

Translating Laboratory Research of BIOCERAMIC Material, Application on Computer Mouse and Bracelet, to Ameliorate Computer Work-Related Musculoskeletal Disorders

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Abstract

We investigated the effects of a room temperature-emitting far infrared ray ceramic material (BIOCERAMIC) on computer work-related pain and coldness. Thirty-two computer users reporting complaints in upper extremities and shoulders were assigned to play 30-cycles of specially-designed computer game. Each subject was provided with a normal and BIOCERAMIC-made mouse for the game on two different days. When using BIOCERAMIC mouse for the computer game, the most significant improvements among the upper extremity complaints were for wrist, finger, forearm, and partially shoulder soreness. Greater differences in surface temperatures of mouse and hand in BIOCERAMIC group were seen. The most significant difference occurred when using both the BIOCERAMIC cover and bracelet were found to reduce pain sensations. It was concluded that pain intensity and disability were significantly reduced after using BIOCERAMIC mouse for the game. The effect remained during follow-up when using BIOCERAMIC mouse cover and bracelet during their usual computer work.

Keywords: Computer users; BIOCERAMIC; Pain; Room temperature-emitting far infrared ray; Upper extremities

Introduction

Work-related upper extremity and shoulder complaints are common in developed and industrialized countries. In Holland, about 8% employees were not able to work due to different work-related musculoskeletal complaints [1-3] and middle-aged females are more likely to suffer due to computer-related work than males [4,5]. Computer work-related musculoskeletal problems impose economic burdens on a country's productivity and influence a country's gross domestic product. Computer work-related musculoskeletal disorders broadly affect parts of the anatomy, including tendons, ligaments, nerves, muscles, circulation, and pain perception. Musculoskeletal disorders are related to a wide range of inflammatory and degenerative diseases which result in pain and functional impairment that affect the hands, fingers, wrists, forearms, and shoulders. It is necessary to develop method and determine the development and exacerbation of the computer work related suffering [6,7].

Frequently using a computer mouse can cause musculoskeletal discomfort and symptoms in the forearms and shoulders. During use of a computer mouse, muscle activity and loading increase at the extensor carpi ulnaris, extensor digitorum, pronator teres, and upper trapezius muscles, this can be recorded by surface electromyography [8-10].

A previous study found that the muscle metabolic and acid-base status during a wrist extension exercise in the forearm of individuals with work-related myalgia was related to a reduction in the local muscle blood flow in the trapezius and lower capillary-to-muscle fiber area ratios, which may have been a consequence of localized ischemia during prolonged muscular work loading [11]. Ischemia, particularly during contractile activity, is associated with increased levels of Reactive Oxygen Species (ROS), such as the superoxide and hydrogen peroxide (H₂O₂), which are responsible for destructive processes in muscle cells [12-15]. Ischemia also has important consequences for the cellular metabolic status, with a significantly worsened metabolic and acid-base

status when acidosis is predominate in individuals with work-related myalgia [16,17]. There are also some other mechanisms, including a reduction in local muscle blood flow and perfusion, reduction in the rate or contribution of aerobic ATP production, and increased ATP costs of force production. As a result, these are likely to have severe impacts on work tolerance [18,19].

The purpose of this study is whether there is benefit of a room temperature-emitting Far Infrared (FIR) ray ceramic material (BIOCERAMIC) to manufacture computer related apparatus, on work-related musculoskeletal complaints. Since our earlier studies and publications investigating BIOCERAMIC [20-27], mostly focused on basic medical science of cells and animal models, and we had showed that BIOCERAMIC promotes the microcirculation and has other effects by upregulating calcium-dependent nitric oxide and calmodulin in different cell lines, an antioxidant effect by increasing the hydrogen peroxide-scavenging ability of different cells, including murine macrophages (RAW264.7), murine calvaria-derived osteoblast-like cells (MC3T3-E1), NIH3T3 fibroblast cells, and murine myoblast cells (C2C12). In addition, another published data show that BIOCERAMIC irradiation had significant inhibition of PGE-2, COX-2 and iNOS, (inflammatory and pain inducing factors) elevations during

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lipopolysaccharide-induction in both murine macrophages and human chondrosarcoma cell line. We expect that BIOCERAMIC may have the potential, through apply on the computer related devices, that may exhibit effective health promote effect. In order to obtain clinical data base on our previous bio-molecular findings, in this study, we designed a series of experimental method to prove the BIOCERAMIC material on computer work-related related musculoskeletal disorders.

Methods and Materials

Subjects

Subjects for the study cohort were recruited by posting advertisements after the clinical trial was approved by an independent ethics committee of our university hospital with certification by the Institutional Review Board (IRB) approval no. 201007004 (Taipei Medical University--Joint IRB). Candidates mainly suffered from different complaints and locations of computer-work related musculoskeletal diseases which were verified by a questionnaire before our computer work tests took place. Thirty-two subjects (26 women and 6 men) were enrolled as subjects. There were no major diseases except for suffering from computer worked-related complaints of the upper extremities and shoulder. We required that all candidates fill in a short-form pain questionnaire, which mentioned possible locations of musculoskeletal discomfort during and after computer work. They also needed to sign a consent document and gave consent prior to allowing them to play the computer game.

BIOCERAMIC

BIOCERAMIC, the ceramic powder used in this study (obtained from the Department of Radiology, Taipei Medical University Hospital), was composed of micro-sized particles produced from several ingredients, mainly different elemental components (Figure 1). The average emissivity of the ceramic powder was 0.98 at wavelengths of 6–14 μm (determined by a CI SR5000 spectroradiometer), which represents an extremely high ratio of FIR intensity. Three types of BIOCERAMIC devices were used in this study, including computer mouse, silicon rubber mouse cover and silicon rubber bracelet, made of polypropylene pp plastic chips and silicon rubber with BIOCERAMIC powder (Plastics Industry Development Center, Taiwan and YY Rubber company, Foshan, PRC). The above BIOCERAMIC devices underwent specific physical-chemical tests at room temperature in the laboratory of Radiology Department of Taipei Medical University Hospital to guarantee their FIR ray-emitting function [20-27].

Pain assessment

Our questionnaire had 5 major categories that measured a bodily

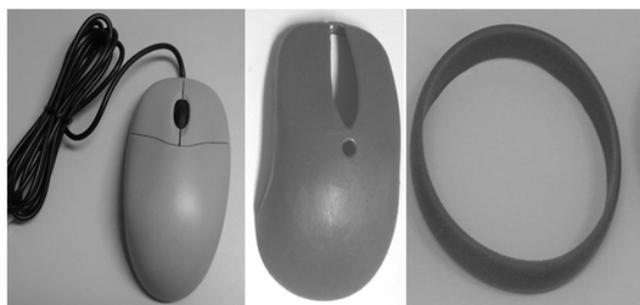


Figure 1: BIOCERAMIC computer mouse (left), BIOCERAMIC silicon rubber mouse cover (middle), and BIOCERAMIC silicon rubber bracelet (right)

pain score about a subject's attitude towards pain. Higher scores reflected more pain and lower scores less pain. Reduced pain was correlated with lower scores. The primary efficacy parameter was a pain severity rating, recorded by candidates in their daily diaries using a 10-point scale (from 0 indicating no pain to 10 indicating the worst possible pain).

Computer game assessment

Subjects were asked to play the computer game on 2 different days Software called 'MSE_Operation3RD' was used as a platform on which subjects could operate, and was make sure that the subjects did not have experiences on this software. Subjects were asked to play the computer game on 2 different days for this study in the same room. The room temperature is keep at lesser than 25 degree with air-conditioned ventilation. Initial check up of hands' temperatures were performed by thermography, in order to make sure that the hands' temperatures were not below the temperature of the room. All the operations were collected on the same mouse without and with BIOCERAMIC, so as to standardize the efficacy of the mouse operation. Besides, the subjects were requested to operate the mouse in their usual postures and their habitually using methods.

On the first day, a normal computer mouse was used for control data. On the second day, a special mouse with BIOCERAMIC material was used, and procedures were the same as on the first day. On each day, as the first step of the computer game operation, a cursor appeared in the upper then lower parts of the picture on the screen, and the subject was asked to press and hold down the left mouse button and drag the image to the trash in the middle of the screen (Figure 2). Then, another image appeared but in a different style, and the candidate again had to move the cursor to the object, press and hold the left mouse button, and drag the image to the trash in the middle of the screen. Eight times of the 'dragging' action were counted as a cycle. The same works were continued and repeated until counted to 15 cycles. After 15 cycles, the candidate was asked to record the soreness of different body parts of the upper extremity. Before the second round of 16~30 cycles, the surface temperatures of the candidate's hand and computer mouse he/she had been using were separately measured using IRISYS IRI 1011 thermal imager (InfraRed Integrated Systems, Northampton, UK).

The game was then continued until 30 cycles had been completed. At the end, the surface temperatures of both the candidate's hand and computer mouse were separately measured. Another part of the questionnaire was then provided (Figure 3). Finally, a BIOCERAMIC mouse cover and bracelet were given to the candidate, and we requested that they use both of them for usual computer work in their office or home. A final questionnaire of, pain score was then finished after this 7-day period had been completed.

Statistical analysis

Paired t-test was used to evaluate the significance of differences between groups (SPSS Inc., IBM, Chicago, IL, USA). A P-value < 0.05 was considered statistically significant.

Results

According to the questionnaire, the most complaints of computer work-related problems of the upper extremities were soreness of the wrist, hand, fingers, forearm, and shoulder.

In the item reflecting 'soreness of wrist' on the subjects, BIOCERAMIC group improved at '1-15cycle' (12.8%, $p = 0.0032$), '16-30 cycle' (15.62%, $p = 0.0013$) and 'after-test' (21.88%, $p = 0.0005$). In the

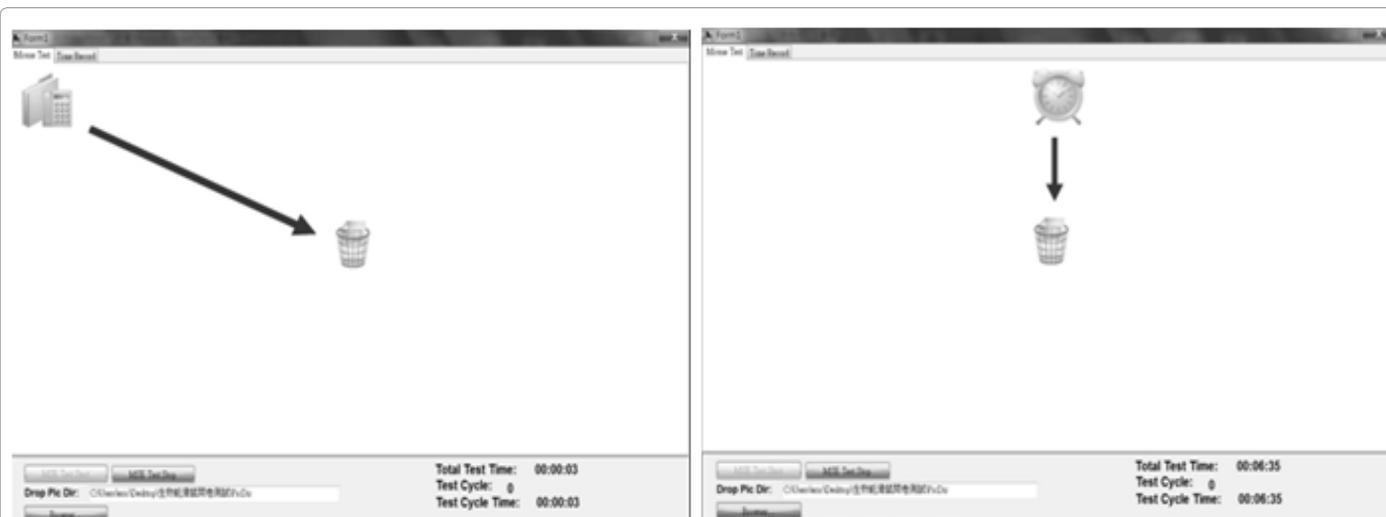


Figure 2: Computer game designed to have a subject repeat precise movements of the fingers, hands, elbows, forearms, and shoulders, to help highlight the weakness, coldness, and soreness of the upper extremities

(A) 請填寫您在第幾次測試時，開始感覺到手(手腕、手臂、手指頭)痠痛? Which cycles you initiate to fell soreness(wrist, forearm or finger)? _____ * ..

(B) .

1 第 1-15 次循環(遊戲) Cycles 1-15(Game) .

手腕痠痛感 wrist soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

肩頭痠痛感 shoulder soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

使用滑鼠的 手指頭痠痛感 soreness of the PC mouse using fingers (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

手臂(前臂、上臂) forearm soreness 有幾分酸痛感 (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

手部是否感覺冰冷 hand coldness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

2、第 15-30 次循環(遊戲) Cycles 15-30 (Game) .

手腕痠痛感 wrist soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

肩頭痠痛感 shoulder soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

使用滑鼠的 手指頭痠痛感 soreness of the PC mouse using fingers (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * | .

手臂(前臂、上臂) forearm soreness 有幾分酸痛感 (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

_____ * ..

手部是否感覺冰冷 hand coldness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

3、30 次循環(遊戲)後之整體感受 Sensation after 30 cycles .

1、請填寫現在您 手部有幾分冰冷感 Hand coldness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

2、請填寫現在您 手腕有幾分酸痛感 wrist soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

3、請填寫現在您 手臂(前臂、上臂)有幾分酸痛感 forearm soreness (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

4、請填寫現在您 肩頭有幾分酸痛感 shoulder soreness (10 分 → 最酸痛, 0 分 → 沒感覺)? _____ * ..

5、請填寫現在您 手指頭有幾分酸痛感 (使用滑鼠的那隻手) soreness of the PC mouse using fingers (10 分(score) → 最酸痛 mostly; 0 分(score) → 沒感覺 no complain)? _____ * ..

Figure 3: The questionnaire using for assessment of pain score in this study

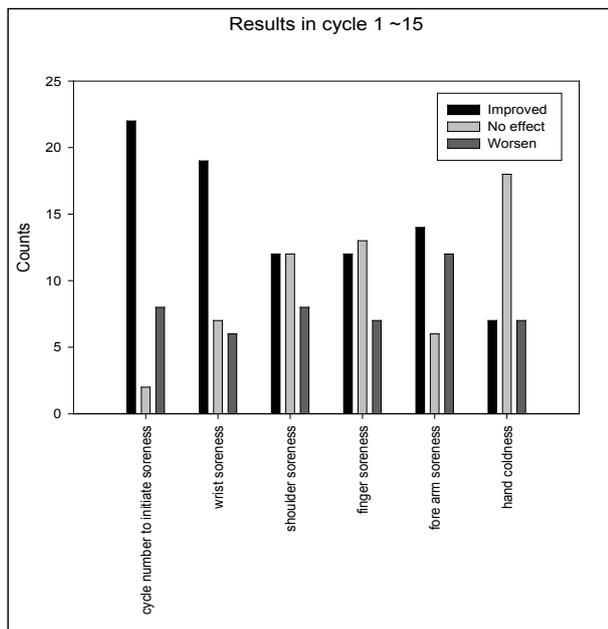


Figure 4a: Results of questionnaire for the 1-15 cycles, the overall improved cases were found more than the worsen cases in BIOCERAMIC group, the group was found tolerated more cycles of games to initiate feeling soreness. The number of cases improved on BIOCERAMIC group on soreness of wrist was the most significant. The improved cases of finger and forearm soreness were also out number than worsen cases

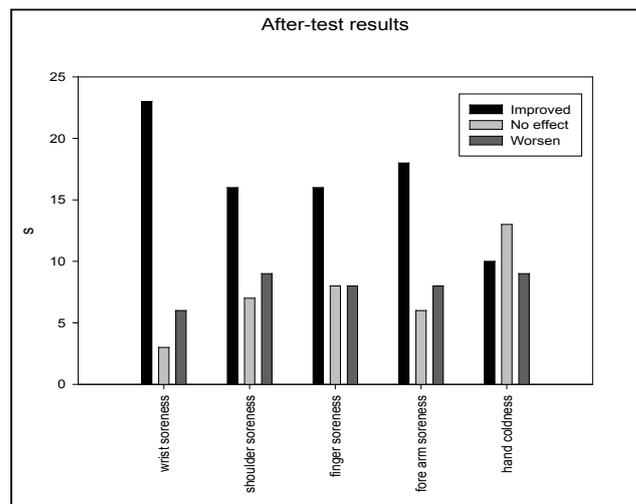


Figure 4c: Results of questionnaire for the 'after test', the overall improved cases were found more than the worsen cases in BIOCERAMIC group. The soreness of wrist and forearm were the most significantly improved. The number of cases improved in BIOCERAMIC group on soreness of shoulder and finger were also out number than worsen cases

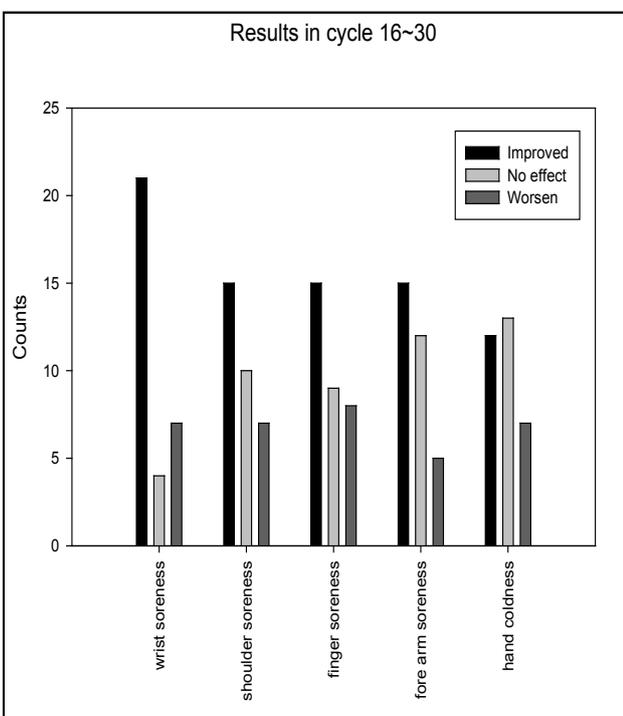


Figure 4b: Results of questionnaire for the 16-30 cycles, the overall improved cases were found more than the worsen cases in BIOCERAMIC group; the soreness of wrist was the most significantly improved. The number of cases improved in BIOCERAMIC group on soreness of wrist was the most significant. The improved cases of shoulder, finger, forearm and hand soreness were also out number than worsen cases

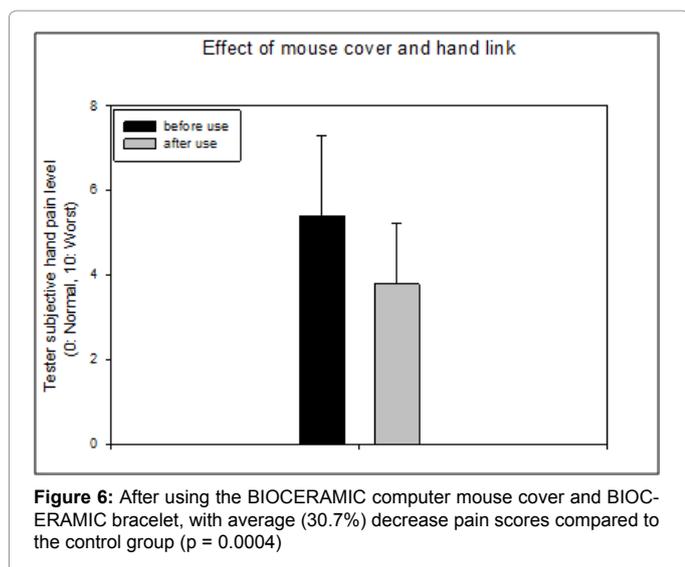
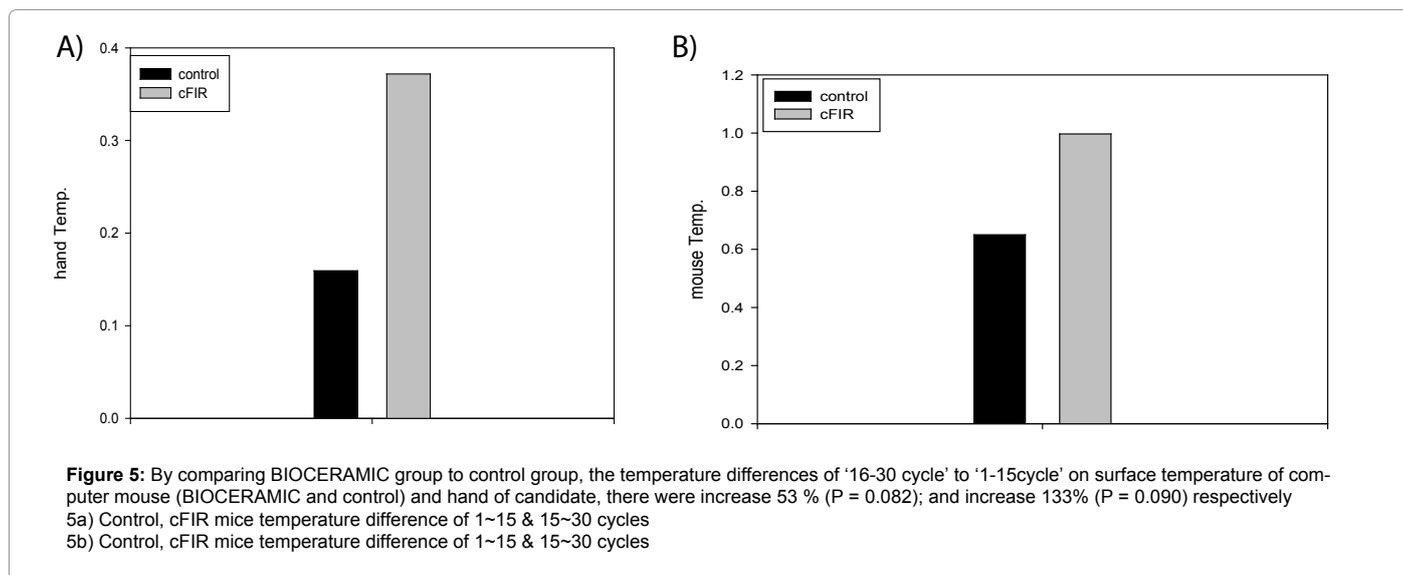
item reflecting 'soreness of shoulder' on the subjects, BIOCERAMIC group improved at '1-15cycle' (4.69%, $p = 0.1592$), '16-30 cycle' (8.13%, $p = 0.0550$) and 'after-test' (8.75 %, $p = 0.0601$). In the item reflecting 'soreness of finger' on the subjects, BIOCERAMIC group improved at '1-15cycle' (4.688%, $p = 0.1592$), '16-30 cycle' (7.81%, $p = 0.0625$) and 'after-test' (10.31%, $p = 0.0402$). In the item reflecting 'soreness of forearm' on the subjects, BIOCERAMIC group improved at '1-15cycle' (3.44%, $p = 0.2299$), '16-30 cycle' (9.38%, $p = 0.0261$) and 'after-test' (16.88%, $p = 0.0055$). In the item reflecting 'coldness of hand' on the subjects, BIOCERAMIC group improved at '1-15cycle' (4.69%, $p = 0.2205$), '16-30 cycle' (8.44%, $p = 0.0462$) and 'after-test' (3.44%, $p = 0.2726$). The above results are demonstrated in Figures 4a-c.

For differences in the surface temperatures of the computer mouse(BIOCERAMIC and control) and 'using hand' of subjects on the '16-30 cycle' to the '1-15cycle', both of the BIOCERAMIC groups (computer mouse and 'using hands;) showed temperature increases, although not reaching significant difference (Figure 5).

After that, a BIOCERAMIC mouse cover and BIOCERAMIC bracelet were given to each of the candidates, and we requested that they use both of them for usual computer work in their office or home. A final questionnaire was then finished after this 7-day period had been completed. According to the results, the BIOCERAMIC group had very significant improvement after the test using both the mouse cover and bracelet during their usual computer work (Figure 6).

Discussion

In the past, the usual management of work-related musculoskeletal problems of the upper extremity included worksite modifications, rest from inciting/aggravating movements, maintenance of central and regional body temperature, ergonomic modifications in work and non-work environments, wrist splinting, physical therapy, anti-inflammatory medication, acupuncture, cortisone injections, and surgical management [27]. However, there are few treatments to help computer work-related complaints of the upper extremity by solely physical effects of a material without invasive methods, chemical drug intake, or electricity supplied by a physical therapeutic



instrument reported in the past. This study investigated the efficacy of a BIOCERAMIC-made mouse, mouse cover, and bracelet that act as a supplement that has direct contact with the hands and wrist, for computer-work related discomfort.

BIOCERAMIC is high performance far infrared ray emitting material and is different from general materials with at least two unique characteristics. Firstly, high performance far infrared ray from BIOCERAMIC's irradiation capable to pass through usual non-metallic material such as cell culture disk and enhanced different intracellular effects [21-25,27,28]. Secondly, BIOCERAMIC emitting material irradiated water exhibited different physical, chemical and biological effects from usual water. Although the BIOCERAMIC-made products were not well designed with an ergonomic approach as to the shape and angle of the mouse while it is being used, the BIOCERAMIC material was proven to enhance microcirculation by upregulating calcium-dependent nitric oxide and calmodulin [20,21,25]. Its antioxidant effect, by increasing the hydrogen peroxide-scavenging ability in different cells, including murine calvaria-derived osteoblast-like cells (MC3T3-E1) [22-25] and murine myoblast cells (C2C12)

[25], was also reported. We also observed that under BIOCERAMIC influence, there were a significant decrease in metabolic acid accumulation and significantly prolonged periods of contractions in isolated frog's muscles [25]. Those data collected by bio-molecules of an experimental cell model and animal experimental model may be adequate to explain the results in this human trial, as microcirculation enhancement, upregulation of calcium-dependent nitric oxide, calmodulin, and antioxidant ability, as well as prevention of metabolic acidosis accumulation, was able to maintain proper skeletal activity or ameliorate chronic musculoskeletal diseases [28-30]. Our published results also found that the beneficial effect of BIOCERAMIC materials against inflammation, through the mechanisms of inhibitory effects on both PGE2 and COX-2, and potential inhibitory effect on iNOS expression. Since the biological effects of BIOCERAMIC occur through physical induction, BIOCERAMIC exhibits similar effects of NSAID and other pain relief remedies, to reduce drug dependency. Besides, by increase local temperature of operating hands could associate with increase microcirculation to against muscular weakness and soreness, especially to the wrist joint. According to our previous human trial by application of BIOCERAMIC necklace, was found successfully to reduce muscle stiffness of neck, which was assessed of severity of pain by using Visual Analogue Scale (VAS) and Pressure-Pain Threshold (PPT) [31]. To explain the results of these two human studies, future investigations on the effects of BIOCERAMIC on inflammatory pain or inflammatory arthritis should be more concentrated on the bio-molecular level.

Conclusions

Based on the results of the present study, for over half of our candidates (female predominant), pain intensity and disability of computer related musculoskeletal discomfort were likely to reduce after using BIOCERAMIC mouse to continuously and intensive play a special computer game. The effect remained at follow-up using a BIOCERAMIC mouse cover and bracelet during subjects' usual computer work. As far as we know, the current study is the first to explore possible beneficial effects of a BIOCERAMIC-made mouse, mouse cover, and bracelet, to ameliorate computer work-related musculoskeletal disorders. It is another example of translating laboratory developed BIOCERAMIC material into medical application.

Acknowledgments

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References

1. Bongers PM, Kremer AM, ter Laak J (2002) Are psychosocial factors, risk factors for symptoms and signs of the shoulder, elbow, or hand/wrist?: A review of the epidemiological literature. *Am J Ind Med* 41: 315-342.
2. Juul-Kristensen B, Kadefors R, Hansen K, Byström P, Sandsjö L, et al. (2006) Clinical signs and physical function in neck and upper extremities among elderly female computer users: the NEW study. *Eur J Appl Physiol* 96: 136-145.
3. Huisstede BM, Wijnhoven HA, Bierma-Zeinstra SM, Koes BW, Verhaar JA, et al. (2008) Prevalence and characteristics of complaints of the arm, neck, and/or shoulder (CANS) in the open population. *Clin J Pain* 24: 253-259.
4. Buckle PW, Devereux JJ (2002) The nature of work-related neck and upper limb musculoskeletal disorders. *Appl Ergon* 33: 207-217.
5. Ketola R, Toivonen R, Häkkinen M, Luukkonen R, Takala EP, et al. (2002) Effects of ergonomic intervention in work with video display units. *Scand J Work Environ Health* 28: 18-24.
6. Waersted M, Hanvold TN, Veiersted KB (2010) Computer work and musculoskeletal disorders of the neck and upper extremity: a systematic review. *BMC Musculoskelet Disord* 11: 79.
7. Eltayeb S, Staal JB, Kennes J, Lamberts PH, de Bie RA (2007) Prevalence of complaints of arm, neck and shoulder among computer office workers and psychometric evaluation of a risk factor questionnaire. *BMC Musculoskelet Disord* 8: 68.
8. Chen HM, Leung CT (2007) The effect on forearm and shoulder muscle activity in using different slanted computer mice. *Clin Biomech (Bristol, Avon)* 22: 518-523.
9. Samani A, Fernández-Carnero J, Arendt-Nielsen L, Madeleine P (2011) Interactive effects of acute experimental pain in trapezius and sore wrist extensor on the electromyography of the forearm muscles during computer work. *Appl Ergon* 42: 735-740.
10. Fagarasanu M, Kumar S, Narayan Y (2004) Measurement of angular wrist neutral zone and forearm muscle activity. *Clin Biomech (Bristol, Avon)* 19: 671-677.
11. Raymer GH, Green HJ, Ranney DA, Marsh GD, Thompson RT (2009) Muscle metabolism and acid-base status during exercise in forearm work-related myalgia measured with ³¹P-MRS. *J Appl Physiol* (1985) 106: 1198-1206.
12. Howard C, Ferrucci L, Sun K, Fried LP, Walston J, et al. (2007) Oxidative protein damage is associated with poor grip strength among older women living in the community. *J Appl Physiol* 103: 17-20.
13. Jakeman P, Maxwell S (1993) Effect of antioxidant vitamin supplementation on muscle function after eccentric exercise. *Eur J Appl Physiol Occup Physiol* 67: 426-430.
14. Manuel y Keenoy B, Moorkens G, Vertommen J, De Leeuw I (2001) Antioxidant status and lipoprotein peroxidation in chronic fatigue syndrome. *Life Sci* 68: 2037-2049.
15. Vecchiet J, Cipollone F, Falasca K, Mezzetti A, Pizzigallo E, et al. (2003) Relationship between musculoskeletal symptoms and blood markers of oxidative stress in patients with chronic fatigue syndrome. *Neurosci Lett* 335: 151-154.
16. Larsson SE, Cai H, Oberg PA (1993) Microcirculation in the upper trapezius muscle during varying levels of static contraction, fatigue and recovery in healthy women—a study using percutaneous laser-Doppler flowmetry and surface electromyography. *Eur J Appl Physiol Occup Physiol* 66: 483-488.
17. Oskarsson E, Gustafsson BE, Pettersson K (2007) Decreased intramuscular blood flow in patients with lateral epicondylitis. *Scand J Med Sci Sports* 17: 211-215.
18. Wakefield E, Holtermann A, Mork PJ (2011) The effect of delayed onset of muscle soreness on habitual trapezius activity. *Eur J Pain* 15: 577-583.
19. Lee TH, Huang SM (2006) Effects of wrist rest and forearm support on muscle activity. *Percept Mot Skills* 103: 873-878.
20. Leung TK, Lee CM, Lin MY, Ho YS, Chen CS, et al. (2009) Far infrared ray irradiation induces intracellular generation of nitric oxide in breast cancer cells. *J Med Biol Eng* 29: 15-18.
21. Leung TK, Lin YS, Chen YC, Shang HF, Lee YG, et al. (2009) Immunomodulatory effects of far infrared ray irradiation via increasing calmodulin and nitric oxide production in RAW 264.7 macrophages. *Biomed Eng Appl Basis* 21: 317-323.
22. Leung TK, Lin YS, Lee CM, Chen YC, Shang HF, et al. (2011) Direct and indirect effects of ceramic far infrared radiation on hydrogen peroxide-scavenging capacity and on murine macrophages under oxidative stress. *J Med Biol Eng* 31: 345-351.
23. Leung TK, Shang HF, Chen DC, Chen JY, Chang TM, et al. (2011) Effects of far infrared rays on hydrogen peroxide-scavenging capacity. *Biomed Eng Appl Basis* 23: 99-105.
24. Leung TK, Chen CH, Lai CH, Lee CM, Chen CC, et al. (2012) Bone and joint protection ability of ceramic material with biological effects. *Chin J Physiol* 55: 47-54.
25. Leung TK, Lee CM, Tsai SY, Chen YC, Chao JS (2011) A Pilot Study of Ceramic Powder Far-Infrared Ray Irradiation (cFIR) on Physiology: Observation of Cell Cultures and Amphibian Skeletal Muscle. *Chin J Physiol* 54: 247-254.
26. Leung TK, Yang JC, Lin YS (2012) The physical, chemical and biological effects by room temperature ceramic far-infrared ray emitting material irradiated water: a pilot study. *J Chin Chem Soc* 58: 1-6.
27. Leung TK, Liu YC, Chen CH, Fang HN, Chen KC, et al. (2013) In vitro cell study of the possible anti-inflammatory and pain relief mechanism of far-infrared ray emitting ceramic material (BIOCERAMIC). *J Med Biol Eng* 33: 179-184.
28. Akimoto T, Ribar TJ, Williams RS, Yan Z (2004) Skeletal muscle adaptation in response to voluntary running in Ca²⁺/calmodulin-dependent protein kinase IV-deficient mice. *Am J Physiol Cell Physiol* 287: C1311-1319.
29. Fox AJ, Murrell GA (2007) Nitric Oxide and Tendon Healing, Techniques. in. *Orthopaedics*. 22: 14-19.
30. Murrell GA (2007) Oxygen free radicals and tendon healing. *J Shoulder Elbow Surg* 16: S208-214.
31. Lai CH, Leung TK, Peng CW, Chang KH, Lai MJ, et al. (2013) Effects of Far-Infrared Irradiation on Myofascial Neck Pain: A Randomized, Double-Blind, Placebo-Controlled Pilot Study. *J Altern Complement Med*.