|  |
| --- |
| **CRITICALLY APPRAISED TOPIC** |

**FOCUSED CLINICAL QUESTION**

|  |
| --- |
| In a person who has undergone an amputation, is mirror therapy as effective as TENS for relief/management of phantom pain? |

**AUTHOR**

|  |  |  |  |
| --- | --- | --- | --- |
| **Prepared by** | James Bryan Mull | **Date** | 11-22-2014 |
| **Email address** | james\_mull@med.unc.edu | | |

**CLINICAL SCENARIO**

|  |
| --- |
| In my previous clinical rotation at HealthSouth Inpatient Rehabilitation Hospital – Columbia, South Carolina, I encountered a patient that experienced intense residual limb pain (phantom limb pain or PLP) following a below knee amputation. The patient’s wound site was not healing properly, thus they were not an appropriate candidate for application of TENS electrodes. Seeking an alternative intervention, mirror therapy (MT) was used with minimal success at managing the patient’s pain. Answering this clinical question will help direct my clinical practice by deciding whether to continue implementing mirror therapy in the future as a viable alternative means of pain management in patients with compromised skin integrity where placement of an electrode would be contraindicated. |

**SUMMARY OF SEARCH**

Best evidence appraised and key findings

|  |
| --- |
| * Fourteen studies were identified that met the inclusion and exclusion criteria, comprising 3 systematic reviews, 3 randomized control trials, 1 controlled crossover design, and 7 lower quality uncontrolled clinical studies. No studies were identified that directly compared the two interventions of interest. Three studies (2 RCTS, 1 systematic review) are critically appraised below * MT, when delivered for more than two treatment sessions, showed some potential to decrease intensity and duration of PLP, though no evidence has yet defined the long-term benefits of this intervention. Several adverse side effects have also associated with receiving this intervention, including grief, increased pain, and increased swelling in the involved extremities. No standard protocol has been established for administering MT in this patient population. * There is little evidence to support the use of low-frequency TENS to manage PLP. There were clinically significant improvements in amputation site healing in subjects that received this indication, which may be a better indication for use of this intervention in the clinic. Future research should focus on high-frequency TENS for reducing PLP, as there is some anecdotal support behind the efficacy its use for this purpose in this patient population. |

**CLINICAL BOTTOM LINE**

|  |
| --- |
| Even the best evidence on this clinical topic is lacking in several regards. Neither intervention has been validated with high quality evidence that establish a standardized protocol for use with patients in the clinical setting. More support has been published to indicate the use of MT, administered over multiple treatment sessions, to manage PLP. However, patients should be monitored closely for adverse symptoms as a result of this intervention. Further research is needed for both interventions, specifically to document risk of adverse effects for MT, efficacy of high-frequency TENS to manage PLP, and establish more specific protocols for use in this patient population. |

|  |
| --- |
| ***This critically appraised topic has been individually prepared as part of a course requirement and has been peer-reviewed by one other independent course instructor*** |

**SEARCH STRATEGY**

|  |  |  |  |
| --- | --- | --- | --- |
| **Terms used to guide the search strategy** | | | |
| **P**atient/Client Group | **I**ntervention (or Assessment) | **C**omparison | **O**utcome(s) |
| Patients with Acute Amputation | Mirror Therapy | TENS | Phantom pain relief |

**Final search strategy:**

1. (Amputat\* or Amputee\*)
2. Mirror OR “Mirror Box” OR “Mirror Therapy” OR MT
3. TENS OR “Transcutaneous electrical stimulation” OR “electric\* stimul\*”
4. Pain OR “Phantom Pain” OR “Phantom Limb Pain”
5. “Residual Pain” OR “Residual Limb Pain” OR “Neuropathic Pain”
6. #1 AND #2
7. #1 AND #3
8. (#1 AND (#4 OR #5) AND (#2 OR #3))
9. #1 AND #2 AND #3 AND #4 AND #5

|  |  |  |
| --- | --- | --- |
| **Databases and Sites Searched** | **Number of results** | **Limits applied, revised number of results (if applicable)** |
| 1. **The Cochrane Library** 2. **CINAHL** 3. **Pubmed** | **1. Three**  **2. Six**  **3. Twenty Four** | **1. No limits applied - Three**  **2. Excluded Case Studies/Reports, revised number: Four**  **3. Excluded Case Studies/Reports, revised number: Seven** |

## INCLUSION and EXCLUSION CRITERIA

|  |
| --- |
| **Inclusion Criteria** |
| -Systematic Reviews, RCTs, controlled trials, uncontrolled trials  -Published up to September 2014  -Pain as outcome measure |
| **Exclusion Criteria** |
| -Subjects with history of non-amputation related acute pain (i.e. fibromyalgia, OA, RA)  -Case studies, expert opinion, abstracts, etc. |

**RESULTS OF SEARCH**

|  |  |  |
| --- | --- | --- |
| A total of | \_14\_\_ | Fourteen relevant studies were located and categorised as shown in the following table (based on Levels of Evidence, Centre for Evidence Based Medicine, 2011) and *The Quality Index* quality assessment rating scale. *A Measurement Tool to Assess Systematic Reviews (AMSTAR)* for Systematic Reviews. |

**Summary of articles retrieved that met inclusion and exclusion criteria**

|  |  |  |  |
| --- | --- | --- | --- |
| **Author (Year)** | **Study quality score** | **Level of Evidence** | **Study design** |
| Moseley, GL (2006) | 19/32 | 1b | Randomized Control Trial |
| Mulvey, MR (2006) | 16/32 | 2b | Uncontrolled Clinical Study |
| Finsen, V (1988) | 18/32 | 1b | Randomized Control Trial |
| Kawamura, H (1997) | 11/32 | 2b | Uncontrolled Clinical Study |
| Katz, J (1991) | 16/32 | 2b | Controlled Crossover Design |
| Foell, J (2014) | 17/32 | 2b | Uncontrolled Clinical Study |
| Hunter, J (2003) | 12/32 | 2b | Uncontrolled Clinical Study |
| Darnall, B (2012) | 14/32 | 2b | Uncontrolled Clinical Study |
| Sumitani, M (2008) | 15/32 | 2b | Uncontrolled Clinical Study |
| Brodie, EE (2007) | 20/32 | 1b | Randomized Control Trial |
| Mercier, C (2009) | 16/32 | 2b | Uncontrolled Clinical Study |
| Rothgangel A (2011) | 8/11 AMSTAR | 1a | Systematic Review |
| Mulvey, MR (2011) | 4/11 AMSTAR | 1a | Systematic Review |
| Ezendam D (2009) | 7/11 AMSTAR | 1a | Systematic Review |

**BEST EVIDENCE**

The following 3 studies were identified as the ‘best’ evidence and selected for critical appraisal. Reasons for selecting these studies were:

|  |
| --- |
| * Rothgangel A (2011) - The clinical aspects of mirror therapy in rehabilitation: a systematic review of the literature   + This study was selected due to it being the highest rated systematic review on mirror therapy use * Brodie, EE (2007) **-** Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement   + This study was selected due to it receiving the highest rating among randomized control trials. * Finsen, V (1988) - Transcutaneous electrical nerve stimulation after major amputation   + Despite being published in 1988, this was the highest rated, highest level of evidence identified for use of TENS in patients following amputation. |

**SUMMARY OF BEST EVIDENCE**

**(1) Description and appraisal of Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a ‘virtual’ limb upon phantom limb pain, sensation and movement by E. Brodie, A. Whyte, and C. A. Niven, 2007**

|  |
| --- |
| **Objective of the Study:** |
| To assess the effect of seeing a “virtual limb” move (mirror therapy) while attempting to move both the residual and uninvolved limb on phantom limb pain, movement, and sensation in lower limb amputees. |
| **Study Design** |
| * Non-blinded randomized controlled trial * Subjects were randomly allocated to experimental and control groups via computer generated ‘pseudo’ random series. * This study was conducted during one treatment session. * Outcome measures assessed immediately pre- and post-intervention, no follow-up. * Outcomes were subjective, questionnaire-based |
| **Setting** |
| Subjects participated in the study while receiving outpatient services from two different hospitals:   * Westmarc Prosthetic Fitting Centre at the Southern General Hospital in Glasgow, Scotland * The Donald Tod Rehabilitation Centre, Fazakerley Hospital in Liverpool, England |
| **Participants** |
| * 80 subjects total participated in the study   + 40 subjects from Westmarc Prosthetic Fitting Centre - Southern General Hospital, Glasgow   + 40 subjects from The Donald Tod Rehabilitation Centre - Fazakerley Hospital, Liverpool * Subjects were recruited to participate if they had lower limb amputations (trans femoral or trans tibial), reported sensation of a phantom limb, and attended either of the two clinics during the time of the study (convenience sample). * 63 total males (35 in treatment group, 28 in control group), 17 females (6 in treatment group, 11 in control group); Mean age 55 years (range of 20-83 for treatment group, 25-80 years for control group); Mean 9 years post-amputation (range 1-50 years for treatment group, 3-47 years for control group); History of phantom limb pain: 68 subjects (35 subjects in treatment group, 33 subjects in control group) * Only 15 of the 80 total subjects reported the presence of phantom limb pain (PLP) prior to participation on the day of the study, despite 68 having a history of PLP experiences. * Only 43 of the 80 total subjects reported the presence of phantom limb sensations (PLS) prior to participation on the day of the study. * Subjects in both the test and control groups were comparable at baseline with regards to “gender, age, age at amputation, years since amputation, and self reported ability to move the phantom leg” (Brodie, 2007, pg. 431) |
| **Intervention Investigated** |
| *Control* |
| * 39 subjects – 28 males, 11 females   + 19 trans femoral   + 20 trans tibial * The control group performed the same intervention, same set-up, with the same movements as the experimental group. The lone exception was the subjects looked at their intact limbs with the mirror obscured to hide the ‘virtual limb’ reflected image. |
| *Experimental* |
| * 41 subjects – 35 males, 6 females   + 16 trans femoral   + 25 trans tibial * Subjects stood in a ‘virtual limb box’ (4 sides with open front and top). A mirror was placed at the patient’s midline in the sagittal plane so the intact limb was on one side of the mirror with the residual limb on the other side of the mirror. The side of the virtual limb box with the residual limb was hidden from view of the subject and they were instructed to gaze into the side with the intact limb and reflective mirror surface. The limbs were aligned so that the reflected image of the intact limb lined up with the residual limb, producing a ‘virtual’ limb when the subject looked down at the reflected image in the mirror. * A researcher instructed each subject to perform the following ten movements for ten repetitions each with both limbs.   “1. Slowly straighten and then bend your legs at the knee at the same time.  2. Slowly straighten and then bend your legs at the knee alternately as if walking.  3. Point your feet upwards, and then point your feet downwards at the same time.  4. Turn your soles in towards each other and then away from each other.  5. Move your feet around in a circle, to the left and to the right.  6. Lift your feet off the ground in a walking movement.  7. Point your toes upwards, and then downwards whilst trying to keep your ankle and foot still.  8. Clench and unclench your toes.  9. Spread out your toes and then relax them.  10. Point up your big toe and point down the other toes, then reverse it so that your big toe is pointing down and your other toes are pointing up” (Brodie, 2003, pg. 168)   * Between each of the above movement steps, the subject was asked to describe, via questionnaire, any changes in sensation of their phantom limb pain (PLP) or phantom limb sensation (PLS). The subject was given the option to stop the intervention proceedings if their PLP or PLS became uncomfortable. In this study, PLS is defined as “perception of non-painful sensations such as heat, cold or itch in the phantom leg. PLP is defined as "the perception of painful sensations in the phantom leg.”1   The series of movements were performed once during the lone treatment sessions conducted as a part of this study. |
| **Outcome Measures** |
| * Visual Analogue Scale (VAS) – Range 0 to 100. Measures for PLP and PLS intensity ratings assessed via verbal patient response * McGill pain questionnaire (MPQ) – The MPQ has a scoring range of 0 to 78, with higher scores indicating more intense pain. The subjects circled a variety of words to describe the quality of their pain researched tallied the number of their pain. The researches also used the MPQ to count the number of words chosen (NWC) to assess the individuals’ intensity of pain. The words chosen were categorized into sensory descriptors, ‘affective’, ‘evaluative’, and ‘miscellaneous’ to more accurately record and describe the nature of the PLP and PLS experiences during the study. * Total Pain Ranking Index (PRI) – calculated from conventional analysis of MPQ data. * Outcomes were assessed by an individual researcher with undisclosed training or discipline (i.e. physical therapist). |
| **Main Findings** |
| * There were significant reductions in PLS for both test groups, but no significant difference between the intervention and control groups. <<Put all of these remarks at the beginning of this section, followed by the supporting data>> * There were significant reductions in PLP for both groups in the study, but no significant difference between the intervention and control groups. * In this study power failed to reach the benchmark of 80% in any of the significant findings documented below.   Pre-intervention (±SD) Post-intervention (±SD)  MPQ:   * PLP NWC: Mirror (n=7)- 9.57 ±4.43 5.43 ±6.83  95% CI- 8.21-10.93 3.34-7.52   Control (n=8)- 7.38 ±3.78 3.38 ±3.42  95% CI- 6.19-8.57 2.3-4.46   * PLP Total PRI: p<0.05  Power: 70% (pg. 432)      * PLP VAS: Mirror (n=7)- 57 ±24.2 40 ±41.0  95% CI- 49.59-64.41 27.45–52.55  Control (n=8)- 33 ±21.0 29 ±31.9  95% CI- 26.41-39.59 18.99-39.01  p<0.05   Power: 68% (pg. 433)  Both the control and mirror groups had a significant decrease in NWC and VAS post-intervention compared to the pre-intervention baseline for their PLP, p<0.05. However, power reached only 68% for both findings (Brodie, 2007, pg. 432). There was also no significant difference between the NWC or VAS changes between groups, suggesting that using a mirror to view a phantom limb is no better than attempted movement alone at reducing the quality or intensity of PLP.  Pre-intervention (±SD) Post-intervention (±SD)   MPQ:   * PLS NWC: Mirror (n=21)- 5.33 ±5.05 4.05 ±4.41  95% CI- 3.78-6.88 2.7-5.4   Control (n=22)- 6.91 ±4.84 5.32 ±4.57  95% CI- 5.39-8.43 3.89-6.75  p<0.05  Power: 72% (pg. 431)   * PLS Total PRI: p<0.05  Power: 61% (pg. 431) * PLS VAS: Mirror (n=21)- 48.85 ±30.18 37.60 ±36.05  95% CI- 39.61-58.09 26.57-48.63  Control (n=22)- 49.22 ±27.74 44.08 ±31.81  95% CI- 40.51-57.93 34.10-54.06  p < 0.05   Power: 63% (pg. 431)  Both the control and mirror groups had a significant decrease in NWC and VAS post-intervention compared to the pre-intervention baseline for their PLS, p<0.05; but power reached only 72% and 63%, respectively (Brodie, 2007, pg. 431). There was also no significant difference between the NWC or VAS changes between groups, suggesting that using a mirror to view a phantom limb is no better than attempted movement alone at reducing the quality or intensity of PLS. |
| **Original Authors’ Conclusions** |
| * “The mirror condition increased significantly the ability of all amputees to move their phantom leg, over and above that of the control condition.” (pg. 434) * “The visual feedback of a moving virtual limb does modify the experience of a phantom limb. Although it need not abolish PLP in all amputees, it has the potential for reversing both the acute or chronic cortical reorganization thought to subserve PLP.” (pg. 434) |
| **Critical Appraisal** |
| **Validity** |
| The Quality Index: 21/32 based on Objective Described: Yes; Outcome Measures Described: Yes; Subject Demographics: Yes; Interventions Described: Yes, Principle Cofounders: Yes; Main Findings: Yes; Estimates of Random Variability: Yes; Adverse Events: Yes; Patients Lost to Follow-up Detailed: Yes; Probability Values: No; Representative Sample From Recruitment Population: Yes; Representative Sample From Total Population: No; Setting Representative: No; Blinded Subjects: No; Blinded Measurer: No; Data Dredging: Yes; Same Follow-up: Yes; Appropriate Statistical Tests: Yes; Subject Compliance: Yes; Valid and Reliable Outcome Measures: Yes; Intervention Groups Recruited From Same Population: Yes; Recruited Over Same Period of Time: Yes; Randomization Private: Unable To Determine/No; Adjustment for Confounding: Yes; Losses to Follow-up Accounted For: Yes; Sufficient Power: No  There was no follow-up or long-term intervention protocol to see if there was an additive effect of mirror therapy to aid in symptom reduction for patients experiencing phantom limb pain or sensations. The study only included one session featuring a 10-repetetions of the aforementioned exercises. This intervention protocol and the duration of the study did not allow for sufficient additive effects of the treatments to take hold. The majority of the participants were not even experiencing their PLP or PLS on the day that the study was conducted. This brief window does not adequately describe how a typical patient who may be experiencing these symptoms would respond to mirror therapy treatment to reduce their symptoms. Though the study included 80 test subjects, far fewer were included in many of the analyses due to the lack of symptoms present pre-intervention for most of the participants. This created a small sample size and contributed to a lack of power for the findings in this study. |
| **Interpretation of Results** |
| * The results of the study show that attempting to move one’s residual limb can reduce the intensity of PLP. * This study suggests that while attempting to move one’s residual limb, there is no advantage to viewing a virtual limb in reducing PLP. * Viewing a virtual limb made it easier for subjects to successfully ‘move’ their phantom limb, based on subjective reports. This, however, did not contribute to a greater decrease in PLP or PLS over attempting to move it without mirror therapy/seeing a virtual limb. * The power level in the study failed to reach 80% for all of the outcomes measured in the study. * To reach 80% power, the sample size in the study should have been increased from 80 subjects to 146 subjects (73 for both intervention and control groups * While there were significant treatment effects for reducing PLP and PLS in both groups, no greater treatment effect was seen for mirror therapy compared to the controlled intervention |

**(2) Description and appraisal of Transcutaneous Electrical Nerve Stimulation After Major Amputation by V. Finsen, L. Persen, M. Lovlien, E.K. Veslegaard, M. Simensen, A.K. Gasvann, P. Benum, 1988**

|  |
| --- |
| **Objective of the Study:** |
| This study sought to compare the effects of low frequency transcutaneous electrical nerve stimulation (TENS), chlorpromazine, and a ‘sham’ placebo intervention on phantom pain and incision healing in individuals following lower extremity amputation. |
| **Study Design** |
| * Single, partially blinded randomized control trial. * Subjects were recruited for and participated in the study over a two year period * Study participants were followed for at least one year, until re-amputation or death. (Finsen, 1988, pg. 110) * Subjects were randomized to three intervention groups following their surgical procedure:   + Group A - Sham TENS treatment and chlorpromazine   + Group B – Sham TENS only   + Group C – Low-frequency TENS (Finsen, 1988, pg. 109) * The authors did not disclose the protocol used for random allocation to the three study groups. * Groups B and C were blinded from the other group’s intervention. The authors were unclear as to whether Groups A, B, and C were aware that one group was receiving chlorpromazine, thus this determination that the study contained only a partially blinded protocol, at best. |
| **Setting** |
| This study was conducted at Trondheim University Hospital in Trondheim, Norway. The authors made no mention if this was a rural, community, or metropolitan hospital or what the setting within the hospital the subjects were housed (inpatient rehabilitation, outpatient clinic visits, etc.). |
| **Participants** |
| * A sample of 52 total subjects was recruited, presumably, from patients of Trondheim University Hospital. The authors did not specify how subjects were recruited for participation. However, subjects were eligible if they received through-knee (TK), below knee (BK), or trans-ankle/disarticulation (Syme’s amputation) secondary to diabetic complications or atherosclerosis. Subjects who received “traumatic amputation and re-amputation at a higher level,” non-compliant patients, “and those who were to be returned to a nursing home soon after operation” were excluded from participation.3 One subject from group B was removed from the study after being transferred to another division of the hospital, leaving 51 remaining participants in the study. * Demographics of 3 study groups:   + Group A: 15 subjects (10 males, mean age 71; 5 females, mean age 78)   Syme’s Amputations: 2  BK amputations: 10  TK amputations: 3  Diabetes: 6  Atherosclerosis: 9   * + Group B: 19 subjects (9 males, mean age 69; 10 females, mean age 80)   Syme’s Amputations: 4  BK amputations: 13  TK amputations: 2  Diabetes: 7  Atherosclerosis: 12   * + Group C: 17 subjects (8 males, mean age 68; 9 females, mean age 79)   Syme’s Amputations: 1  BK amputations: 11  TK amputations: 5  Diabetes: 6  Atherosclerosis: 11   * The groups were not uniform with regard to amputation level, but the dispersion of subjects with diabetic and atherosclerosis was equal. * Seven of the 51 initial subjects were on pain medication for unrelated medical issues and therefore not included in the data pertaining to dosages of analgesic medication taken post-surgery. * Two subjects, one from Group A with a TK amputation and one from Group C with a BK amputation, passed away within the first three weeks of the study. Thus 49 subjects remained in the study available and for follow-up. * 18 months after the start of the study, the authors determined that the three groups did not have an equal distribution of amputation levels in the treatment groups. (Finsen, 1988, pg. 110) |
| **Intervention Investigated** |
| *Control* |
| * Group B   + The 19 subjects in this group received sham TENS treatment, administered by research study clinicians. * The shame TENS treatment applied to the amputated limb side for 30 minutes, twice daily for the first two post-operative weeks. * Regardless of amputation level, electrodes were placed over the femoral and/or sciatic nerve. The electrode leads were plugged into an inactive channel on a Tenzcare brand TENS device. The device was set to the one position with lights flashing/displayed to give the illusion to the test subjects that the TENS unit was active and working. * Group A -   + The 15 subjects in this group received identical sham TENs intervention as documented above, with the addition of receiving chlorpromazine prophylactically to prevent phantom pain, 10 mg 3x daily, increased to a maximum of 25 mg if necessary, for a range of 5 to 28 weeks post-surgery. * Subjects were given analgesic medications upon request for management of post-operative pain. * The dosage of medication received during the first four weeks following their surgical procedure was recorded. * Study participants in Group A and B who were enrolled and followed during the first year were reviewed at 16 weeks post-surgery and at 1-year. * Study participants in Group A and B who were enrolled and followed during the second year were reviewed at the end of each of the first four weeks post-surgery, at 16 weeks, and again at 1-year. Participants in the study during the second year were able to provide information about subjective effects of TENS treatment, phantom limb pain, and wound pain during the first four weeks post-surgery. (Finsen, 1988, pg. 110) * All group subjects wore a plaster cast on the involved limb for the first three weeks post-operatively. * No description was provided for the training or credentials of the staff that supervised/administered the aforementioned intervention. |
| *Experimental* |
| * Group C   + The 17 subjects in this group received active, low frequency (7 pulses at 100Hz, 90 nanosecond wavelength) TENS via a Tenzcare brand unit. This unit had two independently controlled channels. One channel (2 electrodes) was applied over the sciatic nerve on the involved side and one channel was applied over the femoral nerve on the involved side.   + The above intervention was applied 30 minutes, twice daily during the first two post-operative weeks. * Study participants in Group C who were enrolled and followed during the first year were reviewed at 16 weeks post-surgery and at 1-year. * Study participants in Group C who were enrolled and followed during the second year were reviewed at the end of each of the first four weeks post-surgery, at 16 weeks, and again at 1-year. Participants in the study during the second year were able to provide information about subjective effects of TENS treatment, phantom limb pain, and wound pain during the first four weeks post-surgery (Finsen, 1988, pg. 110) * All group subjects wore a plaster cast on the involved limb for the first three weeks post-operatively. * No description was provided for the training or credentials of the staff that supervised/administered the aforementioned intervention. |
| **Outcome Measures** |
| * Post-operative pain   + Number of analgesic doses requested and taken by study participants during the first four post-operative weeks. The medications were presumably prepared and administered to subjects by a ‘state registered nurse’, as several of the studies’ authors have this designation. However, the authors do not explicitly state who administered and recorded the data. * Phantom pain   + Respondents in the second year of the study provided subjective reports of the presence of phantom limb pain after each of the first four weeks, at 16 weeks, and 1-year post-surgery. The authors state that the subjects were “directly asked” whether or not they experienced phantom pain. No indication was given that any formal outcome measure or intensity rating scale was used to document the presence or absence of this pain other than “yes” they have experienced it or “no” they have not. * Stump healing   + Subjective determination by research staff from observations of the amputation site for closed, “healed” sutures free from “crusts and scabs.” (Finsen, 1988, pg. 110)   + Only BK amputee patients were included in this outcome assessment |
| **Main Findings** |
| * Post-operative pain:  |  |  |  |  | | --- | --- | --- | --- | | Median # of analgesic medications taken (95% CI) | | | | |  | Group A (Chlorpromazine + Sham TENS) | Group B  (Sham TENS) | Group C  (Active TENS) | | Week 1 | 10 doses (2-15) n=14 | 10 doses (4-17)  n=14 | 5.5 doses (2-17)  n=14 | | Week 2 | 2 doses (0-8)  n=13 | 8 doses (0-12)  n=13 | 2 doses (0-8)  n=13 | | Week 3 | 2 doses (0-3)  n=11 | 2.5 doses (0-9)  n=12 | 0.5 doses (0-5)  n=12 | | Week 4 | 1 doses (0-6)  n=10 | 1.5 doses (0-13)  n=10 | 0 doses (0-7)  n=12 |  * + “The median number of analgesic doses was some-what lower in Group C patients than in the other two groups, but there were very great variations in analgesic consumption within each group and differences were not statistically significant” (Finsen, 1988, pg. 111)   + The sample size from each group reduced over the weeks as the subjects in the group required re-amputation or began analgesic medication for a separate medical condition, and thus was excluded from the following week’s data.3   + “All of the patients in Group C who were asked at the end of the second week said that TENS had an analgesic effect, but half of the 20 patients who had received sham TENS also thought that the stimulation had been of value.” (Finsen, 1988, pg. 111) * Stump healing (ONLY among BK amputees):  |  |  |  |  | | --- | --- | --- | --- | |  | Healed | Not Healed | Re-amputated | | **3rd week** |  |  |  | | Groups A+B (Sham TENS) | n=10 | n=11 | n=2 | | Group C (Active TENS) | n=6 | n=4 | n=0 | | **6th week** |  |  |  | | Groups A+B (Sham TENS) | n=13 | n=6 | n=4 | | Group C (Active TENS) | n=8 | n=1 | n=1 | | **9th week** |  |  |  | | Groups A+B (Sham TENS) | n=14 | n=4 | n=5 | | Group C (Active TENS) | n=9 | n=0 | n=1 |  * + By weeks 6 and 9 post-amputation, there was a significantly higher proportion of healed amputation sites among individuals with BK amputations in the Group C (n=10) compared to Groups A and B (n=23), p<0.05. By week 9, only 1 individual with a BK amputation needed an amputation revision after receiving active TENS, while 5 individuals required revision after receiving sham TENS, p<0.05. * Chronic phantom pain:   + Four Weeks post-surgery: “No significant difference in the proportion of patients in each group who complained of phantom pain.” (Finsen, 1988, pg. 110)   + 16 weeks post-surgery:     - Group A: 4 out of 11 subjects report phantom pain     - Group B: 7 out of 12 subjects report phantom pain     - Group C: 0 out of 10 subjects report phantom pain     - Significantly lower incidence in phantom pain amongst study subjects receiving active low-frequency TENS at this follow-up period (p<0.05)   + 1 year post-surgery     - Group A: 3 out of 8 subjects report phantom pain     - Group B: 5 out of 9 subjects report phantom pain     - Group C: 3 out of 8 subjects report phantom pain     - Of the only remaining 25 of the original 51 study participants available for inclusion at the 1-year follow-up (secondary to death or re-amputation), there was no significant difference between intervention or control groups for incidence of phantom pain. |
| **Original Authors’ Conclusions** |
| * “There was however, a statistically significant higher number of healed stumps, even when re-amputations were excluded, in Group C after both six and nine weeks. This is probably due to the vasodilatation which low frequency TENS” (Finsen, 1988, pg. 111) * “TENS had a considerable placebo effect with respect to pain.” “However, in our series, the subjective analgesic effect of active stimulation and the placebo effect of sham stimulation were not reflected in a reduced requirement for analgesia. This lack of an objective effect may be due to the use of low frequency stimulation; this is less well documented than high frequency as an analgesic for postoperative pain.” (Finsen, 1988, pg. 111) * Chlorpromazine also had no significant affect on the requirement for analgesia. * With prophylaxis TENS use, “we found no long-term difference between stimulated and control groups. The transitory reduction in phantom pain in the stimulated group is difficult to explain, there being no difference in the prevalence of phantom pain during stimulation, nor any significant change in analgesic consumption. Since none of our patients suffered significantly from chronic phantom pain, it is possible that prophylaxis is not really necessary.” (Finsen, 1988, pg. 111) |
| **Critical Appraisal** |
| **Validity** |
| The Quality Index: 17/32 based on Objective Described: Yes; Outcome Measures Described: Yes; Subject Demographics: Yes; Interventions Described: Yes, Principle Cofounders: Yes; Main Findings: Yes; Estimates of Random Variability: Yes; Adverse Events: No; Patients Lost to Follow-up Detailed: Yes; Probability Values: No; Representative Sample From Recruitment Population: No; Representative Sample From Total Population: No; Setting Representative: No; Blinded Subjects: Yes; Blinded Measurer: No; Data Dredging: No; Same Follow-up: Yes; Appropriate Statistical Tests: Yes; Subject Compliance: Yes; Valid and Reliable Outcome Measures: No; Intervention Groups Recruited From Same Population: Yes; Recruited Over Same Period of Time: No; Randomization Private: Unable To Determine/No; Adjustment for Confounding: Yes; Losses to Follow-up Accounted For: Yes; Sufficient Power: No  There are numerous noteworthy weaknesses in the design and methodologies that the authors employed during the execution of this study. For the interventions chosen in the study, the authors do not validate the use of chlorpromazine in this patient population. Their only mention to the efficacy of this medication was “we have used chlorpromazine on an empirical basis to treat (phantom pain after an amputation).” (Finsen, 1988, pg. 109) The authors also discuss that high frequency TENS has more research to support its use in this patient population to manage post-amputation pain, but they chose to use low frequency TENS in this study. The authors do not describe their participant selection protocol or discuss the method of randomizing subjects into the three different groups. It was only after 18 months that the authors identified that the intervention groups were not equal with regards to their level of amputation. Perhaps TENS is more effective for higher-level amputations (i.e. TK vs. Syme’s) and a more distributed sample would have yielded a higher treatment effect.  The authors also fail to mention the clinical reasoning behind some patients receiving chlorpromazine for 5 weeks and some patients receiving it for up to 28 weeks. A longer dosage period of chlorpromazine may have led to a larger treatment effect for managing phantom limb pain. In addition to providing no detail on the clinical reasoning behind the chlorpromazine dose period, the authors did not elaborate on whether all analgesic medications the patients received were of the same drug and/or potency.  The validity and reliability of the “outcome measures” chosen in this study were not described. Using the number of analgesic medication dosages requested by patients in each group to determine post-surgery pain may not be an effective outcome assessment. This does not account for the individual pain tolerances of each subject or the possible hesitation of an individual to take pain narcotics secondary to a history of drug abuse. Perhaps this is why the authors chose to report the median dosage of pain medications as opposed to the mean, which could have influenced the data.  Lastly, different periods of the study (i.e. year 1 vs. year 2) featured different follow-up methods for outcome assessment regarding post-operative and phantom limb pain. There is less information from subjects during the first year of the study pertaining to their acute experiences following their amputation. Subjective pain reports from these patients are not available until 16 weeks post-operatively, whereas enrolees in the second year of the study were able to provide their subjective pain experiences weekly for the first four weeks post-surgery. This decreases the actual sample size that contributed to the data used to determine the effect of TENS during the acute post-amputation period. |
| **Interpretation of Results** |
| This study only minimally supports the use of active, low frequency TENS for the management of post-surgical wound or phantom limb pain. Low frequency TENS is may be a more indicated intervention for promoting wound healing secondary to its reported vasodilation effects. The use of low frequency TENS leads to better healing of the amputation site in the residual limb compared to placebo TENS treatment with or without the addition of chlorpromazine medication. Low frequency TENS can reduce the prevalence of phantom pain during a brief period (between 4 months to 1-year) following lower extremity amputation, but no appreciable treatment effects can be expected to be maintained after 1 year post-surgery. |

**(3) Description and appraisal of The clinical aspects of mirror therapy in rehabilitation: a systematic review of the literature by A. Rothgangel, S. Braun, A. Beurskens, R. Seitz, and D. Wade, 2011**

|  |
| --- |
| **Objective of the Systematic Review:** |
| This systematic review aims to evaluate and determine the clinical efficacy of mirror therapy (MT) in patients who have experienced stroke, phantom limb pain (PLP) following amputation, or complex regional pain syndrome (CRPS). |
| **Study Design** |
| * Systematic review and attempted meta-analysis of 10 randomized controlled trials, 7 case series, and 4 case studies. * Meta-analysis was unable to be completed due to the included studies having insufficient reports of various components, such as detailed treatment protocols and potential side effects of treatment. * Methods:   + Search strategy:     - Computer search of Cochrane Database of controlled trials, PubMed/MEDLINE, CINAHL, EMBASE, PsycINFO, PEDro, Rehabtrials, DIMDI, and Rehadat.4     - Keywords used: “imagery, mirror, feedback/psychological, rehabilitation, therapy, stroke, amputation, phantom limb, complex regional pain syndromes and reflex sympathetic dystrophy” (Rothgangel et al., 2011, pg. 2)     - Studies were excluded if the protocol only included two or less sessions of MT. Each study’s intervention had to feature a prolonged intervention exposure to MT, defined as more than two sessions by the review authors4   + Data collection and analysis:     - Two researchers performed independent literature searches. A third researcher settled any discrepancies in study selections if the first two researchers were not in agreement.   + Assessment of risk of bias and quality of evidence:     - The authors utilized the Amsterdam–Maastricht Consensus List (AMCL) for Quality Assessment, in addition to looking for detailed interventions, side effects, sample size a priori, and adequate statistics, to appraise the RCTs. The AMCL scores range from 0-11, with a higher score indicating a higher quality of evidence.     - Researches set an arbitrary threshold of 6/11 on the AMCL for studies to be deemed “sufficient methodological quality” (Rothgangel et al., 2011, pg. 4)     - A third researcher resolved any disagreements on AMCL scores for the included studies.   + Data extraction:     - Two researches used a standardized form to extract study data on the basis of “design, population, interventions, and outcomes.”4 |
| **Setting** |
| The authors did not specify the setting for the majority of studies included in this systematic review. The lone setting identified for studies that pertained to this clinical question was for Chan et al, 2007: military hospital. |
| **Participants** |
| * All studies featured participants over the age of 18 years who have experienced a stroke, PLP post-amputation, or CRPS. * The authors of this systematic review did not report any pooled participant demographics for any or all of the patient populations (sufferers of stroke, CPRS, or PLP). The instead reported the participant demographics for each of the 21 studies included. * Participants for the included studies that pertained to this clinical question:   + (Moseley et al., 2006):     - 51 total participants: 37 with CRPS diagnosis, 9 post-amputation (upper or lower extremity) with PLP, 5 with brachial plexus avulsion injuries (BPAI). Mean age: 41 years old Mean duration of symptoms: 14 months   No other patient demographics (i.e. gender, group baseline demographic homogeneity, etc.) reported4   * + (Chan et al., 2007):     - 18 total participants experiencing traumatic amputation of lower limb, military background No other patient demographics (i.e. gender, group baseline demographic homogeneity, etc.) reported4   + (Mercier and Sirigu, 2009):     - 8 total participants: 6 subjects with BPAI, 2 subjects post-amputation of upper extremities Mean age: 37 years old (19-54 years old) Mean duration of symptoms: 6.75 years (1-16 years) No other patient demographics (i.e. gender, group baseline demographic homogeneity, etc.) reported4   + (Maclachlan et al., 2004):     - 1 participant, post-through hip amputation Male, 32 years old, “chronic phase”, unspecified post-amputation duration4   + (Darnall, 2009):     - 1 participant, traumatic above knee amputation Male, 35 years old, “chronic phase”, 1 year post-amputation4 |
| **Intervention Investigated** |
| *Control* |
| * Control interventions for the included studies that pertained to this clinical question:   + (Moseley et al., 2006), RCT:     - Physical Therapy session at least 1x/week for 6 weeks     - Additional home exercise plan with similar load/intensity as experimental group     - Control group did not perform any exercises that closely mimicked MT   + (Chan et al., 2007), RCT:     - Control group I: performed same movements, same frequency/repetitions as experimental group, but did not look at reflection of virtual limb in the mirror     - Control group II: Mental practice- Subjects imagined voluntary movement of the amputated limb, eyes closed, same frequency/repetitions as experimental group’s intervention   + (Mercier and Sirigu, 2009), case series:     - No control intervention   + (Maclachlan et al., 2004), case study:     - No control intervention   + (Darnall, 2009), case study:     - No control intervention |
| *Experimental* |
| * Experimental interventions for the included studies that pertained to this clinical question:   + (Moseley et al., 2006), RCT:     - MT/Graded Motor Imagery (GMI) performed at home, daily, for 6 weeks     - 1 weekly PT consult in clinic to monitor home exercise plan with MT     - Subjects performed tasks divided into three two-week stages as follows:       * Stage 1: look at a mean of 107 pictures per day of various hand/foot (depending on subjects amputation site) positions to “recognize limb laterality”(preference for one side of the body vs. the other)4       * Stage 2: Mental practice: subjects imagined voluntary movement of amputated limb into mean of 40 different positions/postures as seen on provided photographs       * Stage 3: MT: mirror placed in sagittal plane so orientation of reflection of unaffected limb lined up as a ‘virtual limb’, Subjects viewed virtual limb and mimicked 20 positions viewed on provided HEP materials, each position performed for 10 repetitions on both involved and uninvolved limb. Subjects performed this 20 set, 10-repetition exercise once per hour throughout day.4   + (Chan et al., 2007), RCT:     - MT: mirror placed in sagittal plane as detailed in Moseley et al. study.     - Subjects attempted to perform unspecified movement of both the amputated and unaffected lower extremities while looking at a reflection of the unaffected limb oriented as a virtual limb.     - Frequency: 15 min/day, 4 weeks     - Location: military hospital     - Unspecified if concurrent interventions were being give to experimental and/or control groups4   + (Mercier and Sirigu, 2009), case series:     - Two 30-60 min sessions/week for 8 weeks. 10 different tasks were performed for 10 repetitions each as follows: gross arm/hand movements, fine motor tasks, functional tasks.     - Subjects performed the above tasks, clinicians recorded movements of unaffected limb, footage played back while being reflected/superimposed via mirror as virtual limb for subject to view.4   + (Maclachlan et al., 2004), case study:     - MT and mental practice: 2-3x/day, 10 different movements for 10 repetitions each for 3 weeks.     - Authors of this review did not specify the movements     - First week: subjects performed movements under direct supervision of PT daily, performed at home as HEP on weekends.     - Second week: PT supervision reduced to 3-4 days, HEP performed daily     - Third week: Same movements/frequency but without mirror or PT supervisions (mental practice)4   + (Darnall, 2009), case study:     - MT and mental practice: MT performed at home 3x/week, 20-30 min sessions, progressed to 30 min/day for 3 months after unspecified timeframe. Subject also attended five hour-long psychology sessions during initial three months of study.     - Self-directed motions performed at discretion of subject, no specific movements prescribed for HEP.     - Subject performed daily progressive muscle relaxations and breathing techniques, 25 minutes.     - Subject performed mental practice similar to Maclaclan et al. study while at work/when without his MT setup |
| **Outcome Measures** |
| * All included studies were assessed using the AMCL for Quality Assessment to appraise evidence quality * All included studies in this systematic review were, at a minimum, required to include at least one outcome measure for activity level in subjects with a stroke diagnosis, or a measure of pain for subjects with CRPS or PLP. * Outcome Measures for the included studies that pertained to this clinical question:   + (Moseley et al., 2006):     - Numeric Pain Scale, Numeric Rating Scale, McGill Pain Questionnaire, Visual Analogue Scale (VAS), Graded Motor Imagery     - Above outcome measures were recorded once before (baseline) and immediately after the study period, once after 6 weeks of therapy, and once at a 6-month follow-up     - No details, score range, administration, or location information was provided by the authors   + (Chan et al., 2007):     - VAS, number and duration of painful episodes     - Above outcome measures were recorded once before the study, once after each week of therapy, and once after the 4-week study period, no follow-up     - No details, score range, administration, or location information was provided by the authors   + (Mercier and Sirigu, 2009):     - “Short-term pain relief at every session; long-term pain relief over intervention period’ daily pain diary (background pain; paroxysms during day; number and duration)”. (Rothgangel et al., 2011, pg. 9)     - Above outcome measures were recorded as during a baseline period prior to beginning the study (this period varied between 1-5 weeks for test subjects), at the end of each week during study period, during 8-week study period, at immediately following study participation, and once at 4-week follow-up     - No details, score range, administration, or location information was provided by the authors   + (Maclachlan et al., 2004):     - Numeric Rating Scale (NRS) of motor control over phantom limb, 0-100%     - Above outcome measure was recorded once as baseline prior to intervention and once immediately following the three week intervention period, no follow-up     - No details, administration, or location information was provided by the authors   + (Darnall, 2009):     - Brief Pain Inventory, Numeric Rating Scale     - Above outcome measure was recorded once as baseline prior to intervention and once immediately following the three month intervention period, no follow-up     - No details, score range, administration, or location information was provided by the authors |
| **Main Findings** |
| * Main Findings for the included studies that pertained to this clinical question:   + (Moseley et al., 2006), RCT:     - AMCL score: 8/11 – high quality methodological rating     - Significant improvement of VAS in experimental compared to control group (24 millimetre (mm) pain reduction vs. 10.5 mm in control group). The authors of this review provided no context for what clinical significance or meaning was associated with each millimetre improvement on the VAS for pain rating.     - Significant improvement in NRS of experimental group compared to control group, “mean improvement of +2.2 points in (experimental group) vs. +0.6 points in control group after 6 weeks therapy and at follow-up” (Rothgangel et al., 2011, pg. 6)     - The authors again provided no context or evaluation of the clinical significance in the NRS outcome measure.   + (Chan et al., 2007), RCT:     - AMCL score: 2/11 – low quality methodological rating     - Significant improvement of VAS pain rating in experimental group compared to control group following MT, median improvement- 24 mm (range 13-54 mm)     - No data/outcomes provided for control group in the original study     - 100% of patients in intervention group reported decrease in frequency and duration of painful episodes compared to 17% in control group I and 33% in control group II.     - 33% of subjects in experimental group reported adverse effects from mirror therapy treatments. “Adverse effects” not defined by reviewing authors.   + (Mercier and Sirigu, 2009), case series:     - 5 of 8 patients showed “significant pain improvement” – 30% or more, range 13.8%-93.5% pain reduction.     - There were no correlations with long-term pain relief and the duration of patient’s symptoms4     - There were no correlations with type of phantom limb sensations and outcome measures4   + (Maclachlan et al., 2004), case study:     - Pain intensity: significant reduction, patient reported no longer suffering from any phantom limb pain4   + (Darnall, 2009), case study:     - Significant reduction in pain intensity for subject. Patient reported being pain-free.     - Patient reported that there was a strong relationship between how frequently he performed MT and how intense the pain was (more MT, less pain and vice versa)4 * The authors of this systematic review did not report detailed findings from each of the included studies, as seen above. No p values, confidence intervals, mean differences, or treatment effects were provided from the studies, if they were even available * MT appeared to have a moderate treatment effect |
| **Original Authors’ Conclusions** |
| * “Included studies did not provide sufficient information on the clinical protocols used.” (Rothgangel, 2011, pg. 12) * “Consequently, given the moderate quality of evidence for beneficial effects one cannot support widespread uncritical clinical use of this technique (MT) until there is stronger evidence of benefit and evidence that it outweighs any risk or harm.”4 (Rothgangel, 2011, pg. 11) |
| **Critical Appraisal** |
| **Validity** |
| AMSTAR: 1. A Priori design- yes; 2. Duplicate study selection and data extraction- yes; 3. Comprehensive literature search- yes; 4. Status of publication used as selection criterion- no; 5. List of included and Excluded studies provided- no; 6. Characteristics of included studies provided- yes; 7. Scientific quality of the included studies assessed and documented- yes; 8. Scientific quality of the included studies used appropriately in formulating conclusions- yes; 9. Methods used to combine the findings of studies appropriate- yes; 10. Likelihood of publication bias assessed- no; 11.Conflict of interest included- yes.  The researchers that authored this systematic review were unable to pool together many of the findings due to the heterogeneity and poor methodological quality of the studies that met their inclusion criteria. Meta-analyses were unable to be performed and the findings of each study were largely taken at face value on an individual basis for the three different patient populations treated with mirror therapy. The authors did not report many of the specific results from each study (i.e. p-values, confidence intervals, and/or effect sizes), instead choosing to generalize the overall result of the studies findings on the treatment effect of MT to improve pain and function.  The authors did not appraise the methodological quality of the ‘lower tiered evidence’ (case series and case studies) with a standardized tool the same way they did for the randomized controlled trials. Since these studies still met their inclusion criteria, the quality of these studies should have been objectively assessed and quantified in some standardized manner, as was done with the ‘higher tiered evidence.’  The authors did not validate or discuss any of the outcome measures that the included articles used to assess the effects that MT or the control interventions had on study subjects. This diminishes the ability of the ready to understand and apply the findings of this review to other patient presentations. |
| **Interpretation of Results** |
| * As it pertained to this clinical question, this systematic review did not provide many specific objective results that enable determination of the magnitude of the treatment effect for MT to manage PLP symptoms in patients. * This review’s included studies lacked sufficient methodological quality, such as vague intervention protocols, patient demographics, and validated outcome measures. This makes it hard to interpret and apply the findings. * Despite the poor quality of the studies, long-term MT intervention led to significant reductions in PLP for patients post-amputation. This could be a practical, efficient, cost-effective intervention to use for this patient population but more high quality research studies should be conducted to determine the treatment effect of MT for PLP in patients who have undergone an amputation. |

**IMPLICATIONS FOR PRACTICE and FUTURE RESEARCH**

|  |
| --- |
| **Current implementations to practice:**  Based on the literature search and subsequent findings for this clinical question, TENS and MT may have some minimal efficacy for reducing PLP in patients who have undergone an amputation. However, there was vast heterogeneity in the protocols and outcome measures used to validate these claims. In many of the studies, the investigators did not validate the outcome measures that were used to substantiate the claims. There was great variance in the length of time that the two interventions, TENS and MT, were prescribed with sometimes no follow-up to assess the long-term abilities to decrease PLP. For TENS, the only high-quality evidence identified tested low-frequency charges despite there being some support behind the efficacy of high-frequency TENS for reducing pain in this patient population.  Investigators also sparingly discussed the risks and adverse effects associated with receiving these interventions, especially for MT. Chan et al. reported that of the subjects receiving MT for PLP, 33% (2 of 6) reported adverse effects during treatment. Casale et al. reported in a retrospective study of subjects receiving MT for PLP pain, 88% (29 of 33) subjects “withdrew from MT treatment because of side effects such as grief, confusion or dizziness.”5 Several other studies also report findings of adverse effects with this condition, including increased pain and swelling.4 If using this intervention in the clinical setting, it is important for clinicians to be aware of these potential implications and discuss the importance with patients to monitor for these adverse symptoms so that alterations can be made to the treatment protocol.  Both interventions are cost effective and utilize low-budget, readily available equipment in most rehabilitation clinics/settings. Until better quality evidence and more specific protocols are defined, any therapist considering the use of these interventions to help treat PLP should consider these and similar research studies to make the best evidence-based decision for identifying the proper protocol to use for their individual patient’s clinical presentation.  **Current implementations to research:**  There are many different levels and types of amputations that patients can receive and, if a patient does develop PLP, it is often a unique presentation to that individual. All research available on TENS and MT for management of these conditions utilizes the two interventions in varying ways (to address acute pain, chronic PLP, wound healing, swelling reduction, etc.) with no standardized protocol.  TENS for use in this patient population has seemed to lost favour with many clinicians and researchers, with most of the high quality evidence on it published 20+ years ago. There are more recent studies looking into the treatment effects of MT, but quality and homogeneity of the intervention protocols is lacking. Rothgangel et al. adds that “there is a need of multicenter studies using a smaller number of standardized and clinically relevant outcome measures that investigate the effects of MT in routine clinical settings” (pg. 12)  In the future it would be beneficial for high-quality, controlled research would be done that directly compare the effects of multiple interventions that target PLP, including MT and TENS. This research should investigate any risks or adverse effects that arise from the various treatment options that are available to patients with PLP. From this, better clinical judgment can be made when establishing a plan of care and selecting the most appropriate, safe, and evidence-based interventions for this patient population. |

**REFERENCES**

|  |
| --- |
| 1. Brodie E. Analgesia through the looking-glass? A randomized controlled trial investigating the effect of viewing a 'virtual' limb upon phantom limb pain, sensation and movement. *European journal of pain.* 2007-05;11:428-436. 2. Brodie E. Increased motor control of a phantom leg in humans results from the visual feedback of a virtual leg. *Neuroscience letters.* 2003-05-01;341:167-169. 3. Finsen V. Transcutaneous electrical nerve stimulation after major amputation. *Journal of bone and joint surgery. British volume.* 1988-01;70:109-112. 4. Rothgangel A. The clinical aspects of mirror therapy in rehabilitation: a systematic review of the literature. *International journal of rehabilitation research.* 2011-03;34:1-13. 5. Casale R. Mirror therapy in the rehabilitation of lower-limb amputation: are there any contraindications? *Am J Phys Med Rehabil.* 2009;88:837–842. |