A Pilot Study to Determine the Effect of Different Dosage Regimens of High Energy Acoustic Shockwaves in Treating Diabetic Foot Ulcers

Poznan University of Medical Science

Professor Doctor Tomasz Banasiewicz (Poland)+ and Iulian Cioanta, Ph.D. (U.S.A.)++

+ Department and Clinic of General, Endocrinological and Gastroenterological Oncology, Poznan University of Medical Sciences, Poznan, Poland

++ Chief Science and Technology Officer, SANUWAVE Health Inc., Suwanee, Georgia, U.S.A.

Background and Aims:

The objective of this clinical study is to assess in diabetic foot ulcers (DFUs) patients the effects of three (3) different regimens of shockwave pulses delivered in up to ten (10) treatment sessions using the proprietary Extracorporeal Shockwave Technology (ESWT), known as Pulsed Acoustic Cellular Expression (PACE®) Technology, employed by the dermaPACE® System provided by SANUWAVE® Health Inc.

Methods:

Shockwave pulses per treatment session, together with energy setting, and shockwave frequency represent the DOSAGE for one PACE® treatment. The three different shockwave regimens are determined based on wound area plus adding 2 cm in each direction from the perimeter of the wound bed, area also known as periwound area. The total shockwave number per one treatment session is established based on the chosen shockwave number delivered per each centimeter square of the wound and periwound area, as follows:

- Group 1 – starts at 1000 shockwaves (1 cm^2 wound) and with increments of 100 shockwaves for 1 cm^2 increase in wound area.
- Group 2 – starts at 1250 shockwaves (1 cm^2 wound) and with increments of 150 shockwaves for 1 cm^2 increase in wound area.
- Group 3 – starts at 1500 shockwaves (1 cm^2 wound) and with increments of 200 shockwaves for 1 cm^2 increase in wound area.

Total duration of the study is 15 weeks with one (1) week of screening at the beginning of the study, a total of ten (10) treatment sessions (if needed) with a frequency of one treatment per week, and four (4) weeks of follow-up at the end of the study. The goal is to enroll a total of 60 patients, with 20 for each group. The energy setting used was E2, frequency of 4 shockwaves per minute (4 Hz) and the shockwave regimens from above.

All subjects received standard of care wound bed preparation and then dermaPACE ® System treatment. Subjects included were male or female 18 years and beyond, having Type I or Type II diabetes, who have at least 1 chronic ulcer for more than 30 days. Those subjects who presented with ABI ≤0.70, wound Wagner grade 3 or greater, pregnancy, with active infection, and/or Charcot Foot, were excluded.

Wound areas were measured using a mobile and tablet software App from Tissue Analytics, Inc., U.S.A., which is an automatic tool HIPAA compliant, registered and listed with the FDA.

This clinical study has enrolled to date twenty (20) DFU subjects with wounds ranging from 1 cm^2 to 16.9 cm^2 distributed evenly among the three dosage groups.

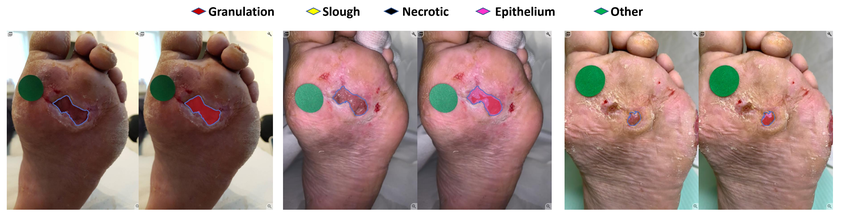
Results

All participant patients had wound pictures taken, laboratory tests, X-rays, bacterial genotyping material collected, blood tests, biofilm evaluation (using MolecuLight device), and quality of life assessment.

Out of 19 patients enrolled so far, 16 displayed wound area reduction and granulation within 2 to 4 treatments, 2 were too early to assess, and 1 had initial area reduction and then wound area increased. Wound area reduction was evident within the first two treatments. The significance of the PACE® treatment was well tolerated and patients were relatively compliant.

The study was finished so far by 10 patients and out of them 6 healed, 2 from Group 1 after 7 and 11 weeks, 3 from Group 2 after 11, 12, and 13 weeks, and 1 from Group 3 after 6 weeks. The remaining 4 patients that finished the study, 1 (Group 1) had a decrease in wound area of 89%, 1 (Group 2) had an increase of 43.5%, 1 (Group 2) had a decrease of 61%, and 1 (Group 3) shown a decrease of 69.6%. The remaining 9 patients enrolled in the study are continuing treatments and all are showing wound area reduction and granulation.

Below there is an example of patient that had 10 treatments with dermaPACE® System and went through 12 weeks of the study, which means that it has 11 weeks since the beginning of the dermaPACE ® System treatments (1 week was used for screening of the wound).



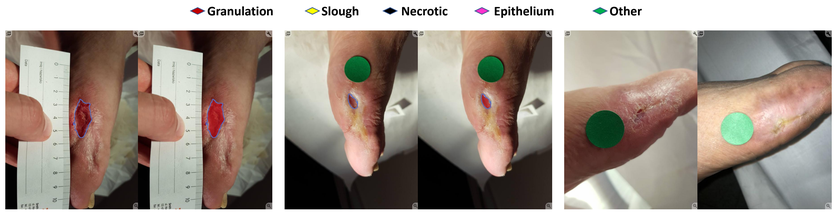
Visit 2
Wound area 2.41 cm^2

Visit 6
Wound area 1.93 cm^2

Visit 12
Wound area 0.47 cm^2

Area reduction is 80.5% and the remaining wound exhibits only granulation tissue, which is an indication of future healing.

The next example is a patient from Group 1 who had 10 treatments with dermaPACE® System and completely healed 12 weeks into the study, which means 11 weeks since the beginning of the dermaPACE ® System treatments.



Visit 2
Wound area 1.13 cm^2

Visit 6
Wound area 0.45 cm^2

Visits 12 and 13
Wound area 0.00 cm^2

Conclusions

For the FDA clearance study SANUWAVE® used only 500 shockwaves for wounds with area less than 16.9 cm^2, as the ones included in this new study. In the authors' opinion, the dermaPACE® System used at three (3) different enhanced dosages shown significant improvements in wound healing, as a non-invasive advanced modality that it is easy to administer, is well tolerated by patients, and does not show any adverse effects. Shockwaves produce revascularization with subsequent improved circulation and oxygenation, inflammation modulation, and trigger the body's natural healing process via different growth factors, which ultimately results in tissue regeneration and chronic wounds healing. The participating patients had a variety of other modalities utilized on their wounds and there had been no improvement. The dermaPACE® therapy was the only treatment that resolved their wounds. Results also indicate that PACE® technology for regenerating healthy tissue is suitable to increase the healing rate of chronic wounds and ulcers, in less of 14 weeks from the beginning of the treatment. The device was easy to apply by clinicians in a Community Clinical setting. During the PACE® treatment there was no treatment-related toxicity, infection, or deterioration of any kind.

References:

[1] Houtum, WHV, Lavery, LA, Armstrong, DG. Risk Factors For Above-Knee Amputations in Diabetes Mellitus. Southern Medical Journal. 1998. 35:528-531.
[2] Brodsky, JW. The Diabetic Foot. In: Coughlin, MJ, Mann RA, eds. Surgery of the Foot and Ankle. St. Louis: Mosby Inc. 1999: 895-969.
[3] McCallon, SK. Vacuum-assisted closure versus saline-moistened gauze in the healing of postoperative diabetic foot wounds. Ostomy Wound Manage. 2000. 46(8):28-34.
[4] Frykberg, RG. Diabetic Foot Ulcers: Pathogenesis and Management. Am. Fam. Physician 2002. 66:1655-62.
[5] Abetz, L, Sutton, M, Brady, L, McNulty, P, Gagnon, DD: The Diabetic Foot Ulcer Scale (DFS): a quality of life instrument for use in clinical trials. Practical Diabetes Int. 2002. 19(6):167-175.
[6] The Wound Management Manual, Editor: Bok, Y. Lee, McGraw-Hill, New York, 2005.
[7] Kuo, Y-R, Wu, W-S, Hsieh, Y-L, Wang, F-S, Wang, C-T, Chiang, Y-C, Wang, C-J: Extracorporeal Shock Wave Enhanced Extended Skin Flap Tissue Survival via Increase of Topical Blood Perfusion and Associated with Suppression of Tissue Pro-inflammation. J. of Surgical Research. 2007. 143(2):385-392.
[8] Kuo, Y-R, Wang, C-T, Wang, F-S, Yang, K, Chiang, Y-C, Wang, C-J: Extracorporeal Shock Wave Treatment Modulates Skin Fibroblast recruitment and Leukocytes Infiltration for enhancing Extended Skin-Flap Survival. Wound Repair and Regeneration. 2009. 17:80-87.
[9] Krokowicz, L, Cwykiel, J, Klimczak, A, , Mielniczuk, M, Siemionow, M: Pulsed Acoustic Cellular Treatment Induces Expression of Proangiogenic Factors and Chemokines in Muscle Flaps. The Journal of TRAUMA Injury, Infection, and Critical Care. 2010. 69(6):1448-1456.
[10] Krokowicz, L, Mielniczuk, M, Drews, M, Siemionow, M: Long-Term Follow Up of the Effects of Extracorporeal Shockwave Therapy (ESWT) on Microcirculation in a Denervated Muscle Flap. Polish Surgical Review. 2011. 83(6):591-605.
[11] Wang, C-J, Ko, J-Y, Kuo, Y-R, Yang, Y-J: Molecular Changes in Diabetic Foot Ulcers. Diabetes Research Clinical Practice. 2011. 94:105-110.
[12] Krokowicz, L, Klimczak, A, Cwykiel, J, Mielniczuk, M, Siemionow, M: Pulsed Acoustic Cellular Expression as a Protective Therapy Against I/R Injury in a Cremaster Muscle Flap Model. Microvascular Research. 2012. 83:213-222.

SANUWAVE®