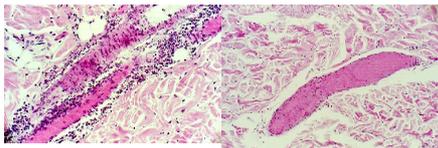


# A comparative study of intravenously administered BMOV versus control infusion in a deep dermal contact-burn model in pigs

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## HISTOPATHOLOGICAL EVALUATION

### Postburnday 1; wound centre; stasis zone; HE 10x



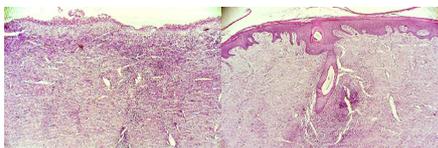
Placebo

BMOV-treated

Many of the capillaries in the stasis zone are obstructed by microthrombi. Moreover, the vessels are often damaged, containing fibrin in their walls, while under attack of neutrophils. This vasculitis often persists beyond post burn day 4.

Here too, many of the capillaries in the stasis zone of the wound centre are occluded by microthrombi. However, the inflammatory component and the damage of the vascular walls are strongly reduced. In the following few days at least some of these capillaries appear to re-open.

### Postburnday 21; wound centre; surface; HE 4x



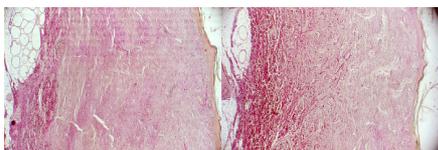
Placebo

BMOV-treated

In the wound centre the dislodged crust leaves a denuded granulation tissue surface covered by a thin fibrinous layer. No follicular recovery is seen in this area at post-burn day 21.

The central wound bed has been completely resurfaced. Recovered follicles clearly contribute to the neo-epidermis.

### Postburnday 43; wound centre; overview; HE 2.5x



Placebo

BMOV-treated

After wound closure by neo-epidermis the underlying scar tissue (yellowish pink) is broad, containing few collagen remnants of the original dermis (darker red zones).

After wound closure by neo-epidermis the underlying scar tissue (yellowish pink) is thinner containing more collagen remnants of the original dermis (darker red zones).

## Introduction

After a major burn, various inflammatory and physiological mechanisms are initiated in the affected tissues. Although the primary injury is caused directly by heat, this is followed by secondary or indirect injury, induced by the release of various mediators such as cytokines, interleukines, free radicals, etc. at the wound site. These cellular mediators initiate micro-thrombi and vascular inflammation in areas of apparently viable dermis which are nevertheless at risk of denaturation. This vascular trauma results in a delayed destruction of the blood vessels and further deepening of the burn wound (Watts, A. et al., 2001) and can be a major obstacle to wound healing.

Various growth factors, such as insulin-like growth factor (IGF) and epidermal growth factor (EGF), may reduce the further deepening of the burn by helping to preserve the underlying vascular plexus. Bis(maltolato)oxovanadium (BMOV), an organic vanadium compound, mimics insulin, IGF, and EGF, and has been shown to inhibit the cellular mediators mentioned above, thus potentially reducing indirect injury as well as facilitating wound healing by preservation of the blood vessels. BMOV has already been used in man for many years as a food supplement and in weight-reducing products. The aim of this study was to determine the effect of BMOV in an animal model for deep dermal contact burns.

## Materials & methods

In Dutch Landrace pigs, 12 contact burns, six on each flank were induced by application of a brass block of 6.8 x 6.8 cm, at a temperature of 170°C for 15 seconds (Hoekstra, M. J. et al., 1993). The epidermal remnants of skin were removed after infliction of burns. Three groups of two pigs each received three intravenous slow bolus injections of BMOV at three different doses (0.05, 0.1 or 0.25 mg/kg body weight). The first dose was given 30 min after inflicting the last burn wound and the other two on the following two days; another group of pigs received an injection of control treatment (vehicle only). All burn wounds were treated topically with silversulfadiazine cream.

Physical appearance and histopathology of all the wounds were evaluated in a blind way at defined post-burn intervals. The following macroscopic parameters were examined: vascularisation, re-epithelialization, hair growth, contraction and pliability of the scar. The following histopathological parameters were evaluated from wound biopsies: degree of necrosis and preservation of the dermis, re-epithelialization and contraction, quality of the scar, the appearance of the vascularisation, and the presence/recovery of hair follicles and sweat glands.

## Results

In the control pigs, much of the initially viable-appearing dermis was lost after an extensive vasculitis in the stasis zone underlying the wound. This delayed microvascular damage resulted in a rapid and extensive replacement of the original dermis by fibro-vascular tissue. The development of granulation tissue was more extensive than in treated animals, which probably facilitated the initially faster growth of neo-epithelium. The appearance of this neo-epithelium was, however, fragile.

In comparison, the treated pigs showed greater preservation of the blood vessels and the development of granulation tissue was less extensive; in addition, there was greater preservation of hair follicles and sweat glands and the neo-epithelium appeared to be healthier. The re-epithelialization of the wound was also more rapid in BMOV-treated animals. The magnitude of this effect appeared to be dose-related.

## Conclusion

Intravenous administration of BMOV shortly after deep dermal burn injury in pigs resulted in more extensive preservation of the blood vessels and hair follicles, which appeared to reduce the secondary injury induced by dermal burns. The treated pigs showed greater preservation of the dermis, faster epithelialization, better vascularisation, less contraction, and the formation of more pliable scars, compared with control treatment.

## MACROSCOPICAL EVALUATION

### Postburnday 1



Placebo

BMOV-treated

The burns on the control and treated pigs look much the same. The wound of the treated pig may be a slightly brighter red

### Postburnday 21



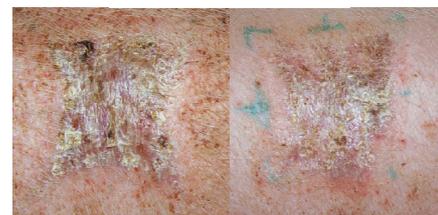
Placebo

BMOV-treated

Vascularisation is poor with much granulation tissue. The wound is not entirely epithelialized.

Well-vascularised wound with little granulation tissue. Almost completely epithelialized.

### Postburnday 43



Placebo

BMOV-treated

The skin surface still appears raw. The scar tissue is thicker and the scar is more contracted than that of the treated pig. The tattoo marks are hardly visible, presumably due to the severity of the injury, even at the edges of the wound.

The scar tissue is thin and supple, and appears well-vascularised. There is little contraction and some hair growth towards the edge of the wound (within the tattoo marks). The skin at the edge of the wound appears to have healed almost without scarring, only slight damage to the epithelium is visible.

Hoekstra, M.J., Hupkens, P., Dutrieux, R.P., Bosch, M.M., Brans, T.A. and Kreis, R.W., 1993. A comparative burn wound model in the New Yorkshire pig for the histopathological evaluation of local therapeutic regimens: silver sulfadiazine cream as a standard. *Br J Plast Surg*, 46(7): 585-589.

Watts, A., Tyler, M., Perry, M., Roberts, A. and McGrouther, D., 2001. Burn depth and its histological measurement. *Burns*, 27(2): 154-160.

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