#### A 9 Year Clinical Experience with Kelo-cote © The Role of topical silicone in wound healing

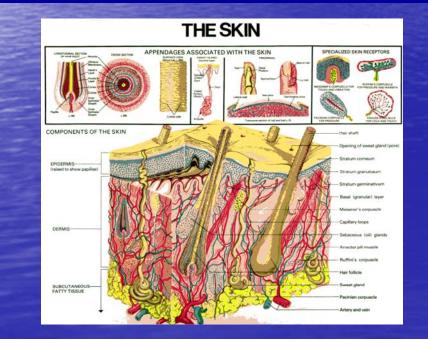
**Rex Moulton-Barrett, MD** 

**Plastic and Reconstructive Surgery** 

Oakland, California

### Not all wounds are created equally

- Fresh surgical: sharp edges, tensionless epidermis, layered dermal repair
- Traumatized tissue: crushed irregular edges, tension
- Thermal and chemical burns: basal layer and dermis may be absent
- Post-scar ( hypertrophic/keloid ) excision: tendency to recur
- Scar prone locations: chin to xiphoid, intra-mucosal
- Scar prone races: related to Fitzpatrick skin types: tan easily=scar easily



Epidermis: 40 - 150 microns Dermis: 140 - 400 microns E & D: 180 >/= 550 microns



### Choices In Topical Therapy Dry Wounds



- Tapes: control tension, shear through surface protection, hydration
- Oil based antibiotic ointments: Polymyxin, Bacitracin, Bactroban, Neosporin
- Skin substitutes: Biobrane, Alloderm
- Silicone gel: Kelo-cote, Scarfade, Mederma
- Silicone gel sheeting: Cica-care, Epiform, Mepilex, Mepitel, Silgel
- Collagens: Clayton Chagall
- Tissue adhesives: cyanoacrylate-Dermabond, Epiglu, Indemil, Liquiband
- Barrier films: fast drying carrier solvent: Cavillon, Comfeel, Superskin



### Choices In Topical Therapy Wet Wounds



- Silver dressings: Acticoat, Actisorb, Avance, Flamazine
- Foams: absorptive for exudates-Allevyn, Flexipore
- Alginates: seaweed based very absorptive- Meligisorb, Algisite, Sorbsan
- Hydrogels: >70% water, minimally absorptive- Aquaform, Intrasite, Nu-Gel
- Hydrocolloids: semi-permaeable-Aquacel, Cutinova
- Vapour permaeable films: semi-permeable, fluid accululates-Tegaderm
- Low-Adherance Dressings: Telfa, Medipore, Cutilin, Xeroform
- Multi-layer bandages: useful for venous ulceration- Profore

### **Components of Normal Wound Healing**

### Coagulation process

#### A) Immediate to 2-5 days

 Inflammatory process  B) Hemostasis : Vasoconstriction , Platelet aggregation , Thromboplastin clot
 C) Inflammation: Vasodilation , Phagocytosis

 Migratory/ Proliferative process

Remodeling

process

#### A) 2 days to 3 weeks

- B) Granulation: Fibroblasts lay collagen, Fills & new capillaries
- C) Contraction: Wound edges pull together to reduce defect
- D) Epithelialization: Crosses moist surface up to 3 cm

#### A) 3 weeks to 2 years

B) New collagen forms which increases tensile strength

#### C) Scar tissue is only 80 percent as strong as original tissue

Injury: hours / days

weeks

# **Biochemical Differences**

**Chronic** wounds

### Healing wounds

- cell mitosis
- pro-inflammatory cytokines
- matrix metalloproteinases
- growth factors
- cells capable of responding to healing signals

Repeated trauma Local tissue ischemia Necrotic tissue Heavy bacterial burden Tissue breakdown

Chronic wound delayed healing

Prolonged inflammation Stimulation of macrophage and neutrophils to wound bed

Degrades ECM
impaired cell migration
impaired connective tissue deposition
Degrades growth factors

Release of pro-inflammatory cytokines

Production MMPs and TIMPs

### TIME Principles of Wound Bed Preparation Wound bed preparation accelerates healing

issue non viable or deficient	nfection or inflammation	Moisture imbalance	dge of wound non advancing or undermined
Defective matrix and cell debris	High bacterial counts or prolonged inflammation	Desiccation or excess fluid	Non-migrating keratinocytes Non-responsive wound cells
Debridement	↓ Antimicrobials	Dressings compression	Biological agents Adjunct Therapies Debridement
Restore wound base and ECM proteins	Low bacterial counts and controlled inflammation	Restore cell migration, maceration avoided	Stimulate keratinocyte migration

### **Debridement Methods**

Surgical: excise
Mechanical: adherence, sheer, irrigate
Autolytic: topical
Enzymatic: topical
Biological: topical

# Autolytic Debridement

•The process by which the wound bed utilizes phagocytic cells and proteolytic enzymes to remove debris

•This process can be promoted and enhanced by maintaining a moist wound environment



### Autolytic Debridement Considerations

- Less aggressive
- Slower
- Easy to perform
- Little or no discomfort
- Performed in any setting
- Contraindication: infection

# **Enzymatic Debridement**

•The use of topically applied chemical agents to stimulate the breakdown of necrotic tissue

#### Common Topical Agents

- Papain-Urea
- Papain-Urea-Chlorophyllin
- Collagenase



## **Enzymatic Debridement**

#### Collagenase

- Derived from Clostridium Hystoliticum
- Highly specific for peptide sequence found in collagen
- Less aggressive debridement
- Site of action collagen fibers anchoring necrotic tissue to the wound bed

### Enzymatic Debridement

#### Papain-Urea

- Proteolytic enzyme derived papaya<sup>6</sup>
- Urea is added as a denaturant<sup>6</sup>
- Site of action cysteine residues on protein<sup>8</sup>

### **Enzymatic Debridement Considerations**

- Should be painless
- Less traumatic than surgical or mechanical debridement
- Easy dressing change
  Observe caution with infected wounds

- Consider for individuals who:
  - Cannot tolerate surgery
  - long-term-care facility
  - home care\*

#### Collagenase Papain-Urea-Chlorophyllin

#### Autolytic



#### The right method is a <u>clinical decision</u> that requires judgment

# **Bacterial Balance**

- Intact skin is a physical barrier
- Skin secretes fatty acids and antibacterial polypeptides
- Normal flora prevent pathogenic flora from establishing

### **Bacterial Burden**

 Tissue bacterial levels > 10<sup>5/gram</sup> have consistently resulted in impaired healing causing:

Metabolic loadProduces endotoxins and proteases

<sup>3</sup>Robson (1997) <sup>14</sup>Dow (2001)

### Efficacy of traditional topical antibiotics

- Leyden & Kligman, 1979: Neomycin contact sensitivity < 1% skin testing</li>
- Booth, etal,1994: Minimum Inhibitory Concentration mg/L

Bacteria	A:Neomycin	B:Bacitracin	C:Polymyxin B	(TAO): A+B+C
Staph Aureus	1	54	61	synergy
Pseudomonas aerug.	32	>6917	8	synergy
Enteric bacillus	8	>6917	1	synergy

• Dire, et al, 1995: Uncomplicated sutured soft tissue trauma wounds

Topical Agent	Infection Rate	
Bacitracin Zinc	5.5%	
TAO	4.5%	
Petroleum	17.6%	

### 3 "Rules" for Topical Antimicrobial Agents ?

 Do not use antibiotics that are used systemically – ability to breed resistant organisms (topical gentamicin, tobramycin)

Do not use agents that are common allergens (neomycin, gentamicin, amikacin, tobramycin, bacitracin, lanolin)

• Do not use agents that have high cellular toxicity in healable wounds (povidone iodine, chlorhexidine, hydrogen peroxide)

# Topical Antimicrobials: Silver

#### Centuries of use

- Cytotoxicity associated with carriers not silver ex. Silver nitrate, Silver sulfadiazine
- Traditional delivery required repeated applications due to binding with chlorine and proteins
- New silver dressings allow for continued silver release in to the dressing - up to 7 days

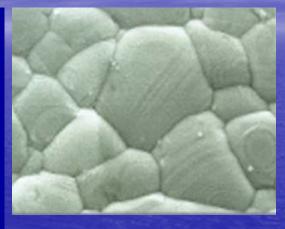
### Why Silver for Wound Bed Preparation?

- Broad spectrum antimicrobial: yeasts, molds & bacteria, including MRSA
- Kills microbes on contact: inhibition cellular respiration denatures nucleic acids alters cell membrane permeability
- Does not induce resistance: if used at adequate levels
- Low mammalian cell toxicity

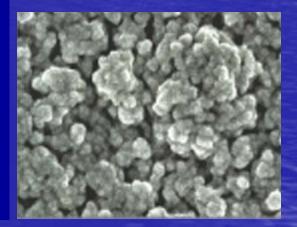
### Nanocrystalline Silver

 Decreased size of silver particles leads to increased proportion of surface atoms

 The nanocrystalline structure is responsible for the rapid and long lasting action<sup>15</sup>



Magnification of normal Silver



<sup>17</sup>Demling and DeSanti (2001)

Magnification of Nanocrystalline Silver (< 1 micron)

### **Evaluating Silver Products**

Minimum bactericidal concentration (MBC) - amount of antimicrobial agent required to kill a given microbe MBC is represented by a log reduction of 3

Stratton et al (1991)

 The silver required varies from 5ppm - 50+ ppm for clinically relevant microbes

Yin et al (1999) & Hall (1987)

- MBC of silver for MRSA = 60.5 ppm

Calculated from Maple et al (1992)

# Moist Wound Environment

### Additional benefits

- Faster healing
- Capacity for autolysis
- Decreased rates of infection
- Reduced wound trauma
- Decreased pain
- Fewer dressing changes
- Cost effective

### **Exudate from a Chronic Wound**

- Different from acute wound
- Imbalance of growth factors and pro-inflammatory cytokines



- Excessively high levels of proteases
- Degrades ECM and selectively inhibits proliferating cells

# Managing Moisture Imbalance

#### Exudate amount

• Films	None	Small	Moderate	Large
<ul> <li>Hydrogel</li> </ul>				
<ul> <li>Hydrocolloid</li> </ul>				
<ul> <li>Alginate</li> </ul>				
- Foams				
Specialty Absort	pent			
Suction Vac				

#### **Suction Vac Therapy**

**Management of open wounds** 

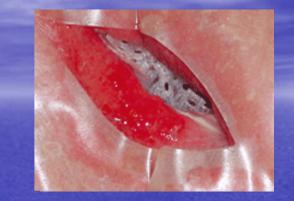
- increases granulation rate > 5x's
- success depends on pore size, -125mmHg
  - reduces wound volume

equires changing every 2 days

vascular ingrowth and healing appear to be due cell deformation

early epithelial cells lack rete pegs and are easily strained to 5-20%, postulated mechanism

Saxena, etal, 2004: PRS 114(5)





### Modern Scar Concepts (1)

- New keratinocytes lack rete pegs, are fragile, deformable and produce many fibrotic growth factors
- Fibroblasts within the injury zone are more sensitive to these and other growth factors
- Sulphated side chains develop from chondroitin produced from these fibroblasts
- The side chains cause water binding and subsequent scar rigidity

### Modern Scar Concepts (2) Collagenesis - Deposition - Resorption

#### Collagenesis

- Scar volume is dependent on the volume of collagen
- Collagen formation: mRNA mediated
- Fibroblast interferon β( IFN- β): inhibitor of collagenesis
- Transforming Growth Factor TGF ß 1 (adult): stimulates collagenesis
- TGF ß 3 (infant): inhibits collagenesis
- Renovo/ Retinae: inhibitors of TGF- ß1 activation: reduced collagenesis improving scars
- Gamma interferons and other cytokines down regulate collagen and matrix synthesis and increase monocyte retention within the wound

# Modern Scar Concepts (3) Collagenesis - **Deposition - Resorption**

#### **Collagen Deposition & Resorption**

- Fibroblast and monocyte collagenase: <u>reduce collagen deposition</u>
- Metalloproteinases inhibit collagenases: promoting collagen deposition
- Expression of fetal metalloproteinase: loss of scarless healing
- Intralesional steroids inhibit fibroblast growth

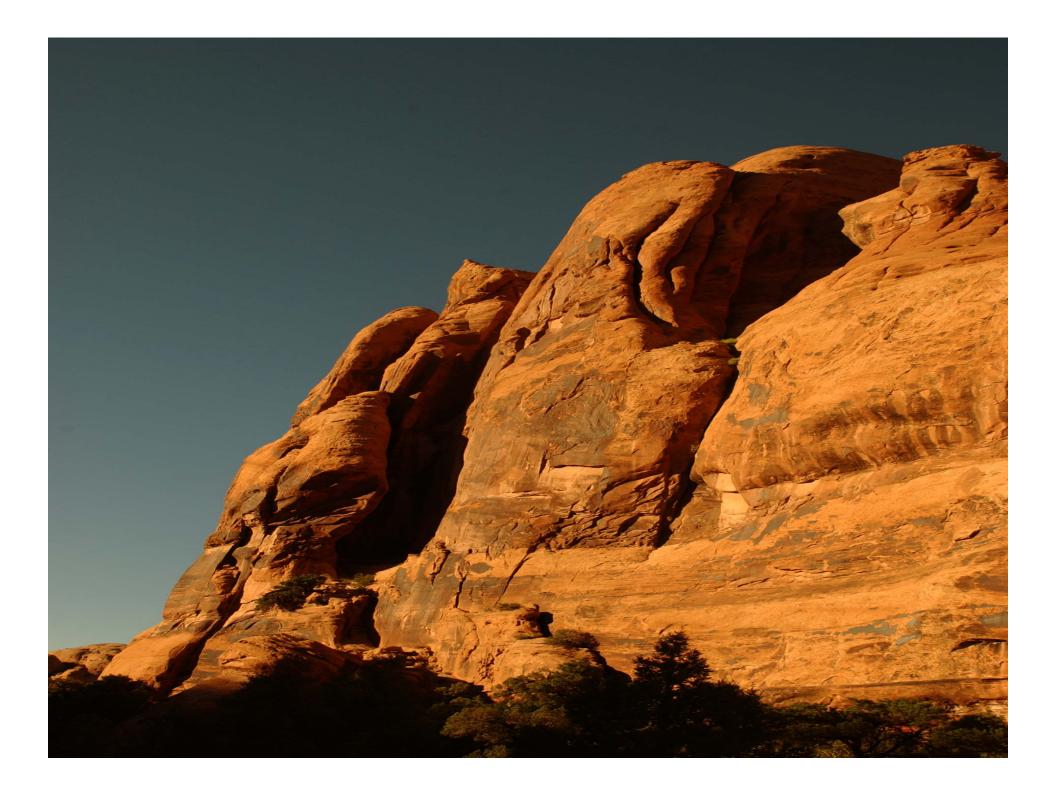
inhibit collagen deposition:

- <u>increase</u> monocyte <u>collagenase</u> secretion
- no influence on metalloproteinase
- no influence on collagen production

# Modern Scar Concepts (4) + The Role of Tissue Hypoxemia -

- impedes epithelialisation
- increases infection: neutrophil dependent
- + reduces collagenesis in an epithelialised wound
- + compression and radiation lead to local fibroblastic hypoxemia
- Compression and radiation should be used <u>after</u> epithelialisation is complete

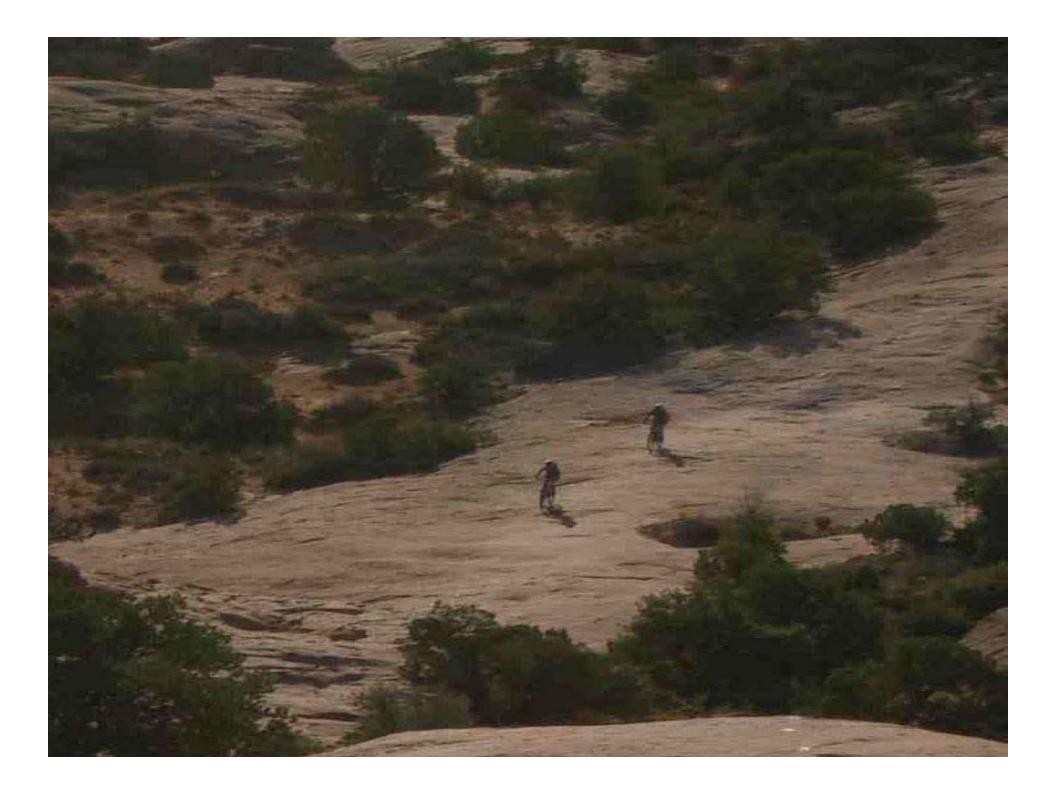












### Summary of Treatments for Hypertrophic Scar and Keloids

- Surgery
- Laser Excision
- Pulse Dye Laser Reduction
- Cryotherapy
- Pressure Therapy
- Radiotherapy
- Steroid, Interferon, 5-FU Injections, Colchicine
- Topical Aldara 5%
- Prolonged taping\*
- Silicone gel/sheeting\*

 k patient controlled inexpensive non-prescription few if any complications well tolerated

## Prolonged Paper Tape To Scar

Atkinson, et al, PRS Nov 2005; 116 (6), 1648-

- 70 pts acute scars: s/p caesarian section, Brisbane, Australia
- Micropore tape to randomized 1/2 pts after staple removal 4-7 days post-op
- Tape applied continuously for 12 weeks
- The control group received no treatment
- Scar volume was assessed by ultrasound
- Scar volume was reduced in the treatment group (p<0.05)</li>
- High correlation between subjective scar rating & intradermal scarring ( p<0.001)</li>
- Authors postulate that tension is the cause of significant scarring

### Management of Common Keloids

#### • Earlobe - If primary excision:

3 x daily peroxide and triple antibiotic remove nylon 5.0 sutures at 10-14 days, then: Dermajet inject Kenalog (trimacinolone 40mg/ml) start Kelo-cote after sutures out for at least 3 months start compressive clamp "ear-ring" : no Nickel return every 6 weeks for further injections

#### Berman B, Bieley HC. Dermatol Surg 1996 Feb;22(2):126-30

- excision alone: 45-100 % recurrence
- excision and Kenalog injection: < 50 % recurrence
- excision and irradiation: < 10% recurrence
- excision and button compression: no recurrences

### www.delasco.com tel: 1 800 320-9612

#### **MadaJet Needle-Free Injector**



#### **Pressure Earrings**

For Post Op Ear Lobe Keloid Treatment

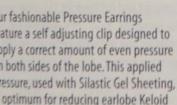








PE-11, PE-12

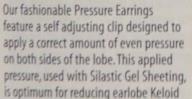


PE-10





PE-1







### **Glori-Sil®** Pressure Earrings



Oval, Sleeper, Square

Glori-Sil Compression earrings are attractively designed plus hypo-allergenic and nickel-free. Fitted with DuraSiL<sup>™</sup>-K silicone sheeting. Clear finish is heat-cured for durability.

**Average Lobe PS-14** Oval



## Management of Common Keloids

Earlobe - if secondary excision: excise and within 14 days: post-op irradiation either one dose of 10 Gy or up to 15 Gy in 2-4 fractions sutures out 14 days post-op Kenalog injection, compressive ear-ring and 6 week follow-up

Klumpar DI, Murray JC, Anscher M. JAm Acad Dermatol 1994 Aug; 31(2 Pt 1):225-31

- Dose irradiation most important factor: give >900c Gy
- Irradiation completed within 1-3 weeks equally effective
- ear lobe 98% successful at > 1 yr follow-up
- small subsequent recurrences can be re-irradiated: 15 Gy

Improvement of Erythematous and Hypertrophic Scars by he 585-nm Flashlamp-pumped Pulsed Dye Laser, Tina Alster. Ann Plast Surg 1994;32:186-190

- 14 healthy subjects with hypertrophic and or erythematous scars as a results of trauma
- Scars were at least 2 years old
- Candela flashlamp-pumped dye laser: 6.5-6.75 J/cm2 1-2 treatments
- 57% improved: lightening and flatter after one treatment
- 83% improved after 2 treatments
- Continued improvement over 6 months
- Improvement was not location specific, depth of scar not assessed



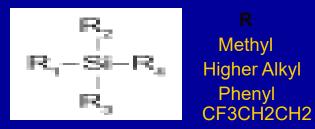
**Irradiation mostly contraindicated Re-resection definitely harmful** Laser excision usually harmful **Pulse Dye lasers not helpful** Aldara 5% not helpful Silicone sheeting not helpful **Steroid injections very helpful Kelo-cote helpful if < 5mm raised** 

## 

- Kelo-cote Composition:
  - Long chain polymers of silicone (Polysiloxanes)
    Minimal Silicone dixoide cross links polymers
    A volatile solvent allows silicone to dry on the stratum corneum in an ultra-thin sheet

## **Silicone Composition**

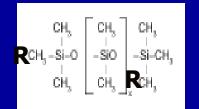
#### Silanes: monomers



#### **Characteristics**

Hydrophobicity & Low surface tension Organic-compatibility and Paintability Thermo-stabile,Organo-compatible, Hydrophobic Solvent resistant

#### Siloxanes: polymers



more crosslinked: more solid recurring silicone / oxygen backbone end / side chains determine functionality **R**: ie.: amine,carboxy, hydroxyl,epoxyl

### Favorable properties related to scar reduction

- Intermediate forms: elastomers: gel, rubber
- Solid-liquid binding requires catalyst 'curing': ie. platinum,

stannous octoate

- Delivery in an evaporative solvent may provide the ability to change the properties of the silicone upon delivery
- Properties influencing scar reduction include:
- Thickness: < 0.254mm
- Moisture vapor transmission rate: <15mg/cm2/day</li>
- Oxygen permeability: > 600cc/100 in.sup.2/day
- High stretch: ,1.5lbs/in stretches > 110% length
- Tensile strength: >100g
- Penetrability: 4-7mm
- Peel strength: 2-6 g

### Potential Theories

- Hydration: increases
- Oxygenation: decreases
- Protection: increases
- Cellular Strain: increases ?
- Modulation of growth factors

### Hydration

- Kelo-cote is semi-occlusive aerating and hydrating
- Silicone absorption is limited to the epidermis
- Stratum corneum regulates fibroblast /collagenesis
- Hydration normalises the collagen synthesis

### Hydration

#### But not all breathable dressings will reduce scars

- In a study comparing silicone and hydrogel dressings, silicone normalised collagen synthesis, other breathable non-silicone dressings did not
- Silicone has a scar reducing characteristic not seen with polyurethanes
- Further research ongoing

### Protection

- Microbial, chemical or physical irritation promote excessive collagen production in early scars:
- Keratinocyte dependent: exposed cell release growth factors
- Fibroblast dependent: Staph epidermidis Immortalization Theory
- Intact dermis is necessary for normal wound healing

### **Modulation Theory**

- Silicones oils and sheeting appear to have an influence on Fibroblast growth factors and transforming growth factors
- Silicone reduces FGF growth factors in vivo, yet ( opposite in vitro )
  - Fibroblast are reduced
  - Collagenase is increased
- "Collagen production is normalised"

### History of Silicone in Scar Reduction

Good review: Mustoe, et al, PRS 2002:110(2) 560-

• Perkins et al, 1983: reported silicone a new treatment for hypertrophic scars

- Ahn, et al, 1989: silicone gel improved texture, color, thickness and itching from small hypertrophic scars
- Sawada & Sone, 1990: 20% silicone gel 82% improved hypertrophic scars and keloids a.c.t. glycerin 22% improved
- Sawada &Sone, 1992: silicone gel an elastomer sheeting vs. petroleum, 6 months f/u silicone group much softer, less red
- Pamieri, et al, 1995: Found Vit E enhanced hypertrophic scar and keloids
- Phillips, et al. 1996: hydrocolloid dressings no evidence to support reduce scarring after hypertrophic scar or keloid established

### Literature lacks double blind placebo controlled studies

### Placebo Controlled Pilot Study Evaluating Kelo-cote in the Reduction of Scarring Following Cleft Lip Repair

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture. QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture. QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.

10 days post-op

QuickTime™ and a TIFF (LZW) decompressor are needed to see this picture.

8 weeks post-op



8 months post-op

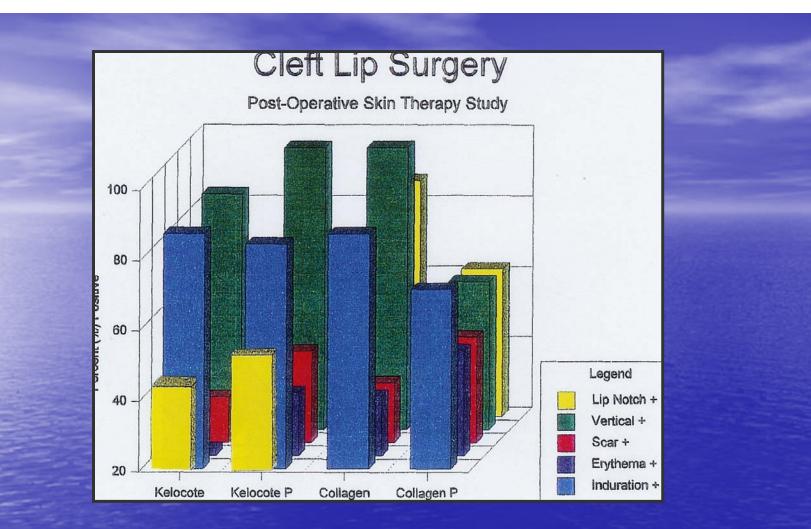
A



33 patients, Santiago, Chile, 1996
 Methods: mm vertical scar shortening (A-B) mm depth lip notch

 \*average width scar mm scar softness 0-3 grade
 scar erythema 0-3 grade

 6 week follow-up results



### Markedly reduced erythema (p< 0.005) Reduced horizontal scar width ( p<0.05)

### Chan, et al, 2005: PRS Sept 15

 Placebo controlled study prospective clinical trial of silicone gel (Scarfade ®) in the prevention of hypertrophic median sternotomy scars

- 100 wounds/50 pts Malaysia
- Reduction of:

pigmentation (p=0.02)vascularity(p=0.001)pliability(p=0.001)height(p=0.001)pain(p=0.001)itchiness(p=0.001)

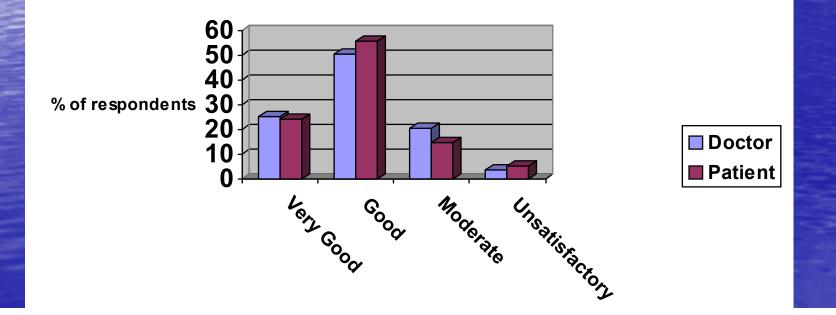
- Non-placebo controlled study Kelo-cote on scars: all-comers, up to 48 month follow-up
  - Data 111 patients Germany, Switzerland & Austria
  - Study: legal requirement for `new' products
  - Independent study
  - Data is on all types of scars
  - Different ages of scars
  - Measurement tool is Vancouver scar scale, which is standard measurement for scars

Patients & physicians assessment of tolerability and efficacy using 4 point scale
Vancouver scar scale

	Score					
	0	1	2	3	4	5
Pigmentation	Normal	Hypopigmentation	Hyperpigmentation			
Vascularity	Normal	Pink	Red	Purple		
Pliability	Normal	Supple	Yielding	Firm	Banding (rope-like)	Contracture
Height	Flat	1 to 2 mm	2 to 5 mm	>5 mm		
Pain	None	Occasional	<b>Requires</b> medication			
Itchiness	None	Occasional	Requires medication			

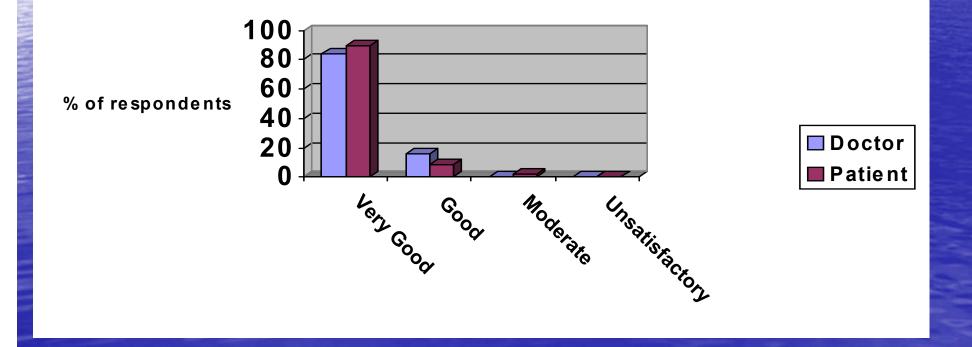
Results of patient and physician assessment - Efficacy

Patient and Physician assessment of efficacy



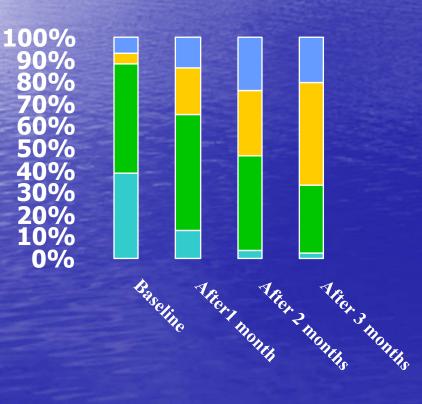
Results of patient and physician assessment - Tolerability

### Patient and Physician assesement of Tolerability



### Decrease in Vancouver Scar Scale - Redness

% of patients (n=111)

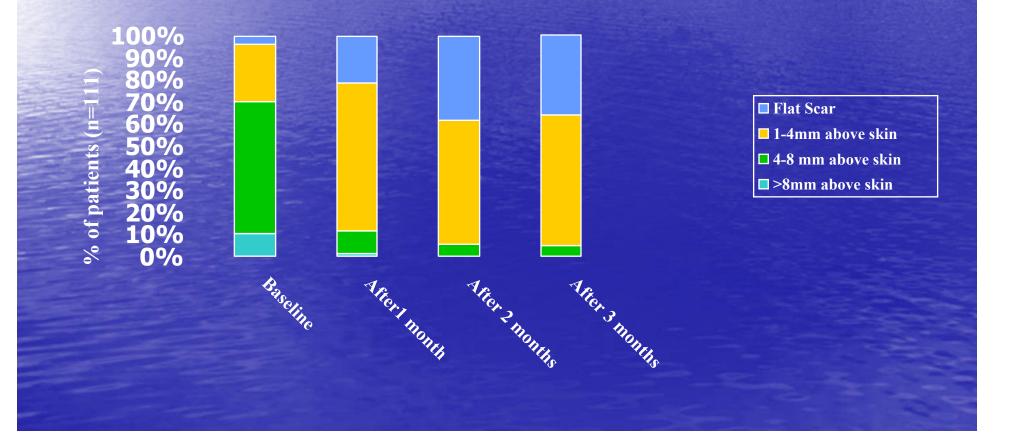


Normal skin

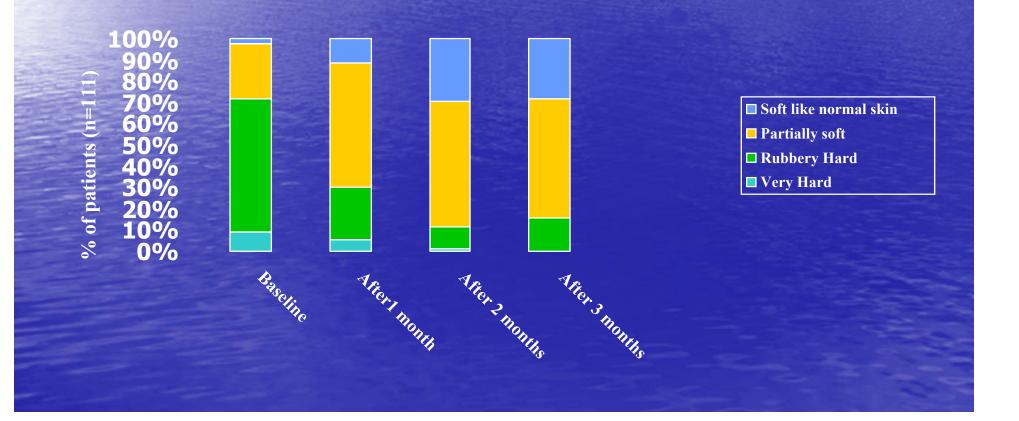
**No redness but dark apperance** 

Redness Dissapears with pressure
 Severe Redness

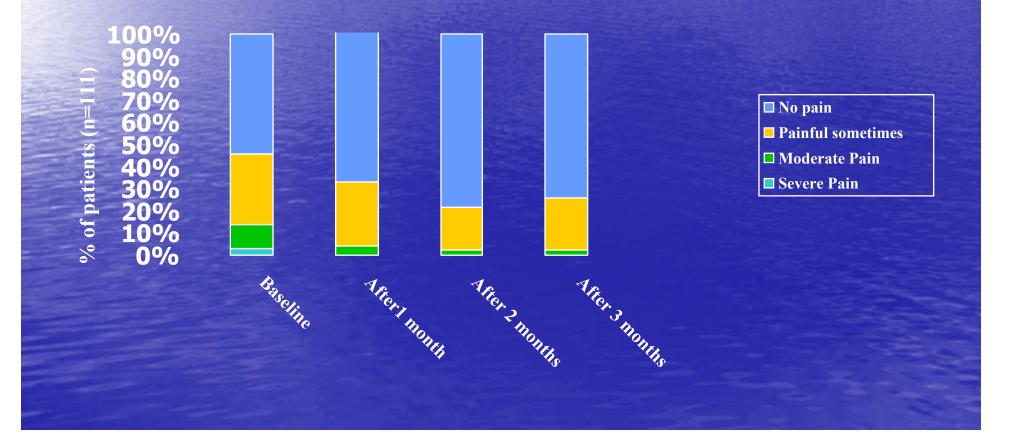
### **Decrease in Vancouver Scar Scale - Elevation**



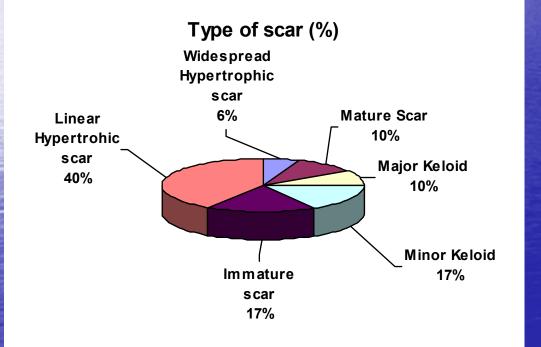
### Decrease in Vancouver Scar Scale - Hardness

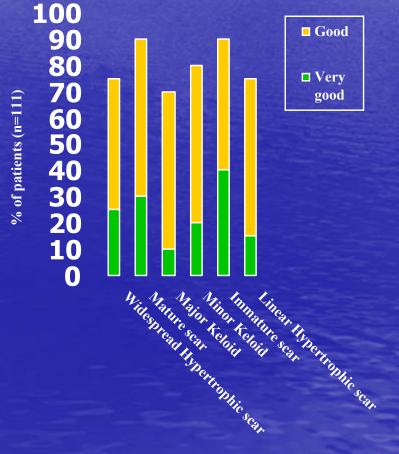


### Decrease in Vancouver Scar Scale - Pain

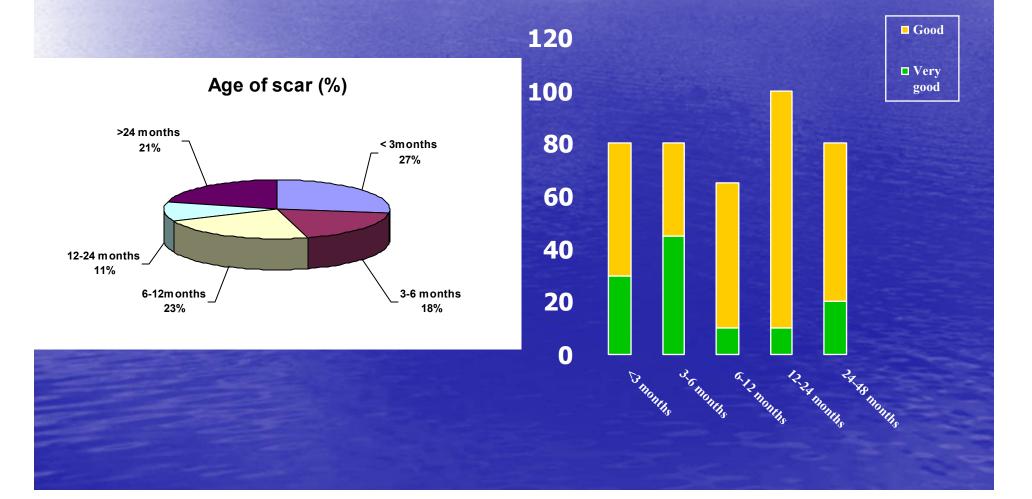


# Sebastian et al, 2005 Results by type of scar





# Sebastian et al, 2005 Results by age of scar



## Summary of study

- Kelo-cote® rated:good/very good > 80% patients & physicians
- Physicians rated tolerability: good/very good 100% of patients
- Kelo-cote® decreased: redness, elevation, hardness, itchiness and pain of scars over a two month period

## Indications for use

- Kelo-cote® is indicated for the management of:
  - Acute healing scars
  - Hypertrophic scars
  - Keloids
- Kelo-cote®<sup>™</sup> has also been used for scars resulting from:
  - Trauma
  - Burns
  - Surgery
  - Acne
  - Post laser erythema

## Length of treatment

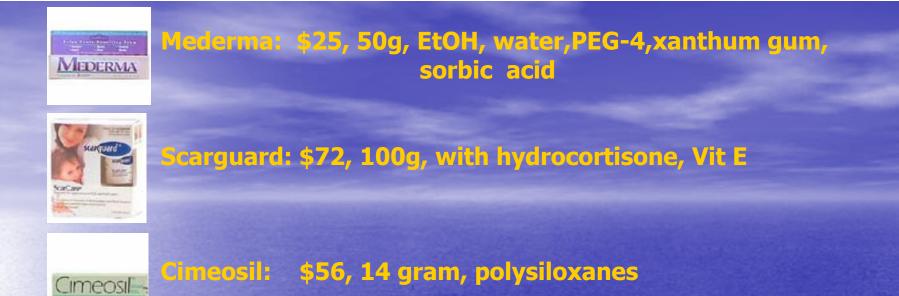
Minimum treatment should be 2 months
Treat larger and older scars >3 months
Active persons apply usually in am
May treat with other topicals in pm

### Instructions for use 0.5 oz Kelo-cote

- Ensure the area is clean and dry.
- Apply a very thin layer and allow to dry
- Apply once daily, or twice daily
- Maximum effect, 24 hours of continuous contact
- Once dry, OK to cover with pressure garments, sun block or cosmetics
- If not dried within 4–5 minutes: too much
- Gently remove the excess and allow the drying
- Larger and older scars > 90 days
- 0.5 oz contains enough Kelo-cote®, for: 7.5–10cm 2x/day for 90 days
- Reduce drying time hotter climates, keep in the refrigerator
- In colder weather, use low setting on hair dryer to reduce drying time

## Warnings and Precautions

- Avoid direct contact with eyes, mucous membranes, & open wounds
- Kelo-cote® may stain clothing if not completely dry
- Store below 77°F (25°C)
- Do not use after the expiration date





Skin Esthetique: \$24, 170g,dimethicone, arnika, copper, seaweed



Scarfade: \$25, 50g, silicone dioxide, micro quartz crystals +/- vit E,K, co-enzyme Q-10

Pro-Sil: \$17.50, glide-on, silicone "creams and oils"

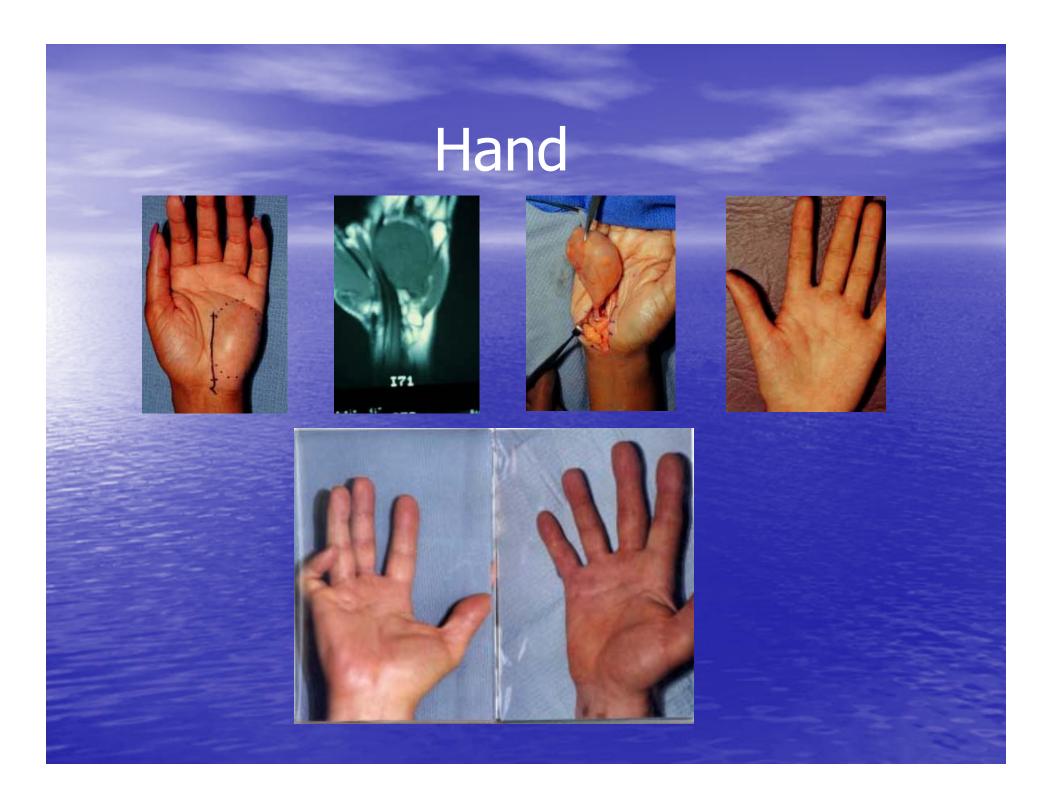


- Kelo-cote

   is a uniqe patent protected silicone gel
- 80% patients rate Kelo-cote® as good or very good in scar reduction
- 100% physicians rate Kelo-cote® good or very good in pt tolerability
- Kelo-cote softens, flattens & reduces the redness of old & new scars
- Kelo-cote® is a comaparatively cost effective treatment

## Clinicial Care: 'Olsen's Rule'

- "Most wounds heal proportionate to the time and attention they are given"
- Steristrip minimum of 4 7 days & then another 5 days after changing strips
- Early application of Kelo-cote, avoid any contact with clothing for 6 weeks minimum: diapers OK
- All open wounds treated with 1/2 peroxide, bacitracin, minimum of twice daily



# **Breast Reduction**









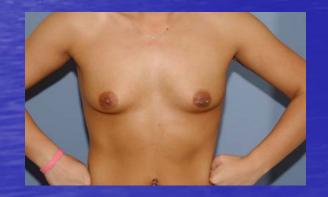




## **Breast Augmentation**













## **Mastopexy Augmentation**





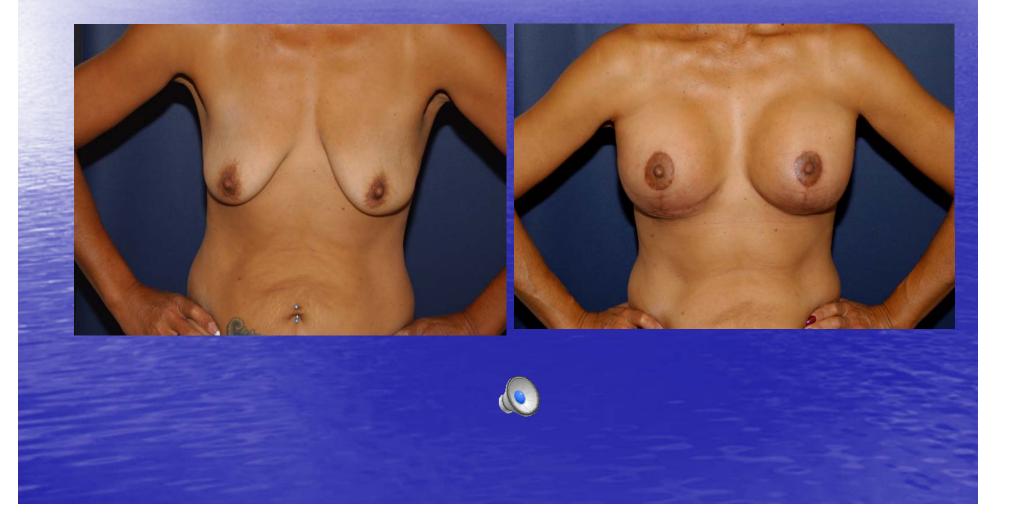








### **Verbal testimonial: Mastopexy Augmentation**



## **Breast Cancer Reconstruction**

#### Bilateral Transverse Rectus Abdominus Myocutaneous Flap





## Abdominoplasty











#### **<Olsen's Rule**



### **Facial Trauma**



## Facelift









## Head and Neck Excisional Surgery



## **Cleft Lip Surgery**













#### **Looking into the Future**



#### **Bioglass and nano crystal Silver Spray**