TENS in Fibromyalgia: From fundamental neurobiology to pragmatic trial

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DJO, Inc TENS units and electrodes
What is fibromyalgia?
  - Central (nocicplastic) pain
  - Basic pain mechanisms

Why TENS?
  - Mechanisms of TENS

Randomized controlled trial
  - FAST

Pragmatic trial
  - FM-TIPS
What is fibromyalgia?

Central (nociplastic) pain syndrome
Diagnosing fibromyalgia

- Symptom of widespread pain
  - “Hurt all over”
  - 1990 ACR Classification Criteria – “Above and below the waist, left and right sides or the body, involving the axial skeleton”
  - 2016 – “Involving 4 of 5 regions from the widespread pain index”
  - Other criteria count number of painful sites

- Symptom/sign of tenderness
  - “Painful with gentle touch”
  - ACR1990 – 11 of 18 tender points (4 kg/cm² pressure)
  - Skin roll or BP cuff tenderness

- Pain worsened with physical activity
Diagnosing fibromyalgia

- Chronic fatigue
- Non-refreshing sleep
- Chronic myofascial/visceral pain
  - Irritable bowel syndrome
  - Interstitial cystitis/bladder pain syndrome
  - Temporomandibular pain
  - Chronic headache (tension, migraine)
  - Etc.
- Depression/anxiety
Somatic Pain
Noxious impulses being received and transmitted by normal components of the sensory nervous system

Neuropathic Pain
Noxious impulses originating from an abnormality in neural structures

Central (Nociplastic) Pain
Innocuous impulses perceived as noxious due to physiologic alterations of neural structures
Nociplastic Pain

Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain.

IASP Definition 2017
Is the Pain “Real”?

Evoked Pain Testing in Nociplastic Pain

- **Pain response**
- **Stimulus intensity**

- **Non-painful stimuli**
- **Normal pain response**
- **CS pain response**
- **Hyperalgesia**
- **Allodynia**

CS shifts pain threshold downwards leading to greater response to given stimuli.
Basic Pain Mechanisms
Transmission

Perception
Central Pain Pathways

- Sensory discriminative
  - Somatosensory cortex

- Motivational-Affective
  - Cingulate and insular cortex

- Fear-Emotion
  - Amygdala

- Planning, decision-making, social behavior
  - Prefrontal cortex
Descending Inhibition

- Via RVM and PAG
- Endogenous opioids
- Serotonin

K. Sluka
Steps in Central Sensitization

- Nociceptive Transmission
  - Requires nociceptive input (peripheral pain generator)
  - Dependent on excitatory amino acids, tachykinins, substance P

- Acute Phase Central Sensitization
  - Release in block of NMDA receptors
  - Activation of kinases via NMDA, NK1, TrkB receptors

- Late Phase Central Sensitization
  - Gene transcription locally and diffusely
  - Activation of microglia

- Disinhibition
  - Altered inhibitory and facilitatory controls from CNS

Why TENS?

Mechanisms suggesting potential benefit in central (nociceptive) pain
What is TENS?

- Transcutaneous Electrical Nerve Stimulation

TENS is expected to be effective mainly when the unit is active.
High Threshold Neuron

Wide Dynamic Range Neuron

TENS Reduces Central Excitability


Ma and Sluka, 2001; Sluka et al., 2005; Garrison and Foreman, 1994, 1996
TENS Activates Endogenous Inhibition: Opioids and Serotonin

Mixed frequency, low and high, prevents analgesic tolerance
TENS Opioid Effects in Humans

Solomon et al., 1980, Leonard et al., 2010; Sjolund and Eriksson, 1974
TENS for Chronic Musculoskeletal Pain

- Meta-analysis with data from 29 randomized trials
  - Patients had pain from back, hip, neck, and knee
  - 335 placebo, 474 TENS

- TENS had favorable pooled effect vs placebo (p<0.0005)

- Out of favor as pain treatment in PT
Why TENS in Fibromyalgia?

- Reduces central excitability at the level of the dorsal horn
  - High threshold neurons AND wide dynamic range neurons
  - Reduces neuronal activation to BOTH innocuous and noxious stimuli
  - Reduces excitatory amino acid (glutamate) release

- Activates descending inhibitory pathways
  - PAG-RVM-spinal cord
  - Uses endogenous opioids and serotonin
Randomized, Controlled Trial

Fibromyalgia Activity Study with TENS (FAST)

Arthritis Rheumatol. 2020 May;72(5):824-836
Treatment

- Active TENS parameters
  - Butterfly electrodes cervical and lumbar placement
  - Asymmetrical biphasic waveform
  - Modulating frequency 10-125 Hz
  - Variable pulse duration
  - Highest “strong but comfortable” intensity

- Instructed to apply at least 2 hours/day during activities
Placebo and Blinding

- Used Placebo TENS
  - Transient unit with short-duration of stimulation of 45s that ramped down over last 15s
  - Blinding script

- Included a No TENS group with Mock TENS during assessments

- Assessors remained blinded to Active TENS (45% correct), Placebo TENS (13% correct), and Mock TENS (20% correct)

- Participants blinded to Placebo TENS (49% correct), but Active TENS correctly identified by 70%
Main Inclusion Exclusion Criteria

- **Inclusion**
  - Women between 18-70 years old
  - Met 1990 criteria for classification of fibromyalgia
  - Average pain rating ≥ 4 over last 7 days by NRS at Visit 1
    AND Visit 2

- **Exclusion**
  - TENS use in last 5 years
  - Contraindications to TENS use
All participants received 4 weeks of Active TENS between Visit 3 and Visit 4.
**Outcome Measures**

**Primary**

- Pain during movement measured by NRS during 6-minute walk test (6MWT) of the ITT population
  - Comparing before/during TENS at study visits

**Secondary**

- Resting pain pre/post TENS during visits
- Disease activity/impact (FIQR)
- Pain intensity/interference (BPI: Brief Pain Inventory)
- Pain self-efficacy (PSEQ)
- Pain catastrophizing (PCS)
- Fatigue during movement and at rest
- Multidimensional fatigue (MAF)
- Sleep (PSQI)
- Fear of movement (TSK)
- PROMIS-Anxiety
- PROMIS-Depression
- Quality of life (SF-36)
- Self-report physical function (FIQR-function)
- Performance based physical function (6WMT, 5TSTS)
- Patient global rating of change
Participants

Completed Visit 4: Active TENS (n=75), Placebo TENS (n=73), No TENS (n=84)

Exclusion criteria met (n=468)
- Previous TENS use (n=136)
- Pain <4 (n=134)
- Assistive device for walking (n=80)
- Inflammatory Disease (n=58)
- Spinal Fusion (n=48)
- Neuropathic pain (n=43)
- Allergy to nickel/adhesive (n=10)
- Implanted metal device (n=6)
- Inclusion criteria not met (n=60)
- Declined (n=85)
- Lost to follow up (n=81)

Enrolled
n=352

Randomized
n=301

Assessed for eligibility
n=1046

Exclusion criteria met (n=20)
- Inclusion criteria not met (n=5)
- Withdrew (n=17)
- Lost to follow up (n=6)
- Terminated, change in health status (n=2)
- Terminated, serious adverse event (n=1)

Active TENS
n=103

Completed Visit 3
n=87
- Lost to followup (n=1)
- Withdrew (n=15)

Placebo TENS
n=99

Completed Visit 3
n=84
- Lost to follow-up (n=2)
- Withdrew (n=11)
- Terminated (n=1)

No TENS
n=99

Completed Visit 3
n=94
- Withdrew (n=4)
- Terminated (n=1)
<table>
<thead>
<tr>
<th>Demographic Variables*</th>
<th>Active TENS n=103</th>
<th>Placebo TENS n=99</th>
<th>No TENS n=99</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>44.7 (14.3)</td>
<td>47.2 (12.6)</td>
<td>48.6 (11.8)</td>
<td>0.10</td>
</tr>
<tr>
<td>Race, White</td>
<td>92%</td>
<td>92%</td>
<td>92%</td>
<td>0.99</td>
</tr>
<tr>
<td>Ethnicity, Not Hispanic</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>0.99</td>
</tr>
<tr>
<td>Married / Living with partner</td>
<td>33%</td>
<td>51%</td>
<td>52%</td>
<td>0.01</td>
</tr>
<tr>
<td>Less than college graduate</td>
<td>61%</td>
<td>61%</td>
<td>64%</td>
<td>0.48</td>
</tr>
<tr>
<td>Working</td>
<td>55%</td>
<td>45%</td>
<td>58%</td>
<td>0.42</td>
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<tr>
<td>Health Variables</td>
<td></td>
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<tr>
<td>Never smoked</td>
<td>82%</td>
<td>80%</td>
<td>70%</td>
<td>0.16</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>34.8 (8.7)</td>
<td>33.7 (8.8)</td>
<td>34.0 (8.9)</td>
<td>0.65</td>
</tr>
<tr>
<td>Duration of fibromyalgia (yrs)</td>
<td>7 (3-12)</td>
<td>7 (2-14)</td>
<td>7 (4-15)</td>
<td>0.47</td>
</tr>
<tr>
<td>Opioids for pain^</td>
<td>27 (26%)</td>
<td>26 (26%)</td>
<td>26 (26%)</td>
<td>--</td>
</tr>
<tr>
<td>Baseline Measures</td>
<td></td>
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</tr>
<tr>
<td>Pain at rest (NRS)</td>
<td>6.2 (1.5)</td>
<td>5.9 (1.4)</td>
<td>6.1 (1.6)</td>
<td>0.33</td>
</tr>
<tr>
<td>Fatigue at rest (NRS)</td>
<td>6.8^a (2.0)</td>
<td>6.1^b (1.8)</td>
<td>6.4^ab (2.0)</td>
<td>0.08</td>
</tr>
<tr>
<td>FIQ-R 7-day pain</td>
<td>6.7 (1.8)</td>
<td>6.0 (1.6)</td>
<td>6.15 (1.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>FIQ-R</td>
<td>59.2^a (16.8)</td>
<td>53.7^b (15.9)</td>
<td>55.6^ab (16.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>SF-36 MCS</td>
<td>38.7 (10.0)</td>
<td>40.2 (10.2)</td>
<td>39.5 (10.6)</td>
<td>0.57</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>32.7 (6.4)</td>
<td>33.3 (6.2)</td>
<td>32.7 (6.6)</td>
<td>0.72</td>
</tr>
<tr>
<td>PSQI, z-score</td>
<td>12.6 (3.8)</td>
<td>12.0 (3.8)</td>
<td>11.9 (3.4)</td>
<td>0.38</td>
</tr>
<tr>
<td>PCS</td>
<td>23.1 (13.0)</td>
<td>20.4 (12.5)</td>
<td>20.8 (12.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>PSEQ</td>
<td>28.2 (13.3)</td>
<td>29.9 (13.1)</td>
<td>29.0 (13.2)</td>
<td>0.67</td>
</tr>
<tr>
<td>TSK</td>
<td>36.5 (7.7)</td>
<td>37.1 (8.0)</td>
<td>37.4 (8.3)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

^Enrollment stratified by site and by opioid use
Movement and Resting Pain/Fatigue

A. Movement Pain 6MWT
   - Before
   - During
   - Visit 2
   - Visit 3
   - Active TENS
   - Placebo TENS
   - No TENS

B. Movement Pain 5TSTS
   - Before
   - During
   - Visit 2
   - Visit 3

C. Resting Pain
   - Before
   - During
   - Visit 2
   - Visit 3

D. Movement Fatigue 6MWT
   - Before
   - During
   - Visit 2
   - Visit 3
   - Active TENS
   - Placebo TENS
   - No TENS

E. Movement Fatigue 5TSTS
   - Before
   - During
   - Visit 2
   - Visit 3

F. Resting Fatigue
   - Before
   - During
   - Visit 2
   - Visit 3
<table>
<thead>
<tr>
<th>Patient-reported outcomes</th>
<th>Active TENS n=103</th>
<th>Placebo TENS n=99</th>
<th>No TENS n=99</th>
<th>Group Mean Difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Active vs PLACEBO</td>
<td></td>
</tr>
<tr>
<td>FIQ-R</td>
<td>-8.48 (-12.92, -4.04)^^^</td>
<td>-3.42 (-6.54, -0.30)^</td>
<td>-1.39 (-4.40, 1.62)</td>
<td>-5.06 (-10.44, 0.32) 0.073</td>
<td></td>
</tr>
<tr>
<td>FIQ-R Pain</td>
<td>-1.3 (-1.8, -0.7)^^^</td>
<td>-0.4 (-0.9, 0.2)</td>
<td>-0.1 (-0.6, 0.4)</td>
<td>-0.9 (-1.7, -0.1) 0.018</td>
<td></td>
</tr>
<tr>
<td>BPI-Interference</td>
<td>-0.94 (-1.40, -0.48)^^^</td>
<td>-0.26 (-0.73, 0.21)</td>
<td>-0.29 (-0.74, 0.16)</td>
<td>-0.68 (-1.33, -0.01) 0.044</td>
<td></td>
</tr>
<tr>
<td>BPI-Intensity</td>
<td>-0.75 (-1.08, -0.43)^^^</td>
<td>-0.26 (-0.59, 0.07)</td>
<td>0.15 (-0.17, 0.46)</td>
<td>-0.49 (-0.96, -0.02) 0.035</td>
<td></td>
</tr>
<tr>
<td>MAF GFI</td>
<td>-4.63 (-6.42, -2.84)^^^</td>
<td>-1.46 (-3.29, 0.37)</td>
<td>-0.26 (-1.98, 1.47)</td>
<td>-3.17 (-5.73, -0.61) 0.009</td>
<td></td>
</tr>
<tr>
<td>PSQI (z-score)</td>
<td>-0.88 (-1.67, -0.10)^</td>
<td>-0.87 (-1.68, -0.09)^</td>
<td>-0.07 (-1.03, 0.49)</td>
<td>-0.01 (-1.11, 1.12) &gt;0.99</td>
<td></td>
</tr>
<tr>
<td>PSEQ#</td>
<td>3.16 (0.75, 5.57)^^^</td>
<td>1.51 (-0.94, 3.96)</td>
<td>0.82 (-1.5, 3.15)</td>
<td>1.65 (-1.79, 5.09) 0.745</td>
<td></td>
</tr>
<tr>
<td>PCS</td>
<td>-3.38 (-5.32, -1.45)^^^</td>
<td>-3.12 (-5.09, -1.15)^^^</td>
<td>-1.39 (-3.26, 0.48)</td>
<td>-0.26 (-3.03, 2.50) &gt;0.99</td>
<td></td>
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<tr>
<td>TSK</td>
<td>-0.73 (-2.04, 0.59)</td>
<td>-0.34 (-1.68, 1.00)</td>
<td>-0.18 (-1.45, 1.09)</td>
<td>-0.39 (-2.26, 1.49) &gt;0.99</td>
<td></td>
</tr>
<tr>
<td>SF-36 MCS#</td>
<td>2.32 (0.21, 4.43)^</td>
<td>1.24 (-0.91, 3.39)</td>
<td>-0.04 (-2.08, 2.00)</td>
<td>1.08 (-1.94, 4.09) &gt;0.99</td>
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<tr>
<td>SF-36 PCS#</td>
<td>2.37 (1.05, 3.70)^^^</td>
<td>1.15 (-0.20, 2.50)</td>
<td>1.37 (0.09, 2.65)</td>
<td>1.22 (-0.67, 3.12) 0.359</td>
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<tr>
<td>PROMIS-Anxiety</td>
<td>-1.07 (-2.59, 0.46)</td>
<td>-0.57 (-2.12, 0.98)</td>
<td>-0.66 (-2.14, 0.82)</td>
<td>-0.05 (-2.68, 1.68) &gt;0.99</td>
<td></td>
</tr>
<tr>
<td>PROMIS-Depression</td>
<td>-2.84 (-4.18, -1.49)^^^</td>
<td>-0.09 (-1.47, 1.28)</td>
<td>0.38 (-0.92, 1.68)</td>
<td>-2.71 (-4.66, -0.82) 0.002</td>
<td></td>
</tr>
</tbody>
</table>

**P-values:**
- **<0.0001** indicates statistical significance at the 0.0001 level.
- **0.0006** indicates statistical significance at the 0.0006 level.
- **0.005** indicates statistical significance at the 0.005 level.
- **0.018** indicates statistical significance at the 0.018 level.
- **0.035** indicates statistical significance at the 0.035 level.
- **0.044** indicates statistical significance at the 0.044 level.
- **0.047** indicates statistical significance at the 0.047 level.
- **0.073** indicates statistical significance at the 0.073 level.
- **0.09** indicates statistical significance at the 0.09 level.
- **0.15** indicates statistical significance at the 0.15 level.
- **0.26** indicates statistical significance at the 0.26 level.
- **0.38** indicates statistical significance at the 0.38 level.
- **0.745** indicates statistical significance at the 0.745 level.
- **0.99** indicates statistical significance at the 0.99 level.
- **<0.0001** indicates statistical significance at the 0.0001 level.
- **0.0006** indicates statistical significance at the 0.0006 level.
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- **0.38** indicates statistical significance at the 0.38 level.
- **0.745** indicates statistical significance at the 0.745 level.
- **0.99** indicates statistical significance at the 0.99 level.
|                           | Active TENS  
n=103 | Placebo TENS  
n=99 | No TENS  
n=99 | Group Mean Difference (95% CI) | P-value |
<table>
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<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Active vs No TENS</td>
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<tr>
<td><strong>Self-report function</strong></td>
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<td></td>
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<tr>
<td>outcomes</td>
<td></td>
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<td></td>
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<tr>
<td>FIQ-R Function</td>
<td>-2.71 (-4.00, -1.42)^(^{\wedge})</td>
<td>-1.38 (-2.70, -0.06)^(^{\wedge})</td>
<td>-0.56 (-1.81, 0.68)</td>
<td>-1.33 (-3.18, 0.51) 0.073</td>
<td>-2.15 (-3.94, -0.36) 0.005</td>
</tr>
<tr>
<td>SF-36 Physical Function</td>
<td>1.39 (0.10, 2.69)^(^{\wedge})</td>
<td>0.53 (-1.79, 1.84)</td>
<td>0.75 (-0.50, 2.00)</td>
<td>0.86 (-0.98, 2.71) &gt;0.99</td>
<td>0.65 (-1.15, 2.44) &gt;0.99</td>
</tr>
<tr>
<td><strong>Performance-based function outcomes</strong></td>
<td></td>
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<tr>
<td>6MWT</td>
<td>0.06 (-0.49, 0.61)</td>
<td>-0.11 (-0.66, 0.44)</td>
<td>-0.34 (-0.87, 0.19)</td>
<td>0.17 (-0.61, 0.95) &gt;0.99</td>
<td>0.40 (-0.36, 1.17) &gt;0.99</td>
</tr>
<tr>
<td>Functional reach</td>
<td>0.16 (-0.42, 0.74)</td>
<td>0.04 (-0.55, 0.63)</td>
<td>-0.13 (-0.69, 0.44)</td>
<td>0.29 (-0.60, 1.18) &gt;0.99</td>
<td>0.29 (-0.60, 1.18) &gt;0.99</td>
</tr>
</tbody>
</table>
TENS improves global rating of change

NNT=3
<table>
<thead>
<tr>
<th>Responder Definitions</th>
<th>Active TENS n=103</th>
<th>Placebo TENS n=99</th>
<th>No TENS n=99</th>
<th>P-value (adjusted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥30% Reduction pain</td>
<td>44% (34-53)</td>
<td>22% (15-31)</td>
<td>14% (9-22)</td>
<td>0.004  &lt;0.001</td>
</tr>
<tr>
<td>≥20% Reduction fatigue</td>
<td>45% (35-54)</td>
<td>26% (19-36)</td>
<td>23% (16-33)</td>
<td>0.019  0.004</td>
</tr>
<tr>
<td>≥20% Reduction function</td>
<td>38% (29-48)</td>
<td>36% (28-46)</td>
<td>28% (20-38)</td>
<td>0.974  0.319</td>
</tr>
<tr>
<td>≥30% Reduction pain + ≥20% fatigue</td>
<td>29% (21-39)</td>
<td>13% (8-21)</td>
<td>13% (8-21)</td>
<td>0.018  0.018</td>
</tr>
</tbody>
</table>

Strongest predictor of pain response was reduction of MEP during first TENS treatment
Other Results

- No difference in ITT compared with per protocol analysis
  - PP: At least 30 min/d for 8 sessions over 4 weeks

- Placebo TENS and No TENS groups had similar beneficial results after 4 weeks open-label Active TENS

- Active TENS group had sustained/improved outcome after an additional 4 weeks open-label treatment

- No significant reduction in effectiveness of TENS in opioid versus non-opioid strata

- TENS-related adverse effects
  - Skin irritation from electrodes
  - Anxiety, nausea
  - Pain (muscle spasm, unspecified)
  - NNH between 20 and 100
Summary

- Active TENS improves resting and movement-evoked pain and fatigue acutely
  - No TENS tolerance develops over 4-8 weeks of treatment

- After 4 weeks of treatment, there was evidence of a chronic TENS effect with a reduction in baseline pain and fatigue

- Active TENS resulted in global improvement of disease impact

- There was improvement in one measure of depression, but no significant effect of TENS on measures of function, sleep, or other clinical domains

- There were minimal adverse effects associated with TENS treatment
Pragmatic Trial

Fibromyalgia – TENS in Physical Therapy Study (FM-TIPS)
Study Team
Goal:
- Demonstrate the feasibility of adding TENS to treatment of patients with FM in a real-world Physical Therapy practice setting and
- Determine if addition of TENS to standard Physical Therapy for FM reduces pain, increases adherence to PT and allows patients with FM to reach their specific functional goals with less drug use.

Hypothesis
- Using TENS in a Physical Therapy setting is feasible and that FM patients using TENS are more likely to reach their therapeutic goals.
Specific Aims

**Aim 1:** Determine if addition of TENS to routine PT improves movement-evoked pain

**Aim 2:** Determine if addition of TENS to routine PT improves 1) disease activity, 2) likelihood of meeting patient-specific functional goals, 3) adherence to PT, and 4) medication use

**Aim 3:** Examine feasibility of implementing TENS into routine PT care for FM using semi-structured exit interviews of patients and PTs

- Cluster-randomized pragmatic trial
- Routine PT with or without TENS for FM
- Enroll ~600 people with FM
Study Design

- Physical therapy setting
  - PT are familiar with TENS
  - TENS may be most helpful when used during movement
  - More frequent “touches” with patients may facilitate compliance

- Cluster randomized
  - Five PT health systems – Iowa, Illinois, Tennessee
  - Twenty-four PT sites
  - Each site randomized to TENS + PT or PT only
  - Stratified randomization by health system and site size
    - Versus constrained randomization

- Pragmatic design
  - Inclusion/exclusion criteria
  - Minimal interference with usual care
  - Emphasis on PRO

- Intervention
  - TENS (Quell) x 2 applied to cervical/low back regions recommended for 2h daily during activity
  - Mixed frequency, strong but comfortable intensity
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<th>PT V1</th>
<th>Home</th>
<th>PT V2</th>
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<th>PT V3-PT completed</th>
<th>Home Days 30, 60, 90, 180</th>
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<td>• Primary endpoint Day 60</td>
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<td>• TENS provided to no-TENS randomized participants if data completed</td>
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Pre-Resting NRS pain/fatigue, Pre-MEPT with NRS mvmt pain/fatigue, TENS applied for 1st full treatment (or not) x 30 min, Demographic data, 2016 FM criteria, FIQR, MAF, BPI, PROMIS PhysFunc, PROMIS Sleep, Sleep Duration, PCS, PHQ-8, GAD-7, TAPS1, Medications, RAPA, Post Resting NRS pain/fatigue, Post MEPT with NRS mvmt pain/fatigue, Adverse event, Barriers to TENS
Outcome measures

- **Primary outcome:** Movement evoked pain
  - Baseline: Five times sit-to-stand pre-TENS
  - Primary endpoint: 5TSTS after 30-min TENS at day 60
  - TENS + PT vs PT only
  - Power analysis → 600 participants

- **Secondary outcomes**
  - Other PRO
  - PT adherence

- **Descriptive comparisons**
  - Baseline vs days 90, 180: TENS + PT (long-term use) and PT-only followed by TENS started at home
Challenges

- PT sites not used to conducting embedded research
- Multiple different EHR
  - Data collection limited
- COVID impact on free-standing PT practices
  - Changes in volumes, financial issues
  - Rolling starts of PT systems
Conclusions

- TENS can be safely used in addition to other treatments to improve pain and fatigue in women with fibromyalgia in the setting of an RCT.

- Practicality of using TENS for patients with fibromyalgia referred for PT needs to be determined.
  - Is TENS uptake improved if applied during PT treatment?

- Effectiveness of TENS in a real-world type setting remains to be determined.
Comments or Questions?