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Australia and New Zealand Horizon Scanning Network

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TERRITORY GOVERNMENTS OF AUSTRALIA
AND THE GOVERNMENT OF NEW ZEALAND

Horizon Scanning Technology Prioritising Summary

Shock wave therapy for wound healing

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**Australian
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PRIORITISING SUMMARY

REGISTER ID S000095

NAME OF TECHNOLOGY DERMAGOLD™ SHOCK WAVE THERAPY

PURPOSE AND TARGET GROUP TO TREAT PATIENTS WITH SOFT TISSUE WOUNDS

STAGE OF DEVELOPMENT (IN AUSTRALIA)

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- Yes
- No
- Not applicable

INTERNATIONAL UTILISATION

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Austria	✓		
USA	✓		

IMPACT SUMMARY

Shock wave therapy has been used for more than two decades to break down renal calculi and treat various musculoskeletal conditions. Shock wave therapy may also be useful for treating wounds by stimulating tissue regeneration and wound healing, and Dermagold™ shock wave therapy (Tissue Regeneration Technologies, Woodstock, GA) has been developed specifically to treat dermatologic indications. This technology is yet to emerge in Australia.

BACKGROUND

Wound healing disorders may have associated burdens including increased morbidity, prolonged hospital stay, increased treatment costs and lower patient satisfaction (Dumfarth 2008). The type and aetiology of a wound determines its treatment, with wounds broadly classified as either acute or chronic (Werdin 2008). Acute wounds are those in which the normal healing process is expected to take place, whereas chronic wounds are those which have not achieved anatomic and functional integrity after 3

months (Knox et al 2007; Werdin 2008). Common chronic wounds include venous and arterial ulcers, diabetic ulcers, and pressure sores (Werdin 2008).

Depending on the aetiology and severity of wound, treatments may include:

- Antibiotics
- Vacuum assisted closure: removal of excess wound fluid, allowing improved oxygenation and peripheral blood flow (Enoch et al 2006)
- Hyperbaric oxygen: an adjunctive therapy where the atmospheric pressure is increased (Enoch et al 2006)
- Pharmacology: improved circulation, controlled inflammatory response, and promotion of angiogenesis, collagen synthesis and epithelialisation (Enoch et al 2006)
- Antimicrobials: used for infected wounds, may include iodine or silver based preparations (Enoch et al 2006)
- Debridement: removal of devascularised tissue and necrotic material, without damaging healthy tissue
- Dressings:
 - Hydrogels for the debridement stage
 - Foam for the granulation stage
 - Hydrocolloids and low-adherence dressings for the epithelialisation stage (Werdin 2008)

DermaGold™ has been introduced as an alternative method of encouraging wound healing. DermaGold™ uses low-energy shock waves composed of heat, electromagnetic, acoustic and light energies to encourage tissue regeneration (Speed 2004; DermaGold™ website). The action of shock waves on wound healing is unknown, but thought to include neovascularisation, disintegration of calcium, neural effects, nitrous oxide and growth factor promotion, stem cell migration, and antibacterial effects (Speed 2004, DermaGold™ website). However, shock waves may also have adverse effects on soft tissues, as they may damage tissue during their passage which can result in localised bleeding.

DermaGold™ may be used prophylactically for surgical wounds or to actively treat acute and chronic wounds. It is a non-invasive therapy which requires no anaesthesia and may be performed as an outpatient procedure. The number of shock wave treatments needed varies, depending on the indication and the wound surface (DermaGold™ website)

CLINICAL NEED AND BURDEN OF DISEASE

The burden of disease is difficult to quantify as there is a wide range of acute and chronic wounds. In the identified studies shock wave therapy was used to treat surgical wounds, wounds with disturbed healing, post traumatic necrosis, venous stasis ulcer, decubitus ulcer, plaster cast pressure ulcer, arterial insufficiency ulcer, and burn wounds.

DIFFUSION

Shock wave therapy has been used since the mid-1980's for many different indications including kidney stones, treatment of un-united fractures, plantar fasciitis, calcifying tendonitis of the rotator cuff and humeral epicondylitis. Although shock wave therapy is not a new technology, its use in the treatment of wounds is novel. The Dermagold™ system has been developed specifically for dermatological treatment. At the time of writing Dermagold™ was an investigational device only, and not listed on the US Food and Drug Administration (FDA) or the Australian Therapeutic Goods Administration (TGA). Several clinical trials of the Dermagold™ technology for wound healing are currently underway in the United States.

COMPARATORS

Dermagold™ may be used as an adjunctive to wound closure treatments such as vacuum assisted closure (VAC), debridement, skin grafting or flap coverage, or dressings. It may also be used prophylactically, and comparators include other methods to promote epithelialisation such as hyperbaric oxygen therapy.

SAFETY AND EFFECTIVENESS ISSUES

Study description

Randomised controlled trial

This prospective randomised study enrolled 100 consecutive patients undergoing elective coronary artery bypass graft (CABG) surgery at one hospital department. Patients were randomly allocated to the treatment and control groups, although the method of randomisation was not reported. Excluded patients were emergency cases as well as those patients who tested positive for hepatitis C and HIV. The groups appeared to be well matched for age, gender, body mass index, risk factors for wound healing disorders, and history of impaired wound healing. Vein grafts were harvested from both groups and wound closure was performed using absorbable cutaneous sutures and staples. All patients received intraoperative antibiotic treatment. The treatment group received low-energy shock wave therapy (Dermagold) after wound closure. A total of 25 impulses (0.1 mJ/mm²; 5Hz) per centimetre of wound length were applied to the wounds. Patients in the control group did not receive shock wave therapy. The follow up was seven days. In this study, shock wave therapy was studied as a prophylactic treatment (Dumfarth et al 2008).

Case series

This study prospectively enrolled 208 patients between August 2004 and June 2006. Eligible patients had either "...acute or chronic complicated, non-healing wounds of various aetiologies including trauma, failure of primary closure following operation, venous or arterial insufficiency, pressure necrosis, or burn in the absence of extension to underlying bone or associated bone disruption." The most common wounds were surgical wounds which had failed to heal and wounds resulting from direct trauma associated with necrosis of the epidermis. Excluded patients were those who were pregnant, had stage I and stage IV decubitus ulcers, superficial first- and second-degree or circumferential

burns, compartment syndrome, necrotising fasciitis, or lymphoedema. Further exclusions were patients participating in another clinical study, those with physical or mental disability, or those who were not located close to the study and may not have been available to follow up. All patients received shock wave therapy (Dermagold) in conjunction with wound debridement and dressing. According to the wound size, patients received 100 to 1000 pulses at 0.1mJ/mm (100 pulses/cm²). Although no patients were removed from the study due to wound progression or deterioration, 32 patients (15.4%) dropped out of the study and were analysed in the incomplete healing group. The mean follow-up was 6.3 weeks (Schaden et al 2007).

Safety

Randomised controlled trial

A total of three patients died (3%, 3/100): two in the control and one in the treatment group. The causes of death included multiorgan failure, haemorrhagic stroke, and pulmonary embolism. There were no severe wound infections during the seven day follow up. No haematoma formations, skin lacerations or postoperative pain were observed after low-energy shock wave therapy (Dumfarth et al 2008).

Case series

There were no reported cardiac, neurological, dermal, thermal or allergic reactions or adverse events. Further, no clinically evident wound infections developed, and no wounds deteriorated in this study. During follow-up there was no treatment-related toxicity, no infection, and no deterioration of shock wave therapy-treated wounds (Schaden et al 2007).

Effectiveness

Randomised controlled trial

The primary outcome, wound healing, was measured using the ASEPSIS (Additional treatment, presence of Serous discharge, Erythema, Purulent exudate, Separation of the deep tissue, Isolation of bacteria, and duration of patient Stay) score. Wounds were assessed from postoperative days 3 to 7 by a blinded investigator. The ASEPSIS score was significantly lower in the treatment group than in the control group from postoperative day 3 to day 7 ($p < 0.05$ for each day). ASEPSIS scores were then analysed in five classes (satisfactory healing, disturbance of healing, minor wound infection, moderate wound infection, and severe wound infection). When analysed in this manner, there was more satisfactory healing in the treatment group ($p < 0.05$). There were significantly higher disturbances of healing, and minor and moderate wound infection in the control group ($p < 0.05$ for each). The secondary outcomes included the need for surgical revisions of the wound; and the need for new antibiotic treatment for wound healing disturbances of the vein graft harvesting site. The control group required more surgical revisions than the treatment group (control: 10% vs. treatment: 2%, $p = 0.092$) but this was not statistically significant. However, the control group required significantly more antibiotics than the treatment group (4 vs. 22; $p = 0.015$) (Dumfarth et al 2008).

Case series

The majority (75%, 156/208) of patients enrolled in the trial achieved 100% wound epithelialisation. Of the 176 patients who completed the trial, 88.6% (156/176) showed complete healing. No wound deteriorated with shock wave therapy. Complete wound epithelialisation was significantly associated with wound size (81.0% for wounds ≤ 10 cm² surface area vs. 61.8% for versus ≥ 10 cm² surface area, $p=0.05$) and duration (83.0% for wound ≤ 1 month old vs. 57.1% for wound ≥ 1 month old, $p<0.001$). Acute wounds were found to be significantly more likely to heal than chronic wounds (81.0% acute versus 56.3% chronic; $p=0.001$), and complete epithelialisation was significantly less likely and healing time prolonged in patients with large (>10 cm²) chronic (>1 month) wounds ($p<0.005$). Wound healing was significantly better in younger than in older patients (complete epithelialisation 57.7 ± 1.5 years vs. less than complete epithelialisation 69.1 ± 2.6 years, $p<0.001$). The wounds which demonstrated the worst overall healing rates were venous stasis ulcers (36.0% vs. 66.0% for all other wounds; $p=0.001$) (Schaden et al 2007).

COST IMPACT

At the time of writing, the cost for DermaGold™ was not available, as the device was still under clinical investigation. Shock wave therapy is proposed to reduce length of hospital stay and associated costs through several mechanisms including reducing the need for operative debridement of wounds; provision of treatment in an outpatient setting; and promotion of wound healing.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No other issues were identified from the retrieved studies.

OTHER ISSUES

Two authors of the randomised trial, Dr. Grimm and Dr. Schaden, disclosed a financial relationship with the manufacturer of Dermagold™ (Tissue Regeneration Technologies, Woodstock, GA). Dr. Schaden was also an author on the case series study and it is likely that this financial relationship was applicable, although no disclosure was made.

SUMMARY OF FINDINGS

Both studies applied shock wave therapy at 0.1 mJ/mm² with the case series applying 100 pulses per cm² and the RCT applying 25 pulses per centimetre of wound length. One patient receiving shock wave therapy died, as did two control patients. No other serious side effects were reported. Both studies reported that shock wave therapy was effective in treating various wounds including surgical, post-traumatic, venous stasis ulcer, decubitus ulcer, plaster cast pressure sores, arterial insufficiency ulcers, burns, and wounds with disturbed healing. However, further comparative trials are required and it is unclear whether the technology will be effective or safe in treating other types of wounds.

HEALTHPACT ACTION

The evidence available on shock wave therapy for wound healing is limited. Furthermore, the comparator utilised within the randomised trial was a control rather than an active

comparator such as hyperbaric oxygen therapy. There was no cost information available; however, it may be assumed that a shorter length of hospital stay due to complete wound healing may represent economic benefits. Based on the available evidence, shock wave therapy for wound healing will be monitored for 12 months.

NUMBER OF STUDIES INCLUDED

Total number of studies: 2

Level II and IV intervention evidence

REFERENCES

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Knox KR, Datiashvili RO, Granick MS Surgical wound bed preparation of chronic and acute wounds. *Clinics in Plastic Surgery* 2007; 34: 633-641

Shrivastava SK and Kailash Shock wave treatment in medicine. *Journal of Bioscience* 2005; 30: 269-275

Speed CA Extracorporeal shock-wave therapy in the management of chronic soft-tissue conditions. *Journal of Bone and Joint Surgery* 2004; 86: 165-171

Werdin F, Tenenhaus M, Rennekampf H-O Chronic wound care. *Lancet* 2008; 372: 1860-1862

SEARCH CRITERIA TO BE USED

Shock wave therapy AND (tissue OR wound)

PRIORITISING SUMMARY (2010 UPDATE)

NAME OF TECHNOLOGY

SHOCK WAVE THERAPY FOR WOUND HEALING

PURPOSE AND TARGET GROUP

TO TREAT PATIENTS WITH SOFT TISSUE WOUNDS

2010 SAFETY AND EFFECTIVENESS ISSUES

Study descriptions

A search of the literature identified eight new studies on shock wave therapy for wound healing. Of these, three trials, two randomised (Moretti et al 2009, Larking et al 2010) and one case series study (Arno et al 2009) on human subjects were retrieved for inclusion in this update. Several animal studies were identified but were excluded from this update.

The prospective randomised controlled trial by Moretti et al (2009) recruited 30 patients with diabetic foot ulcers, lasting at least 6 months, with wound area wider than 1cm². All patients have had peripheral neuropathy, defined as insensitivity to a 10g monofilament and vibration perception threshold measure at the malleolus of at least 25 volts. Exclusion and inclusion criteria were clearly listed. However, method of randomisation to standard therapy (n=15) and shock wave therapy (n=15) groups was not explicitly stated. Patients in the shock wave therapy group received three applications of shock wave therapy in addition to standard therapy. Treatment lasted 1-2 minutes and was administered over the course of 3 sessions (every 72 hours, 100 pulses per 1cm²). Subjects were evaluated over 20 weeks (Moretti et al 2009).

The randomised crossover trial, performed by Larking et al (2010), attempted to determine the efficacy of shock wave therapy to encourage healing of chronic skin ulceration in patients (n=9; mean age: 63.3 years; range: 42 to 83 years) with severe and complex neurological disabilities. Ulcers were randomised (shuffled cards method) to shock wave therapy (treatment group, n=4) or placebo (control group, n=5) shock wave therapy, one session per week for four weeks. Shock waves were applied at a rate of 5 per second for 200 impulses + 100 impulses per cm² at 0.1J/mm². All ulcers received one period of shock wave therapy/placebo each week for four weeks. Assessors were blinded to the treatment administered. The treatment and control groups were crossed over at 6-weeks (Larking et al 2010).

Arno et al (2009) evaluated the potential of shock waves as a method to treat severe burns. This pilot study involved 15 patients with acute deep partial or full thickness burns affecting less than 5% of their total body area. All paediatric patients and pregnant women were excluded. In addition, patients with burns located in the genitalia, thorax, face or neck regions were considered unsuitable for this trial. Shock wave therapy was administered on the third and fifth days after injury. Subjects were reviewed weekly over 1 month, followed by monthly evaluations (Arno et al 2009).

Safety

Moretti et al (2009) reported 2 incidences of local infection (peri-lesional erythma and oedema), one from each patient group, which required oral antibiotics for 10 days. Both incidences were resolved within 7 days and patients remained in the study (Moretti et al 2009). Meanwhile, Arno et al (2009) noted that shock wave therapy was well tolerated and there were no observed adverse side effects, such as bleeding, petechiae, haematoma or seroma. Three patients (20%) reported some pain during treatment, but all VAS scores were below 3. There were no cases of infection or wound deterioration (Arno et al 2009). Tinazzi et al (2009) did not provide any details on adverse events or side effects that may be associated to shock wave therapy.

Effectiveness

In 20 weeks, Moretti et al (2009) reported that the foot ulcers of 53.33% of shock wave therapy patients and 33.33% of standard care patients were healed ($p < 0.05$). Mean healing times were 60.8 ± 4.7 days (mean \pm standard deviation) and 82.2 ± 4.7 days for shock wave and standard care patients, respectively ($p < 0.001$). The re-epithelialisation index was significantly better for shock wave therapy patients compared to standard care patients (2.97 ± 0.34 mm²/die vs. 1.3 ± 0.26 mm²/die; $p < 0.001$) (Moretti et al 2009).

Similarly, Larking et al (2010) noted that after a 3-week observation period (to ensure ulcers are not healing spontaneously without treatment), the introduction of shock wave therapy appeared to encourage healing. Three ulcers actually increased in size at the initial stages of shock wave therapy, but rapidly healed at later stages. One ulcer appeared to deteriorate after 12 weeks of improvement, but this was reversed with the re-introduction of treatment. The authors reported that shock wave therapy appeared to have a debriding effect as well. It is interesting to note that both placebo-first and treatment-first groups achieved significant healing at 6 and 8 weeks following start of shock wave therapy. The ulcers subjected to placebo-first did not improve until the cross-over phase where shock wave therapy was introduced, suggesting that the treatment had a true effect on healing. Mean ulcer size was significantly smaller for both patient groups within 4 weeks post end of the shock wave therapy phase (placebo-first: -0.71 cm²; shock wave-first: -0.78 cm²) and continued to improve up to 8-weeks post end of the shock wave therapy phase (placebo-first: -1.15 cm²; shock wave-first: -0.83 cm²) (Larking et al 2010).

Arno et al (2009) reported that after one shock wave treatment session, burns had a significant increase in acute perfusion, determined by laser assessment on the fifth day (no actual data presented). The investigators observed a progressive decrease of deeper wound zones in favour of an increase size of superficial areas and that 80% (12/15) of patients achieved spontaneous healing within 21-days post-treatment. After healing, patients were instructed to use hydrating cream and silicone sheeting or pressure therapy. The resulting burn scars were not pruritic or painful in 75% of patients, while 5% of patients developed hypertrophic scarring (Arno et al 2009).

2010 SUMMARY OF FINDINGS

The retrieved studies demonstrated positive outcomes for patients with diabetic/chronic ulcers and burns after shock wave therapy. Compared to standard care or placebo, the use

of shock wave therapy for the treatment of ulcers resulted in significantly faster healing rates. However, the evidence to date remains limited to small patient cohorts.

2010 HEALTHPACT ACTION

Given the promising results to date and the potential economic benefits, it is likely that this technology will continue to be trialled in the near future. This technology has been noted by HealthPACT, but additional updates are not necessary at this time.

2010 INCLUDED STUDIES

Total number of studies	3
Level II intervention evidence	2
Level IV intervention evidence	1

2010 REFERENCES

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Larking AM, Duport S, Clinton M, Hardy M, Andrews K. Randomized control of extracorporeal shock wave therapy versus placebo for chronic decubitus ulceration. *Clinical Rehabilitation* 2010 [Epub ahead of print].

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