatabaiee et al[58] (2019)	Patients with myofascial trigger points in the upper trapezius muscle participated	Group 1: Pressure release Group 2: Phonophoresis with betamethasone Group3: Dry needling	60	Pain: VAS, pain threshold algometer Active cervical range of motion	Significant pain decrease, active cervical range of motion, and pain pressure threshold increase were observed in the 3 groups ($P < .001$). The dry needling and phonophoresis groups reported more significant improvement compared with the pressure release group ($P < .001$). NS diff. between the dry needling and phonophoresis groups.
Takla and Rezk-Allah[59] (2018)	Patients with acute mechanical neck pain and myofascial trigger point in the upper trapezius	Group 1: Diclofenac phonophoresis and TENS Group 2: Diclofenac phonophoresis Group 3: US Control group: sham US	100	Pressure threshold algometer Active lateral cervical flexion	Statistically significant improvements in pressure pain threshold and range of motion values in treatment groups ($P < .0001$). Phonophoresis with TENS was superior over phonophoresis in pain reduction ($P < .0001$). Phonophoresis was superior over US in pain reduction.
Akinbo et al[61] (2009)	Adult patients with knee OA	Group 1: Dexamethasone sodium phosphate (DEX-P) phonophoresis (PH) Group 2: 0.4% DEX-P iontophoresis therapy	50	WOMAC scores 20 m ambulatory time knee range of motion	Significant improvement in both groups ($P < .001$) NS diff. between groups
Wu et al[62] (2019)	Adult patients with knee OA (systematic review and meta-analysis of RCTs on OA)	Randomized controlled trials comparing therapeutic US with sham US and phonophoresis with conventional US	1074	VAS, WOMAC, Knee ROM, Lequesne index	TUS significantly reduced pain ($P < .00001$) and (WOMAC) physical function score ($P = .03$) and increased ROM and Laseque index Phonophoresis US illustrated significantly lower VAS scores compared with TUS ($P = .009$)
Altan et al[63] (2019)	Adult patients with acute low back pain	Group 1: US with diclofenac + thiocolchicoside gel for 10 minutes and for a total of 10 sessions Group 2: Therapeutic US with contact gel protocol was applied with the same setting and timing with group 1 using US gel that does not contain any pharmaceutical ingredient	60	Visual numeric scale (VNS), Oswestry Disability Index (ODI), and Shober lumbar flexion test	Significant improvement in both groups ($P < .05$) Phonophoresis is statistically significant and more effective than TUS in short-term ODI and in pain reduction long term

Abbreviations: US, ultrasound; OA, osteoarthritis; TENS, transcutaneous electrical stimulation; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster University Osteoarthritis Index; NS, not significant; ROM, range of motion; RCT, randomized-controlled trial.

offer any benefit in treating wound pain—which is an area of interest to readers of this journal? US is used in wound debridement, which reduces pain and benefits healing as argued in another part of this issue: improving the understanding of TUS may have benefits for wound healers.

Among the other value of US is its portability, lending itself to home care when offered by a trained physiotherapists/clinicians. This could become especially valuable when home care is preferred to clinic visits as observed during the current crisis resulting from COVID-19.

Additionally, there are no known reported adverse effects of TUS application. Hence, it can be applied safely, either alone or in conjunction with other techniques, taking of course into account all indications and precautions as described elsewhere.[10]

Declaration of Conflicting Interests

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