TISSUPOR

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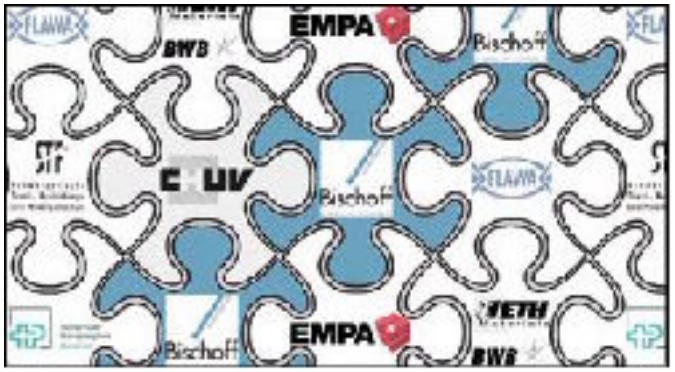

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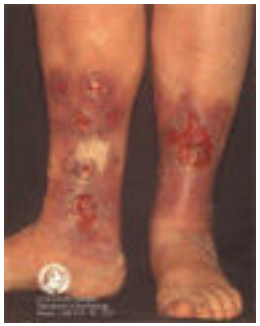
TISSUPOR: Development of a structured wound dressing based on a textile composite functionalised by embroidery technology

Introduction

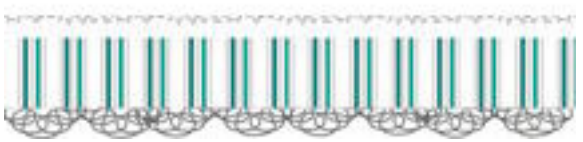


Motivation

The aim of this project is the development of a new, textile based wound dressing system to be applied for chronically non healing wounds e.g. ulcus cruris and pressure sores. Non healing wounds have a great economic impact because they need intensive wound care for very long periods, often disabling the patient and causing high health care costs.

Approach

Textile wound dressing system in three layers:



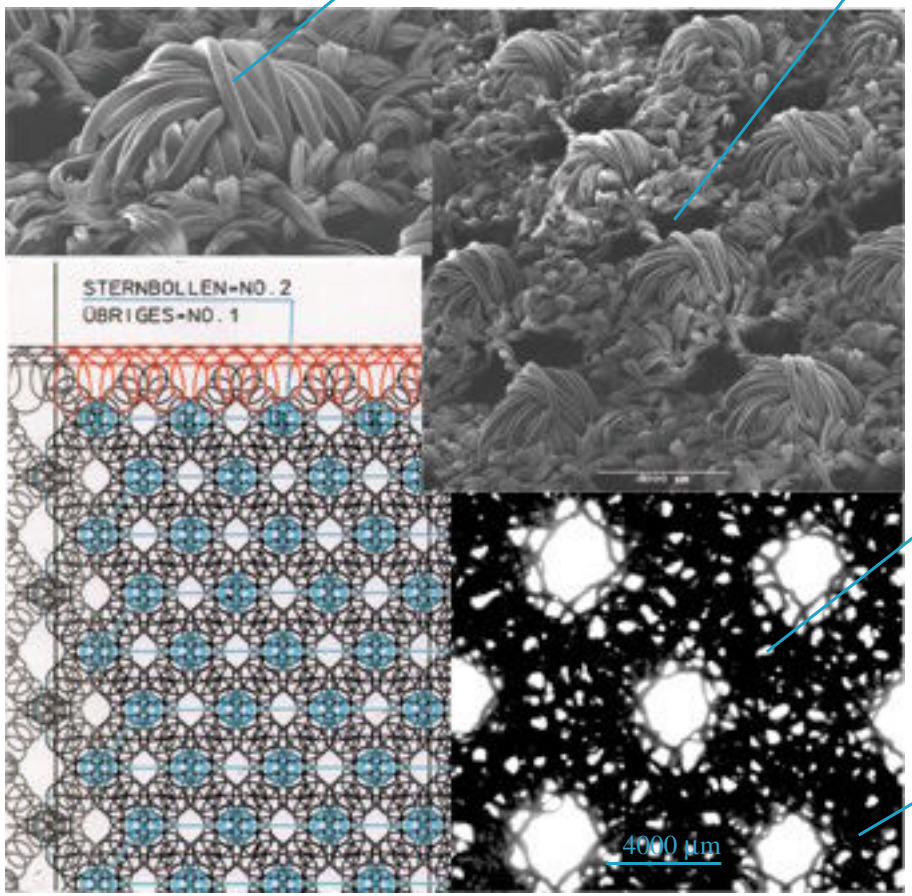
Layer	Functions	Materials
A	• Mechanical and biological protection • Control of humidity and gas transport	• Dense, multilayered nonwoven fabric (PET,PP, cotton)
B	• Mechanical protection by shear compliance • Transfer of compressive forces • Absorption and accumulation of wound exudates	• Spacer fabric (PET monofil, PP, cotton) • SAP, K-polyacrylate
C	• Angiopolar layer for tissue ingrowth and directed angiogenesis • Locally controlled mechanical stimulation of wound area	• Embroidered textile layer (PET, PA)

Design of technical embroidery for the wound dressing

One of the key issues in tissue regeneration of chronically non healing wounds is controlled revascularisation of the epidermal tissue. In textile implant materials tissue formation and vascularisation depend on the size and distribution of pores and fibers. An arrangement of pores of different orders of magnitude, ranging from 1µm to 1000µm will favour the tissue ingrowth and the formation of new blood vessels and capillaries [1]. Embroidery technology allowed to achieve a 3-dimensionally structured textile architecture that combines pores for directed angiogenesis and elements for local mechanical stimulation.

Integrated stiff elements for mechanical stimulation of the wound (Polyamide monofilament, 150µm Ø).

Pore sizes 500µm to 3000µm: Uptake of blood coagula and formation of granulation tissue.



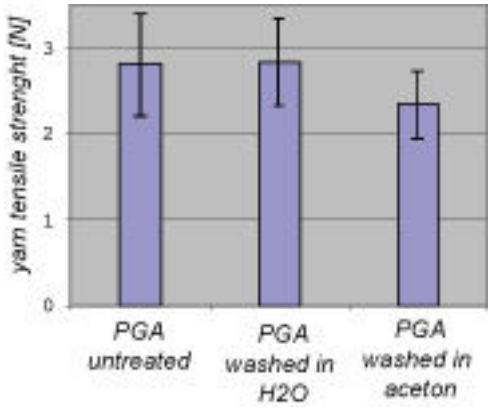
Pore sizes 100µm to 500µm: Ingrowth of blood vessels.

Pore sizes of 10µm to 100µm: Ingrowth of cells and small capillaries.

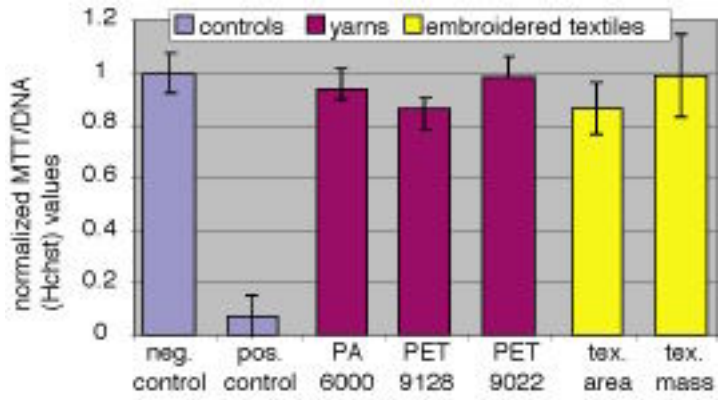
Technical CAD drawing of the embroidered textile

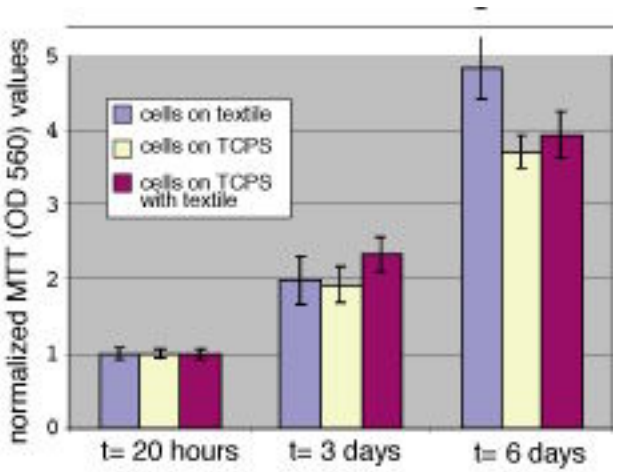
Biodegradable embroidered textiles

Degradation of yarn material is a key question in the design of textile cell carriers for tissue engineering. To demonstrate the use of embroidery technology as a tool for processing of biomaterials we used poly(glycolic acid) (PGA) yarns (left). The removal of the base cloth did not change the tensile properties of the yarn if we stiched onto a nonwoven poly(venyl alcohol) tissue which was washed out in water at ambient temperature for several hours.



Cytotoxicity tests

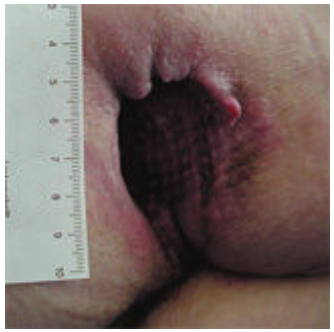




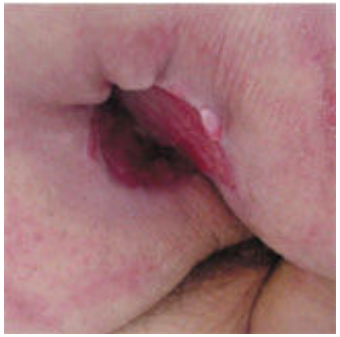
The adaptation of the industrial embroidery process to medical textiles requires thorough biocompatibility testing to find possible toxic effects of chemical residues from machine, base cloth or yarn sizing. We performed basic cytotoxicity assays using a 3T3 fibroblast cell line. In direct (right) and indirect (left) exposure methods, endpoints of mitochondric activity (MTT) and cell mass (DNA) were measured. In both experiments no significant toxic effects could be detected.

Clinical experiences

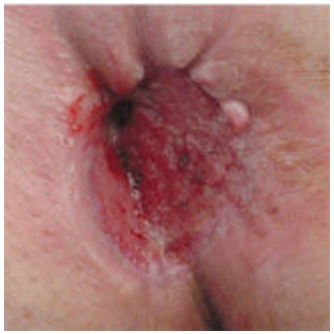
Decubitus was treated at the wound care clinic of the Swiss Paraplegic Centre, Nottwil, according to internal protocols. After initial debridement wounds were treated with TISSUPOR until 50 % wound surface reduction was achieved. First results show a comparable healing rate compared to conventional moist wound care. However the concept of TISSUPOR resulted in much less frequent dressing changement (2 times per week instead of twice a day). Our working hypothesis of induced bleeding during dressing changement could be veryfied. Right side: Example of wound treatment with TISSUPOR. Female patient, age 69, with decubitus. Wound volume after one week was 80ml. The dressing was changed twice a week. The wound was surgically closed after 3.5 weeks.



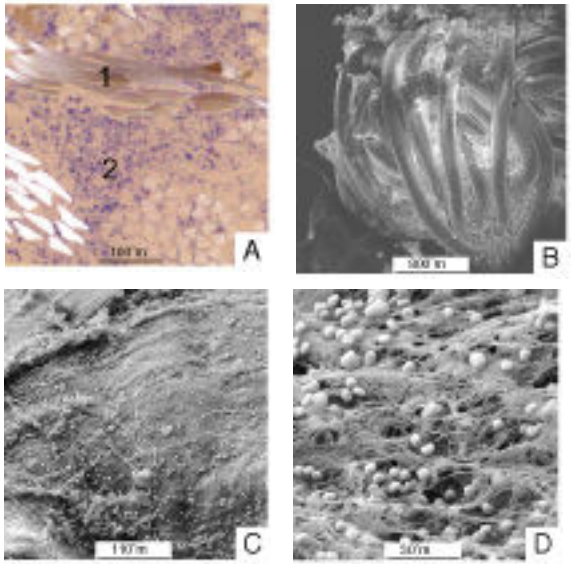
application time 2 weeks
wound volume 40ml



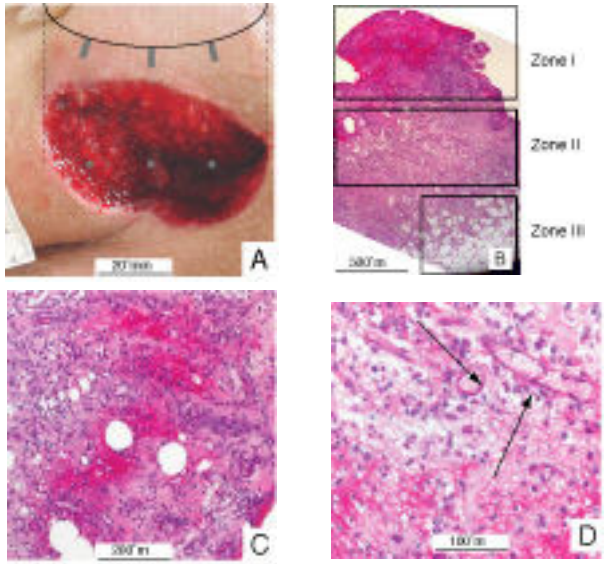
application time 3 weeks
wound volume 22ml



application time 3.5 weeks
wound volume 11ml



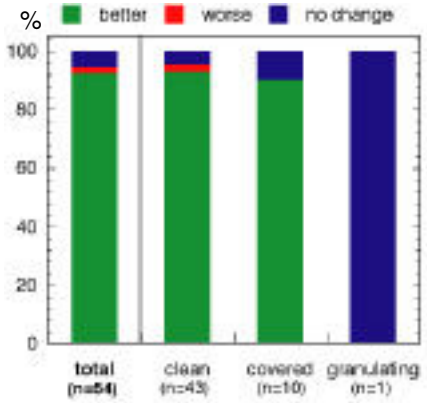
Appearance of the embroidered textile layer of TISSUPOR after removal: In the histologic section (A) the fibers (1) are infiltrated with a mixture of fibrin, necrotic cells, leucocytes and erytrocytes (2). similar observations were made by SEM (B, C, D). The textile structure is covered with a dense fibrin matrix in which erytrocytes and cell debris is trapped.

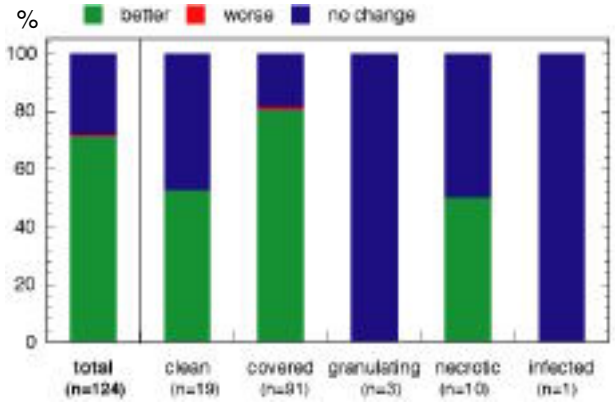


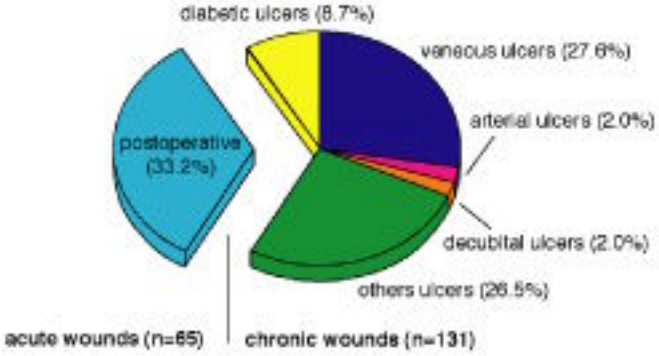
Histological analysis of the wound after removal of TISSUPOR: Punch biopsies from the wound base (A) show three histologically distinct zones (B). The granulation tissue (C, D, taken from zone II) contains a dense network of capillaries (arrows in D).

Clinical screening study: in-use test covering various indications

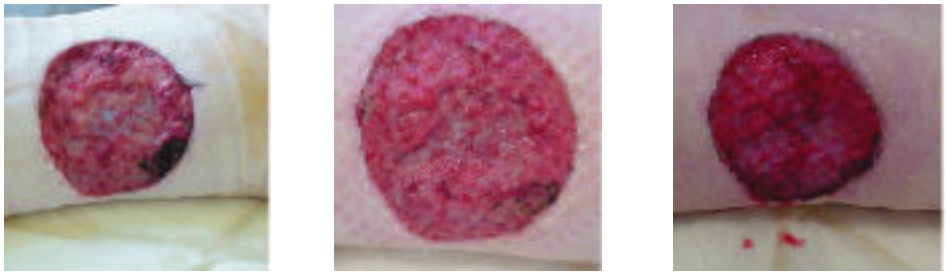
The aim of this study was to screen possible applications of the embroidered wound dressing and to define the most promising indications for successful treatment.
Additionally the combination with standard therapies such as vacuum therapy was of special interest. A total of 196 patients were treated in different European clinics. The study covered mostly chronic wounds, but also post-operative acute wounds e.g. after tumor excision were treated. The wound dressing was applied according to the protocols of the individual clinic. In all cases the state of the wound was documented at each wound pad exchange. The average treatment time was 25 days, ranging from 6 days to 8 weeks.







For acute wounds (left chart) a positive effect of the wound dressing was observed in over 90% of the cases. The application of TISSUPOR was found to rapidly induce new granulation tissue which represents a vital base for surgical wound closure. In chronic cases (right chart) the strongest effect was seen in fibrin covered wounds. Almost 80% of these wounds were clean or granulating at the end of the therapy. No improvement was found in necrotic and infected wounds.

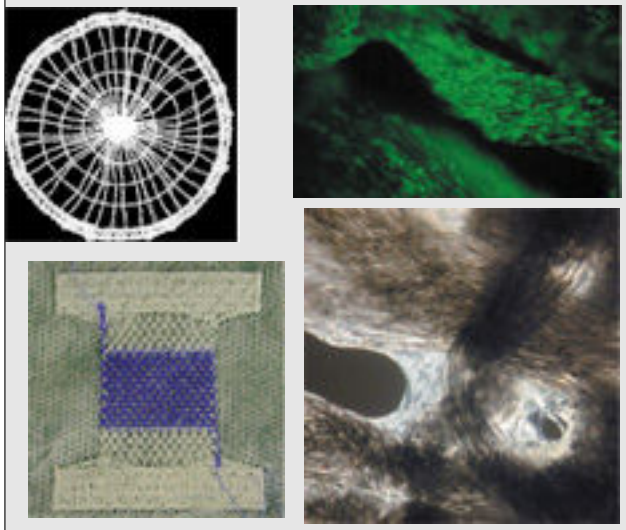


Treatment of large skin defect with TISSUPOR after skin tumor excision.
A: state of the wound at begin of therapy.
B: state at first dressing exchange after 7 days: initiation of wound granulation is observed. The skin around the wound edge is slightly irritated.
C: wound state at second exchange after 14 days: intensive granulation is observed.

Treatment of large defect due to phlegmone and necrotic osteomyelitis. The embroidered wound dressing was combined with vacuum therapy.
A: state of the wound at begin of therapy.
B: first dressing exchange after 3 days shows intensive granulation. The imprint of the embroidered textile structure is clearly visible.
C: after 24 days the wound area is significantly reduced and vital granulation tissue is visible

Outlook

Tissue Engineering



Embroidered scaffolds serve as test systems to study cell/textile interactions in vitro. Influence of mechanical stimulation and material degradation (bottom, left) is investigated. Primary rat tendon fibroblasts (right, top and bottom) are cultured on a circular scaffold that is designed to fit into standard cell culture plates (top, left).

Further development of TISSUPOR

Investigation of the biological effects of TISSUPOR

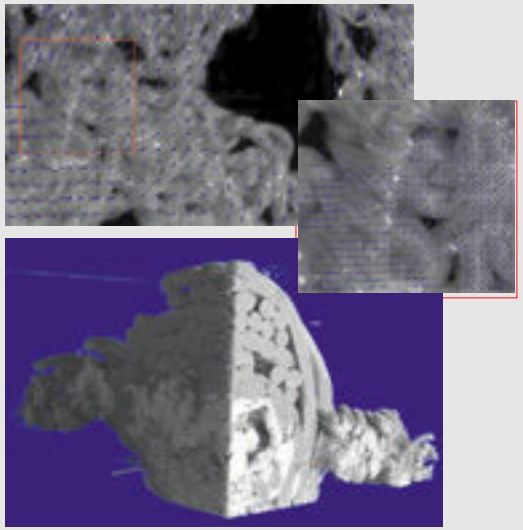
Further clinical and biological studies must concentrate on direct comparison with established therapies to quantitatively analyze a clinical benefit. The biological effect of mechanical stimulation on the formation of granulation tissue remains unclear. Therefore the interactions of the textile structure and the wound dressing have to be further investigated on a cellular and molecular level in order to define the biomechanical factors which are inducing the prominent angiogenesis. Furthermore, the quality of the developing connective tissue with respect to possible scar formation remains an open question.

Evaluation of strategies for wound epithelialization

Different approaches will be investigated in feasibility studies to define an optimal concept for wound closure after formation of highly vascularized granulation tissue with TISSUPOR. Possible further developments include the local delivery of angiogenic, antibiotic or pain reducing factors from degradable yarns. Additionally, the possibility to stitch with conductive fibers in a defined pattern opens new ways in electrotherapy.

Textile structure and mechanics

Image analysis methods are investigated to quantify strain patterns in textiles. Synchtrotron µ-CT is used to measure structural parameters like porosity or specific surface structure.



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Acknowledgements

µ-CT measurement and reconstruction by P. Thurner (ETH-BWB) and F. Beckmann (HASYLAB, Hamburg)