



PLASTIC, AESTHETIC AND
RECONSTRUCTIVE SURGERY GRAZ



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The use of Keratinocytes: Things we should keep in mind!

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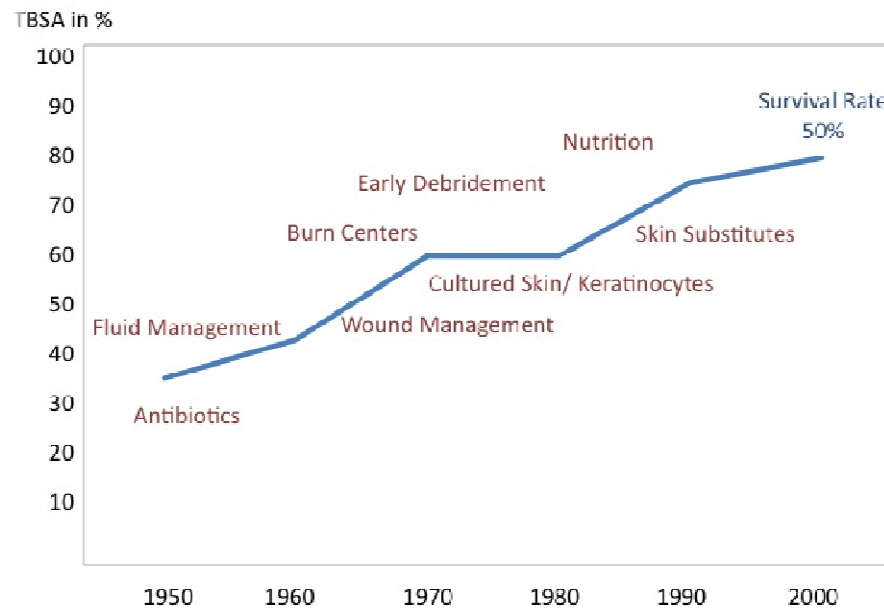
The most common cause of severe skin loss is the thermal injury.





The possibility of surviving severe burn injuries has changed dramatically over the past decades.

One of the milestones was a more aggressive approach concerning surgery; **early wound debridement** and **early wound coverage** has led to a higher survival rate.





- Over the past decades, extraordinary advances have been made in the understanding of cellular and molecular processes involved in burn wound healing.
- This knowledge has led to wound care innovations and new developments concerning burn care; burn care has improved to the extent that persons with burns can frequently survive.
- The trend in current treatment extends beyond the preservation of life; the ultimate goal is the return of burn victims, as full participants, back into their families and communities.

Kamolz LP.

Burns: learning from the past in order to be fit for the future.

Crit Care. 2010;14(1):106.



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- In the acute stage rapid and effective burn wound closure is one of the most important aspects in the treatment of burn patients, because the patient is in a sub-septic condition until all skin defects are closed.
- Exact evaluation of the burn wound (TBSA and burn depth)
- Timing of Surgery
- Burn depth specific treatment

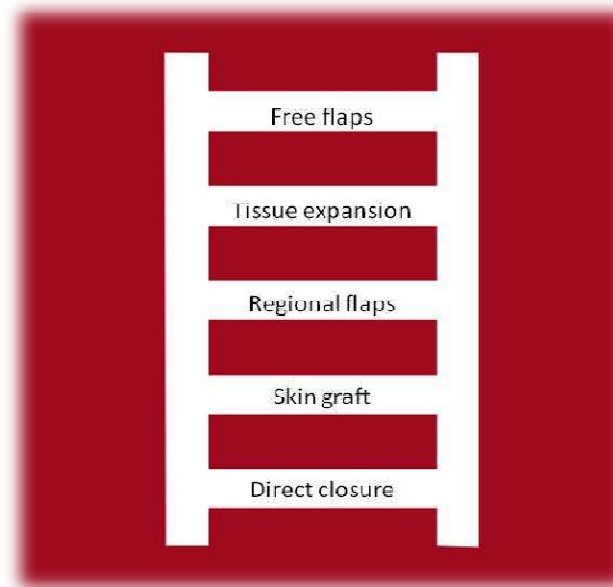
Lumenta DB, Kamolz LP, Frey M.

Adult burn patients with more than 60% TBSA involved-Meek and other techniques to overcome restricted skin harvest availability--the Viennese Concept.

J Burn Care Res. 2009 Mar-Apr;30(2):231-42.



- Mathes and Nahai have used the metaphor of the reconstructive ladder in 1982 in their book: Clinical application for muscle and musculocutaneous flaps. They used the term „**The Reconstructive Ladder**“ in order to integrate the free flap into the reconstructive repertoire.





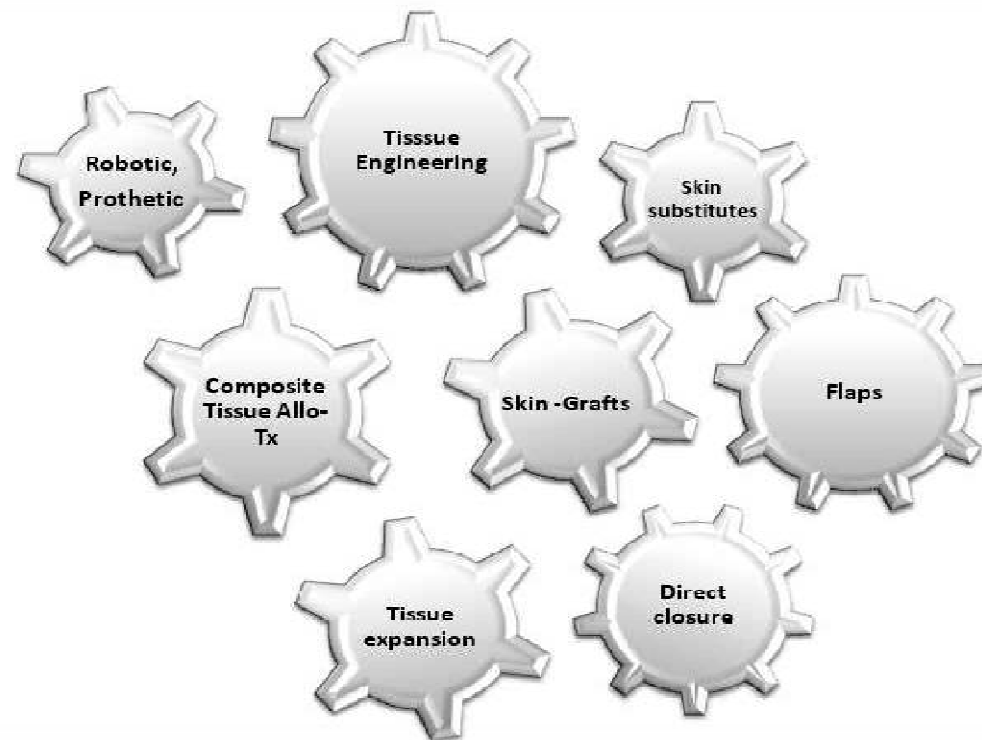
The Reconstructive Elevator:

- With the advancement in the understanding of the anatomy, operative techniques, instrumentation, and surgical skill, complex procedures are no longer considered as last resort procedures only.
- „In the quest to provide optimal form and function, it should be currently be accepted to jump several rungs of the ladder, with the knowledge that some defects require more complex solutions.“
- The reconstructive elevator allows one to ascend from the simplest to the more complex techniques, with the freedom to ascend directly to the chosen level of complexity.



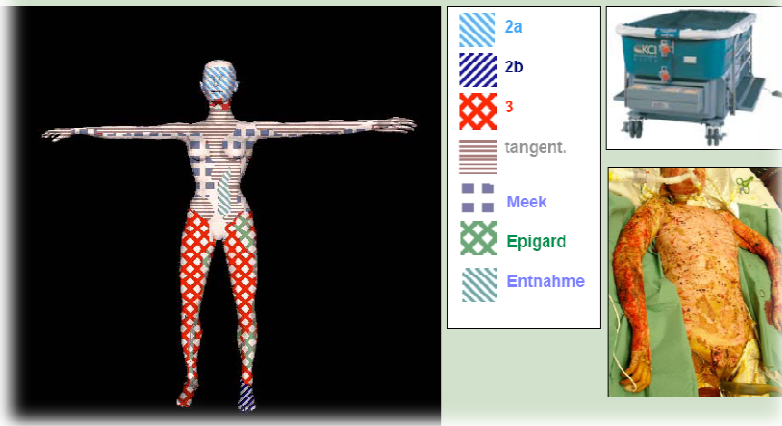
The new Reconstructive Clockwork of the 21st century:

- **Combination of the different reconstructive procedures.**

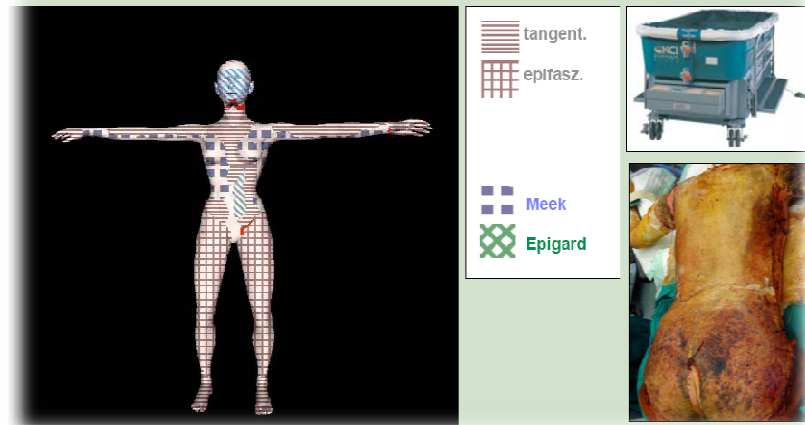




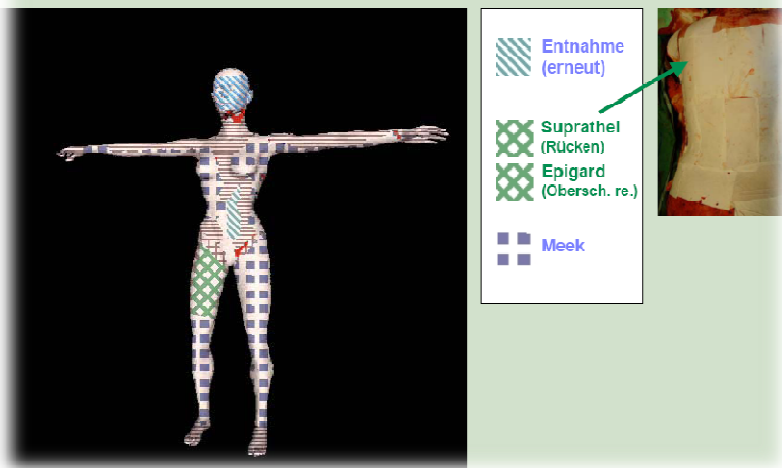
Fallbeispiel: F, 36 Jahre, Ambustio 90% KOF 2B-3 (II)



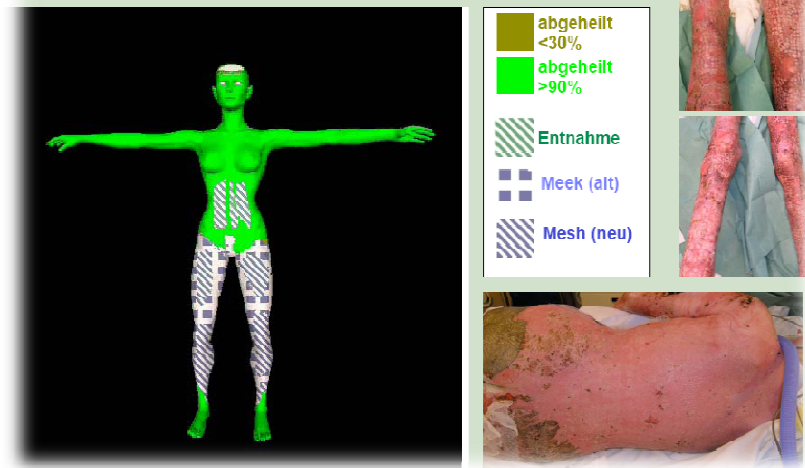
Fallbeispiel: F, 36 Jahre, Ambustio 90% KOF 2B-3 (III)



Fallbeispiel: F, 36 Jahre, Ambustio 90% KOF 2B-3 (IV)



Fallbeispiel: F, 36 Jahre, Ambustio 90% KOF 2B-3 (V)





The Techniques of Reconstruction:

There are several techniques routinely used to reconstruct deformities and to close defects.

Principally, they are:

- direct closure techniques,
- closure with a skin graft with or without the use of a dermal substitute,
- closure with local and regional flaps,
- closure with free flaps,
- closure with tissue expansion,
- closure by use of composite tissue allo-transplantation,
- improvements due to the use of robotics and prosthetics,
- closure and improvements by use of tissue engineering.



➤ The questionnaire:

19 questions: single choice, multiple choice, open text

Questions	Answers	Answer type
1. How important do you consider sk in substitute s for burn patients suffering from medium size burns (between 20% and 60% TBSA)?	Essential, Desirable, Neutral, Seldom required, Never Required	Single choice
2. How important do you consider sk in substitute s for burn patients suffering from severe burns (>60% TBSA)?	Essential, Desirable, Neutral, Seldom required, Never Required	Single choice
3. Do you use sk in substitutes in clinical practice?	No, Allografts, Xenografts, Synthetic materials, Biological and Synthetic	Single choice
4. Do you think that using biological materials on wounds pose a real risk to patients?	Yes, No	Single choice
5. In severe burns (>large 50% TBSA) do you prefer using biological or synthetic skin substitutes in clinical practice?	Biological, Synthetic	Single choice
6. Which of the following represents most likely the main indication for the clinical use of skin substitutes in your institution?	Superficial dermal burns, Deep dermal burns, Full thickness burns, Other	Open text Single choice
7. How important do you consider the factor cost for clinical application of skin substitutes (eg. affordable price)?	Essential, Neutral, Not important	Single choice
8. How important do you consider the factor biological use in the context of clinical application of skin substitutes?	Essential, Desirable, Neutral, Seldom required, Never Required	Single choice
9. How important do you consider the factor "ready availability" (always accessible) in the context of clinical application of skin substitutes (eg. no outstation time needed)?	Essential, Desirable, Neutral, Seldom required, Never Required	Single choice
10. In what further specialization would you like skin substitutes to be available for you?		Open text
11. Do you use Dermal Replacements in clinical practice (e.g. Integra®, Matriderm®...)?	Yes, No	Single choice
if yes, which one do you use?		Open Text
12. Do you use Epidermal Replacements in clinical practice (e.g. Keratocytes, Supathel®...)?	Yes, No	Single choice
if yes, which one do you use?		Open Text
if no, why?		
13. Do you think that an ideal skin substitute is already available?	Yes, No	Single choice
if yes, which one?		Open text
15. Why?		Open text
16. Do you use xenografts?	Yes, No	Single choice
if no, why?		Open text
18. If yes, what is your main indication for applying xenografts in clinical practice?	As a dressing for partial thickness burns, As a BMO (BT) coverage of full thickness wounds, Other	Single choice

➤ We followed the CHERRIES (Checklist for Reporting Results of Internet Surveys) checklist as well as checklist items listed in SURGE (Survey Reporting Guideline) analysis for reporting quality. Study design comparable to *

* Selig MF, Lumenta DB, Giretzlehner M, Jeschke MG, Upton D, Kamolz LP.

The properties of the "ideal" burn wound dressing – What do we need in daily clinical practice?

Results of a worldwide online survey among burn care specialists.

Burns. 2012; 38: 960-966.



111 respondents (response rate 22.2%) from 37 countries within a 1 month study period.

- Surgeons 87.4%
- Anesthetists/ Intensivists 1.8%
- Others 10.8%

Europe	54.1%
North America	28.8%
Asia	13.5%
Central America	0.9%
South America	0.9%
Australia and New Zealand	0.9%
Africa	0.9%

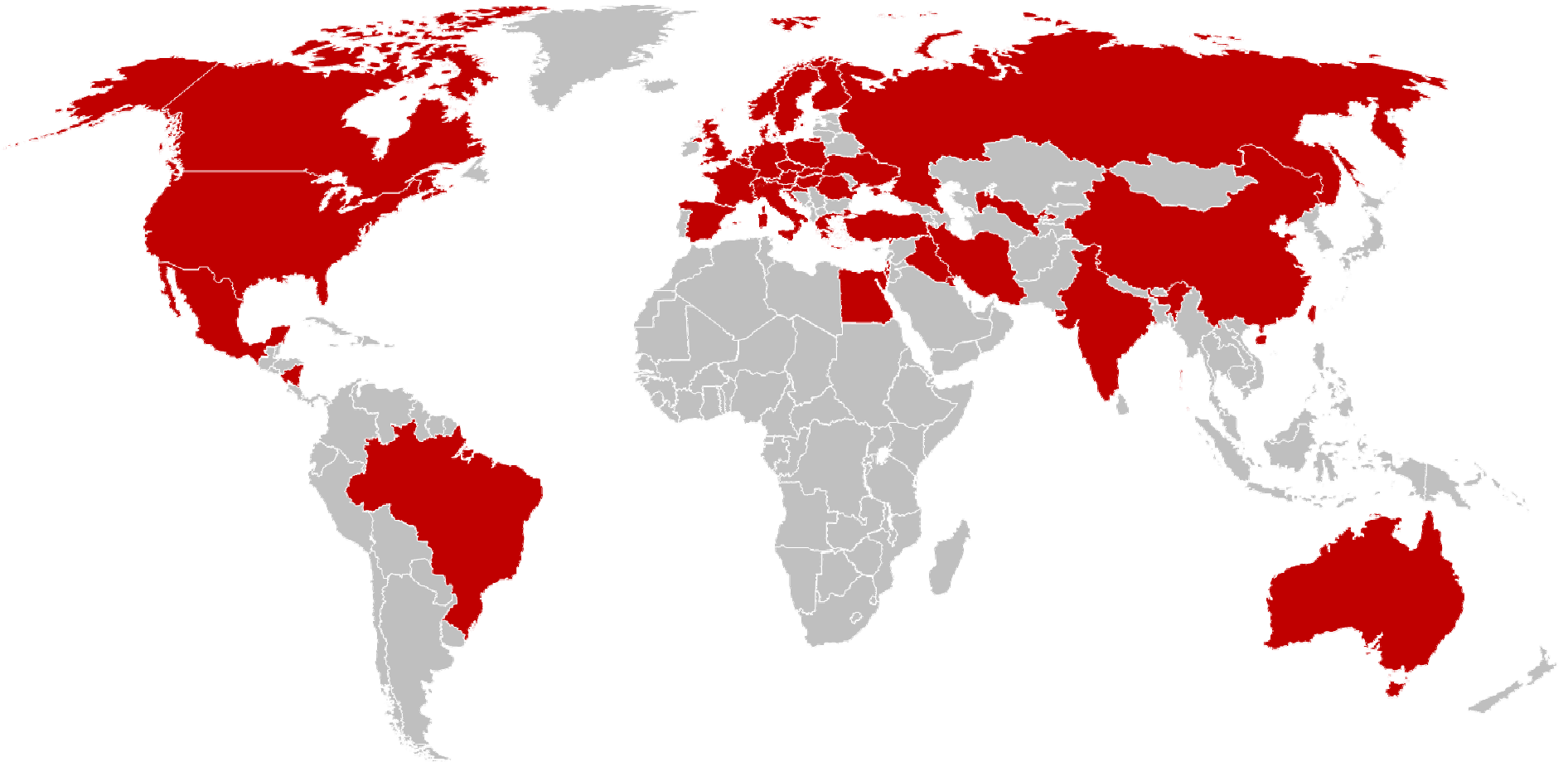
Country	N	%
Australia	1	0,90
Austria	4	3,60
Belgium	4	3,60
Brazil	1	0,90
Canada	2	1,80
China	4	3,60
Croatia	1	0,90
Czech Republic	3	2,70
Egypt	1	0,90
Finland	3	2,70
France	3	2,70
Germany	4	3,60
Greece	1	0,90
Hungary	1	0,90
India	2	1,80
Iran	1	0,90
Iraq	3	2,70
Israel	2	1,80
Italy	6	5,41
Kuwait	1	0,90
Mexico	1	0,90
Netherlands	1	0,90
Nicaragua	1	0,90
Norway	1	0,90
Poland	2	1,80
Romania	3	2,70
Russia	3	2,70
Slovakia	1	0,90
Spain	3	2,70
Sweden	3	2,70
Switzerland	1	0,90
Taiwan	1	0,90
Turkey	5	4,50
Ukraine	2	1,80
United Kingdom	5	4,50
USA	29	26,13
Uzbekistan	1	0,90
Total	111	100



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➤ **Do you use skin substitutes in clinical routine?**

Yes: 94.6%

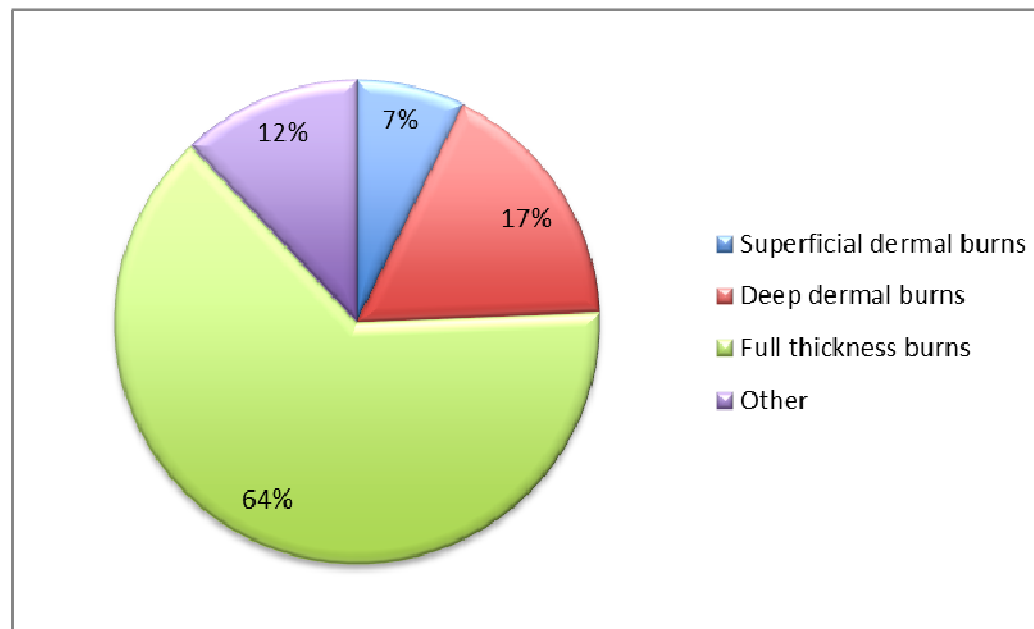
➤ **How important are skin substitutes?**

In medium burns (20 – 60% TBSA): 27.0% essential
55.9% desirable

In large burns (> 60% TBSA): 81.1% essential
14.4% desirable



- Which of the following represents most likely the main indication for the clinical use of skin substitutes in your institution?





Synthetic materials	8.1%
Xenografts	9.9%
Allografts	24.3%
Biological and Synthetic	53.2%

- Do you use Epidermal Replacements (e.g. Keratincytes, Suprathel[®],..) in clinical routine?

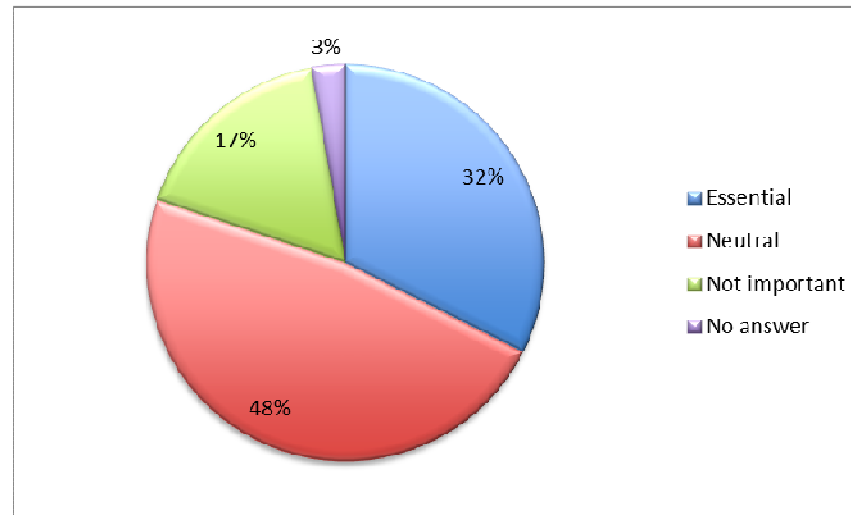
Yes: 46.9%

- Do you use Dermal Replacements (e.g. Integra[®], Matriderm[®],...) in clinical routine?

Yes: 73.0%



- **How important do you consider the factor biological risk in the context of clinical application of skin substitutes?**

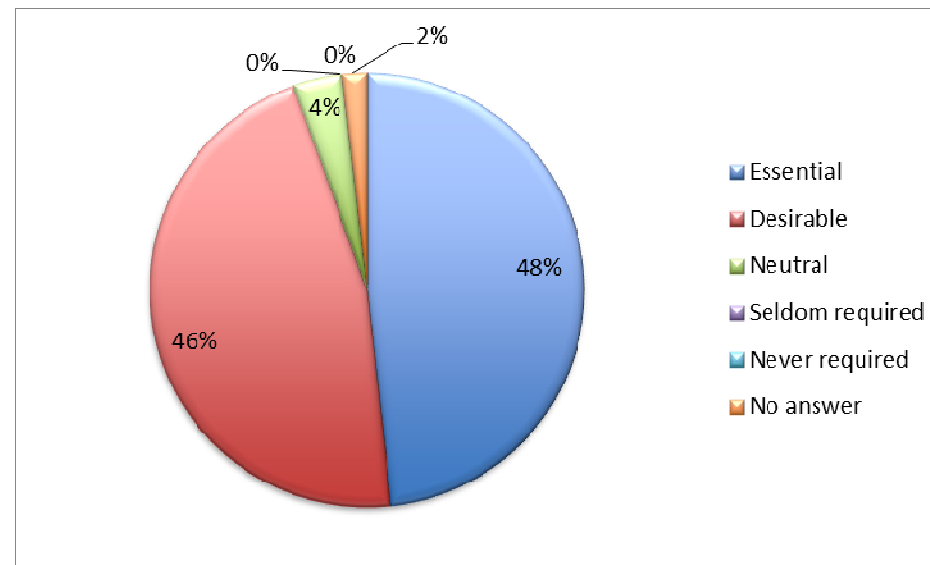


- **Do you think that using biological materials on wounds pose a real risk to patients?**

No: 85.6%



➤ How important do you consider the factor "ready availability (always accessible)" in the context of clinical application of skin substitutes (eg. no cultivation time needed)?





➤ **Do you use Xenografts?**

Yes 48.7%

➤ **If yes, what is your main indication for applying xenografts in clinical practice?**

Temporary coverage of full thickness wounds

Coverage of partial thickness wounds

➤ **What kind of materials do you use for temporary coverage in clinical practice?**

Allografts 50.5%

Xenografts 19.8%

Other 29.7%

➤ **87.4% think that the “ideal” skin substitute is not “on the market” yet.**



The advent of tissue-engineered skin replacements revolutionised the therapeutic potential for burn wounds.

Two major approaches, in vitro and in vivo, have been utilized to develop tissue engineered constructs:

- The **in vitro method** has attracted considerable attention due to its attempts of creating organs in cultures for out-of-the-shelf implantation and replacement.
- In contrast, the **in vivo approach** aims to create a matrix, which contains a scaffold capable of stimulating cell recruitment, inducing cell differentiation, and finally forming the desired “neo-tissue”.

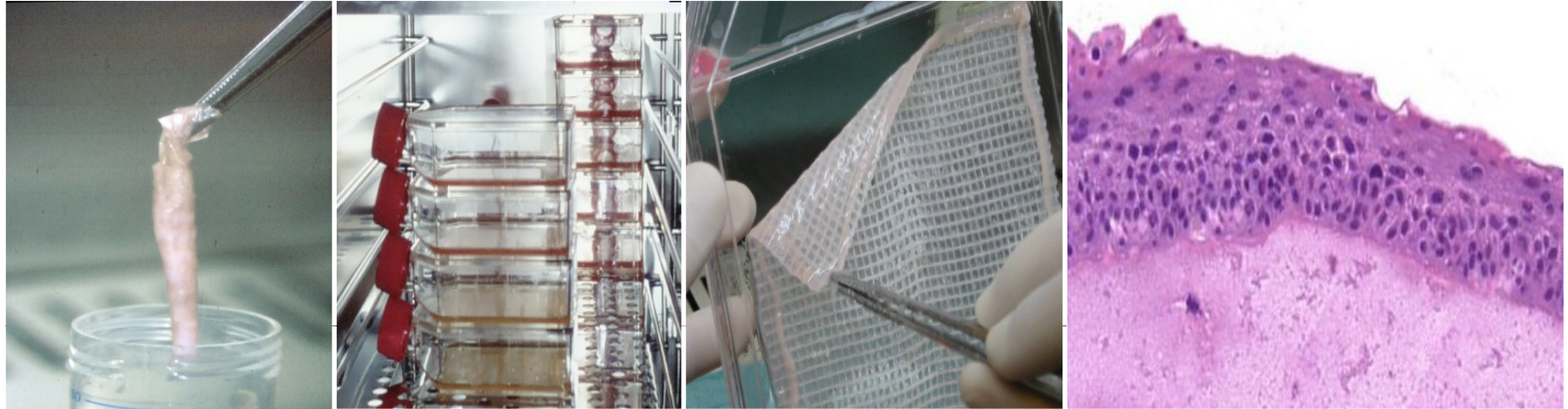
Beier JP, Boos AM, Kamolz L, Vogt PM, Koller R, Horch RE.
Skin tissue engineering--from split skin to engineered skin grafts?
Handchir Mikrochir Plast Chir. 2010 Dec;42(6):342-53.



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600 allogeneic keratinocyte sheet-grafts 75-100cm²/ year
grouped into: CMV +/-

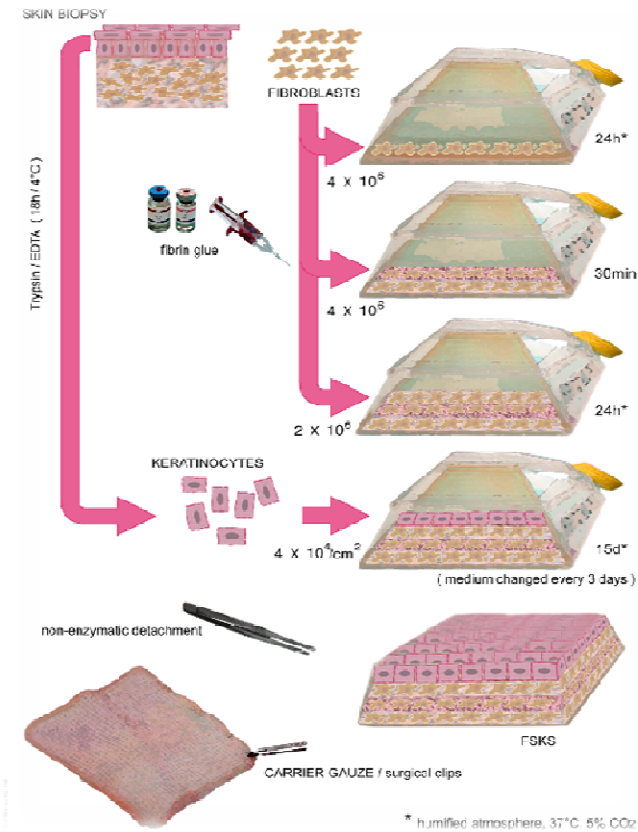
tested for:

HIV

Hepatitis

CMV

Syphillis



Kamolz LP, Luegmair M, Wick N, Eisenbock B, Burjak S, Koller R, Meissl G, Frey M.

The Viennese culture method: cultured human epithelium obtained on a dermal matrix based on fibroblast containing fibrin glue gels.

Burns. 2005 Feb;31(1):25-9.



Clinical study: allogeneic keratinocytes vs. autologous skin graft

36 children:

22 children (18,5% TBSA) [keratinocyte group](#)

14 children (17,2% TBSA) [skin graft group](#)

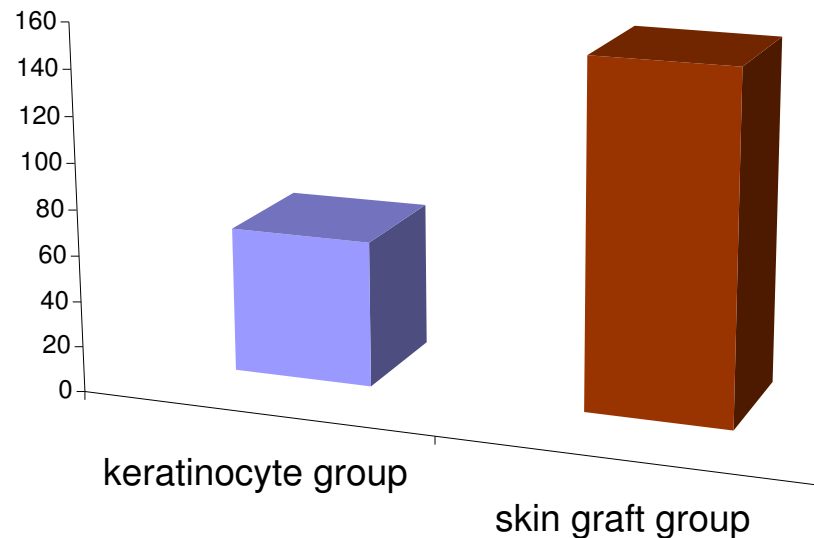
Sorting into one group after tangential debridement of deep partial thickness areas depended on:
actual *presence or lack* of
CMV-negative keratinocytes
in our skin bank.

Scalded areas (full thickness burns),
which had to be excised to the subcutaneous tissue
were covered in both groups with split thickness skin grafts.



Successful wound healing after coverage in both groups, but:

Erythrocyte concentrate transfusion



significantly reduced demand for erythrocyte concentrate transfusions (63.9 +/- 83.6 ml keratinocyte vs. 151.4 +/- 154.7 ml skin graft group)

1/2 of keratinocyte group
-> no blood transfusion

2/3 of skin graft group
-> blood transfusion



Clinical example: skin graft group



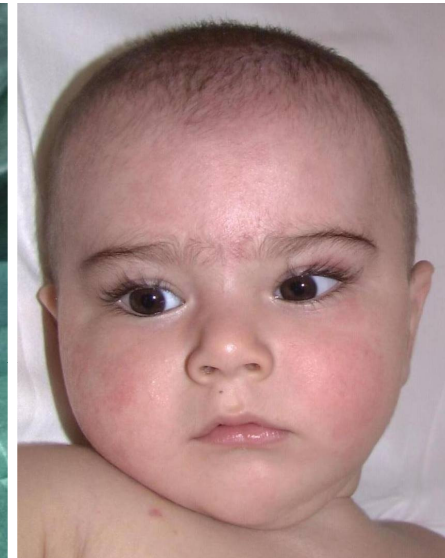
24 month-old girl after scald injury
with 30% TBSA affected
coverage with autologous
split-thickness skin graft



10 days



3 months post-OP



12 month-old boy after scald injury
with 25% TBSA affected
coverage with allogeneic keratinocytes

3 months post-OP

Rab M, Koller R, Ruzicka M, Burda G, Kamolz LP, Bierochs B, Meissl G, Frey M.
Should dermal scald burns in children be covered with autologous skin grafts or with allogeneic cultivated keratinocytes?—
"The Viennese concept".
Burns. 2005 Aug;31(5):578-86.



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Over time limitations became evident

- Demanding infrastructural requirements
- High costs
- Lack of „ ex vitro“ stability
- Additional requirement for dermal support
- Absence of other skin cell types and appendages

Limited the introduction in daily clinical routine

In case of...

- ... lack of CMV-negative keratinocytes?
- ... limited donor sites (large burns)?

Alternatives?



Suprathel

- Polylactic acid (degradation in 4 weeks)
- Synthetical and resorbable
- Bactericide (reduce risk of infection)
- Alloplastic resorbable skin replacement



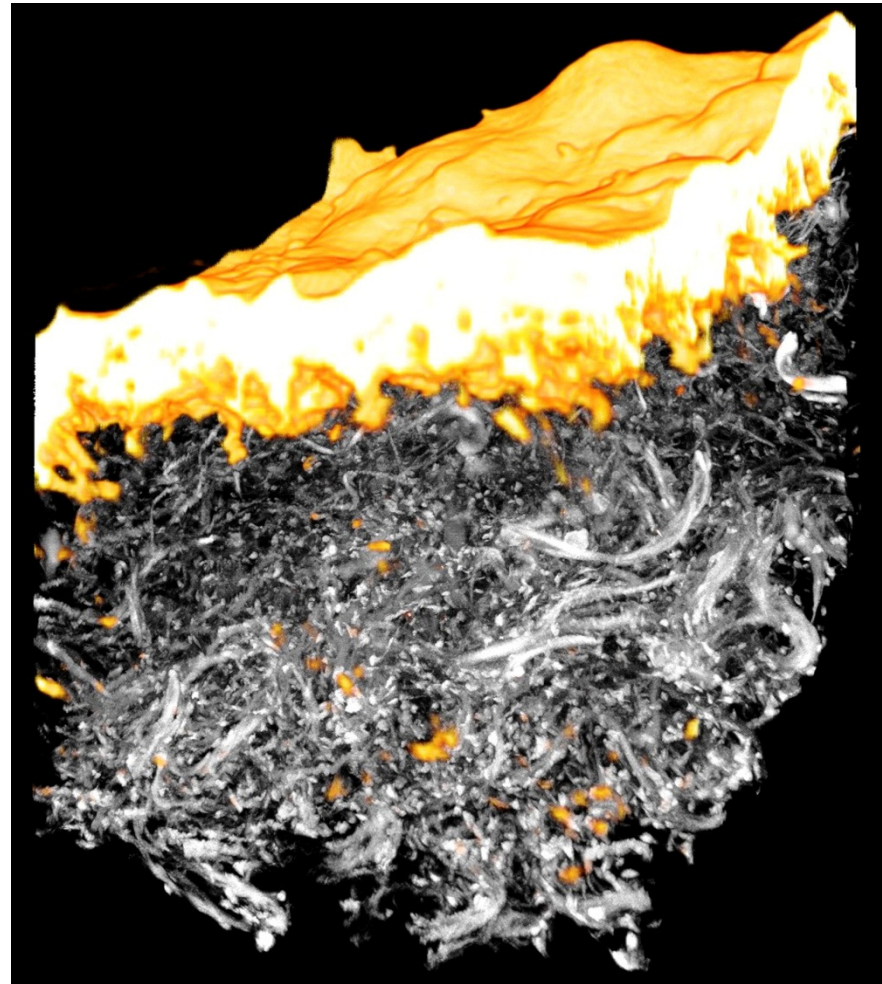
Keck M, Selig HF, Lumenta DB, Kamolz LP, Mittlböck M, Frey M.
The use of Suprathel® in deep dermal burns: first results of a prospective study.
Burns. 2012 May;38(3):388-95.



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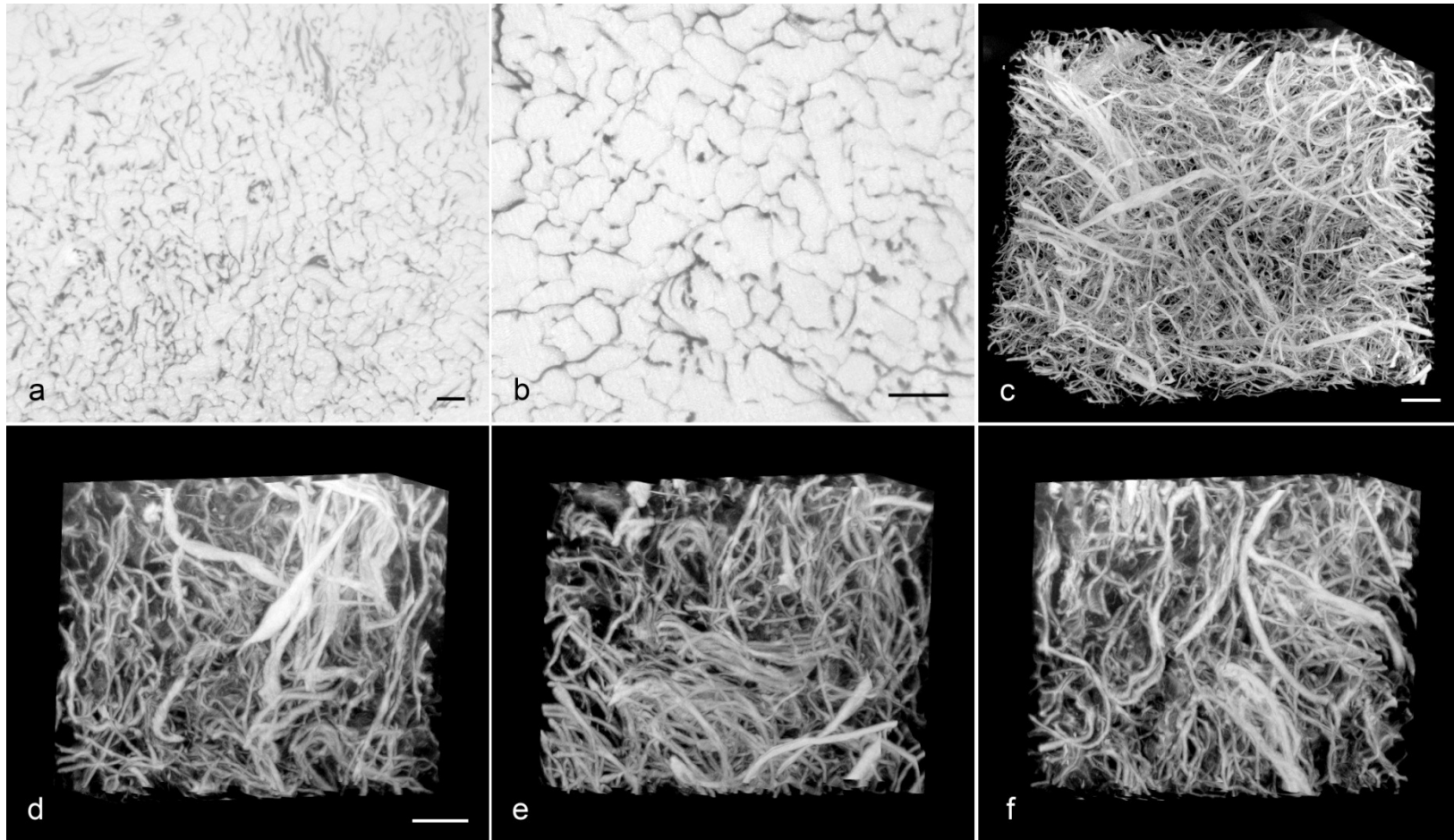


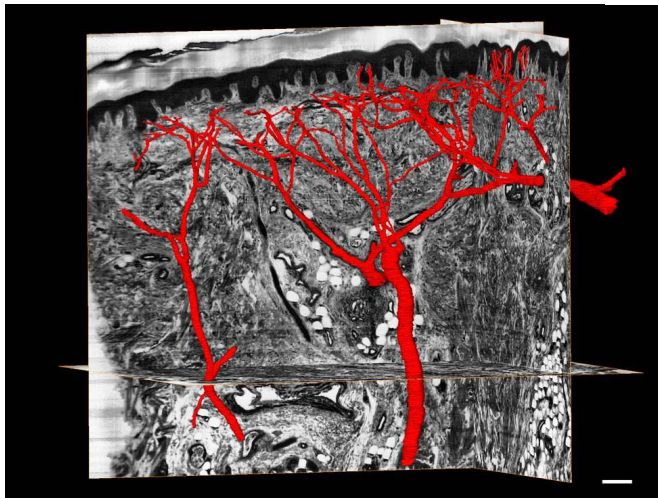


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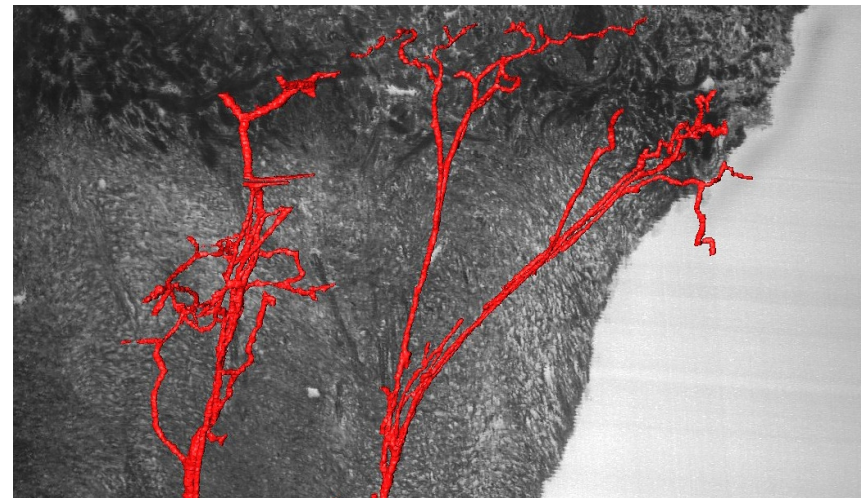


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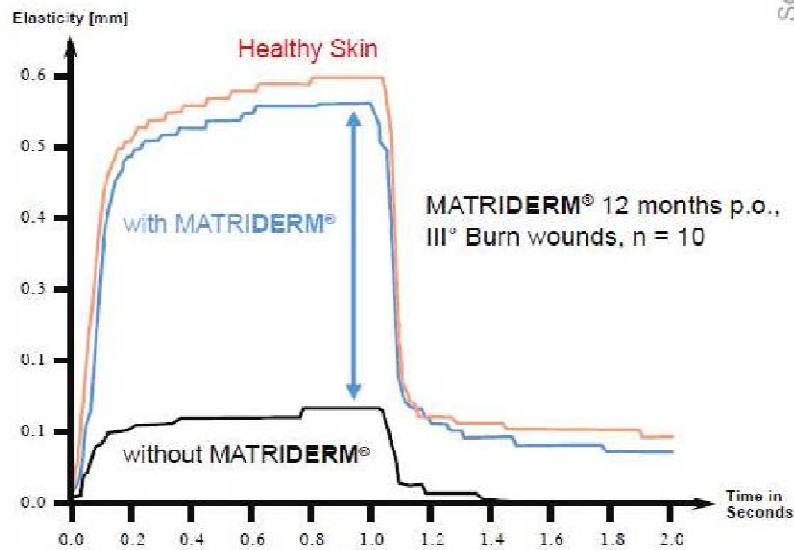
Normal skin



After transplantation of
Matriderm® and STSG
(day 10)



Determination of skin elasticity via cutometer-measurement



Source 16

Long-term outcome:



- Excellent elasticity and pliability



- Full range of motion

Haslik W, Kamolz LP, Manna F, Hladik M, Rath T, Frey M.
Management of full-thickness skin defects in the hand and wrist region: first long-term
experiences with the dermal matrix Matriderm.
J Plast Reconstr Aesthet Surg. 2010 Feb;63(2):360-4.



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3 Layer Skin Substitute:

Fat-Transplantation

Dermal Matrix

Split Thickness Skin Graft



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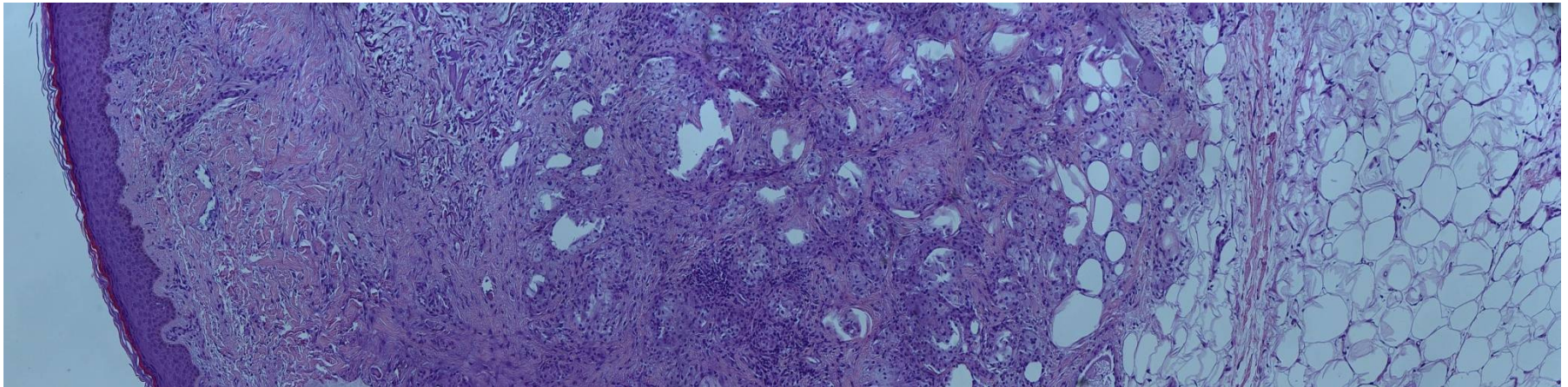




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Epidermis

Dermis

Hypodermis



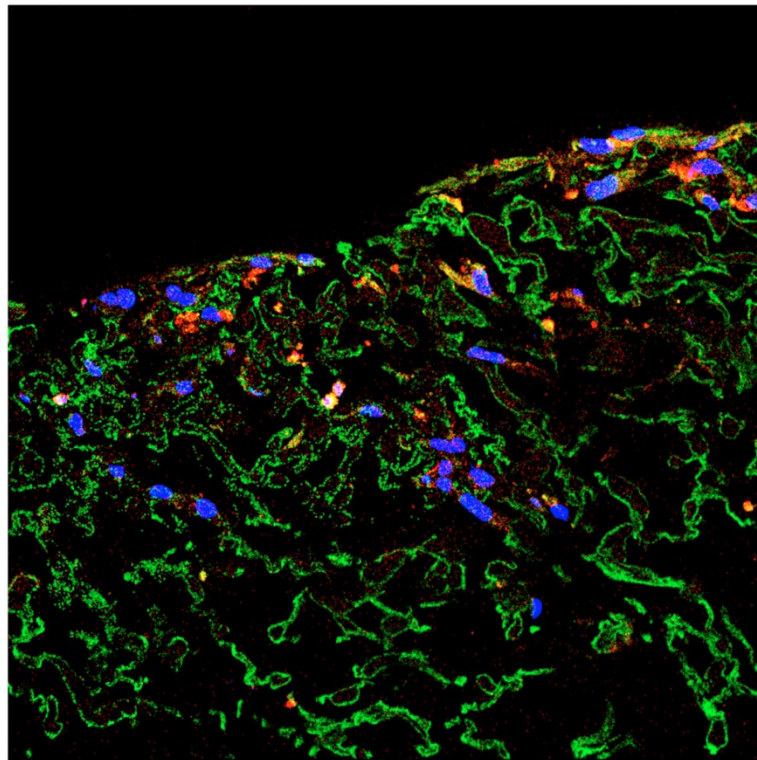
Regeneration – Tissue engineering

Tissue regeneration and Tissue Engineering has gained relevance for reconstructive surgery.

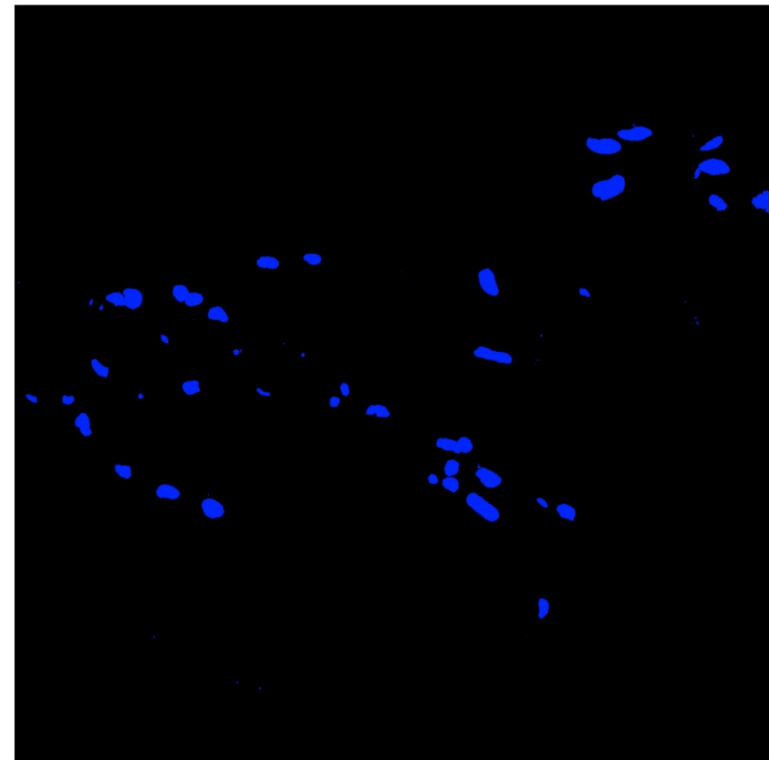
- Fat cell transplantation is not only able to improve volume and contour defects, but also skin quality.
- Recently, fat transplantation or lipo transfer is of utmost interest. In 2001 it was demonstrated that beside fat cells also "adipose-derived stem cells" (ADSC) beside other cell populations in the fatty tissue are usable for these purposes.

Keck M, Zeyda M, Burjak S, Kamolz LP, Selig H, Stulnig TM, Frey M.
Coenzyme Q10 does not enhance preadipocyte viability in an in vitro lipotransfer model.
Aesthetic Plast Surg. 2012 Apr;36(2):453-7.

Keck M, Zeyda M, Gollinger K, Burjak S, Kamolz LP, Frey M, Stulnig TM.
Local anesthetics have a major impact on viability of preadipocytes and their differentiation into adipocytes.
Plast Reconstr Surg. 2010 Nov;126(5):1500-5.



(a)



(b)

Keck M, Haluza D, Selig HF, Jahl M, Lumenta DB, Kamolz LP, Frey M.

Adipose tissue engineering: three different approaches to seed preadipocytes on a collagen-elastin matrix.

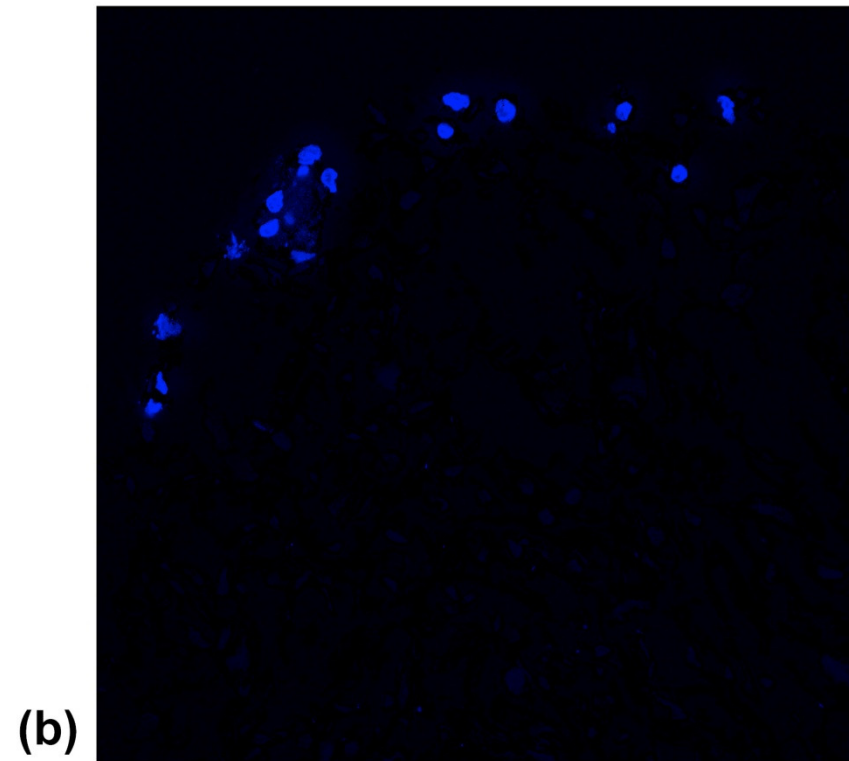
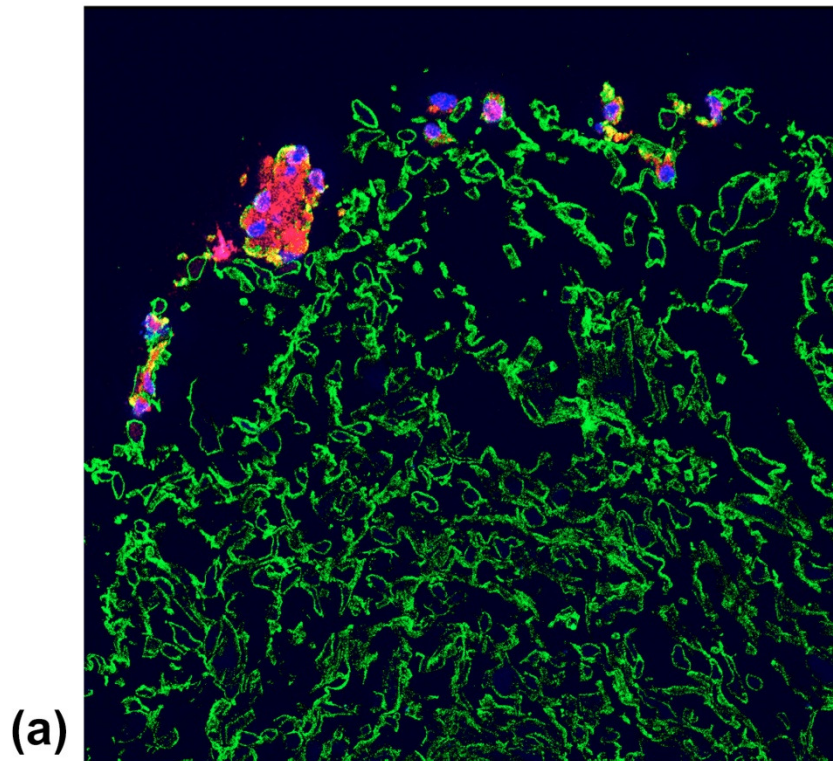
Ann Plast Surg. 2011 Nov;67(5):484-8.

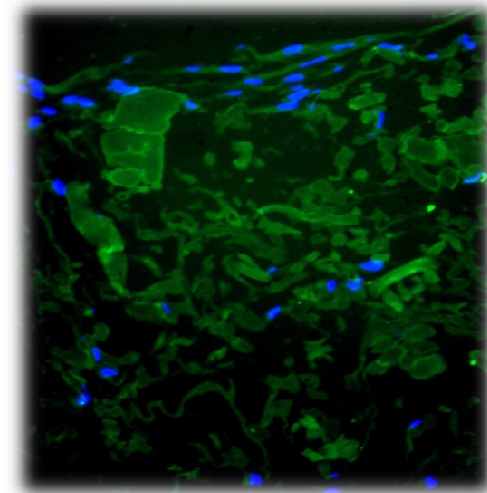
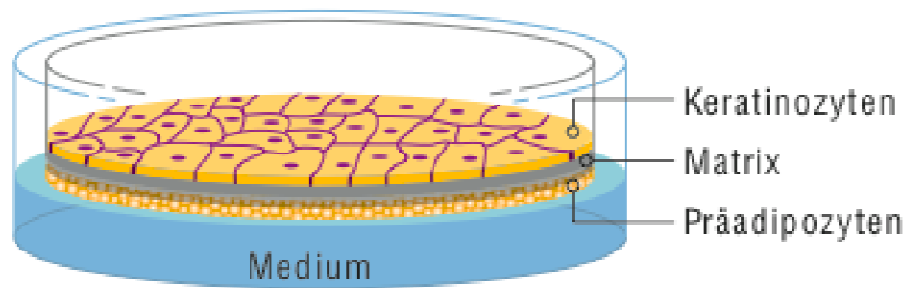


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Keck M, Haluza D, Lumenta DB, Burjak S, Eisenbock B, Kamolz LP, Frey M.
Construction of a multi-layer skin substitute: Simultaneous cultivation of keratinocytes and preadipocytes on a dermal template.
Burns. 2011 Jun;37(4):626-30.



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Deep dermal burn

Keratinocytes (autologous/ allogeneic)

Autologous skin grafts

Allografts/ Xenografts

Epidermal replacements



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Full thickness burn

Autologous Skin Grafts (Unmeshed, Mesh, Meek,..)

Autologous Skin Grafts in combination with Allografts/ Keratinocytes

Allografts/ Xenografts

Dermal and Combined Replacements



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