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# Monopolar capacitive coupled Radiofrequency (mcRF) and ultrasound-guided Platelet Rich Plasma (PRP) give similar results in the treatment of enthesopathies: 18-month follow-up*

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## ABSTRACT

**Introduction: Emergent technologies, *i.e.*, monopolar capacitive coupled Radiofrequency (mcRF) and Platelet Rich Plasma (PRP) are now available to treat conditions characterized by a failed Wound Healing Response. Both mcRF and PRP positively influence the chemical/cellular inflammatory cascade to promote healing. mcRF application results in temperature elevation at the targeted structure up to 50˚C stimulating heat shock proteins, thus inciting the Wound Healing Response. Ultrasound-guided PRP injections results in an inflammatory/reparative reaction through cytokinin release. Methods: Sixty-eight patients who have failed previous conservative treatment for tendinopathies and chronic ligament conditions of the elbow, hip, knee and ankle/foot, were treated either with mcRF or PRP. Treatments were delivered directly by the investigator, and patients were followed prospectively for an average of 19.7 months (range 15 to 24 months). Results: Average age for the mcRF cohort was 53 years (range 17 to 88). Average age for the PRP group was 58 (range 19 to 90). The male to female ratio for both groups was 1/1. 33 of 42 patients treated with mcRF experienced marked improvement (78%), while in the PRP group 19 of 26 patients experienced marked improvement (73%) as self-assessed by study subjects. Discussion/Conclusion: Results of this study are in agreement with reports on the use of both technologies; however, this is the first time that a side-by-side comparison is established. PRP and mcRF represent a new approach to musculoskeletal pathology; both modalities aim at inducing a biological response and are considered at the frontier of regenerative therapeutics. The high safety profile suggests that these, non-invasive (mcRF) and minimally invasive (PRP), office-based alternatives for the management of musculoskeletal conditions are valuable tools and should be used in accordance with a clear understanding of the underlying pathology.**

**Keywords:** Heat-Shock; RelēF; Tendinosis; Wound Healing Response (WHR); Tendinopathy; Microtenotomy; Antinociceptive; Thermal Field

## 1. INTRODUCTION

Tendinopathies, chronic ligament failures and similar musculoskeletal conditions are painful pathologies whose symptoms can be debilitating and refractory to traditional treatment modalities. Emergent technologies, *i.e.*, monopolar capacitive coupled Radiofrequency (mcRF) (RelēF Technology, Alpha Orthopaedics, Inc. Oakland, CA) and Platelet Rich Plasma (PRP) are now available to treat conditions characterized by a failed Wound Healing Response.

Although the pain associated with tendinopathies and fasciopathies is generally self-limiting, symptoms often times persist [1]. Outcomes of current non-invasive treatment modalities are similar to a “wait and see” approach [2-4] indicating of a low level of effectiveness. The cost of these pathologies in terms of lost productivity and health care is significant with a clear association with work-related activities with an annual incidence of

*Level of Evidence: Level II-2: Evidence obtained from prospective side-by-side cohorts comparative studies.

59 per 10,000 workers [5]. England reviewed 108 consecutive patients with confirmed diagnosis of elbow tendinopathy [6]. These patients had failed to respond to a range of treatments over time and had persistent symptoms for an average of 4.6 years; most cases had lasted for two or more and up to 19 years. Of the patients who were operated on, 50% stopped working, 29% changed jobs, and 9% retired. Only 12% returned to their preoperative employment. In the non-operative patients, only 21% remained at their original job. Based on published data, it is apparent that these entities are frustrating issues for patients who in many cases end up living with the pain, changing their lifestyle, or accepting the need for a surgical intervention.

Tendinopathies [7,8] and chronic ligament failures [9] could result from a single traumatic situation, but more often than not, are the result of repeated small traumatic events. Microscopic examination of tissues shows dense populations of fibroblasts, vascular hyperplasia, disorganized collagen, and a typical absence of acute inflammatory cells [10]. These conditions are believed to be due to a failed WHR [11]. A successful long-term outcome requires an adequate wound healing process. This may explain why many non-operative treatments are not successful [2-4], and why surgical interventions are deemed successful [12,13]. The low level of effectiveness of non-operative treatments appears to be related to the non-inflammatory nature of this condition aggravated by the poor blood supply [14-16] as well as repeated use and failure to rest. Non-steroidal anti-inflammatory drugs (NSAIDs) have detrimental effects on human tendon fibroblasts [17]. Corticosteroid injections may have transient short term benefits, limited long term improvement [18], outcomes worse than placebo [2], and increased risk of tendon ruptures [19] as established by randomized clinical trials and systematic reviews [2,3, 19,20]. Physical therapy modalities are of no benefit [4]. Extracorporeal shock wave therapy has not been successful [21-24].

Minimally invasive alternatives such as the injection of water and botulinum toxin [25-27] have had some success. Similar outcomes have been reported without injecting any substance by needle tenotomy [28].

Non-invasive mcRF, working above 6 Mhz, has the ability to generate deep penetrating electric and thermal fields, resulting in supra-physiological temperatures within tendons and ligaments in the form of a heat-shock [29,30]. The collagen matrix in diseased heat-shocked tissues are partially denatured without damage to adjacent structures [30], and a WHR induced [31-33]. Heat-shock applied at the injured site will renew and accelerate the overall healing process [34]. Three to five days following treatment, immature macrophages are present. Between 3 and 14 days post-treatment, alkaline phosphatase-positive mast cells become active. Blood vessel increase beginning at 7 days post-treatment, fibroplasia begins at 7 days, becoming more pronounced 21 days following treatment. By 14 or 21 days following mcRF treatment, collagen compaction and new collagen appears [31].

Platelet Rich Plasma works by activating platelets granules, which results in an inflammatory/reparative reaction through release of growth factors, chemokines and cytokines that regulate biological responses critical for effective wound healing. Platelet factor 4 (PF-4), vascular endothelial growth factor (VEGF), transforming growth factor beta (TGF-$\beta$), epidermal growth factor (EGF), and fibroblast growth factor (FGF) are some examples of proteins released by platelets to control the migration of cells, stimulate the formation of new blood vessels (angiogenesis), cell growth, cell differentiation and deposition of new tissue [35].

Both mcRF [31] and PRP [36] positively influence the chemical/cellular inflammatory cascade to promote healing. mcRF accomplishes this through the release of heat shock proteins and PRP through the release of cytokines [37].

Due to the mechanism of action, office-based minimally invasive treatment (PRP) and non-invasive treatment (mcRF) should offer more predictable clinical outcomes than current non-invasive alternatives [38].

## 2. METHODS

The objective of the present study was to establish a prospective side-by-side comparison of these new treatment modalities when utilized for the treatment of Enthesopathies. Study inclusion criteria included failure to respond to traditional conservative treatment such as cortisone injections and physical therapy and willingness to refrain from using NSAIDs and comply with study follow-up visits. Treatment options were presented as equal and patients were allowed to self-selected their-group. Group selection criterion by patients was mainly based on preconceived notions of PRP (press references to PRP) vs. preference for treatments that include no needles. In addition, the post-treatment morbidity associated with PRP was a factor in the decision making process.

From the sixty-eight patients enrolled 42 elected mcRF and 26 ultrasound-guided PRP preferring mcRF in a proportion of 1.6 to 1. All treatments were delivered directly by the investigator and patients were followed prospectively for an average of 19.7 months (range 15 to 24 months).

Statistical analysis involved counts and percentages. Study subjects that failed to return were handled under the basis of intent to treat (ITT). Patient satisfaction was established with a Likert scale and results incorporated in overall success analysis.

The treatment protocol for mcRF has been published elsewhere [30,39]. The area to be treated was identified by ultrasound and the most tender point to the medical examination was defined as the center or hub for the delivery of radiofrequency pulses. Depending on anatomical location, a 2 × 3 or 3 × 3 removable ink grid was applied to the skin (**Figure 1**). Rapid and precise pulses of energy were delivered covering the area in a staggered fashion three times. Ten additional pulses were finally delivered directly to the point of maximum tenderness (total of 100 pulses). No local anesthetic or particular preparation for the treatment was used.

The PRP was prepared by drawing 20 cc's of whole blood from the patient. Utilizing a dedicated centrifuge (Harvest Technologies, Plymouth, MA) platelets were separated and concentrated in plasma so that platelet count was at least four times or greater above baseline (**Figure 2**). The 20 cc's of whole blood yield about 2 - 3 cc's of Platelet Rich Plasma. Injection of the PRP was accomplished under ultrasound guidance to ensure exact delivery of the concentrate to the targeted structure (**Figure 3**).

## 3. RESULTS

Average age for the mcRF cohort was 53 years (range 17 to 88). Average age for the PRP group was 58 (range 19 to 90). Male to female ratio for both groups was 1/1. Based on demographics and treatments received prior to study enrollment it was considered that the groups were comparable. 33 of 42 patients treated with mcRF experienced marked improvement (78%) **Table 1**, while in the PRP group 19 of 26 patients experienced marked improvement (73%) **Table 2**.

## 4. DISCUSSION

In the current health-care environment, patients suffering from enthesopathies reach physicians' offices only after they have endure a period of "wait and see", self-medication with NSAIDs, and changes in occupational or recreational activities without success. Patients seek care when they are unable or unwilling to accept the pain and/or reduced function associated with their condition [1]. Until now these individuals had been offered a set of poor choices, either non-invasive alternatives that for the most part have been ineffective, or invasive options which for the most part are considered effective. These new treatment alternatives, mcRF and PRP, allow physicians to offer non-invasive or minimally invasive effective options that are safe. In fact, no adverse events were found on either cohort during the follow-up period.

In the present study, patients treated with mcRF ob-

**Figure 1.** Delivery of mcRF.

**Figure 2.** Preparation of the PRP concentrate.

**Figure 3.** Ultrasound determination of the area to be injected.

**Table 1.** Outcomes of mcRF cohort.

| Diagnosis | *N* = | Success | Failure |
|---|---|---|---|
| Elbow tendinosis lateral | 8 | 6 | 2 |
| Elbow tendinosis medial | 2 | 1 | 1 |
| Functional ankle instability | 19 | 16 | 3 |
| Achilles tendinopathy | 6 | 4 | 2 |
| Plantar fasciopathy | 7 | 6 | 1 |
| **Total** | 42 | 33 | 9 |
| Percentage | 100 | **78%** | **22%** |

 

**Table 2.** Outcomes PRP cohort.

| Diagnosis | *N* = | Success | Failure |
|---|---|---|---|
| Elbow tendinosis lateral | 7 | 7 | 0 |
| Rotator cuff tendinopathy | 12 | 8 | 4 |
| Gluteus medius/ minimustendinopathy | 3 | 2 | 1 |
| Quadriceps tendinopathy | 3 | 2 | 1 |
| Patellar tendinopathy | 1 | 0 | 1 |
| **Total** | 26 | 19 | 7 |
| Percentage | 100 | **73%** | **27%** |

tained a level of success that is similar to those obtained by other authors [37,39] and by this author on a different indication [40]. The level of success of PRP is similar or better than published [36,38,41-43]. For both technologies the correct diagnosis and exact location of the area of tendinosis or fasciosis is essential to their success. In PRP, proper preparation and precise injection in the area of tendinosis or fasciosis is mandatory. Unlike other PRP published studies, all patients in the PRP cohort where injected under ultrasound guidance.

As discussed there are many similitudes in these two alternatives; however they differ in other aspects. On the one hand, mcRF generates rapid and precise electric and thermal fields inducing supra-physiological temperatures in the form of a heat-shock (electrocoagulation) [39]. Physical benefits above the induction of the Wound Healing Response may include the denaturation of damaged collagen fibers [44-49] and the elimination of nociceptive fibers [48]. Nociceptor axons are lightly myelinated or unmyelinated. RF generated non-ablative thermal fields have a selective effect on small unmyelinated nerve fibers [50]. Motor axons are myelinated and are not as susceptible to electric fields since myelin is dielectric (electrically insulating) [31,49,51-53]. Recent research has also shown that heat-shock stimulates Myogenic Precursor Cells (MPCs), protein synthesis and stimulates an over-expression of HSPs [34,35].

On the other hand, PRP is indicated for the treatment of some early forms of osteoarthritis for which mcRF offers no benefit, and the treatment of deep structures, which cannot be reached with the commercial probes currently available for mcRF.

Overall patient satisfaction with mcRF tends to be higher than those of patients treated with PRP. This may be due to the pain during the initial weeks post-treatment; nonetheless, long-term success is comparable.

Strengths of this study include its prospective nature, sample size, and the prospective side-by-side comparison of like treatment modalities. Weaknesses of the study include lack of formal randomization and its single-center nature.

## 5. CONCLUSION

Results of this study are in agreement with published data on the use of both technologies; however, this is the first time that a prospective side-by-side comparison is established. PRP and mcRF represent a new approach to musculoskeletal pathology; both modalities aim at inducing a biological response and are considered at the frontier of regenerative therapeutics. The risk/benefit ratio found suggests that these non-invasive or minimally invasive, office-based alternatives for the management of musculoskeletal conditions are valuable tools and should be used based on a clear understanding of the underlying pathology.

## REFERENCES


[1] Hudak, P.L., Cole, D.C. and Haines, A.T. (1996) Understanding prognosis to improve rehabilitation: The example of lateral elbow pain. *Archives of Physical Medicine and Rehabilitation*, **77**, 586-593. doi:10.1016/S0003-9993(96)90300-7

[2] Bisset, L., Smidt, N., Van der Windt, D.A., *et al.* (2007) Conservative treatments for tennis elbow do subgroups of patients respond differently? *Rheumatology*, **46**, 1601-1605.

[3] Bjordal, J.M., Lopes-Martins, R., Joensen, J., *et al.* (2008) A systematic review with procedural assessments and metaanalysis of low level laser therapy in lateral elbow tendinopathy (tennis elbow). *BMC Musculoskelet Disord*, **9**, 75.

[4] Smidt, N., Assendelft, W.J., Arola, H., *et al.* (2003) Effectiveness of physiotherapy for lateral epicondylitis: A systematic review. *Annals of Medicine*, **35**, 51-62. doi:10.1080/07853890310004138

[5] Kivi, P. (1983) The etiology and conservative treatment of humeral epicondylitis. *Scandinavian Journal of Rehabilitation Medicine*, **15**, 37-41.

[6] Kay, N.R. (2003) Litigants' epicondylitis. *Journal of Hand Surgery*, **28**, 460-464. doi:10.1016/S0266-7681(03)00162-1

[7] Faro, F. and Wolf, J.M. (2007) Lateral epicondylitis: Review and current concepts. *Journal of Hand Surgery*, **32**, 1271-1279. doi:10.1016/j.jhsa.2007.07.019

[8] Nirschl, R.P. and Pettrone, F.A. (1979) Tennis elbow. The surgical treatment of lateral epicondylitis. *The Journal of Bone & Joint Surgery*, **61**, 832-839.

[9] Weil, L.J.R., Glover, J.P. and Weil, L.S.S.R. (2008) A new minimally invasive technique for treating plantar fasciosis using bipolar radiofrequency: A prospective analysis. *Foot & Ankle Specialist*, **1**, 13-18.

[10] Nirschl, R.P. (1995) Tennis elbow tendinosis: Pathoanatomy, nonsurgical and surgical management. In: *Repetitive Motion Disorders of the Upper Extremity*. American Academy of Orthopaedic Surgeons, Rosemont.

[11] Kraushaar, B.S. and Nirschl, R.P. (1999) Tendinosis of the elbow (tennis elbow). Clinical features and findings


 

of histological, immunohistochemical, and electron microscopy studies. *The Journal of Bone & Joint Surgery*, **81**, 259-278.

[12] Dunn, J.H., Kim, J.J., Davis, L. and Nirschl, R.P. (2008) Ten- to 14-year follow-up of the Nirschl surgical technique for lateral epicondylitis. *The American Journal of Sports Medicine*, **36**, 261-266. doi:10.1177/0363546507308932

[13] Meknas, K., Odden-Miland, A., Mercer, J.B., Castillejo, M. and Johansen, O. (2008) Radiofrequency microtenotomy: A promising method for treatment of recalcitrant lateral epicondylitis. *The American Journal of Sports Medicine*, **36**, 1960-1965. doi:10.1177/0363546508318045

[14] Almekinders, L.C. and Temple, J.D. (1998) Etiology, diagnosis, and treatment of tendonitis: An analysis of the literature. *Medicine & Science in Sports & Exercise*, **30**, 1183-1190. doi:10.1097/00005768-199808000-00001

[15] Schmidt-Rohlfing, B., Graf, J., Schneider, U. and Niethard, F.U. (1992) The blood supply of the Achilles tendon. *International Orthopaedics*, **16**, 29-31. doi:10.1007/BF00182980

[16] Yepes, H., Tang, M., Morris, S.F. and Stanish, W.D. (2008) Relationship between hypovascular zones and patterns of ruptures of the quadriceps tendon. *The Journal of Bone & Joint Surgery*, **90**, 2135-2141. doi:10.2106/JBJS.G.01200

[17] Almekinders, L.C., Baynes, A.J. and Bracey, L.W. (1995) An *in vitro* investigation into the effects of repetitive motion and nonsteroidal antiinflammatory medication on human tendon fibroblasts. *The American Journal of Sports Medicine*, **23**, 119-123. doi:10.1177/036354659502300120

[18] Smidt, N., Assendelft, W.J., van der Windt, D.A., Hay, E.M., Buchbinder, R. and Bouter, L.M. (2002) Corticosteroid injections for lateral epicondylitis: A systematic review. *Pain*, **96**, 23-40. doi:10.1016/S0304-3959(01)00388-8

[19] Fisher, P. (2004) Role of steroids in tendon rupture or disintegration known for decades. *Archives of Internal Medicine*, **164**, 678. doi:10.1001/archinte.164.6.678-a

[20] Newnham, D.M., Douglas, J.G., Legge, J.S. and Friend, J.A. (1991) Achilles tendon rupture: An underrated complication of corticosteroid treatment. *Thorax*, **46**, 853-854. doi:10.1136/thx.46.11.853

[21] Buchbinder, R., Green, S., White, M., Barnsley, L., Smidt, N. and Assendelft, W.J. (2002) Shock wave therapy for lateral elbow pain. *Cochrane Database of Systematic Reviews*, **1**, CD003524.

[22] Buchbinder, R., Green, S.E., Youd, J.M., Assendelft, W.J., Barnsley, L. and Smidt, N. (2005) Shock wave therapy for lateral elbow pain. *Cochrane Database of Systematic Reviews*, **4**, CD003524.

[23] Buchbinder, R., Green, S.E., Youd, J.M., Assendelft, W.J., Barnsley, L. and Smidt, N. (2006) Systematic review of the efficacy and safety of shock wave therapy for lateral elbow pain. *The Journal of Rheumatology*, **33**, 1351-1363.

[24] Staples, M.P., Forbes, A., Ptasznik, R., Gordon, J. and Buchbinder, R. (2008) A randomized controlled trial of extracorporeal shock wave therapy for lateral epicondylitis (tennis elbow). *The Journal of Rheumatology*, **35**, 2038-2046.

[25] Keizer, S.B., Rutten, H.P., Pilot, P., Morre, H.H., van Os, J.J. and Verburg, A.D. (2002) Botulinum toxin injection versus surgical treatment for tennis elbow: A randomized pilot study. *Clinical Orthopaedics and Related Research*, **401**, 125-131. doi:10.1097/00003086-200208000-00015

[26] Morre, H.H., Keizer, S.B. and van Os, J.J. (1997) Treatment of chronic tennis elbow with botulinum toxin. *Lancet*, **349**, 1746. doi:10.1016/S0140-6736(05)62958-3

[27] Placzek, R., Drescher, W., Deuretzbacher, G., Hempfing, A. and Meiss, A.L. (2007) Treatment of chronic radial epicondylitis with botulinum toxin A. A double-blind, placebo-controlled, randomized multicenter study. *The Journal of Bone & Joint Surgery*, **89**, 255-260. doi:10.2106/JBJS.F.00401

[28] McShane, J.M., Nazarian, L.N. and Harwood, M.I. (2006) Sonographically guided percutaneous needle tenotomy for treatment of common extensor tendinosis in the elbow. *Journal of Ultrasound in Medicine*, **25**, 1281-1289.

[29] Whipple, T. and Steinmann, S. (2012) Mechanism of action of non-invasive monopolar radiofrequency: Technology review. *Open Journal of Orthopedics*, **3**, 23-28.

[30] Whipple, T. and Villegas, D. (2010) Thermal and electric energy fields by noninvasive monopolar capacitive-coupled radiofrequency: Temperatures achieved and histological outcomes in tendons and ligaments. *PM&R*, **2**, 599-606.

[31] England, L., Egbert, B. and Pope, K. (2005) Wound healing in an animal model following thermage treatment. *Wound Repair and Regeneration*, **13**, A28-A48. doi:10.1111/j.1067-1927.2005.130216k.x

[32] England, L.J., Egbert, B.M. and Pope, K. (2005) Dermal wound healing in an animal model following monopolar radiofrequency treatment. *Wound Healing Society Meeting*, Chicago.

[33] Whiiple, T. and Villegas, D. (2011) Bioactive radiofrequency effects on ligament and tendon injuries. In: Mahmut Nedim Doral, M., Reha, N., Tandogan, M., Gideon Mann, M. and Rene Verdonk, M., Eds., *Sports Injuries—Prevention*, *Diagnosis*, *Treatment and Rehabilitation*. 1st Edition, Springer-Verlag, Berlin, 1193-1200.

[34] Hayashi, A. (2008) Getting athletes back in the game: A global view. *AAOS Now*, **2**, 1-6.

[35] Werner, S. and Grose, R. (2003) Regulation of wound healing by growth factors and cytokines. *Physiological Reviews*, **83**, 835-870.

[36] Mishra, A. and Pavelko, T. (2006) Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *The American Journal of Sports Medicine*, **34**, 1774-1778. doi:10.1177/0363546506288850

[37] Weber, T. and Kabelka, B. (2012) Non-invasive monopolar capacitive-coupled radiofrequency (mcRF) for the treatment of elbow lateral tendinopathies: 1-year follow-up. *PM&R*, **4**, 176-181. doi:10.1016/j.pmrj.2011.11.003

[38] Foster, T.E., Puskas, B.L., Mandelbaum, B.R., Gerhardt, M.B. and Rodeo, S.A. (2009) Platelet-rich plasma: From basic science to clinical applications. *American Journal*

 

*of Sports Medicine*, **37**, 2259-2272. doi:10.1177/0363546509349921

[39] Whipple, T.L. (2009) From mini-invasive to non-invasive treatment using monopolar radiofrequency: The next orthopaedic frontier. *Orthopedic Clinics of North America*, **40**, 531-535. doi:10.1016/j.ocl.2009.06.006

[40] Cronkey, J. and LaPorta, G. (2012) Rating systems for evaluation of functional ankle instability: Prospective evaluation in a cohort of patients treated with mcRF. *Foot and Ankle Specialist*, **5**, 293-299.

[41] de Vos, R.J., Weir, A., van Schie, H.T., *et al*. (2010) Platelet-rich plasma injection for chronic Achilles tendinopathy: A randomized controlled trial. *Journal of the American Medical Association*, **303**, 144-149.

[42] Hall, M.P., Band, P.A., Meislin, R.J., Jazrawi, L.M. and Cardone, D.A. (2009) Platelet-rich plasma: Current concepts and application in sports medicine. *Journal of the American Academy of Orthopaedic Surgeons*, **17**, 602-608.

[43] Hildebrand, K.A., Woo, S.L., Smith, D.W., *et al*. (1998) The effects of platelet-derived growth factor-BB on healing of the rabbit medial collateral ligament. An *in vivo* study. *The American Journal of Sports Medicine*, **26**, 549-554.

[44] Allain, J.C., Le Lous, M., Bazin, S., Bailey, A.J. and Delaunay, A. (1978) Isometric tension developed during heating of collagenous tissues. Relationships with collagen cross-linking. *Biochimica et Biophysica Acta (BBA)-Protein Structure*, **533**, 147-155. doi:10.1016/0005-2795(78)90558-5

[45] Allain, J.C., Le Lous, M., Cohen, S., Bazin, S. and Maroteaux, P. (1980) Isometric tensions developed during the hydrothermal swelling of rat skin. *Connective Tissue Research*, **7**, 127-133. doi:10.3109/03008208009152104

[46] Arnoczky, S.P. and Aksan, A. (2000) Thermal modification of connective tissues: Basic science considerations and clinical implications. *Journal of the American Academy of Orthopaedic Surgeons*, **8**, 305-313.

[47] Ochiai, N., Tasto, J.P., Ohtori, S., Takahashi, N., Moriya, H. and Amiel, D. (2007) Nerve regeneration after radiofrequency application. *The American Journal of Sports Medicine*, **35**, 1940-1944. doi:10.1177/0363546507304175

[48] Takahashi, N., Tasto, J.P., Ritter, M., *et al*. (2007) Pain relief through an antinociceptive effect after radiofrequency application. *The American Journal of Sports Medicine*, **35**, 805-810. doi:10.1177/0363546506297085

[49] Wright, N.T. and Humphrey, J.D. (2002) Denaturation of collagen via heating: An irreversible rate process. *Annual Review of Biomedical Engineering*, **4**, 109-128. doi:10.1146/annurev.bioeng.4.101001.131546

[50] Letcher, F.S. and Goldring, S. (1968) The effect of radiofrequency current and heat on peripheral nerve action potential in the cat. *Journal of Neurosurgery*, **29**, 42-47. doi:10.3171/jns.1968.29.1.0042

[51] Grellner, W., Georg, T. and Wilske, J. (2000) Quantitative analysis of proinflammatory cytokines (IL-1beta, IL-6, TNF-alpha) in human skin wounds. *Forensic Science International*, **113**, 251-264. doi:10.1016/S0379-0738(00)00218-8

[52] Grose, R., Werner, S., Kessler, D., *et al*. (2002) A role for endogenous glucocorticoids in wound repair. *EMBO Reports*, **3**, 575-582. doi:10.1093/embo-reports/kvf119

[53] Hubner, G., Brauchle, M., Smola, H., Madlener, M., Fassler, R. and Werner, S. (1996) Differential regulation of pro-inflammatory cytokines during wound healing in normal and glucocorticoid-treated mice. *Cytokine*, **8**, 548-556. doi:10.1006/cyto.1996.0074

 