Kelo-cote® is the only topical scar treatment...

**PROVEN** Clinically Effective in the Improvement of Hypertrophic and Keloid Scars.¹

**PROVEN** Effective in the Prevention of Excessive and Abnormal Scar Formation.²

**PROVEN** Equivalent to Silicone Gel Sheeting in Efficacy, but Preferred by Patients for Ease of Use.³

Unique Patented Formula of Pure Silicones.

**PROVEN** Worthy of Your Recommendation.


Since the first SCAR meeting in 2006, there have been exciting developments in the management of scars and our knowledge of the field has expanded considerably. This area of largely unmet medical need has benefited immensely from greater efforts dedicated to research and development and notably, the potential success of products in clinical trials.

A major turning point in the management of scars has involved the change in perception that the majority of scars should be treated by surgeons to the realisation that real benefits can be achieved in the treatment of some scars with biochemical products. For instance, the use of antimitotic agents in patients with hypertrophic scars has shown great potential, as has novel anti-scarring agents based on transforming growth factor. Knowledge of the wound healing process has been harnessed to create these innovative products, which are currently being investigated in clinical trials. In addition, our understanding of treatment techniques and products, such as silicon, skin substitutes and radiotherapy continues to grow, leading to yet further advances.

Despite these positive changes, the issue of reimbursement of dressings and devices persists. This continues to be hampered by a lack of agreed methodology for evaluating and defining scars, therefore the efficacy of products cannot be adequately assessed in a controlled environment. The SCAR Club hopes to continue the discussion on reimbursement in countries worldwide.

The future management of scars is likely to involve less emphasis on surgery, while a greater prominence will be given to biochemical agents that interfere with the healing process, thus preventing or reducing the formation of scars. It is hoped that the SCAR Club will play a pivotal role in helping to create further advances in the field by forming a platform for sharing ideas and promoting discussion. In this regard, the launch of the SCAR Journal during this second meeting creates a unique and focussed forum enabling the dissemination of research results and ideas.

Over the next three days, we will listen to plenary presentations on the latest advances in the management of scars and get involved in workshop and interactive sessions to discuss important topics in the field of excessive scarring and patient case studies. I do hope that you enjoy this interesting and stimulating meeting and that you also enjoy your visit to Montpellier.

Luc Téot

Scientific Board

Luc Téot
Kenneth Dolynchuk
Mark Ferguson
Wei Liu
Esther Middelkoop
Tom Mustoe
Rei Ogawa
Fiona Wood

Auspices

This meeting is being organized under the auspices of:

- Wound Healing Societies (WUWHS)
- European Tissue Repair Societies (ETRS)
- French Wound Healing Society (SFFPC)
- French Dermatology Society (SFD)
- Centre National de la Recherche Scientifique (CNRS)
SCIENTIFIC PROGRAMME AT A GLANCE

THURSDAY 25 SEPTEMBER 2008

08h30-09h00 Welcome and Introduction
Auditorium
09h00-09h30 Keynote Presentation
New potential anti-scarring approaches
Speaker: Wei Liu (Shangai, China)
Auditorium
09h30-10h45 Mechanical Tension in Scarring
• Dermal origin
Speaker: Dennis Orgill (Boston, USA)
• Control of cell orientation and migration by substratum nanotopography and DC electric fields
Speaker: Ann Rajnicek (Aberdeen, UK)
• Electrical signals generated naturally at a wound regulate the cell biology of wound healing
Speaker: Colin McCaigh (Aberdeen, UK)
• The role of cutaneous innervation in scarring
Speakers’ presentation through telephone conference: Fiona Wood (Perth, Australia)
Auditorium
10h45-11h15 Coffee Break
Exhibition Area
11h15-12h30 Updates in Scarring: Biological Aspects
• When fibroblasts turn wrong: the bad influence of their environment
Speaker: Boris Hinz (Lausanne, Switzerland)
• Tumors: wounds that do not heal. Similarities between tumor stroma generation and wound healing
Speaker: Alexis Desmoulière (Limoges, France)
• Fibroblasts are not equal in front of wound healing: new cell therapy strategies
Speaker: Bernard Coulomb (Paris, France)
• Cell therapy and wound healing: new therapeutical approach in the treatment of severe radiation burn
Speaker: Marie Prat (Paris, France)
Auditorium
12h30-14h00 Lunch
Exhibition Area
14h00-14h30 Keynote Presentation
Facial allotransplantation – follow-up after 3 years
Speaker: Bernard Devauchelle (Amiens, France)
Auditorium
14h30-16h30 Parallel Sessions
Non Surgical Techniques
• Treatment of abnormal scars. The role of silicones
Speaker: Jean Guilbaud (Paris, France)
• Corticosteroid treatment for keloids
Speaker: Rei Ogawa (Tokyo, Japan)
• The plastic surgeon’s perspective on intralesional liposomal cortisone injections in the context of scar revisions: clinical and experimental results
Speaker: Raymund Horch (Erlangen, Germany)
• Compressive garments
Speaker: Claude Roques (Lamalou les Bains, France)
Auditorium
14h30-16h30 Scar Evaluation
• Appraising the evidence - classifying scars
  Speaker: Raj Mani (Southampton, UK)
• Cutometer and Dermaspectrometer in clinical research
  Speaker: Esther Middelkoop (Beverwijk, The Netherlands)
• The Patient and Observer Scar Assessment Scale (POSAS):
  a reliable and feasible tool for the evaluation of burn and linear scars
  Speaker: Annekatrien van de Kar (Beverwijk, The Netherlands)

14h30-16h30 Parallel Sessions
The Epidermal Component
• Zesteem (17B Estradiol) for the acceleration of re-epithelialisation,
  particularly of skin graft donor sites
  Speaker: Mark Ferguson (Manchester, UK)
• The role of the epidermis in scar reduction
  Speakers’ presentation through telephone conference: Fiona Wood (Perth, Australia)
• Utilization of actinic keratinocytes for in vitro reconstruction of non
  melanoma skin cancer
  Speaker: Giovanni Abatangelo (Padova, Italy)

Laser
• Excessive scars and lasers: our approach
  Speaker: Paolo Bonan (Florence, Italy)
• 1064nm Nd: YAG laser treatment for keloids and hypertrophic scars
  Speaker: Satoshi Akaishi (Tokyo, Japan)
• Management of excessive scars with pulsed dye lasers and of postburn
  scars with IPL
  Speaker: Regine Bousquet-Rouaud (Montpellier, France)
• Scar prevention by laser-assisted skin healing (lash): a pilot study with
  an 810-nm diode laser system
  Speaker: Gwen Iarmarcovai (Meyreuil, France)

16h30-17h00 Tea Break
17h00-18h30 Free Papers – concurrent sessions
• Research
• Clinical Trials

FRIDAY 26 SEPTEMBER 2008
09h00-09h30 Keynote Presentation
Prevention and reduction of scarring in the skin: discovery, mechanism
and clinical trials of Juvista
Speaker: Mark Ferguson (Manchester, UK)

09h30-10h45 New Anti Scarring Agents
• Low dose 5-FU for keloid therapy and relapse prevention
  Speaker: Wei Liu (Shangai, China)
• Juvista (TGF83) a potential new human pharmacological agent
  for the prevention and reduction of scarring
  Speaker: Mark Ferguson (Manchester, UK)
• Multi-modality scar management program
  Speakers’ presentation through telephone conference: Alan Widgerow
  (Johannesburg, South Africa)

10h45-11h15 Coffee Break
11h15-13h00 Interactive Session with Patients
- Introduction
  Speaker: Luc Teot (Montpellier, France)
- Insights into differences in physicians’ and patients’ perceptions about scarring
  Speaker: Leroy Young (Saint Louis, USA)
- Live Presentation of Cases

13h00-14h30 Lunch

14h30-15h00 Keynote Presentation
  The role of the epidermis in the regulation of scarring
  Speaker: Tom Mustoe (Huron, USA)

15h00-16h30 Non Cellularised Dermal Substitutes
- Development of a dermal substitute
  Speaker: Esther Middelkoop (Beverwijk, The Netherlands)
- One single procedure using dermal matrix in skin replacement
  Speaker: Luc Teot (Montpellier, France)
- Introduction of artificial dermis ‘Pelna®’
  Speaker: Shuji Kawabata (Tokyo, Japan)

Cellularised Dermal Substitutes
- In vitro reconstruction of vascularised skin
  Speaker: Giovanni Abatangelo (Padova, Italy)
- Allogeneic cell therapy from the bench to commercialization
  Speaker: Vincent Ronfard (Canton, USA)

Extra Cellular Matrix Promoters
- Extracellular matrix and usage of amelogenin treatment in chronic wounds
  Speaker: Magnus Agren (Copenhagen, Denmark)

16h30-17h00 Tea Break

17h00-18h30 Parallel Sessions
- Workshop on Laser - DEKA on laser and acne scars:
  Speakers: Paolo Bonan (Florence, Italy) & Anne Le Pillouer-Prost (Marseille, France)
  Postacne scars: Classification and grading
  Post acne scars: Algorithm of treatment

  - Traditional and fractional ablative lasers
  - Personal experience with the fractional CO2 smartxide DOT (DEKA-Italy)
    with video demonstration
  - Traditional and fractional non ablative lasers
  - Other technologies: LEDs, radiofrequency

- Free Papers
  Clinical Case Reports
SATURDAY 27 SEPTEMBER 2008

09H30-10H00 Aging and Scars  
Speaker: Sylvie Meaume (Ivry, France)

10h00-10h30 Anti scar therapies in burn wounds: from start to finish !  
Speaker: Stan Monstrey (Gent, Belgium)

10h30-11h00 Coffee Break

11h00-12h00 Round Table

12h00-12h30 Scar Club Consensus & End of the Meeting
NEW POTENTIAL ANTI-SCARRING APPROACHES

Wei Liu, MD, PhD, Department of Plastic Surgery, Shanghai 9th People's Hospital Shanghai Jiao Tong University School of Medicine, National Tissue Engineering Center of China, Shanghai, China

Scarring could cause severe physiological and psychological suffering of wounded patients who deserve a better life quality. Although scarring was considered essential for saving life of wounded wild animals, such a healing pattern is no longer necessary for human being living in a modern society. Searching for potential anti-scarring strategies would thus be the goal of both physician and scientists for the sake of the patients. Pioneered by Professor Mark Ferguson, anti-TGF-beta strategy becomes the first scar manipulation and reduction approach that brings the hope to both patients and physicians. It seems that anti-scarring approaches might fall into two categories: scar prevention and scar remodeling. Obviously, anti-TGF-beta approach remains the mainstream strategy of scar prevention and reduction. This can be achieved by protein neutralization or gene transfection and manipulation or blocking signaling. In addition, growth factors or cytokines other than TGF-beta also seem to play a role in fetal scarless wound healing. Therefore, it might be worth trying to use these factors for scar reduction. Recently, tissue regeneration has become a new means of tissue/function restoration. From this point of view, scarring should be considered as the opposite side of tissue regeneration. Thus, promoting tissue regeneration of wounded skin might also become the new approach by using stem cell and other technologies. Finally, for already formed scar, how to remodel it into relatively normal skin might also be a potential approach.

FACIAL ALLOTRANSPLANTATION FOLLOW UP AFTER 3 YEARS

Bernard Devauchelle, Head of the Department of Oral and Maxillofacial Surgery at Amiens University Hospital, Amiens, France

« To be conscious that to be oneself is to perpetually change and accepts oneself as changing ». That could be the summary of what it could be learned from the first facial transplant. Beyond its mediatic dimension, the first facial allotransplantation of composite tissue still remain a scientific adventure futuring many extrapolations in very different fields but also linked like:

- the tissues and scar healing around defects and flaps
- the reconstructive microsurgery in all technical aspects
- immuno-suppression and tolerance
- cutaneous and mucosal pathology
- nervous regeneration and cortical integration
- psychologic and social integration of the recomposed body
- ethics and medias (ethic of the mediatisation and mediatisation of ethics)
- organ donation and philosophy of the transplantation

All that subjects are not specific of facial transplant but more acute in that purpose. Those problems are also changing according the fourth dimension, that is to say “time running”.
Scarring is a major clinical problem resulting in adverse aesthetic, functional and psychological sequelae. Many years ago we discovered that experimental skin wounds made on experimental animal embryos healed perfectly with no scars. We investigated the cellular and molecular basis of scar free healing, asking fundamental questions such as, when during embryonic development does scar free healing turn into scar forming healing and what are the cellular and molecular correlates? In mice, skin wounds made on or before embryonic day 16 heal without a scar, whereas those made thereafter scar. There are many cellular and molecular differences between embryonic day 16 wounds, which heal without a scar and those made later which scar. But the question is which of these are epiphenomena e.g. related to development of the embryo and which are causative of the scar free healing.

We have shown that members of the Transforming Growth Factor Beta family are particularly important for the scar free healing phenotype. Specifically embryonic wounds that heal without a scar have high levels of TGFb3, whereas adult wounds which scar have much lower levels. TGFb3 is an endogenous molecule, important in the development of the skin. Skin volume in the developing mouse embryo increases rapidly and one of the important morphogenetic factors involved is TGFb3. Experimental addition of human recombinant TGFb3 to skin wounds (incisions and excisions) in adult mice, rats and pigs, results in wounds which heal with markedly improved scarring compared to placebo treated controls. Furthermore, wounds on mouse embryos, genetically null for TGFb3, made on or before embryonic day 16, heal with a scar by contrast to a wound on a normal mouse embryo (with normal levels of TGFb3) which heal without a scar. These observations have confirmed the importance of TGFb3 in the scarring process and have allowed us to investigate the underlying cellular and molecular effectors. TGFb3 increases migration of both fibroblasts and keratinocytes. It does so by stimulating the Ras GTPase CD42 which induces filopodia formation on the surface of the cells and rapid random migration in all directions (motogenic, chemokinetic). This random migration results, in the case of fibroblasts, in the deposition of extracellular matrix in a normal basket weave organisation. By contrast, in adult wounds, fibroblasts under the influence of TGFb1/TGFb2, which comes from degranulating platelets and monocytes / macrophages, form stress fibres in their cytoplasm (myofibroblasts) and line up in a row at the wound margins, migrating into the wound on mass, which results in the deposition of an abnormal parallel organisation of extracellular matrix, which results in a scar.

We have developed human recombinant TGFb3 as a potential human therapeutic (Juvista). Early clinical trials investigated the optimal dose and dosing regimens for Juvista in human incisions, excisions and skin graft donor sites. We have shown that the effective dose range is 50 – 500ng/100 L/cm of wound margin. The drug is most effective when administered twice, once at the time of surgery and once 24 hours later. Single administration at the time of surgery is efficacious, but there is an additional efficacy benefit from the second injection, 24 hours later. In early clinical trials, we excised the scars 6 – 12 months after dosing, performed histological analysis and demonstrated restoration of a more normal dermal structure in the Juvista treated wounds compared to placebo. Scarring has been assessed at various times post wounding, but typically the endpoint is 12 months post wounding with a follow-up every year for 5 years. The beneficial effects of Juvista first become obvious around 2 – 3 months post surgery, where there is a marked improvement in the Juvista treated scars: the scars are typically less red, less elevated above the skin, narrower, blend in better and have an appearance that is more similar to the surrounding skin compared to placebo treated scars in the same individuals. This benefit is maintained out to 12 months and the longest follow-up to date is 3 years. At which time the Juvista treated scars are still significantly improved compared to the placebo and the magnitude of the effect is similar to that seen at 12 months. On the basis of these observations, plus the histological evidence of the regeneration of a more normal skin structure, we believe that Juvista causes an earlier and permanent improvement in scar appearance. Recently we reported a positive clinical trial in scar revision surgery. These were long and poor scars, where again Juvista resulted in a marked improvement in the subsequent scar compared to placebo treated controls. To date, we have dosed approximately 1,500 patients with Juvista and the safety profile is very favourable. Bioavailability is less than 0.1%, which probably explains the excellent systemic safety record, whilst there are no adverse local tolerability issues at the wound site: if anything, there is evidence of a slight acceleration of healing/maturation. Juvista continues its development in a number of Phase 2 trials and the Phase 3 programme should commence in the European Union in 2008.

We believe this represents a new pharmaceutical approach to the prophylactic reduction of scarring following wounding, which will augment current good surgical technique, suturing and bandaging practices and hopefully bring benefit to both patients and surgeons.
THE ROLE OF THE EPIDERMIS IN THE REGULATION OF SCARRING

Tom Mustoe,  
Professor MED-Surgery, Northwestern University, Huron, USA

The manifestation of excess scarring is excess collagen accumulation in the dermis, and current therapeutic approaches have largely focused on direct efforts to control collagen synthesis, or indirectly via control of growth factor pathways that impact collagen synthesis such as TGFβ. The role of the epidermis in the control of scarring has poorly defined.

The impact of perturbations in the epidermis on inflammation in the dermis has long been recognized and the focus of a very large body of research in the dermatologic diseases, but its role in scarring has been less well studied. A commonly used therapy for hypertrophic scarring has been silicone gel in its various forms, but its mechanism of action has been poorly understood. Our laboratory and others have established the role of silicone gel and other occlusive dressings in influencing epidermal proliferation, synthesis of inflammatory cytokines, and through those effects presumably regulating collagen synthesis. The specific pathways involved are still not worked out, but it is anticipated that increased understanding of these pathways will provide new targets for control of scarring mediated by the epidermis. Recent studies will be highlighted which provide evidence for the importance of the epidermis in the control of scarring.
MECHANICAL TENSION IN SCARRING
DERMAL ORIGIN

Dennis Orgill, Brigham and Women’s Hospital, Harvard Medical School, Surgery Department, Boston, USA

Scarring is a mammalian adaptation to injury. Rather than regenerate, the wound rapidly produces a connective tissue matrix with fibers that are more oriented and smaller than mature dermal connective tissue fibers. This change in fiber morphology results in a connective tissue matrix that is stiff with a lower yield strength than normal dermis. The orientation of the fibers is related to tension applied in wounds. Specific to humans is abnormal scarring including hypertrophic scarring and keloid formation which appear to have a genetic basis, yet within a specific individual the scar reaction appears to be dependent on body location. Mechanical tension appears to be an important risk factor in developing abnormal scarring which may be frequency dependent. Experimental evidence in animal models suggests that tension applied to wounds can result in a rapid change in skin vasculature that is frequency dependent. Mechanical tension also appears to be a model to produce heavier scarring in experimental models. The application of micromechanical forces in wounds appears to be a new method to induce more rapid wound closure. Dermal scarring can be reduced by dermal replacement technologies including fabrication of dermal extracellular matrix analogs. These devices are biodegradable scaffolds that can allow controlled infiltration of cells with a directional matrix production. Rapid epidermal closure also appears to a necessary element for reduction in dermal scarring. Dermal scarring is a central aspect of surgery. A better understanding of scar formation, methods to induce a regenerative response, and better uses of mechanical forces may increase safety and decrease scarring in surgery.

CONTROL OF CELL ORIENTATION AND MIGRATION BY SUBSTRATUM NANOTOPOGRAPHY AND DC ELECTRIC FIELDS

Ann M. Rajnicek, Institute of Medical Sciences, University of Aberdeen, Aberdeen AB25 2ZD, United Kingdom

Successful healing requires efficient cell migration directed toward the wound site during re-epithelialisation. Cells accomplish this within the complex wound milieu, in which multiple, superimposed, and potentially contradictory cues are detected and interpreted by cells. Subtle electric fields (EFs) are generated within wounded tissues and the endogenous EF directs migration toward the wound (the cathode) (see McCaig et al., 2005 for review). Epithelial cell migration and the axis of cell alignment (Rajnicek et al., 2008) are also influenced by the nanotopography of the substratum on which the cells migrate. Since variation in extracellular matrix shape and EFs co-exist at wound edges, we explored the hierarchy of electrical and topographical cues in directing cell migration. Cells from the limbal region of the bovine cornea were plated onto custom-made quartz microscope slides etched with a repeating series of parallel grooves 130 nm deep and 1, 2 or 4 μm across. Cells aligned their long axis parallel to the groove axis and they migrated predominantly parallel to the grooves (contact guidance). When exposed to a DC EF similar to that found in epithelial wounds (150 mV/mm) cells migrated toward the cathode (electrotaxis). However, when an EF was applied at a right angle to the grooves, many cells were recruited from contact guidance, to cathodal electrotaxis, suggesting that the EF is a more potent guidance cue than nanotopography. Pharmacological modulation of rho GTPase signalling indicates that migrating epithelial cells use a cdc42/rho A “molecular switch” to sort vectoral cues, with cdc42 controlling electrotaxis and rho A controlling contact guidance (Rajnicek et al., 2007). Selective manipulation of these signals has potential clinical use for controlling wound re-epithelialisation.

References
ELECTRICAL SIGNALS GENERATED NATURALLY AT A WOUND REGULATE THE CELL BIOLOGY OF WOUND HEALING

Colin McCaig, University of Aberdeen, Scotland

Epithelial tissues such as skin and cornea maintain a steady gradient of voltage across the epithelial barrier layer. This is called a trans-epithelial potential difference (TEPD). Across human skin, it is around +100mV with the inside (extracellular spaces) positive with respect to the outer skin surface. One functional consequence is that wounding the epithelium short-circuits the TEPD, which instantly drops to zero at the wound edge. However, non-wounded epithelial cells maintain their metabolic and electrical activities and this sustains the TEPD of +100mV, one millimetre or so back from the wound edge. The net result is that ionic currents flow continuously out of the wound. Because currents travel through tissues which have a specific resistance to current flow, a steady and persistent voltage gradient is established below and within the multi-cellular epithelial layers. The vector of this voltage gradient is oriented laterally, with the negative pole (cathode) at the wound edge. It is therefore perpendicular to the vector of the TEPD, has a field strength of about 100mV/mm and persists until the epithelium re-seals.

Many cell behaviours that are required co-ordinately for normal wound healing are regulated by this wound-induced electrical signal (McCaig et al, 2005). These include, directed epithelial cell migration, increased epithelial cell proliferation, directed epithelial cell division, directed fibroblast migration, directed endothelial cell elongation and migration and directed neuronal sprouting. Enhancing or suppressing the natural electrical signal at a corneal wound respectively increased or reduced the rate of wound healing. These electrical signals also regulate growth factor release and growth factor receptor expression, both of which play roles in scarring. Whether this naturally occurring electrical signal plays a role in wound scarring is unexplored.

Reference


THE ROLE OF CUTANEOUS INNERVATION IN SCARRING

Fiona Wood
Director of the Burns service of Western Australia

The extent of peripheral nerve damaged as a result of burn injury is dependent on injury type and severity. Investigation of peripheral neuroanatomy and sensory function after burn injury in both the scar and in contralateral or adjacent uninjured tissue was undertaken. A battery of functional tests together with immunohistochemistry of tissue biopsies were used to research the links between neuroanatomy and functional outcome. Sensory function was significantly deficient in scar tissue when compared to controls, with increased threshold for sensation, reduced protective sensation and worse 2-point discrimination. However, total nerve density, when measured using the pan-neuronal marker Protein Gene Product 9.5 (PGP), was the same in both scar and matched site normal skin. Sensory fibre density was measured using Substance P (SP) and Calcitonin gene related peptide (CGRP) immunohistochemistry. Neither of these labels showed significant difference between scar and control tissue.

Total nerve density in scar tissue and control undamaged skin also decreased with severity of injury. These findings demonstrate that loss of sensory function in scar tissue is not related to nerve density and strongly suggests there is a systemic response of the peripheral nervous system to localized injury that reduces peripheral nerve density. This has significant implications for our understanding of the peripheral nervous system response to injury, to the development of potential therapeutics to improve sensory function of scar tissue and to the optimal methodology used for measuring neuroanatomical changes in response to injury.
UPDATES IN SCARRING: BIOLOGICAL ASPECTS

WHEN FIBROBLASTS TURN WRONG:
THE BAD INFLUENCE OF THEIR ENVIRONMENT

Boris Hinz, Laboratory of Cell Biophysics, Ecole Polytechnique Federale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland (boris.hinz@epfl.ch)

Novel strategies are required to counteract tissue contractures characteristic for organ fibrosis, stroma reaction to tumors, host reaction to implants, and formation of hypertrophic scars as after burns. Key element for the development and progression of these pathologies is the excessive contractile force generated by myofibroblasts. Indeed, the contractile state of fibroblastic cells is one parameter to diagnose the progress of wound healing and of fibrotic lesions. I will review different methods to qualitatively and quantitatively assessing cell-generated forces on the level of tissues, of individual cells and of subcellular structures. This includes the wrinkling silicone assay, traction force microscopy, and different varieties of three-dimensional collagen gel contraction. Myofibroblasts do not only exert force but up-regulate contractile features according to the level of stress in their microenvironment. We modulate myofibroblast tension using collagen gels of different stiffness and mechanical load, innovative silicone substrates with tunable compliance, stretchable culture membranes and cell shape restriction by microcontact printing. On the molecular level, we specifically interfere with the contractile apparatus, matrix-adhesion, cell-adhesion and growth factor activation of myofibroblasts. I will present recent findings that both the contractile state of fibroblastic cells and the mechanical microenvironment play crucial roles in activating transforming growth factor beta 1 (TGFβ1) from the ECM. TGFβ1 is essential to convert fibroblasts into contractile myofibroblasts. Our data supports that activation of TGFβ1 via integrin-mediated myofibroblast contraction represents a potential checkpoint in the progression of fibrosis, restricting autocrine generation of myofibroblasts to a stiffened ECM. Because reduced intracellular stress always leads to de-differentiation and/or apoptosis of myofibroblasts, interfering with their stress-perception apparatus emerges as novel strategy to eliminate fibrogenic cells.

TUMORS: WOUNDS THAT DO NOT HEAL.
SIMILARITIES BETWEEN TUMOR STROMA GENERATION
AND WOUND HEALING

Prof. Alexis Desmoulière, Department of Physiology, and EA 3842 (IFR 145), Faculty of Pharmacy, University of Limoges, 2 Rue du Docteur Marcland, 87025 Limoges cedex, France. Tel: (33) 555 43 58 73 / Fax: (33) 555 43 59 50 / E-mail: alexis.desmouliere@unilim.fr

The cooperation between epithelial and mesenchymal cells is essential for embryonic development and certainly plays an important role in pathological phenomena such as abnormal wound healing and tumor progression. Many epithelial tumors are characterized by the local accumulation of connective tissue cells and extracellular material; this phenomenon has been called stroma reaction which shows many similarities in its organization and evolution with the granulation tissue which develops during tissue repair. Dvorak (N Engl J Med 1986, 315:1650-59) compared the tumor stroma which shows a chronic adaptability to the malignant tumors with granulation tissue of a wound and suggested that the tumor resembles a wound that does not heal. One of the cellular components of stroma reaction is the myofibroblast, a modified fibroblast which acquires the expression of alpha-smooth muscle actin, the actin isoform typical of contractile vascular smooth muscle cells, and which is involved in synthesis of significant amounts of collagen and other extracellular matrix components. The myofibroblast is a key cell for the connective tissue remodeling that takes place during wound healing and fibrosis development. Myofibroblasts are also capable of interaction with epithelial cells and other connective tissue cells and may thus control such phenomena as tumor invasion and angiogenesis. Fibroblasts and myofibroblasts constitute the “desmoplastic reaction” and have been suggested to represent an important player in the development of the invasion process. Desmoplasia is considered a response of host cells to inductive stimuli exerted by tumor cells. The control of the myofibroblast activity is essential to promote wound healing. On this basis, the mechanisms of myofibroblast evolution during normal and malignant conditions and the interaction of myofibroblasts with other cells in order to control tumor progression are also very important processes. We suggest that the myofibroblast may represent a new and important target for antitumor therapy.
FIBROBLASTS ARE NOT EQUAL IN FRONT OF WOUND HEALING: NEW CELL THERAPY STRATEGIES

Bernard Coulomb, PhD, Inserm U849. Université Paris-Descartes, Paris (France)

Immediately after injury, several events occur to repair the damaged tissue. Wound healing is a complex and dynamic process involving soluble mediators, blood cells, extracellular matrix components and resident cells, in particular fibroblasts. Briefly, three interactive phases take place during the wound healing process (inflammation, granulation tissue formation and remodeling). Thus, the “quality” of the healing, i.e. disappearance of scar and recovery of tissue functions, depends on a delicate equilibrium, and the remodeling phase, in which fibroblasts play a key role, is crucial for the rebuilding of the tissue as close as possible with origin. When the injured area is too large, grafting becomes necessary, but in very large skin defects such as in burns, the amount of non-injured available skin is not sufficient. Skin substitutes are then alternative solutions. The minimum requirement is to re-establish a barrier function obtained by the presence of the horny layer of the epidermis but there is a consensus as to the necessity of a dermal component. Various dermal substitutes have been developed. Some are acellular matrices, while others combine fibroblasts and extracellular matrix components. The presence of living fibroblasts has been shown to promote the rapid emergence of a functional dermis and consequently to permit efficient epidermal anchoring. Interestingly, efficiency of healing in adult depends on organs or tissues. Thus, the use of fibroblasts from sources other than the dermis is a promising approach in cell therapy strategies to tend towards embryonic healing without scar and fibrosis

Author for correspondence
Bernard Coulomb
Inserm U849 - Réparation Artérielle
Université Paris Descartes
Faculté Necker - Enfants Malades
156 rue de Vaugirard
75730 Paris cedex 15 – France

Phone: 33 1 40 61 55 88 (direct line)
Phone: 33 1 40 61 56 69 (secretariat)
Fax: 33 1 40 61 56 68
E-mail: bernard.coulomb@univ-paris5.fr

CELL THERAPY AND WOUND HEALING: NEW THERAPEUTICAL APPROACH IN THE TREATMENT OF SEVERE RADIATION BURN

Marie Prat and Jean-Jacques Lataillade, Centre de transfusion sanguine des Armées ‘Jean Juilliard’, Département Recherche et Unité de Thérapie Cellulaire, Clamart, France

The therapeutical management of severe radiation burns remains today a challenging issue. The conventional surgical treatment (excision and skin autograft or flap) often fails to prevent unpredictable and uncontrolled extension of the radiation necrotic process. We report here our second experience of therapeutic management of a radiation accident victim combining surgery and cellular therapy using autologous Mesenchymal Stem Cells (MSC). The patient presented a very severe arm radiation burn, which was treated by several surgical times: iterative excisions, skin graft, latissimus muscle dorsi flap and forearm radial flap). Local autologous MSC were administrated as an adjuvant to improve the surgical approach. The clinical evolution (radiation pain and healing progression) was favourable and no recurrence of radiation inflammatory waves was observed during the eight month patient’s follow-up. Mechanisms by which local stem cell therapy administration improves the healing process remain unclear, whatever, our results suggest that MSC act as “cell drug” in modulating radiation inflammatory processes.
NON SURGICAL TECHNIQUES

TREATMENT OF ABNORMAL SCARS. THE ROLE OF SILICONES

Jean Guilbaud

Amongst the abnormal scars, the hypertrophic scars and the keloids (called raised skin scars) pose specific problems. In this review and analysis of the role of silicones on scar treatment the pathogenesis of raised skin scars, which is a combination of biological, genetic, cellular, immunological and endocrinological factors, is successively recalled.

Current scar evaluation methods through the different tools are evaluated and reviewed. A number of available treatments are considered such as surgery, dermabrasion, corticosteroids, radiotherapy, laser therapy, cryotherapy, hydrotherapy and the use of pressure. Finally a careful analysis of the role of silicones including chemical data, differences in silicone structures and reflections concerning their tolerance and their possible mechanisms of action.

Over a period of more than 25 years, a number of clinical studies have been conducted with the use of silicones, which are then evaluated.

From Perkins who developed the earliest silicone gel sheet in 1982, (primarily used under pressure garments in an effort to apply uniform pressure) to the last improvements in quality, thousands of patients have been treated in different pathologies, on fresh and long standing abnormal scars: after burns, in oncology, after different types of surgery and particularly after median sternotomy, in high risk groups.

The evaluation of the results has gained in precision with the new equipments able to precisely evaluate the different parameters.

The great majority of these studies show that silicones are efficient, well tolerated and that they have evolved with the passing years.

There is actually a good evidence of the efficacy of silicones both in the prevention and treatment of hypertrophic scars and keloids, and silicone gel sheeting has now become the standard of care for plastic surgeons.

A new self-drying silicone gel solves many of the problems encountered during the application and use: it requires no fixation, is invisible when dry, is easy to handle, must be applied according to simple rules and its tolerance is very good.

The evaluation of clinical evidence also demonstrates good clinical efficacy.

CORTICOSTEROID TREATMENT FOR KELOIDS

Rei Ogawa, MD, PhD
Division of Plastic Surgery, Brigham and Women’s Hospital, Harvard Medical School, 75 Francis St., MA 02115, USA
Department of Plastic and Reconstructive Surgery, Nippon Medical School
1-1-5 Sendagi Bunkyo-ku, Tokyo 113-8603, Japan

Synthetic corticosteroids including hydrocortisone (T1/2 = 8-12 hr), methylprednisolone (T1/2 = 12-36 hr), triamcinolone (T1/2 = 24-48 hr), and dexamethasone (T1/2 = 36-54 hr) have been widely used for the treatment of keloids in injection or topical (ointment / tape) form. Moreover, drug therapy alone or in combination with surgery / cryotherapy / Laser etc. can be selected on a case-by-case basis. Their effects to reduce excessive accumulated scars are rapid and clear. It has been suggested that the mechanisms are decreases in inflammatory cytokines, chemokines, adhesion molecules, lysosomal enzymes, fibroblast proliferation, and tissue inhibitor of metalloproteinase (TIMP). It can be suggested that the inhibition of TIMP increases metalloproteinase including collagenase, and the excessively-accumulated collagen are degraded rapidly. The disadvantages of corticosteroid treatment are severe pain due to the injection, and menstrual disorder in women, suppression of adrenal cortical function, cataract / glaucoma as systemic side effects. The local side effects are thinning and atrophy of the skin and subcutaneous tissues, steroid acne, capillary dilatation, hypopigmentation etc. These complications sometimes hamper combination treatments, thus, use of corticosteroids for the treatment of keloids needs to be planned carefully.
THE PLASTIC SURGEON’S PERSPECTIVE ON INTRALESIONAL LIPOSOMAL CORTISONE INJECTIONS IN THE CONTEXT OF SCAR REVISIONS: CLINICAL AND EXPERIMENTAL RESULTS

Raymund E. Horch MD
Department of Plastic and Hand Surgery, University of Erlangen-Nuernberg Medical Center, Germany
(Chairman: Univ.-Prof.Dr. R.E.Horch, MD)
Department of Plastic and Hand Surgery, University Hospital Erlangen, Friedrich-Alexander Universität Erlangen Nuernberg, Krankenhausstrasse 12, D-91054 Erlangen

Introduction
Within non-operative measures to treat scars, cortisone injections have become a clinical standard to ameliorate hypertrophic and keloid scars. Experimentally and scientifically this option has not been widely described in the direct context of scar revision together with simultaneous intralesional cortisone therapy. It therefore remained to be proven if local cortisone administration can reduce the fibroproliferative phase of scarring.

Materials and Methods:
Hypertrophic scars were infiltrated with lidocaine and then liposomal steroids were injected directly into the scar until blanching occurred and the whole scar was sufficiently infiltrated. Injections were reiterated within 4 – 6 weeks for six times in 87 patients (42 female, 45 male) between January 2003 and September 2008. In 17 patients additional scar excision utilizing running W-plasties or Z-plasties with immediate cortisone injection into the wound margins was performed.

In all 17 patients the size of the scar was decreased successfully and within a period of 3 to 27 months and no relapsing hypertrophic scar was noted except a partial relapse in a patient with severe keloids.

To further substantiate this clinical finding an experimental animal model was used to analyse this phenomenon. On the ventral ears of New Zealand rabbits hypertrophic scar formation was surgically induced, extending an area of 1.5 x 5 cm. Scars were treated with a single boost application of dexamethasone using a dermojet 36 days following surgery. Untreated sites served as controls. 2, 4, 6, 8 and 40 days following application scars were excised and analyzed.

Results:
Clinically a significant response was noted in all patients with good clinical results and no relapse within the observation period.

Experimentally in histology, immunohistochemistry, planimetry of scar areas, as well as molecular analyzes, a clear impact of dexamethasone on TGFß1 signalling, deposition of cytokine depending matrix protein expression as well as scar contraction was noted.

The fibroproliferative pathway was distinctly blocked by Dexamethasone during post application days 2, 4 and 6 as compared to control sites. However, there was no significant difference on day 8. Interestingly, 40 days following boost, scar contraction as well as protein expression in dexamethasone treated sites revealed higher levels of TGFß1 depending proteins as well as stronger scar contraction than control sites.

Conclusion:
Our experimental results confirm the clinical findings that tissue infiltration with dexamethasone is effective in reducing hypertrophic scaring. The differences seen within the various time points in our animal experiments may however also indicate that the success of cortisone treatment is depending on the interval of application too. Corticoids may therefore be a highly useful tool to expand modern plastic surgical reconstructive options.

Key words: scars, keloids, cortisone, scar surgery, z-plasty
COMPRESSIVE GARMENTS

Claude Roques, MD
Pediatric rehabilitation center - CSRE Lamalou le Haut
34240 Lamalou les Bains, France

Compressive garments have been used since the 1970s to help in the maturation of burn scars. Few clinical studies proving their efficacy are published; several histological studies confirm the effectiveness of pressure therapy on scar maturation and allow assumptions on its mechanisms of action. Pressure obeys the physical law of Laplace and recommendations made by authors on the optimal level of pressure are diverse. Studies of interface pressure show a wide variation depending on the anatomical area investigated. Finally, concave regions are difficult to compress; we use rigid compression achieved by using splints made with high temperature thermoplastic materials. At the present time, the evolution of compressive garments particularly concerns the quality of the fabrics, which improves patient acceptance and compliance with treatment. Compression has side effects affecting the skeleton, particularly in children; however, few validated studies exist in the literature.

SCAR EVALUATION

APPRASING THE EVIDENCE – CLASSIFYING SCARS

Raj Mani, Consultant in Clinical Sciences and Senior Lecturer, Southampton University Hospitals Trust, Tremona Road, Southampton SO16 6YD, UK
Email: rm1@soton.ac.uk

Scars present a major therapeutic challenge. Scars may occur on any patient though some types of scars affect patients from specific backgrounds. Scars present problems to those who suffer and to those who treat the perception of each group being different. In recent years, there has been a great deal of research on the bench and in the lab to understand the pathogenesis though a great deal remains to be understood. Studies of skin quality and perfusion have been reported alongside painstaking observations and attempts to score scars. Nonetheless a universal system of appraisal eludes us.

This paper will appraise the best reported attempts to classify scars and draw from the experience of introducing measurements into chronic wound healing.
CUTOMETER AND DERMASPECTROMETER
IN CLINICAL RESEARCH

Prof. Dr. E. Middelkoop 1,2
1 Association of Dutch Burn Centres, PO Box 1015, 1940 EA Beverwijk, the Netherlands
2 Dept. Plastic Reconstructive and Hand Surgery, VUmc, Amsterdam
emiddelkoop@burns.nl

Comparative clinical trials with measurable outcome variables are scarce in wound healing studies. Parameters that are frequently used are: wound area (difficult to assess in curved body parts) or time to healing (difficult to assess when wound dressings are still partly in place). Quality of healing is perhaps even more difficult to quantify. Usually subjective scales are used to assess the skin/scar quality, such as the Vancouver scar scale, Manchester scar scale, Patient and Observer Scar assessment scale. Although very useful, these scales are observer dependent and results may also reflect the training (or lack of training) of the observer.

Therefore, objective measurements reflecting one or several aspects of scar quality are very useful as outcome parameters of a clinical trial.

In the past we have used the Cutometer successfully in a clinical trial setting (1), where we demonstrated a 33 to 50% increase in elasticity parameters of the scar, 3 months after treatment with a skin substitute.

Also the dermaspectrometer was tested for scar assessments (2). We recently used this device in a randomized clinical trial comparing silicone gel to a placebo cream (van der Wal, unpublished results).

Since measurements with this device which measures scar/skin erythema and melanin indices are so easy to perform and little time consuming, we also used it to routinely evaluate scar quality in an outpatient setting in our clinic. 291 patients were evaluated at 3 months post burn, 266 at 6 months and 179 were evaluated 1 year post burn.

Overall decline in erythema index was 8% between 3 and 6 months, versus 21% between 3 and 12 months post burn. Melanin index is not associated with scar maturation, as indicated by a total reduction of only 10% between 3 and 12 months post burn (E. Middelkoop, unpublished data).

These findings demonstrate that scar maturation is a slow process, and progresses more rapidly after 6 months than before. Since patients may experience considerable complaints from their immature scars, it is important for them to know when improvements may be expected. The present scar evaluation data allow medical specialists to predict more accurately the general time course of scar maturation and improve their information to patients.

Acknowledgements: This work was carried out thanks to support from:
Red Cross Hospital, Beverwijk; VU Medical Centre, dept Plastic Reconstructive and Hand Surgery, Amsterdam
And research grants from: Dutch Program for Tissue Engineering (DPTE); Dutch Burns Foundation


THE PATIENT AND OBSERVER SCAR ASSESSMENT SCALE (POSAS):
A RELIABLE AND FEASIBLE TOOL FOR THE EVALUATION OF BURN AND LINEAR SCARS

A.L. van de Kar, L. Draaijers, F.R.H. Tempelman, E. Middelkoop, P.P.M. van Zuijlen
Institution: Red Cross Hospital, Beverwijk, The Netherlands
Academic Medical Center, Amsterdam, The Netherlands

Background
Although scar evaluation tools are necessary for evidence based scar management, there is no general accepted tool. The opinion of the patients is frequently neglected. However, the POSAS consists of a numeric scale for observers and patients. The Patient scale, evaluates pain, itching, colour, stiffness, thickness and pliability whereas the Observer Scale, allows evaluation of vascularity, pigmentation, thickness, relief, pliability. The scale was developed for subjective scar evaluation of all types of scars.

Objectives
To prove the POSAS to be a suitable tool for the evaluation of burn scars as well as linear scars. During the developing process some adaptations were made.

Methods
In the first study the POSAS was evaluated on burns it was compared to the Vancouver Scar Scale (VSS) and the consistency and reliability were tested. Four observers assessed 49 burn scar areas. The patient scale was completed by the patient. After gaining experience with the POSAS we found it useful to add an extra item, ‘surface area’. Including this item the scale was tested on linear scars. One hundred linear scars were assessed by three independent observers using the Observer Scale. The patient completed the patient scale simultaneously and two weeks later.

Results
Burn scale: the POSAS had a good internal consistency and a better reliability and agreement than the VSS. The finding of the great impact of thickness and itching in linear regression of the patient's opinion was novel. Linear Scale: The internal consistency of the Patient and Observer Scale was good (Cronbach’s $a=0.90$ and $0.86$). The inter-observer reliability for all items was good if assessed by 3 observers. The patient's intra-observer reliability is good ($r=0.94$, $p<0.001$).

Conclusion
The POSAS offers a suitable and reliable scar tool for the evaluation of burn scars as well as linear scars.
THE EPIDERMAL COMPONENT

ZESTEEM (17ß ESTRADIOL) FOR THE ACCELERATION OF RE-EPITHELIALISATION, PARTICULARLY OF SKIN GRAFT DONOR SITES

Professor Mark WJ Ferguson, Renovo, Manchester Incubator Building, 48 Grafton Street, Manchester, M13 9XX, UK. www.renovo.com

Acceleration of the healing of acute wounds is important in a number of clinical situations e.g. for the re-harvesting of skin graft donor sites, for prevention of infection/rapid gain of wound strength and earlier discharge from hospital, and in medically challenged patients, where such healing may be impaired e.g. diabetic, immuno-compromised individuals, irradiated patients, those taking particular medications etc.

We have demonstrated that intradermal injection of 17ß Estradiol markedly accelerates the healing of acute wounds with pronounced effects on the acceleration of re-epithelialisation. Dose response experiments in animals indicate that the optimal dose is 0.1 g/100 l/linear cm of wound margin. The dose response is bell shaped with lower doses being ineffective, whilst higher doses are not only ineffective, but actually retard healing, due to the engagement of different low affinity Estrogen receptors.

On the basis of these preclinical studies, we have developed a novel formulation of 17ß Estradiol for delivery by intradermal injection called “Zesteem”. A Phase II efficacy study, investigating the healing of punch biopsies in human volunteers was conducted. This tested a range of Zesteem doses, administered in a placebo controlled, within patient trial, where 3mm punch biopsies were made on the inner surface of each upper arm, one such biopsy begin treated with Zesteem, the other with placebo in a double blind randomised fashion. At various times, e.g. days 3, 5 and 7 post wounding, the biopsies were completely excised and serially histologically sectioned. The wound width, distance travelled by the epithelium, percentage re-epithelialisation was measured from these histological sections. This trial met its primary endpoint and showed that 0.1 g/100 l/linear cm of wound margin significantly accelerated the re-epithelialisation of these human biopsy wounds.

Split thickness skin graft studies in pigs demonstrated that intradermal injection of Zesteem, statistically significantly accelerated the re-epithelialisation of the skin graft donor site. Accordingly, a double blind, placebo controlled, Phase III trial, investigating the efficacy of Zesteem or placebo in the acceleration of the re-epithelialisation of split thickness skin graft donor sites is underway in 296 patients recruited at a variety of European Centres.

THE ROLE OF THE EPIDERMIS IN SCAR REDUCTION

Fiona Wood
Director of the burns service of Western Australia

Epidermal cover provides an essential barrier. When injured it has a significant capacity to regenerate. However, when the regenerative capacity of the epidermis is overwhelmed the resulting healing process is scar formation. It is clear that rapid epithelialisation therefore has a key role in scar reduction.

The practice of rapid wound closure is widely practiced, most frequently using a Split thickness autograft. A split thickness skin graft may reduce the scar potential but it will always leave a scar. The concept that it is the “gold standard” needs scrutiny. The skin of the given body site at the given time of life should be the aim – a regenerative repair.

The potential for rapid cover of partial thickness injury with dermal preservation reduces the risk of permanent scarring. Secondary manipulation of scars by resurfacing the epidermis with site match epidermal cells can reduce scar. Tissue guided regeneration using epidermal dermal combination technologies may be the future for full thickness injuries.

The exploration of the clinical indications for the use of cells harvested from the dermal epidermal junction will be discussed.
The identification of genetic changes has led to an increased understanding of tumorigenesis, identifying the involvement of putative oncogenes and tumor-suppressor genes. Such approaches are equally applicable to non-melanoma skin cancer (NMSC), such as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). NMSCs represent the most common types of cancer in white population and the incidence of skin cancer shows a steadily increase, reaching epidemic proportions. It could be therefore possible to investigate the key genetic changes and molecular characteristics of each stage of progression of SCC development. DNA copy number changes represent molecular fingerprints of solid tumors and are as such relevant for better understanding of tumor development and progression. In this study, we applied CGH array to identify gene-specific DNA copy number changes in chromosomal skin cancers. Up to now, many studies on tumor cells have been performed under standard in vitro cultures. In standard culture conditions, neoplastic cells, as expected, can grow only in a two-dimensional array that differs from their native three-dimensional organization in nodules or masses and although interesting results have been obtained, three-dimensional scaffolds would better allow the tumor cells to organize into nodules or masses. With the present project we cultured keratinocytes isolated from skin cancer in 3D conditions by using scaffolds made with hyaluronic acid derivatives. These three-dimensional tumor cell cultures can be used to perform in vitro pharmacological studies of antitumoral drugs. Furthermore, by utilizing in vitro reconstructed actinic skin, it is possible also to study genetic changes and in particular to define genetic profile, cell spatial organization, cell/cell and cell/extracellular matrix interactions of skin cancer keratinocytes.
LASER

EXCESSIVE SCARS AND LASERS: OUR APPROACH

P. Bonan, P. Campolmi, G. Cannarozzo, T. Lotti
Department of Dermatological Science, University of Florence, Italian Society of Laser in Dermatology

Hypertrophic (HS) and atrophic (AT) scars and keloids (KL) are aberrations of the wound healing process. In particular, the histological distinction between HS and KL is still controversial due to the absence of reliable and standardized differential morphologic criteria. Moreover, the terms HS and KL have been used inconsistently and interchangeably by clinicians in describing excessive scarring, despite the fact that both require distinct therapeutic strategies. Fortunately, insight into the differential diagnosis of pathologic scars has recently been obtained via the recognition of distinct histological and immunohistochemical differences between HS and typical KL. Increased cellularity and an imbalance between the synthesis and degradation of extracellular matrix components characterize these two aberrations.

In fact, fibroblast number and activity and TGFs-b1 and bFGF (cytokines with varied properties and pleiotropic activities) balance and other families of substances regulation is compromised.

Lasers and light sources capable of cutaneous application have made rapid progress over recent decades, however it has only been during the last few years that their successful use in many skin defects, including atrophic and hypertrophic scars and other cutaneous conditions, has gained widespread acceptance in dermatology. The flashlamp-pumped pulsed dye laser (PDL), the first laser developed specifically for treating vascular anomalies based on the principle of selective photothermolysis, is considered the laser of choice for most benign congenital and acquired vascular lesions, especially port-wine stains. The use of pulsed dye laser in the treatment of hypertrophic scars and keloids has been well documented since 1993 and has proved to be an effective treatment for certain keloids and hypertrophic scars. The combination of intralesional medium-concentrate intralesional corticosteroid (triamcinolone acetonide) and pulsed dye laser (595 nm) in keloidal treatment, which is extremely effective and more patient-friendly, improves the results and seems to be the best approach for treating keloids. Pretreatment with PDL facilitates steroid injections by making the scar edematous and therefore softer, with “steroid sparing effects” (no cases of skin atrophy, telangiectasia or hypo/hyperpigmentation have been reported) thanks to a reduction in the commonly used dose of triamcinolone.

In other studies, variable clinical results have been obtained with the application of superpulsed CO2 laser in the treatment of HS and KL. Some clinical and laboratory findings on the delivery of specific energy resulted in a change in growth factor profiles.

The results of the new technology have led to the introduction of fractional photothermolysis (FP), in which an array of tiny thermal wounds, called microscopic treatment zones (MTZs), are produced, while the tissue surrounding each wound is spared. The MTZs have specific three-dimensional arrangements that can be modified with the fractional CO2 laser depending on the depth to be reached.

The application of fractional CO2 laser enhances “normal” fibroblast replication by stimulating bFGF secretion and inhibiting TGF-b1 secretion

Given the function of these growth factors, FP may normalize wound healing, which explains the beneficial effects of laser on a cellular level and endorses the use of FP in the management of hypertrophic and keloid scars.

In conclusion, our results illustrate the success of the specific multifaceted laser approach in treating excessive scars with minimal side effects and improved skin texture. Moreover, the use of multiple treatment methods may be the best approach for maximizing therapeutic success and minimizing side effects with keloids.
1064NM ND: YAG LASER TREATMENT FOR KELOIDS AND HYPERTROPHIC SCARS

Satoshi Akaishi, MD, PhD, Rei Ogawa, MD, PhD, Kyouko Koube, MD, Sachiko Koike, MD, Hiko Hyakusoku, MD, PhD
Department of Plastic and Reconstructive Surgery, Nippon Medical School
1-1-5 Sendagi Bunkyo-ku, Tokyo 113-8603, Japan

Background
Lasers have been used in the treatment of hypertrophic scars and keloids since 1980’s. Pulsed dye lasers are currently considered the best choice though many studies were suspicious about the effectiveness of them. The purpose of this study is to investigate the effect of 1064nm Nd:YAG laser on hypertrophic scars and keloids.

Methods
16 keloids and 6 hypertrophic scars of 22 patients were treated with a 1064nm Nd:YAG laser with a 5 mm spot size, fluences of 14 J/cm² and pulse widths of 0.3 msec, every 3 to 4 weeks. The biopsies of treated and untreated region were examined and assessed histologically and microscopically.

Results
After 14.05 treatment sessions on the average, clinical assessments of the scars were improved. Clinical assessment (scar volume, erythema, hardness, itch and pain) were classified from 0 points to 3 points. It had decreased from 9.86 to 6.34 points after laser treatment. Histological and microscopical examination revealed the collagen fibers where laser was applied were disrupted after irradiation.

Conclusion
During laser treatments, a decrease in clinical assessment was reported. Histological and microscopical findings will support the effectiveness of Nd:YAG laser. The optimal laser is currently 585 nm PDL, although the recent results of 1064nm Nd:YAG laser are promising.

MANAGEMENT OF EXCESSIVE SCARS WITH PULSED DYE LASERS AND OF POSTBURN SCARS WITH IPL

Régine Bousquet-Rouaud, Dermatologist, L’Arche Jacques Coeur, 266 Place Ernest Granier 34000 Montpellier, France

Cosmetic appearance after skin surgery or traumatic injuries is a key component of patient satisfaction and various lasers have been used to attempt scar improvement in conjunction with other treatments. Concerning hypertrophic scars and keloids, pulsed dye laser (PDL) has been commonly used and recent studies have shown that this new laser protocol strategy is more efficient since it is based on possible mechanisms: collagen remodelling through cytokine stimulation, decreased cellular activity from laser induced tissue hypoxia, reduction in transforming growth factor -β and extracellular matrix expression. Therefore, the procedure is evolving towards a series of low-energy, subpurpuric, short pulsed-laser treatments started at the time of suture removal and delivered weeks to months apart. Laser settings, skin type and scar location should really be studied further.

In the case of postburn scars, the treatment is even more difficult because of their depth and fibrotic nature, so a proper analysis of each specific component of the scars is necessary to combine laser treatments and obtain some improvement following scar revision. Persistent pigmented scars have been successfully treated with intense pulsed light systems using low fluences and multiple passes 3 to 4 weeks apart. Q: Switched lasers are not indicated as they may increase postinflammatory hyperpigmentation.

Concerning postburn hypertrophic scars, the entire surface of the scar should be treated according to the previous recommendations. In atrophic scars, CO₂ or longer-pulsed Er:Yag systems aim to reduce the depth of the scar borders and to stimulate neocollagenesis to fill the scar depression. IPL has been shown to be a successful alternative when using multiple and low energy passes every 4 to 6 weeks.

To conclude, the scar revision strategy has evolved from a wait-and-see approach to an early treatment of the scarring process.
SCAR PREVENTION BY LASER-ASSISTED SKIN HEALING (LASH): A PILOT STUDY WITH AN 810-NM DIODE-LASER SYSTEM

G. Iarmarcoval, A. Capon¹, A. Gossé¹, A. Cornil¹, S. Mordon³
¹: Ekkyo, Meyreuil, France ; 2: Lille University Hospital CHU, Lille, France ; 3: INSERM-IFR 114, Lille University Hospital CHU, Lille, France

Key Words
Wound healing. Scar management. Heat

Background
Cosmetic results obtained after skin surgery are a key component of patient satisfaction. Objectives: This pilot study aimed at evaluating the 810-nm diode-laser system to accelerate and improve, through a thermal action, the healing process in surgical scars of patients with Fitzpatrick skin type I to IV.

Methods
Laser treatment was divided into two groups: 5 patients were treated with low dose (fluence < 80J/cm²) and 6 patients with high dose (fluence > 80J/cm²). Incision was divided into two fields, with only portions randomly selected receiving laser treatment immediately after skin closure. Scars were evaluated by the surgeon and patients at 10 day, 3 month, and 12 month follow-up using a comparative scar evaluation from -5 (worst) to 5 (best). Wilcoxon signed ranks test analyses were performed.

Results
There were no significant differences in scar appearance at 10 day and 3 month follow-up. At 12 months, the treated portion scored significantly better for the surgeon (P = 0.046) and for patients (P = 0.025) compared with the controls. Patients reported greater satisfaction than the surgeon in the treated scar portions (P = 0.020). Average high dose scores were of 2.5 for the surgeon and 3.2 for patients. No side effects were reported.

Discussion/Conclusion
These results suggest that 810-nm laser treatments can change fundamentally the physiology of wound healing if applied in the early phases. Further studies may be warranted to optimize 810-nm diode laser parameters for scar revision, and to better understand the cellular mechanisms leading to laser-induced wound healing.

NEW ANTI SCARRING AGENTS
LOW DOSE 5-FU FOR KELOID THERAPY AND RELAPSE PREVENTION

Wei Liu, MD, PhD, Department of Plastic Surgery, Shanghai 9th People’s Hospital
Shanghai Jiao Tong University School of Medicine, National Tissue Engineering Center of China, Shanghai, China

Keloid is big challenge to physicians because of its difficulty to cure and high recurrence frequency. The common strategy is to eliminate or demolish keloid tissue, such as surgery, high dose chemotherapy, cryotherapy and radiotherapy. These often lead to high relapse rate simply because trauma is a trigger for keloid development. We employed low does of 5-FU for keloid therapy base on the hypothesis that angiogenesis is the major cause for keloid growth and relapse and low dose 5-FU will demolish capillary network inside the keloid without causing tissue necrosis, and will inhibit fibroblast proliferation and thus to inhibit relapse. To achieve this, 5-FU was diluted in lidocaine or along with triamcinolone acetonide to obtain low concentration between 3.45mg/ml-1.4mg/ml. The therapy was performed via intralesional injection every 3-4 weeks followed by every 6-8 weeks. For most patients, it generally took about 3-5 injections to completely relieve the symptom of pain and itching. After 10-15 injections, the keloid became completely flattened with significantly reduced erythema. In the final stage, another 5-10 injections were needed to control local regrowth in treated keloid area with low dose of both 5-FU and steroid and with prolonged injection intervals. Importantly, by destroying vascularity with 5-FU, injected steroid can be better retained in the injected area and thus to increase drug efficacy and reduce side effect. In several hundreds of treated cases, keloids involve various anatomical locations including chest, earlobe, limbs and others. Most patients could achieve a flattened keloid without obvious recurrence and symptom after long term therapy. In some cases, keloid tissues were remodeled into normal-looking skin.
JUVISTA (TGFβ3) A POTENTIAL NEW HUMAN PHARMACOLOGICAL AGENT FOR THE PREVENTION AND REDUCTION OF SCARRING

Professor Mark WJ Ferguson, Renovo, Manchester Incubator Building, 48 Grafton Street, Manchester, M13 9XX, UK – www.renovo.com

Scarring is a major clinical problem resulting in adverse aesthetic, functional and psychological sequelae. Many years ago we discovered that experimental skin wounds made on experimental animal embryos healed perfectly with no scars. We investigated the cellular and molecular basis of scar free healing, asking fundamental questions such as, when during embryonic development does scar free healing turn into scar forming healing and what are the cellular and molecular correlates? In mice, skin wounds made on or before embryonic day 16 heal without a scar, whereas those made thereafter scar. There are many cellular and molecular differences between embryonic day 16 wounds, which heal without a scar and those made later which scar. But the question is which of these are epiphenomena e.g. related to development of the embryo and which are causative of the scar free healing. We have shown that members of the Transforming Growth Factor Beta family are particularly important for the scar free healing phenotype. Specifically embryonic wounds that heal without a scar have high levels of TGFβ3, whereas adult wounds which scar have much lower levels. TGFβ3 is an endogenous molecule, important in the development of the skin. Skin volume in the developing mouse embryo increases rapidly and one of the important morphogenetic factors involved, is TGFβ3. Experimental addition of human recombinant TGFβ3 to skin wounds (incisions and excisions) in adult mice, rats and pigs, results in wounds which heal with markedly improved scarring compared to placebo treated controls. Furthermore, wounds on mouse embryos, genetically null for TGFβ3, made on or before embryonic day 16, heal with a scar by contrast to a wound on a normal mouse embryo (with normal levels of TGFβ3) which heal without a scar. These observations have confirmed the importance of TGFβ3 in the scarring process and have allowed us to investigate the underlying cellular and molecular effectors. TGFβ3 increases migration of both fibroblasts and keratinocytes. It does so by stimulating the Ras GTPase CD42 which induces filopodia formation on the surface of the cells and rapid random migration in all directions (motogenic, chemokinetic). This random migration results, in the case of fibroblasts, in the deposition of extracellular matrix in a normal basket weave organisation. By contrast, in adult wounds, fibroblasts under the influence of TGFβ1/TGFβ2, which comes from degranulating platelets and monocytes / macrophages, form stress fibres in their cytoplasm (myofibroblasts) and line up in a row at the wound margins, migrating into the wound on mass, which results in the deposition of an abnormal parallel organisation of extracellular matrix, which results in a scar.

We have developed human recombinant TGFβ3 as a potential human therapeutic (Juvista). Early clinical trials investigated the optimal dose and dosing regimen for Juvista in human incisions, excisions and skin graft donor sites. We have shown that the effective dose range is 50 – 500ng/100 μL/cm of wound margin. The drug is most effective when administered twice, once at the time of surgery and once 24 hours later. Single administration at the time of surgery is efficacious, but there is an additional efficacy benefit from the second injection, 24 hours later. In early clinical trials, we excised the scars 6 – 12 months after dosing, performed histological analysis and demonstrated restoration of a more normal dermal structure in the Juvista treated wounds compared to placebo. Scarring has been assessed at various times post wounding, but typically the endpoint is 12 months post wounding with a follow-up every year for 5 years. The beneficial effects of Juvista first become obvious around 2 – 3 months post surgery, where there is a marked improvement in the Juvista treated scars: the scars are typically less red, less elevated above the skin, narrower, blend in better and have an appearance that is more similar to the surrounding skin compared to placebo treated scars in the same individuals. This benefit is maintained out to 12 months and the longest follow-up to date is 3 years. At which time the Juvista treated scars are still significantly improved compared to the placebo and the magnitude of the effect is similar to that seen at 12 months. On the basis of these observations, plus the histological evidence of the regeneration of a more normal skin structure, we believe that Juvista causes an earlier and permanent improvement in scar appearance. Recently we reported a positive clinical trial in scar revision surgery. These were long and poor scars, where again Juvista resulted in a marked improvement in the subsequent scar compared to placebo treated controls. To date, we have dosed approximately 1,500 patients with Juvista and the safety profile is very favourable. Bioavailability is less than 0.1%, which probably explains the excellent systemic safety record, whilst there are no adverse local tolerability issues at the wound site: if anything, there is evidence of a slight acceleration of healing/maturation. Juvista continues its development in a number of Phase 2 trials and the Phase 3 programme should commence in the European Union in 2008.

We believe this represents a new pharmaceutical approach to the prophylactic reduction of scarring following wounding, which will augment current good surgical technique, suturing and bandaging practices and hopefully bring benefit to both patients and surgeons.

MULTI-MODALITY SCAR MANAGEMENT PROGRAM

Professor Alan D Widerower - MBChB; FCS (SA); MMed (Wits)(Plast) FACS
University of the Wiwatersrand and Linksfield Hospital, Johannesburg, South Africa
Presentation through telephone conference
INTERACTIVE SESSION WITH PATIENTS

INSIGHTS INTO DIFFERENCES IN PHYSICIANS’ AND PATIENTS’ PERCEPTIONS ABOUT SCARRING

Leroy Young MD, FACS* and John Hutchison PhD, FRCP**
*BodyAesthetic Research Center, St Louis, MO; **Renovo Ltd, Manchester, UK

Background: A large body of evidence indicates that disfiguring scars have a major psychosocial impact on patients. However, little is known about the impact of scars resulting from routine surgical procedures. To gain greater insights, a semi-quantitative study investigating perceptions about scarring was conducted.

Methods: An independent US/UK-based research organization conducted structured surveys on scarring in two cohorts: 1) US patients who had undergone a surgical procedure within 6–24 months prior to survey (n=97, aged 18–69; 67% female; 52% Caucasian; 27% African American; 12% Hispanic) and 2) physicians (n=24: 19 plastic surgeons, 5 aesthetic dermatologists; 18 based in the USA, 6 in the UK). Patients were recruited by an independent agency that visited hospitals and conducted a screening interview that recorded demographic information. A patient cohort was selected with a demographic profile that was representative of the general community in terms of age, gender and ethnicity. Selected patients were invited to attend a face-to-face interview where they completed a Self Completion Form (SCF). In the SCF, participants were presented with a series of statements and asked to indicate how strongly they agreed with each statement by providing a score ranging from 1 through 7, with “1” indicating strong disagreement and “7” strong agreement. Physicians were recruited and surveyed via telephone interviews using a similar format of questionnaire, but with questions tailored to physicians.

Results: The majority of patients (87%) indicated they had at least one scar that they wished was less noticeable or felt more like the surrounding skin. In addition, 83% agreed that people are very self-conscious about scars on visible body sites, and more than half (55%) agreed with the idea of going to any length to reduce the possibility of scarring. Two-thirds of patients (64%) disagreed that there was no need to hide or medically alter scars. Many patients (59%) felt they were more concerned than their surgeon about scarring from their recent surgery, and approximately half (45%) also perceived that their surgeon was insensitive to their concerns about scarring. However, only 52% discussed the possibility of scarring with their surgeon before surgery, and only 47% discussed the state of their scar after surgery with their surgeon. By contrast, all of the plastic surgeons and aesthetic dermatologists surveyed agreed that scarring on visible body sites is a concern for patients, and say they make every attempt to minimize scarring when performing a surgical procedure. The majority of patients (81%) and physicians (96%) said they would value additional treatments that add to surgical techniques for minimizing scarring. However, results showed that patients value even small improvements in scarring, including some that were not considered clinically meaningful by the physicians surveyed.

Conclusions: These data confirm that patients are highly concerned with the appearance of scars following routine surgical procedures and want less noticeable scars that more closely resemble surrounding skin. Plastic surgeons and aesthetic dermatologists are well aware of their patients’ concerns about scarring, but the study raises questions about whether this is true of the wider population of surgeons. Because patients value even small improvements in scarring, surgeons should be encouraged to discuss their patients’ expectations about scarring, explain what can be expected after surgery, and reflect on their own perceptions about the impact of scarring on their patients.
NON CELLULARISED DERMAL SUBSTITUTES

DEVELOPMENT OF A DERMAL SUBSTITUTE

Prof. Dr. E. Middelkoop 1,2
1Association of Dutch Burn Centres, PO Box 1015, 1940 EA Beverwijk, the Netherlands
2Dept. Plastic Reconstructive and Hand Surgery, VUmc, Amsterdam
emiddelkoop@burns.nl

Keywords: dermal substitute, artificial skin, burns, wound healing

The effects of a dermal substitute on wound healing parameters such as epithelialisation, contraction and scarring are influenced by the physical and chemical properties of the substitute. In cell culture experiments different materials can be screened for basic suitability as dermal scaffolds. Screening methods are available for cytotoxicity, cell proliferation, contraction of the material, degradation, collagen synthesis etc.

We tested several materials with different physical and chemical compositions. Glutaraldehyde treated reconstituted sheep collagen was tested and found cytotoxic for cells (fibroblasts). Degradation of several materials was also established (1).

Immunological and inflammatory reactions that depend on blood circulation can not be mimicked in vitro and have to be studied in vivo. Therefore, we studied materials that showed good characteristics in vitro in our in vivo porcine excisional wound model. In this model up to 14 10 cm² wounds can be evaluated in one animal. Gross giant cell formation and foreign body reactions were noted in reconstituted collagen treated wounds, as well as in wounds treated with several other crosslinked collagens (2).

In further evaluations we focussed on native bovine collagen materials, with or without addition of other extracellular matrix molecules. Dermal regeneration, measured by calculating the area with mature collagen bundles in polarized light microscopy at 6 weeks post wounding, was improved compared to standard treatment of split skin graft only. Wound contraction was reduced, number of myofibroblasts was low and elastin regeneration more advanced in wounds treated with a dermal substitute of native collagen and elastin hydrolysate.

In clinical evaluation, we demonstrated that this same material improved skin elasticity parameters significantly already 3 months post injury in reconstructive wounds and still showed a trend of improvement after 1 year (3). Also long term follow up of Integra artificial skin, which is composed of bovine collagen with chondroitin sulphate, crosslinked with glutaraldehyde, shows better quality of burn scars compared to standard treatment (4).

In conclusion, dermal substitutes have been shown to be successful in the reduction of scarring in clinical settings. Problems associated with their use are: risk of infection, which may cause loss of the material, and slow vascularisation of the substitute. The latter is the reason that for Integra®, usually a 2 step procedure is carried out. Integra® is placed on the wound bed in the first step, allowed to vascularise during some weeks, and afterwards permanent closure of the wound is achieved in a second procedure, in which a graft is placed on top of the dermal substitute. Also for Matriderm®, slow vascularisation may cause a reduction in outgrowth or even reduced take of the graft, even though this material allows a one step procedure. Improvement of vascularisation rates might be found in small adaptations in the material (composition and/or structure) or in the addition of growth factors or cells. Finally, more randomized clinical studies are wanted which compare the use of innovative materials such as dermal substitutes to standard of care, using objective and measurable outcome parameters, to demonstrate effectiveness and show the limitations of these techniques.

Acknowledgements: This work was carried out thanks to support from: Red Cross Hospital, Beverwijk; Vu Medical Centre, dept Plastic Reconstructive and Hand Surgery, Amsterdam And research grants from: Dutch Program for Tissue Engineering (DPTE); Dutch Burns Foundation

References
ONE SINGLE PROCEDURE USING DERMAL MATRIX IN SKIN REPLACEMENT

Luc Téot, Hôpital de Lapeyronie, Montpellier, France

The use of dermal substitute has been popularized after the pioneer works of Burke & Yannas more recently the development of new devices composed of collagen and/or collagen and elastin has been proposed. In this limited series of 20 clinical cases, we describe the interest and limits of the use of Integra single layer and Matriderm in skin reconstruction, in burns as well as in reconstructive surgery. This preliminary series show the possibility of adhesion of this new substitute to the underlying anatomical structure and its capacity to cover noble structures as a freshly exposed bone. Some haemostatic capacities can be observed, as well as the possibility to cover immediately the dermal substitute using a split thickness skin graft. This one single procedure transform the interest of using these materials, limiting the length of stay in the hospital and reducing the cost. Some differences between simple skin graft and single procedure using dermal matrix were observed, mainly time for obtaining a complete healing, varying from 2 to 7 weeks, depending on the patient profile and the use of negative pressure therapy associated to the post operative period.

INTRODUCTION OF ARTIFICIAL DERMIS “PELNAC®”

Shuji Kawabata, Gunze Limited, Tokyo, Japan

PELNAC® is an artificial dermis consisting of an atelocollagen sponge layer with low antigenicity and a silicone layer, which was developed by Gunze Limited, Japan in 1993.

Indications
PELNAC® is used to replace and regenerate damaged or defected dermal layers, and widely used for the granulation in full-thickness skin defects caused by 3rd grade burn injuries, traumatic skin defects, skin defects after excision of tumors or nevus, donor site of skin flap, and so forth. No adverse reactions are reported in the 60 cases included in the clinical trials conducted before Japanese manufacturing approval and 807 patients included in PMS (Post-marketing surveillance) study.

Features
PELNAC® is a ‘freeze-dry’ products (patented manufacturing method), so that very easy to store and transport. It also enables surgeons easily to handle and adapt for the damaged parts without wasting a time.

Marketing status
Since March, 1996, PELNAC® has been in the Japanese market, and it is presently used in the Asian and the Latin American countries, too, as one of the innovative products in the wound management field. The CE marking will be available shortly within 2008.

Products line-up
Now the following types are available:
- Standard Type: 2-layered material consisting of collagen sponge and silicone film.
- Fortified with mesh type: Mesh (Non-adhesive silicone gauze) for reinforcement of tensile strength is inserted into silicone film of PELNAC® standard type. Better for suturing.
For both standard and fortified type, five sizes are available, 40mmx30mm (SSS), 40mmx60mm (SS), 82mmx60mm (S), 82mmx90mm (M) and 82mmx120mm (L).
- Two new types, Mono layered type (Collagen sponge only) and Drain holes type, are under development and these new types will be soon available.
CELLULARISED DERMAL SUBSTITUTES

IN VITRO RECONSTRUCTION OF VASCULARISED SKIN

Giovanni Abatangelo and Barbara Zavan
Dept. of Histology and Medical Biotechnology, Faculty of Medicine, University of Padova-Italy

Background
Successful in vitro reconstruction of skin requires the inclusion of several cell types that give rise in co-culture to the specific elements present in native skin, and the appropriate scaffolding structure to house and support these cells. In addition to the two main structural components, epidermis and dermis, one critical apparatus of the skin is a capillary network that guarantees adequate perfusion of nutrients and oxygen. The aim of the present study was to develop an in vitro co-culture system that assumed the human dermal-epidermal architecture and included a microcapillary network in a three-dimensional biomaterial that guaranteed ease of handling in a clinical setting.

Methods and Results - Endothelialized skin (ES) was prepared by co-culturing three human cell types: keratinocytes, fibroblasts, and endothelial cells, obtained from human full-thickness skin samples, in scaffolds produced from modified hyaluronic acid. Results were evaluated by histological and immunohistochemical analyses at different time points. In vitro, engineered skin obtained with this composite culture developed into a well-differentiated upper layer of stratified keratinocytes lining a dermal-like structure, in which fibroblasts, extracellular matrix and a microvascular network were present.

Conclusions – The most important novel findings are: isolation of three different cell types (keratinocytes, fibroblast and endothelial cells) from a single skin biopsy; and successful enrichment of a biodegradable three dimensional scaffold with an autologous extracellular matrix that supports the proliferation and differentiation of keratinocytes and endothelial cells. Furthermore, the exceptional handling properties of the scaffolds tested should reflect greater facility of handling in the clinical setting, particularly with regard to what has been evaluated clinically up to now. These improvements should facilitate the take of a graft, particularly in full thickness wounds.

ALLOGENEIC CELL THERAPY FROM THE BENCH TO COMMERCIALIZATION

Vincent Ronfard PhD, Organogenesis Inc. Canton MA

Over the last 30 years, applied research has focused on the development of new therapeutic agents to treat skin wounds. Parts of these therapeutic agents were based on cellular and tissue therapy and the novel concept of bioengineered tissue has emerged. These products were initially designed for the treatment of venous leg ulcers and diabetic foot ulcers, there are reports of their application in other indications, such as epidermolysis bullosa, burns and acute wounds. The mechanism of action of these bioengineered products is not fully elucidated, and different products may have different modes of action. This talk will provide an overview of the literature regarding the use of allogenic cells in the fabrication of a bioengineered construct including the importance of cell sourcing, product/process development and manufacturing. Lastly discussion will focus on the future development of allogenic stem cell use.
EXTRA CELLULAR MATRIX PROMOTERS

EXTRACELLULAR MATRIX AND USAGE OF AMELOGENIN TREATMENT IN CHRONIC WOUNDS

Magnus S. Ågren, Department of Surgery K and Copenhagen Wound Healing Center, Bispebjerg Hospital, Copenhagen, Denmark. maa02@bbh.regionh.dk

The molecular mechanisms responsible for non-healing of chronic venous leg ulcers are complex. It is known from several independent investigations that the chronicity of a venous ulcer affects healing, longer duration ulcers being slower to heal. Furthermore, the proportion of senescent non-proliferating fibroblasts increases with ulcer duration, which suggests a possible correlation with the clinical observations. In addition, fibroblasts isolated from chronic venous leg ulcers exhibit impaired extracellular matrix (ECM) remodelling. Angiogenesis, a key component in wound healing, is often impaired in chronic venous leg ulcers.

Amelogenins are ECM proteins that, under physiological conditions, self-assemble into globular aggregates. Attachment by fibroblasts to these structures increases the endogenous secretion of multiple growth factors e.g. of the pro-angiogenic vascular endothelial growth factor (VEGF) and the pro-fibrotic transforming growth factor-β1 (TGF-β1). Amelogenin is the principal component of Xelma® (Mölnlycke Health Care, Gothenburg, Sweden), a novel ECM preparation that restores cellular signalling in chronic wounds. A recent randomised controlled trial concluded that hard-to-heal venous leg ulcers, i.e. ulcers with a surface area ≥10 cm² and duration of ≥6 months, benefited the most of topical application of amelogenin as an adjunct treatment to compression. The cellular mechanisms of action for these positive therapeutic effects are unknown.

Extensive in vitro studies have shown that amelogenin ameliorate the depressed proliferation and remodelling ability by chronic fibroblasts. Amelogenin treatment also switched the chemokine expression by the chronic fibroblasts into one resembling the expression profile of acute normal fibroblasts. Amelogenin significantly increased microvessel outgrowth in the organ-cultured chick aortic arch assay possibly through enhanced VEGF production.

Restitution of fibroblast phenotype and angiogenic response by amelogenin in chronic venous leg ulcers may contribute to the beneficial clinical effects. The experimental basis for these hypotheses will be presented together with background information on the role of ECM in wound healing with emphasis on chronic wounds.
AGING AND SCARS

S Meaume
Dermatologist and gerontologist
Assistance Publique Hôpitaux de Paris
94205 Ivry sur Seine

Aging is a complex problem that result in functional and aesthetic change in the skin; as advance in skin biology have broadened understanding of the aging process, new treatment have been developed to retard aging and rejuvenate skin. As an example, the use of peptides is becoming more popular among consumers seeking effective treatments for aging. Their main function is to control cell proliferation and to stimulate the synthesis of collagen. Peptides also function as cellular communicators by providing instruction as to how specific cellular structures are intended to function. Much what is know about peptides comes from the study of wound healing and studies in fetal skin that show the presence of growth factors, which result in scarless healing and a relative lack of inflammation. This natural healing process is dependent on biologic factors that signal the start of the repair process; macrophages secrete substances such as growth factors that begin a cascade of events leading to wound healing. Because skin aging is partially characterized by decrease in collagen synthesis and increase in collagen breakdown, biologic factors that stimulate collagen should slow or prevent this process. Aging process produces also tiny wounds or microscars, that over a lifetime become macroscars visible in the skin as wrinkles, irregular pigmentation, and a dry, leathery appearance. Sunlight accelerate this genetic destruction, whereas sun protection prevents this damaging process. Relationships between pathologic scars and infection, persistence of inflammation linked to mechanical factors, even rarely observed will be discussed. Some clinical cases of scars in elderly will be presented also to the audience for discussion.

ANTI-SCAR THERAPIES IN BURN WOUNDS:
FROM START TO FINISH!

Stan J. Monstrey, Department of Plastic Surgery, University Hospital Gent, Gent, Belgium

Improved resuscitation techniques and optimal treatment in specialized burn centres have resulted in increased survival of patients with extended and deep burns.

Nowadays, emphasis in burn treatment is shifting towards reducing scar tissue formation.

Anti-scar therapies in burn patients should not only be started after the healing of the burn wound, but already be considered from the time of the injury on. Indeed, cooling of acute burns can make the difference between a superficial and a deep second degree burn, thus avoiding scar formation. Adequate systemic fluid therapy can prevent secondary deepening of burn wounds by improving microcirculation in zones of stasis. An exact assessment of burn depth (and the indication to operate) can be provided with a Laser Doppler Imaging (LDI) thus avoiding unnecessary scar formation caused by grafting superficial wounds or prolonged conservative treatment of deep burn wounds.

The local treatment of burn wound should provide an optimal environment for wound healing and reduce all inflammation while additional anti-infection therapy (silver, iodine, honey) might be required to avoid infection and the risk of deepening of the burn wounds.

Surgical therapy can influence the resulting scar through a precise indication for escharotomy and grafting, by the use of meshed grafts and Meek expansion and by dermal substitutes or flap surgery. Physical therapy can influence early scar formation and local anti-scar therapies such as pressure garment and silicone application are applied in various forms to improve the final scars. Skin hydration and moistening can help to keep the scars supple and prevent itching while sun blocks protect against UV radiation and secondary pigmentation.

An update will be provided on all recent strategies to further improve function and aesthetics of scar formation after burns.
POST ACNE SCARRING: PHYSIOPATHOLOGY, CLASSIFICATION AND LASER MANAGEMENT

Dr LE PIlLOUER-PROST Anne, dermatologist, Marseille, France
doclepillouer@free.fr
Dr BONAN Paolo, dermatologist, Florence, Italy
pbonan@vodafone.it
Thanks to the support of the laser company DEKA
www.dekalaser.com

The real frequency of PAS is difficult to estimate around 14 % PAS for women and around 11 % PAS for men (1999, USA). A basis for developing successful treatments for post acne scarring (PAS) is a greater understanding of its pathogenesis, genetic reasons why certain people scar and others do not, the inflammatory mediators and immunological factors…Classification, grading and scales of both hypertrophic and atrophic disease must be known for an optimum management. It’s also important to have in mind all the therapeutic armamentarium and how to use specific, combined and step by step treatments for each patient.

Vascular lasers, pigmentary lasers, Intense pulsed light sources: Either for red or pigmented persistent mackles, or for hypertrophic or telangiectatic lesions or for remodeling effect. For remodeling, the literature is poor or moreover ambiguous. Currently there is no scientific evidence of their long term efficiency.

Infra-red or « non ablative » lasers (1320, 1450, 1540, 1064 nm)
Used since the years 1998-2000, their principle, thanks to their depth of penetration, is to sufficiently warm the dermis without altering the epidermis. 1320, 1450 and 1540 nm lasers were marketed firstly only for non ablative dermal remodeling (wrinkles and PAS). The results in series remind rather modest, delayed, inconsistent from a patient to another and almost invisible on photos!

1064 nm Nd-YAG lasers seem more interesting in this field: Numerous dermatologists are already equipped with them in their office for other indications and we have rediscovered them with efficiency for dermal remodeling. Personal clinical cases treated with the device “Synchro HP Platform” from DEKA will be presented during the workshop.

Traditional ablative lasers for « resurfacing » (CO2, Erbium)
We shall not return in detail on their principles neither on the per nor post operatively modalities which were already detailed two years ago during the First Scar Meeting of Montpellier ( www.scar-club.com ). They have been used for many years as the “gold standard” for dermabrasion with up-to-date scanners and various numbers of passes per session. Results are almost very good or excellent but there are infrequent but frightening adverse effects.

Fractionated photothermolysis lasers : « fractional lasers »
They undoubtedly represent the most recent and popular technology for atrophic PAS laser management. The leader is the device Fraxel ®, marketed for 4 years in the USA. The principle is to create a dense network of microscopic thermal wounds in “tiny wells” in the dermis. They are called MTZs (micro thermal zones) and are supposed to induce, in and around them, columns of remodeling effect. The depth and width of the columns depend on wavelength and parameters used. By preserving surrounded tissues and epidermal islands, postoperative after-effects are minimized, reepithelialization is quick and we can treat extra facial areas (neck, hands, chest…). For every patient according to the PAS severity, the phototype, the accepted cares and downtime, the budget ...we realize a specific plan of treatment. More and more non ablative and ablative fractional devices are available every month this year!

For the ablative CO2 device SmartXide-dot of DEKA we tested, we obtained constantly, in 3 sessions spaced out from 2 to 4 weeks, without anaesthesia and with 3 to 5 days of desquamation (« sun tanning” appearance), an improvement and a satisfaction of the patient. The main advantages of this device in its “family” of fractional CO2 devices seem to us to be its power (30W), the small diameter of the spot measured at the skin level, the possibility of treating without anaesthesia, easily at a moderate cost. Clinical cases with videos and photos will be presented.

Conclusion: For moderate and severe grades of PAS, if the treatment has historically been limited by the morbidity of most treatments for only partial improvement, now the development of new techniques, notably fractional lasers which offer more favourable benefit/risk profile, will help practitioners to be more involved in the management of this common and stressful disorder.
ORAL PRESENTATIONS

A. Research
Thursday 25 September 2008, 17h00 to 18h30
Main Auditorium

Abstracts: A01, A02, A08, A09, A10, A11, A12, A13, A14, A15, A16, A17

B. Clinical Trials
Thursday 25 September 2008, 17h00 to 18h30
Actes Room

Abstracts: B01, B02, B03, B06, B07, B08, B09, B10, B11

C. Clinical Case Reports
Friday 26 September 2008, 17h00 to 18h30
Actes Room

Abstracts: C01, C02, C03, C04, C05, C06, C07

POSTER PRESENTATIONS

A. Research
Duques Room

Abstracts: A01, A02, A03, A04, A05, A06, A07

B. Clinical Trials
Duques Room

Abstracts: B01, B02, B03, B04, B05

C. Clinical Case Reports
Duques Room

Abstracts: C01, C02, C03, C04, C05

Posters will be on display on the Duques Room on Thursday 25 September, from 09.00 to 18.30 and on Friday 26 September, from 09.00 to 18.30.
A01. Neurogenic inflammation induced by mechanical stretch: study of a fibroproliferative disease mechanism

Oral & Poster Presentation

Michael S. Chin1,3, Rei Ogawa MD PhD1,2, Luca Lancerotto MD1,3, Jasmine C. Mathews1, Satoshi Akaishi MD2, and Dennis P. Orgill MD PhD1

Background: The mechanisms of fibroproliferative diseases (FPD) of the skin, such as keloids and hypertrophic scars, are not completely understood due to the lack of ideal animal models. As mechanical stress appears to be an important role, we are studying mechanotransduction factors in FPD. We propose that mechanical stress increases neuropeptides in the skin, causing neurogenic inflammation. The resulting abnormal collagen production may evoke keloid and hypertrophic scar formation.

Objectives: We studied neurogenic inflammation in vivo with a servo-controlled mouse skin stretch model.

Methods: A computer-controlled device was attached to the dorsal skin of wild-type mice (n=20). We applied stretching force at either 50 gm/cm2 continuous or 50 gm/cm2 cyclically (2 min on/1 min off) for a duration of 4 hours. At 2 and 10 days, skin was harvested for histological and immunohistochemical analysis for neuropeptide and growth factor accumulation: substance P (SP), calcitonin gene-related peptide (CGRP), nerve growth factor (NGF) and transforming growth factor - beta 1 (TGF-B1).

Results: In the epidermis and dermis, both cyclic and continuous stimulation resulted in a significant increase in accumulation of neuropeptides and growth factors at 2 days, returning back to baseline at 10 days. In addition, cyclic stretch led to significantly more expression of SP, CGRP, NGF, and TGF-B1 than continuous stretch at 2 days.

Conclusion: Our results demonstrate that mechanical forces have the potential to induce neurogenic inflammation of the skin, which may be one of the causes of keloids and hypertrophic scars. Our results support previous suggestion that mechanical stress, stimulates mechanosensitive nociceptors on sensory fibers in the skin. While further experimental studies are needed, our hypothesis may provide new insights into the etiology and pathology of FPD.

A02. Skin camouflage therapy in Scar management – The Royal London experience

Oral & Poster Presentation

Davies K, Abreo N, Kulendren D, M Syed , Shibu M
The Royal London Hospital, London, UK

Introduction
Scars can be extremely difficult to treat especially if they are in exposed areas of the body. These visible scars can result in immense psychological trauma resulting in loss of self esteem and can affects the individual's confidence and morale.

Objective: Snapshot evaluation of the Nurse led Skin camouflage service for management of scars

Methods: We present a snapshot evaluation our 2 year experience of cosmetic camouflage in a nurse led setup for the management of surgically not improvable scars. A retrospective evaluation of 25 consecutive patients was done over a four week period by a telephonic survey using a pre-designed service evaluation questionnaire.

Results: The demographics of the evaluated patients were: Male: Female 17: 8; Age range 20-25 years, Ethnic origin: 6 Asian ,8 Afro-Caribbean; Aetiology 18 trauma ,7 elective. A variety of scar types were camouflaged – Hyperpigmented-10, hypertrophic-9,keloid-Hypopigmented-3,flat-1; 76% of patients confirmed that scars affected their self confidence pre-camouflage and 92% of patients confirmed significant improvement in self esteem following camouflage. The average waiting time for treatment was less 2 weeks.

Conclusion: Camouflage therapy is an extremely effective strategy for management of difficult unsightly scars which cannot be surgically improved or masked. Although it is not a permanent solution it is economical, can be easily learnt and done by the patient themselves. This snapshot review of our service confirms that a nurse led perspective for camouflage therapy makes it very economical and efficient service without compromising on quality.

A03. Use of Electronic callipers for assessment of keloid scars-An economical, objective and effective method

Poster Presentation

Jimenez G, Kulendren D,Davies K, Syed M
The Royal London Hospital, WhiteChapel, London, United Kingdom

Background: Management of keloid scars is handicapped by lack of readily available objective tools for the assessment of keloid scars. Although 3D camera provides the best three-dimensional assessment, it is costly and not readily available in clinics.

Objective and Methods: We trialled the use of digital electronic Vernier callipers(Trojan Digimatic callipers 150mm, UK) with specifications: Resolution - 0.01mm (.0005"),Measuring range - 0.01-150mm ,Instrumental Error - + /- 0.03mm ,Repeatability - 0.01mm,Response speed - Up to approx 1600mm/s. The callipers was used to serially measure the maximum length, maximum width and max height of the scar.
Results: The calliper was trialled by three independent practitioners—a plastic surgery registrar, a keloid specialist nurse and an occupational therapist. To validate the instrument 21 individual measurements were performed. The results are tabulated below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean(mm)</th>
<th>Standard Deviation(SD)(mm)</th>
<th>Range(mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length</td>
<td>1.20</td>
<td>0.99</td>
<td>7.90-98.8</td>
</tr>
<tr>
<td>Width</td>
<td>0.73</td>
<td>0.55</td>
<td>6.30-77.24</td>
</tr>
<tr>
<td>Height</td>
<td>0.51</td>
<td>0.40</td>
<td>0.54-4.04</td>
</tr>
<tr>
<td>Overall</td>
<td>0.73</td>
<td>0.30</td>
<td>0.54-98.8</td>
</tr>
</tbody>
</table>

Inter-individual variation

Conclusion: An electronic calliper seems to provide an objective, cheap and reliable method for assessment of keloid scars. Although the measurements are easily and objectively assessed in a 2 dimensional plane, an objective measurement of height could also be measured. Drawing from the findings of our study, the measurements become less reliable when measuring heights; which are usually in the range of 0.5-1cm. We recommend the use of electronic callipers as a basic tool for objective measurement of scars.

A04. Heterogeneity of keloid-derived fibroblasts

Poster Presentation


*Dept. Plastic Surgery, **Dept. Physiol., Aichi Medical University School of Medicine, Aichi, Japan

Background: The characteristic of keloid-derived fibroblasts(KF) has been not fully understood and discrepant results have been in literature with regard to higher levels of collagen and inflammatory cytokines.

Objective: The difference between KF and normal fibroblasts (NF) were investigated by comprehensive protein and cell cycle analyses

Methods: Four patients with keloid and four healthy volunteers were subjects for this study. The morphology of fibroblasts was observed by a phase contrast microscope. The cell cycle of 10,000 fibroblasts was analyzed by flow cytometry, and cells were classified into G0/G1, S, and G2/M phases. With regard to inflammatory proteins, 2x105 fibroblasts were cultured for 5 days, and the culture supernatant was then comprehensively analyzed using the Proteome Profiler TM. IL-6 mRNA was quantified by real-time PCR.

Results: In the morphology analysis, the forward scatter indicated that the histogram of KF shifted to the right as compared to NF. And the side scatter displayed that the histogram of KF shifted upwards. These results showed that KF were morphologically distinct from NF, and also reflected the image of phase-contrast microscopy. With regard to cell cycle analysis, the percentage of KF in the G2/M phase was higher than that of NF, suggesting that the proliferative activity also significantly differ from NF. The protein levels of IL-6, IL-8, IL-12gp70 and GRO-a in KF were higher than NF. Similarly, KF also increased in IL-6 mRNA levels as compared to NF.

Discussion/Conclusion: The results suggest that the production of inflammatory cytokines which are promoting cellular proliferation and migration are elevated in KF. Further analyses of the properties of keloid-derived fibroblasts might be useful in the treatment of keloid.

A05. A NOSF (Nano-OligoSaccharide Factor) lipido-colloid dressing inhibits MMPs in an in vitro dermal equivalent model

Poster Presentation

B. Coulomb(1), L. Couty(1), B. Fournier(1), Ch. Laurensou(2), C. Aiiaud(2), A. Lafont(1), B. Gogly(1)

(1) Inserm U849, Université Paris-Descartes, Paris (France) ; (2) Laboratoires URGO, Chenêve (France)

Background: Chronic wounds are characterised by an increase in metalloproteinases (MMPs) activity in wound exudates, leading to a metabolic imbalance in the damaged tissues and to a slowing down in the healing process.

Objectives: Mechanisms of action on the wound healing process of a new compound, Nano-Oligosaccharide Factor (NOSF), was studied in vitro. The aim of this work was to compare the effects of lipido-colloidal dressings containing or not NOSF on the activity of MMPs.

Methods: Normal human dermal fibroblasts were incorporated within a collagen matrix, i.e. dermal equivalent (DE). Dressings were applied on DE, and the culture medium was assessed at days 2, 4 and 8. MMP-2 and -9 (Gelatinases), MMP-3 (Stromelysin) or MMP-1 and -8 (Collagenases) activities were analysed using zymography techniques with gelatin, casein and collagen gels, respectively.

Results: At Day 4, NOSF clearly inhibited gelatinases (MMP-2 et -9) and collagenases (MMP-1 et -8). Kinetic analysis of NOSF effects demonstrated that the inhibition of gelatinases was slightly (MMP-9) or not (MMP-2) detectable at Day 2, while the effect existing at Day 4 persisted at Day 8. In contrast, concerning collagenases, the inhibitory effects of NOSF were detected as soon as Day 2 but disappeared at Day 8.

Discussion/Conclusion: Using a dermal equivalent made it possible to study the effects of NOSF in vitro but at tissue level, in a close to in vivo dressing application situation. In these conditions, the effects of NOSF on collagenases appeared rapidly but did not persist while those on gelatinases were delayed but were maintained longer. This study is a first step in the understanding of the mechanisms of action of NOSF and contributes to explain the efficient results observed in vivo on chronic wounds.

This study was funded by a grant from URGO Laboratories, France.
A06. **In-vitro quantitative study of intrinsic mechanical strengths developed by fibroblasts isolated from keloids using the GlaSbox® system**  

**Poster Presentation**

L. Lebcira, D. Binda, C. Viennet, P. Tiberghien, S. Robin, P. Humbert  
University of Franche Comté, INSERM UMR 645, LIBC, Besançon, France

**Background:** Keloids result from an excessive wound healing process preferentially occurring on high skin tension areas such as shoulders, anterior chest ... Their development seems to be closely related to mechanical stress and also to an abnormal fibroblastic activity. Indeed fibroblasts are a high mechano-sensitive and responsive cell type.  

**Objective:** The aim of this study was to compare intrinsic mechanical strengths developed by fibroblasts isolated from keloids (KFs) and from neighboring healthy skin (NFs).  

**Methods:** Strengths developed by fibroblasts in tensed lattices were evaluated by the mean of the patented Growing Methods:  

- Strengths developed by fibroblasts in tensed lattices were evaluated by the mean of the patented Growing  
- Methods:  

**Results:** Kinetics of intrinsic strengths developed by fibroblasts is divided in three phases: an initial phase with low values corresponding to lattice polymerization, a second step during which consists in a near linear increase in strength and a last phase of stabilization. Both KFs and NFs develop contractile strengths, but those generated by KFs present a significantly lower intensity compared to NFs from the first hour to the phase of stabilization.  

**Discussion/conclusion:** These results are consistent with the low myofibroblastic differentiation previously described in the literature and will be completed by the assessment of a smooth muscle actin expression and fibroblasts synthesis activity. The GlaSBox® device could represent a useful tool in order to evaluate the potentiality of chemicals as keloids preventive agents.

A07. **Towards new anti-scarring strategies targeting substrate specific stimulation of procollagen processing**

**Poster Presentation**

D.J.S. Hulmes1, D. Kronenberg1, S. Le Goff1, W. Stocker1, R. Farndale2, N. Raynal3, C. Moali1  
Institut de Biologie et Chimie des Protéines, CNRS/UCBL UMR5086, IFR 128, Lyon, France ; Institute of Zoology, Johannes Gutenberg University, Mainz, Germany; Department of Biochemistry, University of Cambridge, UK.

**Background:** Hypertrophic scarring is characterised by an overproduction of extracellular matrix, notably fibrillar collagens. Previous strategies aimed at reducing collagen deposition have targeted enzymes of collagen synthesis and cross-linking but these enzymes are now known to act on other substrates, such that direct enzyme inhibition could lead to unwanted side-effects. We have shown that the protein PCPE-1 is a substrate specific stimulator of fibrillar procollagen processing (Moali et al, 2005, J Biol Chem 280, 24188), thus making it a potential target for controlling collagen deposition.

**Objectives:** The aim of the research is to develop molecules capable of blocking the action of PCPE-1.  

**Methods:** A number of strategies are being investigated, including the use of synthetic peptides, monoclonal antibodies and rational drug design based on three-dimensional structural information.  

**Results:** We have identified key amino acid residues in the CUB1 domain of PCPE-1 that are essential for stimulating activity (Blanc et al, 2007, J Biol Chem 282, 16924). Furthermore, we have shown that stimulating activity requires contiguous CUB1 and CUB2 domains and that these domains bind to sites on the procollagen substrate straddling the procollagen C-proteinase cleavage site. Finally, a trimeric peptide based on a region close to the cleavage site was found to prevent the activity of PCPE-1.  

**Discussion:** The molecules developed here will be tested in an animal model of corneal scarring, in collaboration with the groups of F. Malecaze (Toulouse) and O. Damour (Lyon).  

**Acknowledgements:** Supported by the the Fondation Coloplast and by the ANR.

A08. **Inhibiting scar formation in rat wounds by electroporation-mediated overexpression of soluble TGF-beta Receptor II**

**Oral Presentation**

Zhen Gao, Xiaoli Wu, Nan Song, Yilin Cao, Wei Liu  
Department of Plastic Surgery, Shanghai 9th People’s Hospital, Shanghai Jiao Tong University School of Medicine, China

**Introduction:** Anti-TGF-beta strategy has been employed in scar reduction with success. This includes both gene and protein approaches. Previously, we have shown adeno virus mediated overexpression of truncated TGF-beta receptor II can inhibit rat wound scarring. In order to enhance biosafety of scar gene therapy, we developed a strategy of plasmid based soluble TGF-beta receptor II (stGFBeta RII) gene therapy assisted with electroporation.

**Methods:** Human stGFBeta RII gene was cloned and then constructed into pVAX1 plasmid which is designed for human gene therapy. For in vitro study, COS cells were transfected with pVAX1-stGFBeta RII or pVAX1 blank vector. Transfected cells were harvested at day 2 for overexpression and function analysis. For in vivo study, EGFP was used as a report gene to analyze gene transfer efficiency by electroporation using different voltages and electroporation times. For gene therapy, 100mg pVAX1-stGFBeta RII plasmid in 100ml PBS was injected intradermally at the right side dorsal skin of SD rats (n=17) and 100ml vector plasmid in PBS at the left side skin as a control. The injected skin was electroporated with an electroporator, then a full thickness incisional wound was created on injected skin at day 1 post-injection. Wound tissues were harvested at day 2 (n=3) and day 7(n=3) after wounding for overexpression analysis and day 14 (n=11) for kinetic of intrinsic strengths developed by fibroblasts in tensed lattices were evaluated by the mean of the patented Growing Methods:  

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**Methods:** Human stGFBeta RII gene was cloned and then constructed into pVAX1 plasmid which is designed for human gene therapy. For in vitro study, COS cells were transfected with pVAX1-stGFBeta RII or pVAX1 blank vector. Transfected cells were harvested at day 2 for overexpression and function analysis. For in vivo study, EGFP was used as a report gene to analyze gene transfer efficiency by electroporation using different voltages and electroporation times. For gene therapy, 100mg pVAX1-stGFBeta RII plasmid in 100ml PBS was injected intradermally at the right side dorsal skin of SD rats (n=17) and 100ml vector plasmid in PBS at the left side skin as a control. The injected skin was electroporated with an electroporator, then a full thickness incisional wound was created on injected skin at day 1 post-injection. Wound tissues were harvested at day 2 (n=3) and day 7(n=3) after wounding for overexpression analysis and day 14 (n=11) for
histological and quantitative scar area analysis. **Results:** In vitro results showed that pVAX1- sTGF-beta RII was markedly overexpressed in COS cells at both gene and protein level. The overexpressed protein could promote MV1Lu cells proliferation by neutralizing TGF-beta. In vivo study showed that electroporation with an amplitude of 800 volts per cm area, 6 square wave pulses, each lasting for 20 ms with 200 ms interval, could achieve optimal gene expression by covering a wide area including an incisional wound area and in epidermis, dermal fibroblasts, hair follicle and panniculus carnosus, with a time course lasting about 7 days. Gene therapy results demonstrated that human sTGF-beta RII expression in rat skin was detected at both gene and protein levels. More importantly, the experimental wound at day 14 had much less scar formation than its control wound of the same rats, with an average of 57 percent reduction of the scar area (p <0.05). In addition, treated wound seemed to have a better collagen organization.

Conclusion: Electroporation-mediated sTGF-beta RII gene therapy can reduce scar formation in rat incisional wound. Due to its relative safety, this strategy may potentially be applied to clinical scar treatment.

**A09. High expression of growth differentiation factor-9 in keloid invasive area**

**Oral Presentation**

Zhen Gao, Nan Song, Xiaoli Wu, Yilin Cao, Wei Liu
Department of Plastic Surgery, Shanghai 9th People's Hospital, Shanghai Jiao Tong University School of Medicine, China

**Introduction:** The mechanisms of keloid invasiveness are largely unknown. Although TGF-beta plays very important roles in keloid pathogenesis, whether it plays a role in promoting keloid invasion remains unknown. Based on the clinical observation of keloid lesion that includes peripheral invasive area and central regressive area that is not invasive, we hypothesized that there will be differential gene expression between the fibroblasts of these two areas and thus may find a molecule responsible for keloid invasion.

**Methods:** Keloid, hypertrophic scar or donated normal skin tissues were obtained from patients who underwent plastic surgery and received no previous treatment. Tissues of three keloids were dissected into peripheral “invasive area” and central “regressive area” respectively based on gross morphology and digested to harvest cells. RNA was extracted from the first passage cells and subjected to a microarray chip analysis that contains total 96 genes related to TGF-beta signaling and superfamily. In addition, another 3 keloid along with 3 hypertrophic scar tissue and 3 normal skin tissues were digested with collagenase for cell harvest and RNA digestion. Gene expression of GDF-9 was evaluated with real-time PCR. In addition, these tissues were also frozen sectioned for immunofluorescence staining of GDF-9 expression.

**Results:** The chip analysis revealed differential gene expression pattern between the “invasive areas” and “regressive areas”. Of the differentially expressed genes, the expression of GDF-9, a member of a TGF-beta superfamily, was significantly higher in all 3 tested “invasive areas” than their respective “regressive areas” with an average of 4.66 fold increase. In addition, this differential expression of GDF-9 was also confirmed by real-time PCR. Interestingly, real-time PCR analysis revealed a 300 times more increase of GDF-9 expression in keloid than in hypertrophic scars and normal skins. Furthermore, immunofluorescence showed high protein expression of GDF-9 in keloid tissue, but the expression was not detectable in both hypertrophic scar and normal skin.

**Conclusions:** The differential expression of GDF-9 in keloid between invasive area and regressive area as well as the differential expression between keloid and hypertropic, normal skin indicates that highly expressed GDF-9 may play a role in keloid growth and invasion.

**A10. Comparing natural and synthetic membrane dressings in burn wound healing**

**Oral Presentation**

O Antar, A Moghazy, A Hussein, A El-Labban, O Salah
Faculty of Medicine, Suez Canal University, Ismailia, Egypt

**Background:** As xenografts are not available in most Islamic countries, other modalities of temporary skin substitutes for burn wounds were suggested. Amniotic membrane, for its availability and known efficacy, was chosen to be compared with Polyurethane as representative of synthetic membrane which are supposed to be similarly efficient.

**Objectives:** Comparing wound healing and progression with amniotic (Biomembrane) and polyurethane (Tegaderm) membrane dressings.

**Methods:** Sixty four patients with different types of burn (percentages and degrees) were randomly assigned either to amniotic membrane or polyurethane dressing.

**Results:** Healing time was significantly accelerated in the amniotic membrane group. In addition, this group showed more suppression of bacterial proliferation and elimination of existing bacteria over the polyurethane group. Furthermore, tolerance to pain during dressing change was significantly improved in amniotic membrane group. Finally, amniotic membrane experienced less albumin and electrolyte losses.

**Discussion:** The superiority of amniotic membrane was attributed to pliability and adherent property of the amniotic membrane dressing that inhibited bacterial contamination. Fibrin matrix provided an ideal substratum for migration of phagocytes to wound site. These are supported by the presence of lysozymes and progesterone. Presence of Angiogenic and growth promoting factors promoted active and high quality healing. For the third degree Burns, polyurethane had no effect at all compared with amniotic membrane that assisted high quality complete healing in relatively large areas.

**Conclusion:** Amniotic membrane is an ideal temporary skin substitute as it prevents heat, water and protein loss as well as forming a mechanical barrier against bacterial contamination. In addition, its use before and after grafting promoted graft uptake. It decreased post-operative pain and oozing. This cost-effective dressing uniquely acted on raw areas yielding sound and high-quality scars.
A11. Visualized finite element analysis of the relationship between keloid growth pattern and stretching tension

Oral Presentation

Satoshi Akaishi*, Rei Ogawa*, Masataka Akimoto** and Hiko Hyakusoku*
*Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School Hospital, Tokyo, Japan;
**Department of Plastic and Reconstructive Surgery, Nippon Medical School Chiba Hokusoh hospital, Chiba, Japan

Backgrounds: It is well known that stretching tension of skin, in other words mechanical force on the skin, is an important factor that promotes keloid formation. Thus, we analyzed the relationship between keloid growth patterns and stretching tension using a visualized finite element study.

Materials and Methods: Keloids, normal skin and fat structures were reproduced using DISCUS© software. The contours were transferred to ADINA© analytical software to rebuild and mesh volumes.

Results: 1. High tension was observed at the edges, and not in the entire region, of stretched keloids. 2. Keloid centers were regions of low tension, which helps to explain the healing which generally occurs in the central regions of keloids. 3. Expansion of a keloid occurred in the direction in which it was pulled. 4. The “crab’s claw”-shaped invasion occurred in response to increased stretching tension. 5. Skin stiffness in the circumference of a keloid was associated with greatly increased tension. 6. Fat hardness and thickness did not influence the amount of tension. 7. Adhesion with subcutaneous hard tissue greatly increased the tension in the keloid.

Conclusion: These stretching results have advanced understanding of keloid formation under various conditions. Our results suggest that stretching tension is an important condition associated with keloid growth.

A12. Effects of cyclical tensile force on skin: enhanced cellular proliferation, vascularity, and cutaneous perfusion

Oral Presentation

Michael S. Chin1,2, Rei Ogawa MD PhD3,4, Luca Lancerotto MD4, George Younan MD1, Jasmine C. Mathews1, Kevin T. Schomacker PhD1, Mike Prsa1, Mark Ottensmeyer PhD1, Arístidis Veves MD MSc1, and Dennis P. Orgill MD PhD4
1Tissue Engineering and Wound Healing Laboratory, Division of Plastic Surgery, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, 2Tufts University School of Medicine, Boston, MA, 3Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School Hospital, Tokyo, Japan, 4University of Padua, Padua, Italy, 5HyperMed Inc, Waltham, MA, 6Department of Electronics & Mechanical, Wentworth Institute of Technology, Boston, MA, 7Massachusetts Institute of Technology, Cambridge, MA, 8Joslin-Beth Israel Deaconess Foot Center and Microcirculation Laboratory, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA

Introduction: Mechanical forces have been used empirically for procedures such as tissue expansion and proposed as an underlying mechanism in wound healing. We propose that waveform-specific stretching can stimulate cellular proliferation and vascularity in skin.

Objectives: Using a servo-controlled device, we applied specified tensile forces to the dorsal skin of mice to study changes in cellular proliferation and vascularity.

Methods: A finite element model predicted the force distribution to be nearly uniform. We applied 50 gm·f/cm² cyclically (2 min on/1 min off) or continuously for 1 or 4 hours. At days 2 and 10 after stretch, skin was harvested for immunohistochemical staining including cell proliferation, vascular density, and inflammatory cells (n=40). Cutaneous perfusion was measured with hyperspectral imaging (n=12). Fluorescent corrosion casting was performed to visualize skin microvasculature. Tissue hypoxia was analyzed with pimonidazole hydrochloride staining in 4 hour continuously stretched mice (n=4).

Results: In the epidermis, all stretch groups resulted in a significant increase in cellular proliferation rate over sham controls. Cyclical stretch was more effective than continuous stretch at one hour. In the dermis, vessel count increased nearly 3-fold for stimulated groups when compared to controls. Stretch did not lead to increase in inflammation. Hyperspectral imaging demonstrated a 46% increase in total hemoglobin over baseline following cyclical stretch. Pimonidazole immunohistochemistry revealed dermal hypoxia in stretched tissue.

Conclusion: Our results suggest that cyclical tensile forces applied on skin stimulate epidermal cell proliferation and dermal vascularity partially mediated by hypoxia. Cyclical application of force also increases cutaneous perfusion. Waveform-specific mechanical loads have the potential to produce accelerated tissue regeneration.

A13. Electric field control of wound inflammation

Oral Presentation

Pullar, C. E. University of Leicester, Leicester, U.K.

Background: Chemical, electrical and mechanical cues orchestrate cell migration, proliferation and differentiation to repair adult wounds quickly, but imperfectly. An over-zealous inflammatory response contributes to excessive fibroblast-mediated matrix deposition and remodeling, resulting in scar tissue. The identity of the cue that guides inflammatory cells to the wound within minutes/hours of injury is currently unknown. Altering the wound inflammatory guidance signal could limit the recruitment of inflammatory cells to the wound which would reduce wound scarring.

Objectives: Previous investigations of wound electric currents have suggested the involvement of specific ion channels and pumps in current generation. Here I describe an in vivo study using a zebrafish model to investigate if an electrical cue guides inflammatory cells to tail wounds, within hours of injury.

Methods: Zebrafish larvae, seventy two hours post fertilization, were immersed in pond water containing 2% tricaine and complete transection of the tail was performed with a sterile scalpel blade. Post-wounding the larvae were incubated in the presence or absence of pharmacological agents for 6 hours, washed and stained using a fluorescein-tiyramide
signal amplification method (Perkin Elmer) prior to fixation in 4% paraformaldehyde. Tails were mounted and photographed on a Nikon TE-2000 inverted microscope at 20x magnification. The number of neutrophils recruited to each wounded tail was recorded (n = 15-30).

**Results:** An average of 10 neutrophils were recruited to wounded tails within 6 hours of wounding. Specific ion channel/pump blockade reduced the recruitment of neutrophils to the wound by 45% to 60%.

**Discussion/Conclusion:** Specific ion channels/pumps play a role in generating the zebrafish wound electric field which appears to be an important guidance cue in recruiting neutrophils to the wound site, within hours of injury. The ability to tailor the electric guidance cues in the wound, both pharmacologically and electrically, has potential as a future therapeutic approach to reduce wound inflammation and, therefore, reduce wound fibrosis and scarring.

### A14. Wet wound healing modulates scar formation in the Yorkshire pig

**Oral Presentation**

Richard G Reish, Baraa Zuhaili, Jurí Bergmann, Pejman Afkāli, Taro Koyama, Emily C Waishbren, Feng Yao, Elof Eriksson

Division of Plastic Surgery, Brigham & Women’s Hospital, Harvard Medical School, Boston, MA, USA

**Introduction:** It was hypothesized that the decreased inflammatory response seen in wet wound healing is correlated with diminished scarring. This study seeks to test this hypothesis and to validate a model of scarring in the liquid environment in the Yorkshire pig.

**Methods:** 4 Yorkshire pigs were used to create 36 dorsal wounds per pig (144 wounds total) in the following groups: full thickness excisional wounds, partial thickness, meshed split thickness skin graft (STSG), sheet STSG, minced skin, and incisional wounds. Wounds were randomized into wet and dry wound healing. Wet wounds were enclosed in polyurethane chambers with 2 ml of normal saline. Dry wounds were covered with regular gauze. Terminal biopsies were performed at 72 hours and day 28.

**Results:** The mean macroscopic scar surface area was significantly decreased in full thickness excisional wet wounds compared to dry wounds (61.2 mm2 vs 150.8 mm2, p<0.01). H&E and trichrome histology demonstrated significantly less inflammatory infiltrate, thicker neoepidermis, more pronounced rete ridge formation, and less scar tissue thickness in wet compared to dry wounds. Hydroxyproline content was decreased in full thickness wet compared to dry groups (44.81mg/g vs 62.21mg/g, p<0.01). Tensile strength was 90% greater in all full thickness wet compared to dry groups (p<0.01).

**Conclusion:** Healing in the liquid environment significantly reduced macroscopic scar surface area, histological evidence of scar, hydroxyproline content, and increased the tensile strength of the wound. There was a high degree of correlation (r2=0.99) between the number of acute inflammatory infiltrates at 72 hours postwounding and the final scar width at 28 days. This validated model will allow for future investigation of high dose topical scar modulating agents in the liquid healing environment.

### A15. Itching following burns. Epidemiology and predictors

**Oral Presentation**

MK Nieuwenhuis, NEE van Loey, M Bremer, AW Faber, E Middelkoop

Association of Dutch Burns Centres, Groningen, The Netherlands

**Background:** Itching (pruritus) following burns is a well known clinical problem. However, long-term prospective studies that document the course and the extent of the problem are not available. Studies on risk factors are anecdotic.

**Objectives:** To study self-reported itching in a multi-centre cohort among adults with burns at three, twelve and twenty four months post burn. Further we aim to examine psychological and injury characteristics in relation to itching at these three points in time.

**Methods:** Itching was assessed as part of a self-report scar complaint list in a prospective longitudinal cohort study. Injury characteristics, demographics and self-reported post-traumatic stress symptoms were examined as possible risk factors in three linear regression models.

**Results:** A total of 510 persons participated. The reported prevalence rates of mild to severe itching were as high as 87%, 77% and 67% at the three respective points in time. Significant predictors of itching at all three moments in time were deep dermal injury and early posttraumatic stress symptoms. Along with these, total burned surface area and female gender were predictors at 3 months post burn.

**Discussion / Conclusion:** Itching remains a problem of significant extent over a two-year period. Individuals having undergone surgical procedures and experiencing early post-traumatic distress are more likely to suffer from long-term and persistent itching. Implications regarding practice and research are discussed.

### A16. Honey: a cost-effective environmental-based efficient dressing for the most difficult wounds

**Oral Presentation**

A Moghazy, O Antar, A Hussein, M Shams, W Saleh, I El-Shiek

Faculty of Medicine, Suez Canal University, Ismaïlia, Egypt

**Background:** The cost of wound care is in constant rise. The emergence of resistant strains is a solid evidence of failure of used modalities. Honey emerges as an ideal cost-effective and efficient dressing; even in difficult wounds. It well known “curing” action makes it the perfect environmentally based dressing in our country.

**Objectives:** Itching (pruritus) following burns is a well known clinical problem. However, long-term prospective studies that document the course and the extent of the problem are not available. Studies on risk factors are anecdotic.

**Methods:** Itching was assessed as part of a self-report scar complaint list in a prospective longitudinal cohort study. Injury characteristics, demographics and self-reported post-traumatic stress symptoms were examined as possible risk factors in three linear regression models.

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**Discussion / Conclusion:** Itching remains a problem of significant extent over a two-year period. Individuals having undergone surgical procedures and experiencing early post-traumatic distress are more likely to suffer from long-term and persistent itching. Implications regarding practice and research are discussed.

**Objectives:** Testing the efficacy and cost-effectiveness of honey as local treatment in Diabetic foot infections.

**Methods:** 35 patients with diabetic foot infection were submitted to the study. The University of Texas Diabetic Wound classification was used to assess the stage and grade of the wound weekly for three months.
Results: The mean healing time was 2.3 weeks. Complete healing was achieved in 13% of patients in the first as well as the second months. Further 16% of the patients followed in the third month. 43% of the patients showed partial healing. Two patients were grafted and two were subjected to amputation.

Discussion: Honey was proven to be efficient: in rate and quality of healing. The disappearance of odor and pain, were significantly rapid. The omnipresence of honey and its cheap price, as well as the absence of any side effect helped in the adherence of patients to all instructions of the treatment. Honey failure in two cases was attributed to bad patient compliance as well as the very bad local and general condition of the patients.

Conclusion: Honey is an efficient and cost-effective dressing particularly in low income countries. It had a rapid rate of healing and less rates of surgical procedures. Honey is an environmentally-based treatment as it comes in concordance with most patients’ believes and culture. It has no side effects, adverse reactions or emergence of resistant microorganisms. Honey has very limited value in cases of local extremely bad condition; osteomyelitis and severe peripheral vascular diseases.

A17. An objective measuring device for surface roughness in scars

Oral Presentation

M.C.T. Bloemen\textsuperscript{1}, M.S. van Gerven\textsuperscript{1}, E. Middelkoop\textsuperscript{1,2}

\textsuperscript{1} Association of Dutch Burn Centers, Beverwijk, The Netherlands;
\textsuperscript{2} Department of Plastic and Reconstructive Surgery, VU University Medical Center, Amsterdam, The Netherlands

Background: Burn scars are considered a major medical problem that lead to functional and cosmetic sequelae. Various therapies for the treatment of burn wounds and scars have been developed to improve scar quality. To follow scar maturation and to evaluate the effectiveness and the final outcome of treatment options, valid and reliable objective measurement tools are necessary. The Phaseshift Rapid In vivo Measurement Of the Skin (PRIMOS) is a measuring system, which in vivo produces a three dimensional image of the microtopography of the skin by means of a non-invasive measuring device.

Objectives: The aim of this study is to investigate whether the PRIMOS is a valid instrument for the objective and quantitative measurement of the surface roughness of burn scars.

Methods: In this study 32 burn scars and 32 control areas of 29 patients were measured with the PRIMOS. Additionally, the subjective Patient and Observer Scar Assessment Scale (POSAS), was scored in all patients and applied as golden standard for relief in burn scars. Various surface roughness parameters were obtained from the PRIMOS software (Sa: arithmetic mean of the surface roughness, Sz: mean of five highest peaks and deepest valleys, PC: peak count, number of peaks). Statistical analysis (Wilcoxon signed rank test and linear regression analysis) was performed with SPSS 14.0.

Results: All three parameters of the PRIMOS were significantly different in scar versus control area (Sa 0,000; Sz 0,000; PC 0,000). Furthermore, a significant correlation of 0.631 was found between parameter Sa and the POSAS relief score.

Conclusion: The PRIMOS is a valid tool for the objective non-invasive evaluation of the differences between scar and control area. Currently, further research on the PRIMOS involving scar relief and thickness in burn patients is being performed.
CLINICAL TRIALS

B01. Bismuth subgalate/borneol(suile) results in less scarring than a topical antimicrobial in the human forearm biopsy trial for acute wound healing

T.E. Serena, M.K. Kauffman
NewBridge Medical Research, Gannon University, Erie, Pennsylvania, USA

Background: Bismuth subgalate/Borneol (Suile) has been shown to be superior to Bacitracin in the human forearm biopsy model for acute wound healing.1 It subsequently demonstrated a trend toward more rapid healing when compared to a commonly used topical antimicrobial dressing.2 Anecdotal reports, mostly from Asia, suggest that, in addition to promoting healing, the use of Suile reduces scarring in acute and chronic wounds. The postulated mechanism is a reduction in wound inflammation. In the United States, Suile is a device cleared for marketing by the FDA for partial thickness wounds, 1st and 2nd degree burns, donor sites and abrasions. 

Objective: The objective of this clinical trial was to determine if Suile reduces scarring in the human forearm biopsy model for acute wound healing.

Methods: Twenty-two healthy volunteers who participated in a randomized blinded study comparing Suile to a topical antimicrobial (Acticoat®) were photographed one year after healing of their forearm biopsy wounds. The high quality digital photographs were then evaluated by medical and non-medical reviewers using the Vancouver burn scale.

Results: There was significantly less hyperpigmentation in the Suile vs. non-Suile treated biopsies (p<0.05). There was a trend toward less vascularity. There was no difference in pliability or height between the two groups. There was also no difference in assessment between the medically trained and lay evaluators.

Discussion/Conclusion: The results suggest that Suile decreases the hyperpigmentation associated with scarring in acute wound healing. Moreover, the lack of difference in height and pliability assessments could have been the result of the difficulty in evaluating these parameters using photographs. A follow up study is planned for the fall semester 2008 to evaluate these parameters. In conclusion, Suile should be considered in the treatment of wounds and burns in which scarring and cosmeses are a concern.

B02. A randomised, placebo-controlled phase II study evaluating improvement of scar appearance following intradermal administration of avotermín (Juvista®) following scar-revision surgery

Renovo, Manchester Incubator Building, Manchester, United Kingdom M13 9XX

Introduction: There is a need for effective treatments that reduce scarring following injury or surgery, with patients indicating that they value even small improvements in the appearance of scars. Previous clinical trials have shown that avotermín (transforming growth factor 3; Juvista®) is a new class of prophylactic medicine that promotes regeneration of normal tissue and improves scar appearance.

Aims and Objectives: To investigate the efficacy and safety of avotermín administered intradermally to approximated wound margins following scar-revision surgery.

Methodology: Subjects had mature linear scars (≥5cm long) suitable for revision by excision and direct closure. Scars were divided into 3 sections. The two outer sections were randomised to intradermal injections of 100mL/linear cm/wound margin of either placebo or avotermín (200ng/100mL) immediately post-wound closure and 24-hours later. The middle section (length ≥3cm) was closed but not dosed. The primary endpoint was the difference (avotermín versus placebo) in total scar score (ToScar). ToScar was calculated by summing scores assigned to standardised digital images of each scar at Months 1–7 post-surgery by an Independent External Scar Assessment Panel (comprising lay volunteers) using a 100mm visual analogue scale.

Results: Thirty patients were enrolled (50% females, 90% Caucasians, median age 44 years). Scars ranged 5.2–8.3cm long and 67% were on the abdomen. Analysis of ToScar showed a statistically significant improvement in scar appearance with avotermín compared with placebo (mean within-subject improvement of 33.52mm, p=0.0279). Avotermín demonstrated a similar safety profile to placebo, with no statistically significant differences in the incidences of itch, burn, pain, oedema, exudate or erythema.

Conclusion: Avotermín at 200ng/100 L/linear cm/wound margin administered twice following surgical scar revision achieves a statistically significant improvement in scar appearance over a 7-month time frame compared with placebo. Results suggest that avotermín supplements good surgical technique for the management of unsightly scars, resulting in less-noticeable scars.
B03. Self Drying Silicone Spray and hypertrophic scarring in burned skin

Steinstraesser L, Flak E, Witte B, Steinau HU
Dept. Plastic Surgery, Burn Center, BG University Hospital Bergmannsheil, Ruhr University Bochum, Germany

Introduction: Prevention of hypertrophic scars and keloids in burned patients are still problematic. The combination of compression therapy and silicone sheets is a promising method of Prevention. In this randomized long−term−study the efficacy of a new topical self drying silicon spray preparation in the prevention of hypertrophic scars and keloids combined with compression therapy has been assessed and compared to a control treatment composed of silicone sheeting and compression in split thickness graft burn wounds.

Methods: 40 patients with two comparable areas of split thickness graft burn wounds (wounds sized at least 3 cm x 5 cm each, burn index < 100) have been included into this study. Study design: Design: Open, single−center, randomized controlled study, intra−individual comparison of study preparation and control to standard treatment. Right after split thickness skin grafts were adherent Patients received compression garments and were randomized to two of the following treatment groups a) Self Drying Silicone Spray b) Silicone Sheet or c) no treatment control. Clinical assessment by scores (Vancouver Scar Scale), measurement of scar redness (Chromametry) and height (Profilometry) photo documentation of each treated area are performed at different visits with a long−term follow−up of 18 months.

Results: The preliminary results of this study (20/40 Patient finished the 18 months follow−up) indicate that the efficacy of Self Drying Silicone Spray appears comparable to silicone gel sheeting. The patients’ satisfaction and compliance are higher in the silicone spray group compared to silicone sheeting.

Discussion: This study shows first evidence that the results with Self Drying Silicone Spray treatment are comparable with the current clinical gold standard of silicone sheeting. In contrast to the Silicone Sheet, Self Drying Silicone Spray can be applied easier on uneven and widespread scar areas without touching the wound, the silicone spray layer cannot shift and the procedure of fixing and cleaning of the sheets will be avoided. An advantage regarding better compliance can be expected. Statistical analysis will be performed after all study subjects have terminated the required 18 months follow−up.

B04. Clinical analysis of the burn scar carcinomas

Yumeji Takeichi1, K.Nishihori1, H.Tada1, M.Kato1, M.Oda1, K. Yokoo1
1Department of Plastic and Reconstructive Surgery, Aichi Medical University, Aichi;
2Department of Plastic and Reconstructive Surgery, Wakaba Hospital, Mie, Japan

Background: The malignant tumor after burn scar gives big influence to the prognosis of the patients. Especially, it is a huge problem that the malignant change occurs after long periods.

Objectives: We performed statistical analysis of the burn scar carcinomas, and the treatment of the burn scar carcinomas.

Methods: I analyzed 23 cases of burn scar carcinomas that we have experienced in Aichi Medical University between 18 years from June, 1990 to June, 2008.

Results: The mean periods from burn to malignant change is about 50 years. The older patients were, the shorter the period to change to malignancy tended to be.

Discussion: The burn scar carcinomas often occur in the hard scar tissue, therefore the prognosis of them are relatively good.

With the advancement of plastic surgery, the burn ulcers have become obtained good epithelization. Therefore, the rate of incidence of burn scar carcinomas has been decreased recently.

In the case of limb reconstruction, the thin flap like a dorsalis pedis flap is usefull.

B05. Scar prevention by laser-assisted skin healing (lash): a pilot study with an 810-nm diode-laser system

G. Iarmarcoval1, A. Capon2, A. Gossé1, A. Cornil1, S. Mordon2
1Ekkyo, Meyreuil, France;
2Lille University Hospital CHU, Lille, France;
3INSERM-IFR 114, Lille University Hospital CHU, Lille, France

Key Words: Wound healing. Scar management. Heat.

Background: Cosmetic results obtained after skin surgery are a key component of patient satisfaction.

Objectives: This pilot study aimed at evaluating the 810-nm diode-laser system to accelerate and improve, through a thermal action, the healing process in surgical scars of patients with Fitzpatrick skin type I to IV.

Methods: Laser treatment was divided into two groups: 5 patients were treated with low dose (fluence < 80J/cm²) and 6 patients with high dose (fluence > 80J/cm²). Incision was divided into two fields, with only portions randomly selected receiving laser treatment immediately after skin closure. Scars were evaluated by the surgeon and patients at 10 day, 3 month, and 12 month follow-up using a comparative scar evaluation from -5 (worst) to 5 (best). Wilcoxon signed ranks test analyses were performed.

Results: There were no significant differences in scar appearance at 10 day and 3 month follow-up. At 12 months, the treated portion scored significantly better for the surgeon (P = 0.046) and for patients (P = 0.025) compared with the controls. Patients reported greater satisfaction than the sur-
Results

A wound healing model was used. Starting 10 days after surgery, for the total duration of three months. At postoperative, scar-segments were either treated with calcipotriol or placebo, for the total duration of three months. At 3 weeks, 3 months and 12 months postoperative, the scar histology was examined.

Discussion/Conclusion: These results suggest that 810-nm laser treatments can change fundamentally the physiology of wound healing if applied in the early phases. Further studies are warranted to optimize 810-nm diode laser parameters for scar revision, and to better understand the cellular mechanisms leading to laser-induced wound healing.

B06. Topical application of calcipotriol for preventive treatment of hypertrophic scars: a randomized, double-blind, placebo-controlled trial

Running head: Effect of calcipotriol on hypertrophic scar formation

Oral Presentation

F.B. Niessen, MD, PhD[a], W.M. van der Veer, MSc[b], X.E. Jacobs, MD[b], I.E. Waardenburg, MD[b], M.M. Ulrich, PhD[a]

[a] Department of Plastic and Reconstructive Surgery, VU University Medical Centre, Amsterdam, The Netherlands
[b] Department of Plastic and Reconstructive Surgery, University Medical Centre Groningen, Groningen, The Netherlands
[c] Association of Dutch Burn Centres, Beverwijk, The Netherlands

Background: The epidermis of hypertrophic scars shows histological abnormalities similar to psoriatic lesions. Calcipotriol is widely used for treatment of psoriasis.

Objectives: To investigate the efficacy of topical application of calcipotriol in preventing hypertrophic scar formation.

Methods: In a randomized, double-blind, placebo-controlled trial, 35 women were enrolled. The bilateral reduction mammaplasty wound healing model was used. Starting 10 days postoperative, scar-segments were either treated with calcipotriol or placebo, for the total duration of three months. At 3 weeks, 3 months and 12 months postoperative, the scar aspect was scored, its thickness was measured by ultrasound, and punch biopsies were collected for histological analysis.

Results: After 3 and 12 months, no significant difference in prevalence of hypertrophic scars was observed between the placebo- and calcipotriol-treated scars. At 3 weeks postoperative, the calcipotriol-treated scars contained significantly more epidermal layers (P = 0.017) and proliferating basal keratinocytes (P = 0.029). None of the 3-week-old scars without activated keratinocytes became hypertrophic, whereas 48% of the 3-week-old scars that contained activated keratinocytes did (P = 0.001). After three months, hypertrophic scars contained more epidermal layers than normotrophic scars (P = 0.013).

Conclusions: Topical application of calcipotriol during the first three months of wound healing did not affect the incidence of hypertrophic scar formation. Contrary to its effects in psoriatic lesions, calcipotriol treatment increased proliferation of keratinocytes and the number of epidermal layers. We observed a strong association between keratinocyte activation and hypertrophic scar formation. These findings contribute to the concept of both dermal and epidermal involvement in the aetiology of hypertrophic scar formation.

B07. A randomised controlled trial measuring the effectiveness of tubed silicone gel versus placebo in promoting the maturation of hypertrophic scars

Oral Presentation

M.B.A. van der Wal[a], E. Middelkoop[b]
[a] Burn Center, Red Cross Hospital, Beverwijk, The Netherlands
[b] Association of Dutch Burn Centers, Beverwijk, The Netherlands

Background: Silicone sheets are widely used in the treatment of hypertrophic scars although not all locations on the body seem appropriate for application. When scars are located on or around the joints the sheets tend to restrict movement and may not stay adherent. Also on visible locations the appearance of sheets can decrease patients compliance to therapy. Therefore a tubed silicone gel was developed which is easy to apply in a thin layer whereas it does not restrict motion and is less apparent.

Objective: Methods: Twenty three patients with a mean age of 39.0 years (range 18.0-64.9) were included in a randomized, placebo-controlled, within-subject comparison, double blinded, prospective clinical trial. They were given coded and blinded Dermatix and cetomacrogol cream to apply twice a day on the predetermined locations of two comparable scars and were followed for 1 year. Effectiveness was evaluated by using the objective DermaSpectrometer for erythema and subjective Patient and Observer Scar Assessment Scale. (POSAS) Significance was tested using the Wilcoxon signed rank test for two related samples.

Results: The mean scores for erythema and POSAS were not significantly different for silicone gel and placebo. However, there was a trend versus lower (=qualitatively better) scores for the silicone treated scars, which could mainly be attributed to the components relief and thickness of the POSAS score. At 3 months post inclusion, the relief of Dermatix treated scars was significantly better than placebo (P = 0.034).

Conclusion: Silicone gel from a tube seemed to promote maturation of scars, but was in general not significantly better than placebo. Surprisingly more effects of silicone gel were found on scar relief and thickness than on erythema. Based on our results we advise tubed silicone gel for the treatment of hypertrophic scars if silicone sheets are contraindicated.

B08. Preventing recurrence of surgically removed auricular keloid with intralesional injection of low-dose of 5-fluouracil and corticosteroid

Oral Presentation

Xiaoli Wu, Zhen Gao, Nan Song, Yilin Cao, Wei Liu
Department of Plastic and Reconstructive Surgery, Shanghai 9th people’s hospital, Shanghai Jiao Tong University School of Medicine, China
Objective: We report a clinical therapy for better control of the recurrence of surgically removed auricular keloid.

Methods: This study involved 56 patients with total 126 ear keloids. 23 patients had helix keloids, 31 earlobe keloids, and 2 for both locations. Ear piercing was the main pathology (89.3%). The average suffering time was about 5 years. Keloids were first excised with complete removal of embedded skin and sebaceous cyst followed by contour reconstruction using keloid flap. One month postoperation, all patients received intralesional injection of a mixture of 5-FU (1.19 mg/ml) and corticosteroid (3.33 mg/ml) in 2% lidocaine once a month. Drug concentration decreased with prolonged injection interval if no recurrence was observed before next injection. The therapy finished if no recurrence after 6 month intermission. All patients have either been treated or followed-up for more than 6 months.

Results: The average treatment time for all patients was 7.63 months (2-26 months) with an average follow-up time of 8.8 months (0 to 28 months). In 56 cases, 28 stopped injection for more than 6 months without recurrence after the therapy for an average of 8.53 months. Among them, 9 patients received no treatment for more than 24 months; 6 for 12-24 months and 13 for 6-12 months. For the rest of 28 patients, 9 received no treatment approaching 6 months without signs of recurrence after therapy for average 7.15 months (3-10 months). The other 19 cases needed injection every 1 to 2 months with small amount of diluted drugs to control the residue recurrence after an average 5.53 month treatment, but exhibiting a trend of complete control of recurrence. 90% of patients could retain a normal ear counter achieved by the surgery with drug injection. Interestingly, comparing corticosteroid injection alone in our previous therapy, adding 5-FU could effectively control the angiogenesis, leading to significantly reduced erythema and inhibited regrowth.

Conclusions: Although high variations in therapy time needed, all patients seemed to be able to gain complete control of keloid recurrence given an enough long therapy that is achievable by this reported therapy.

B09. Topical herbal cream for hypertrophic scars: a pilot study

Oral Presentation

Jain Pardeep, Institute of Medical Sciences, Banaras Hindu University, Dept of Plastic Surgery, Varanasi, India
N.G. Kostopoulos, Athens, Greece

Background: The hypertrophic scars, irrespective of the aetiology, are very troublesome and difficult to treat. No single modality of treatment has been found to be fool-proof. Lasers, radiation, interferons and steroids have all been tried with variable outcome and side effects.

Objectives: To find out a single, safe, user-friendly and effective topical treatment modality for hypertrophic scars.

Method: After an informed consent and ethical approval, a topical herbal cream was used as the sole agent for treating hypertrophic scars in 25 patients, 20 with post-burn and 5 with post-traumatic scars (skin graft donor site, post-surgical), all 12 months or more in duration.

Results: Smoothened and shining skin was the first change noticed after 3 weeks of application but itching persisted. After 6 weeks of persistent application, the thickness was reduced and the color changed from hyperemic to normal. The scars softened, and thickness further decreased at 12 weeks. At 16 weeks, the scar regressed dramatically both in volume and texture with tolerable or no itching. All the patients accepted the cream without any untoward effect or complication.

Discussion / Conclusion: The herbal cream used as monotherapy had tremendous success in improving the hypertrophic scars with scar regressing and flattening to great extent. There was slow and steady decrease in itching and either it disappeared completely or persisted within tolerable limit. There were no side effects and the patients’ compliance was good.

These interim results show promising potential for its use as a single agent, cost-effective therapy in management of hypertrophic scars and perhaps keloids as well.

B10. Cardiopulmonary bypass plus perioperative high-dose dexamethasone affect presternal hypertrophic scar formation

Oral Presentation

Frank B. Niessen, M.D., Ph.D. [a], Willem M. van der Veer, M.Sc. [b], José A. Ferreira, Ph.D. [c], Etty H. de Jong, B.Sc. [c], Grietje Molena, Ph.D. [d]
[a] Department of Plastic and Reconstructive Surgery, VU University Medical Center, Amsterdam, The Netherlands
[b] Department of Epidemiology and Biostatistics, VU University Medical Center, Amsterdam, The Netherlands
[c] Department of Plastic and Reconstructive Surgery, University Medical Center Groningen, Groningen, The Netherlands
[d] Department of Pathology and Medical Biology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

Background: Corticosteroids are widely used as treatment for excessive scarring by intralesional injection with variable success. It is conceivable that systemically administered corticosteroids affect a wider range of inflammatory processes that influence wound healing and may be more successful in preventing hypertrophic scar formation.

Objectives: To study the preventive effect of high dose perioperative dexamethasone on the formation of hypertrophic scarring.

Methods: We have used a standardized model of prestenral scars caused by cardiothoracic surgery through a median sternotomy incision. During cardiac surgery with cardiopulmonary bypass, 1 mg/kg dexamethasone was administered preoperative, and 0.5 mg/kg eight hours postoperative. The prestenral scars were evaluated at 2, 4 and 6 weeks, and 3 and 12 months postoperative at standardized measuring points. At 3 and 12 months postoperative, the height and width of the scar were measured with both a slide caliper and a 7.5 MHz ultrasound probe.

Results: Cardiopulmonary bypass was used in 31 of the included 43 patients. 11 patients (35%) in the dexamethasone group developed clinical hypertrophic scars compared to four patients (33%) in the control group. These differences were not statistically significant. Cranial scars were significantly wider in the dexamethasone group compared to the...
control group (p=0.04). At three months scars were significantly higher in the dexamethasone group, both cranial (p=0.05) and caudal (p=0.03). The differences in scar width and height were chiefly present in patients that developed hypertrophic scars.

**Conclusions:** Administration of high-dose perioperative dexamethasone does not prevent hypertrophic scar formation. On the contrary, its use together with the cardiopulmonary bypass did affect scar dimensions negatively up to 12 months following surgery.

**B11. Postoperative electron-beam irradiation therapy for keloid -Analysis of 552 sites followed up over 18 months-**

**Oral Presentation**

Rei Ogawa*, Satoshi Akaishi*, Shimpei Ono*, Shigehiko Kuribayashi**, Tsuguhiro Miyashita**, Hiko Hyakusoku*
*Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School Hospital, Tokyo, Japan; **Department of Radiation Oncology, Nippon Medical School Hospital, Tokyo, Japan

**Backgrounds:** Before 2002, keloids were treated at our facility with postoperative irradiation of 15 Gy (the traditional protocol). Analysis of the therapeutic outcomes of patients treated with this protocol showed that the recurrence rates of keloids in the anterior chest wall, as well as the scapular and suprapubic regions, were statistically higher than at other sites, while the recurrence rates in earlobes were lower. Thus, we customized doses for various sites.

**Patients and Methods:** After 2003, 317 keloids were treated with surgical excision following the new protocol: electron-beam irradiation at total doses of 10, 15, or 20 Gy, depending on the site. The recurrence rates and toxicities were compared with 235 keloids that were treated with the traditional protocol. The minimal follow-up time was 18 months. Statistical analysis was performed using Fisher exact probability test.

**Results:** The recurrence rates in the anterior chest wall and scapular region were statistically reduced. Outcomes of earlobe did not differ between irradiation with 15 Gy and 10 Gy. **Conclusion:** Our results suggest that keloids with a high risk of recurrence should be treated with 20 Gy in 4 fractions over 4 days and that earlobe should be treated with 10 Gy in 2 fractions over 2 days.
C01. Silicon gel dermatix® in management of traumatic nose and midface avulsion

**Oral & Poster Presentation**

Fernández García Á., Guzmán Salinas J.L., Aznar Vicente J., Fernández Pascual C., Alonso Rosa S.
Virgen de la Arrixaca University Hospital. Department of Plastic Surgery and Burns, Murcia, Spain

**Background:** The management of high-energy facial trauma requires the complete repair of anatomical structures whose dynamic function is necessary for the social well-being of the patient.

**Objectives:** The aim of this study has been to value the results obtained in a midface avulsion after silicon gel Dermatix treatment.

**Materials and methods:** A fourteen-year-old female presented with high-energy trauma to the right side of her face. There was partial right midface avulsion with complete avulsion of the nasal pyramid. The wounds were under general anesthesia. The gingival mucosa and the orbicularis oris muscle were repaired. Epi-perineural neurorraphy used nylon 8/0 on severed branches. The nasal pyramid was repositioned and the nasal bones fixed in place. The septal mucosa was closed and the lateral nasal mucosa repaired. The alar and triangular cartilages were reconstructed. Muscle bundles of PLR, LGP and levator labii superioris were repaired. The skin was closed. Venous perfusion improved following surgery. Sutures were removed on postoperative day 10. Dermatix treatment (daily application every 12h for 1 year) was initiated at week 3 as prophylaxis against hypertrophic scarring.

**Results:** On postoperative day 21 the wounds had closed and cutaneous scars showed signs of hypertrophy. The facial contours showed paresis of the elevator muscles of the right upper lip. At 1 year, after continued (Dermatix) treatment, a new picture was performed. These pictures were processed with a computer program. With this system it is possible to know the coordinates that define the colour of the scar and the healthy surrounding skin before and after the treatment. With these coordinates we have defined a scar score SS. The therapeutic benefit TB was defined as the descent in percentage of the initial SS obtained with the therapy.

**Methods:** After the photoprotection treatment, the SS showed a significant improvement of the aesthetic results in both groups, but in the series with Dermatix the differences were more important. The analysis revealed a significantly therapeutic benefit more important in the group with Dermatix in front of the photoprotective treatment.

**Conclusions:** Urgent reconstruction of facial avulsion must be carried out if permitted by the general status of the patient. Return of ischaemic avulsive flaps to their anatomical location, primary neurorraphy of lesioned nerves, and repair of muscle bundles is essential to obtain a dynamic result. Early and prolonged treatment with (Dermatix) provides satisfactory management of cutaneous scarring and gives an aesthetic and functional result.


**Oral & Poster Presentation**

Fernández García Á., Guzmán Salinas J.L., Aznar Vicente J., Fernández Pascual C., Alonso Rosa S.
Virgen de la Arrixaca University Hospital. Department of Plastic Surgery and Burns, Murcia, Spain

**Background:** The objective study of a scar is complex in the clinical practice, due to the inherent subjectivity in any opinion of aesthetic nature.

**Objectives:** The aim of this study has been to compare the results obtained in scars after silicon gel (Dermatix) treatment in front of photoprotector. The valuation of the results was performed using a objective digital colorimetric method.

**Methods:** Twenty patients with scars were divided in two prospective cohorts. Ten patients received Dermatix and the other patients photoprotector. We performed an initial picture in all the patients. Nine months later, after the therapy, a new picture was performed. These pictures were processed with a computer program. With this system it is possible to know the coordinates that define the colour of the scar and the healthy surrounding skin before and after the treatment. With these coordinates we have defined a scar score SS. The therapeutic benefit TB was defined as the descent in percentage of the initial SS obtained with the therapy.

**Results:** After the photoprotection treatment, the SS showed a similar original punctuation (NS: p=0,416). Howevver, the group with (Dermatix) experimented a more important reduction in the punctuation average that the series with photoprotector (p=0,029). The average punctuation of the TB observed in the group with photoprotector (44,47±25,33) was very inferior to the group with (Dermatix) (80,93±16,27). This difference was very significant (p=0,002).

**Conclusions:** The SS showed a significant improvement of the aesthetic results in both groups, but in the series with Dermatix the differences were more important. The analysis revealed a significantly therapeutic benefit more important in the group with Dermatix in front of the photoprotective treatment.

C03. Larges keloids treated with Integra

**Oral & Poster Presentation**

Giovannini Uberto
Hospital Maternité Metz, 1 Place Sainte Croix 57000 Metz, France

**Background:** Keloids are extremely disturbing to patients, both physically and psychologically. The treatment of keloid and hypertrophic scars remains a challenging clinical problem. Simple surgical excision is usually followed by recur-
rence unless adjunct therapies are employed. Integra was initially developed for the primary coverage of acute burns. It acts as a network for dermal reconstruction. An epidermal graft overlay is necessary after 3 weeks to achieve the in vivo reconstruction of a full-thickness skin equivalent.

**Objective:** Our purpose was to determine the benefit of large intralesional excision of the keloid with healing by Integra and secondary autologous skin graft taken from the scalp.

**Methods:** We treated three patients who had keloids with intralesional excision and Integra graft. Three weeks later the silicone layer is removed and replaced with an epidermal autograft taken from the scalp. Follow-up periods were 6 to 18 months.

**Results:** No postoperative complications for the two surgical procedures. After a healing time of 12 to 48 weeks, scars were smooth and painless. No recurrence of keloids has been observed. Range of motion or and aesthetic outcome was rated as good or excellent. All subjects were satisfied with the results of the procedure.

**Conclusion:** Very large keloids may be resistant to medical management, and too aggressive for surgery owing to a high likelihood of recurrence. Integra appears as an alternative in treating keloids. The disadvantages of using Integra are the necessity of two operations. On the other hand, Integra has many advantages including its immediate availability, the availability of large quantities, the simplicity and reliability of the technique, and the minimal morbidity.

**C04. Clinical nurse specialist-led keloid clinic: the royal london experience**

**Nurse-led keloid clinics - The way forward in the management of keloid scars**

**Oral & Poster Presentation**

**Kim Davies**, Barts and the London NHS Trust, Plastic Surgery Department, Royal London Hospital, London, UK

**Background:** Keloid scars are particularly difficult to treat, and require a patient-centred approach. Typically, patients are treated in busy, general Plastic Surgery or Dermatology clinics - environments that are less than ideal because successful treatment can take considerable time and often requires an approach that addresses psycho-social needs. The development of the first United Kingdom dedicated nurse specialistscar management clinic is described and the benefits are evaluated.

**Objectives:** To review the seven year experience of a nurse-led (Kim Davies - KD) specialist scar clinic for scar and keloid management.

**Methods:** A systematic retrospective review of the work carried out in the nurse-led Scar Management Clinic was performed, with emphasis on cost-effectiveness, nature of management, patient outcomes and compliance rates.

**Results:** In the 7 year period 846 new patients were treated. Patients were referred from Consultant clinics and were subsequently managed to the completion of care in the nurse-led clinic unless surgical input was deemed necessary. Treatments offered were tailored to the individual patient and included steroid injections, pressure therapy, silicone gel sheeting, camouflage, micro-pigmentation, combination therapies and referral to occupational therapists (OT). This has resulted in lowered treatment costs, decreased waiting times, attendance rates of around 80%, with better compliance resulting in low recurrence rates of around 15%.

**Conclusion:** In our 7 year experience we have found that a nurse led keloid clinic is a unique concept providing a holistic approach to management of keloids. It serves to provide economical and effective patient centered care in a nurse-led environment. The nurse can provide a battery of treatments and when necessary invoke the services of surgeons, OT and psychologists. The success of our nurse led clinic in terms of its outcomes as attracted other units in UK to follow a similar approach.

**C05. Technological advancements in the management of hypertrophic scars with silicone and pressure modalities**

**Oral & Poster Presentation**

Jonathan Niszczak
Bio Med Sciences, Inc., Allentown, Pennsylvania, USA

**Background:** Hypertrophic scars continue to be a common consequence for individuals who suffer a burn injury or other significant trauma to the epidermis. Effective rehabilitation and management of these scars requires a comprehensive approach to healing that incorporates the use of durable silicone materials and modulated pressure therapy to enhance both functional and cosmetic outcomes. Pressure therapy has long been a mainstay in the management of hypertrophic scars and more recently, the advances in silicone materials have significantly enhanced the ability of the rehabilitation professional to successfully address diverse hypertrophic scar sequelae.1,2 Although the exact mechanism of action still remains elusive, clinical intervention provides significant evidence that the use of these materials reduce the adverse effects of immature scars.1,2

**Objectives:** The objectives of this presentation are to examine the recent history and theory related to pressure and silicone treatments and how they impact hypertrophic burn scar behavior and to discuss technological advancements in silicone materials (Silon®) and how these improvements have assisted in the management of difficult scar deformities, particularly those affecting the face and hands.1,2

**Study Design:** Case presentations will be provided that demonstrate effective minimization of long-term hypertrophic scars and increased functional recovery through the clinical use of these materials as part of a comprehensive scar management practice.

**References**

C06. Use of a collagen-elastin matrix (matriderm) for dermal reparation in a one stage procedure long term results in the treatment of severe hand burn injuries

**Oral Presentation**

DB Lumenta, LP Kamolz, W Haslik, M Frey
Division of Plastic and Reconstructive Surgery, Department of Surgery, Medical University of Vienna, Waehringer Guertel 18-20, A-1090, Vienna, Austria

**Background:** Since ever more patients survive severe burn injuries, the focus of interest has shifted from high survival rates to an improved quality of life. In this regard, restoration of full function and satisfying aesthetic appearance are essential factors.

**Objectives:** Dermal substitutes can be used to minimize scar formation and to restore pliability of the skin, but because of the increased distance between the wound bed and skin grafts until now a two-stage procedure was necessary to allow for sufficient integration of the applied sheets on the wound.

**Methods:** Matriderm is an absorbable collagen-elastin matrix used for dermal reparation capable of being used in a single stage procedure. Until now 8 patients with full thickness dorsal hand burns were treated with Matriderm in our department. After early debridement the matrix was applied to the wound bed and immediately thereafter the unmeshed split skin grafts. Follow-up was performed within the first two weeks and after 12 months.

**Results:** All grafts were adherent to the wound bed during the observation period. After removal of the dressings, an excellent take-rate could be observed. No haematoma occurred and no further grafting was necessary. No signs of topical or systemic allergic reactions were noted. All patients showed very satisfying cosmetic and functional results after 12 months. The pliability of the Matriderm-skin-graft complex was judged by raising a skin fold of the dorsum of the hand, easily achievable in all treated hands. Mean VSS was 2.6 and the ROM was unlimited. There was no need for secondary procedures. No unstable scar formation or blisters could be observed.

**Conclusion:** Matriderm can be used successfully for dermal reparation in hand burns and its application in a one-stage procedure seems to be a major advantage. Our first long term results are promising, but further studies in a prospective randomized setting are necessary to confirm these findings.

C07. Differential diagnosis of diseases that resemble keloid and hypertrophic scars

**Oral Presentation**

Rei Ogawa, Satoshi Akaishi, Hiko Hyakusoku
Department of Plastic, Reconstructive and Aesthetic Surgery, Nippon Medical School Hospital, Tokyo, Japan

**Background:** Previous articles suggested the presence of various kinds of malignant tumors that resemble keloid or hypertrophic scar, including dermatofibrosarcoma protubersans (DFSP), trichilemmal carcinoma, and keloidal basal cell carcinoma (BCC). Thus, we studied our cases that were diagnosed with diseases other than keloid or hypertrophic scar.

**Patients and Methods:** From April 2003 to March 2007, we examined 378 patients self-diagnosed with keloid or hypertrophic scar.

**Results:** We detected four other diseases (1.06%) in the group of patients. All tumors were benign: apocrine cystadenoma, adult-onset juvenile xanthogranuloma, mixed tumor, and chronic folliculitis.

**Conclusions:** Our study led us to the conclusion that differential or exclusive diagnosis of diseases similar to keloid and hypertrophic scar is important. We found the following considerations important in the examination of keloid or hypertrophic scar: 1. biopsy should be conducted in anomalous cases since malignant disease may be the original or secondary problem, 2. steroid injection should be performed only after careful consideration since malignancy or infection may be present, 3. careful differential diagnosis is particularly challenging in African-Americans because skin and tumor color are often similar, 4. the presence of bacterial or fungal infection should be investigated.
Stand 1. LYMED OY
Lymed Ltd.
Pyhäjärvenkatu 5 A
FIN-33200 Tampere
FINLAND
Tel.: +358-3-272 0800
Fax: +358-3-272 0801
www.lymed.fi

Stand 2. MEDICAL Z
Z.I. Saint-Avertin
14, rue Georges Curvier
37172 Chambray-les-Tours-cedex
FRANCE
Tel.: +33 (0) 2 47 71 3333
Fax: +33 (0) 2 47 71 3334
www.medicalz.com

Stand 3. VALEANT
Valeant Pharmaceuticals Ltd
12 Cedarwood
Chineham Business Park
Crockford Lane
Basingstoke
Hampshire
RG24 8WD
UNITED KINGDOM
Tel.: +44 (0) 2 47 71 3333
Fax: +44 (0) 2 47 71 3334
www.dermatix.net

Stand 4. KCI International
KCI Europe Holding B.V.
Parktoen, 6th floor
Van Heuven Goedhartlaan 11
1181 LE Amstelveen
THE NETHERLANDS
Tel.: +31 (0)20 426 0000
Fax:+31 (0)20 426 0099
www.kci-medical.com

Stand 5. ADVANCED BIOTECH
Advanced Bio-Technologies Inc.
14010 Roosevelt Blvd.,
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Florida, 33762
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Fax: +1 727 531 0360
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BELGIUM
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Fax: +32 9 386 16 09
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Fax: +33 (0)4 92 911 530
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Fax: +44 (0) 1223 341 170
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