Ultrasound in Med. & Biol., Vol. ■, No. ■, pp. 1–11, 2015

0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2015.07.028

● *Original Contribution*

EXTRACORPOREAL SHOCK WAVE THERAPY: AN EMERGING TREATMENT MODALITY FOR RETRACTING SCARS OF THE HANDS

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(*Received* 22 *January* 2015; *revised* 22 *July* 2015; *in final form* 27 *July* 2015)

Abstract—Prolonged and abnormal scarring after trauma, burns and surgical procedures often results in a pathologic scar. We evaluated the efficacy of unfocused shock wave treatment, alone or in combination with manual therapy, on retracting scars on the hands. Scar appearance was assessed by means of the modified Vancouver Scar Scale; functional hand mobility was evaluated using a range-of-motion scale, whereas a visual analogue score was implemented for detecting any improvements in referred pain. Additionally, biopsy specimens were collected for clinico-pathologic correlation. For each active treatment group, statistically significant improvements in modified Vancouver Scar Scale were recorded as early as five treatment sessions and confirmed 2 wk after the last treatment session. Analogous results were observed when assessing pain and range of movement. Histopathological examination revealed significant increases in dermal fibroblasts in each active treatment group, as well as in neoangiogenetic response and type-I collagen concentration. (E-mail: saggini@unich.it) © **2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Scarring, Retracting scar, Regeneration, Resolution, Collagen, ESWT, Histopathologic features.**

INTRODUCTION

The cutaneous dermis is a specialized connective tissue consisting of a collagen-rich fibrous network embedded in a ground substance matrix. The proteoglycan-rich matrix is key to skin viscous quality at low loads. On the other hand, the main fibrous constituents of the dermis, namely collagen and elastin, provide structural stiffness and elasticity (Lanir 1981; Smith et al. 1982).

By definition, cutaneous scars develop by means of wound healing through a combined process of regeneration and replacement of the dermal tissue with fibrous tissue. Several sources of damage to the reticular dermis and subcutis may lead to cutaneous scarring, including burns, abrasions, lacerations and surgery. Abnormal wound healing is often characterized by a protraction of the healing process over time, with wounds appearing to be "stuck" in the inflammatory and proliferative phases, which predisposes to excessive accumulation of collagen and pathologic scarring (Roques 2013). Pathologic scars are classified into atrophic and hypertrophic scars, with the latter being further divided into simple hypertrophic scars and keloids (Roques 2013).

Both loco-regional and systemic factors appear to be able to promote pathologic scarring: wound features (*i.e.*, healing by primary or secondary intention, scar orientation, source of primary damage and anatomic site), extent of bleeding, presence of hematoma and/or serum collection, superimposing infection, innervation deficits, constitutional characteristics (*i.e.*, age, gender and race), coexisting administration of drugs (such as corticosteroids, antimetabolite agents or immunosuppressive drugs), disorders of blood supply, lack of nutritional factors and endocrine factors (such as presence of glucose intolerance), among others (Widgerow 2011).

Once formed, pathologic scars may be subject to several changes, including regression, keloid formation, neoplastic degeneration and retraction. Retracting scars are characterized by collagen fibers in a cord-like

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disposition exerting significant traction on surrounding healthy tissues; ensuing functional limitation is especially prominent when scars occur secondarily to deep burns in the neck area or in proximity of appendicular joints. Indeed, retracting scars may cause significant functional deficit (Slemp and Kirschner 2006; Wollstein et al. 2012).

Multiple sources of dermal damage may induce deposition of new collagen through activation of dermal fibroblasts, which are mesenchymal cells that play a critical role in wound healing. Morphologic features of fibroblasts include a spindle-shaped cytoplasm with a central elliptic nucleus and inconspicuous nucleoli. Functional activation induces profound morphologic changes in fibroblasts, including a significant expansion of the rough endoplasmic reticulum as well as expression of different surface markers. Fibroblasts are capable of secreting the precursors of extracellular matrix components, including basal substance, collagen, glycosaminoglycans, reticular and elastic fibers and glycoproteins (Darby et al. 2014).

The circulating precursors derived from bone marrow are an additional source of cells involved in the metabolism of the extracellular matrix and wound healing. Bone marrow–derived circulating precursors may include fXIIIa-positive dendritic cells and CD34-positive fibrocytes. The fXIIIa-positive cells were the first subtypes of cutaneous dendritic cells to be recognized. Antibodies against fXIIIa detect a sub-set of dermal dendritic cells and resident macrophages in the dermis; a higher density of fXIIIa-positive cells in the dermis has been described in a number of metabolic disorders of the extracellular matrix (Yokoyama and Muto 2006), including morphea and systemic scleroderma. Although the origin of CD34-positive cells in the dermis is still considered controversial, CD34-positive fibrocytes appear to result from circulating hematopoietic progenitor cells. It is thought that CD34-positive dermal fibrocytes play a significant role in several conditions associated with excessive collagen deposition and fibrosis, such as nephrogenic systemic fibrosis, scleroderma and graft versus host disease (Oh et al. 2011).

Injury can affect the skin's structure and composition, thereby greatly influencing the biomechanics and directionality of the resulting scar tissue. The characteristics of scars are a result of altered structure and composition in the dermis. Scars typically have fewer blood vessels supplying the denser connective tissue, which is less elastic. A significant difference between normal tissue and scar tissue seems to lie in the orientation of the fibrous matrix. Human scar tissue is characterized by greater collagen density, with larger fibers exhibiting increased alignment compared to normal tissue, although such alignment is not exactly parallel to the skin. Further structural differences between scars and normal tissue include a different ratio of collagen types and a loss of normal hair follicles and sweat glands in scars. Type I and III collagen are formed in human skin in a higher proportion relative to other types and are maintained in a fixed proportion relative to one another in normal skin tissue. However, in human scar tissue, as a result of age or injury, there is alteration in the abundance of type I and III collagen as well as their proportions to one another. Recently, both the abundance and balance of type I and III collagen have received considerable research attention (Feng et al. 2001; Garner et al. 1993; Ghahary et al. 1996; Guan et al. 1997; Guo et al. 2002; Hurley et al. 1993; Ichiki et al. 1997; Kennedy et al. 1995; Linares 1996; Liu et al. 2001; Lu 2003; Shah et al. 1995; Tan et al. 1993; Tang et al. 2004; Thomas et al. 1995; Wan et al. 2001; Wang et al. 1999; Wu et al. 2000; Yin 1999; Zhou et al. 1997).

In healthy human skin, type I and III collagen have relatively substantial roles during collagen formation, comprising 80%–85% and 10%–15% of human skin, respectively (Riita et al. 2002). Newly developed scars undergo a maturation process, with type III collagen being gradually replaced by type I collagen so as to restore normal type I-to-III ratio (which is approximately 5:1). Despite the fact that physiologic healing has been extensively studied, much less is known about the causes and the pathogenetic mechanisms of pathologic scarring (Liu et al. 2001). Collagen is a keystone of skin formation and repair, playing a crucial role in the maintenance of skin tensility and elasticity. Variations in content and ratio provide the basis for hypertrophic scar formation. Collagen fibers within scar dermis show a reduced resistance potential, being only 70% of that of normal skin.

Possible treatment of pathologic, retracting scars currently includes several options, such as intra-lesional corticosteroids, cryotherapy, dermabrasion, excision and scar revision surgery, laser therapy and radiation therapy; likewise, prophylactic strategies may include variable combinations of compression therapy, silicone gel and oral supplements such as flavonoids. Nonetheless, retractive scarring is characterized by a complex etiology related to both local and systemic factors, and the efficacy rate of available treatments is still far from satisfactory. As a consequence, treatment of pathologic scars often requires lengthy and expensive procedures, posing the need for clinical studies aimed at the development of novel therapeutic strategies for pathologic scarring (Faga et al. 2013; Rabello et al. 2014).

The list of emerging therapies for retracting scars currently features, among others, intra-lesional injections of interferon, controlled enzymatic debridement and stem-cell infusion (Bush et al. 2010; Jalali and Bayat 2007; Prado et al. 2005; Reish and Eriksson 2008; Williams and Barbul 2003), as well as extracorporeal