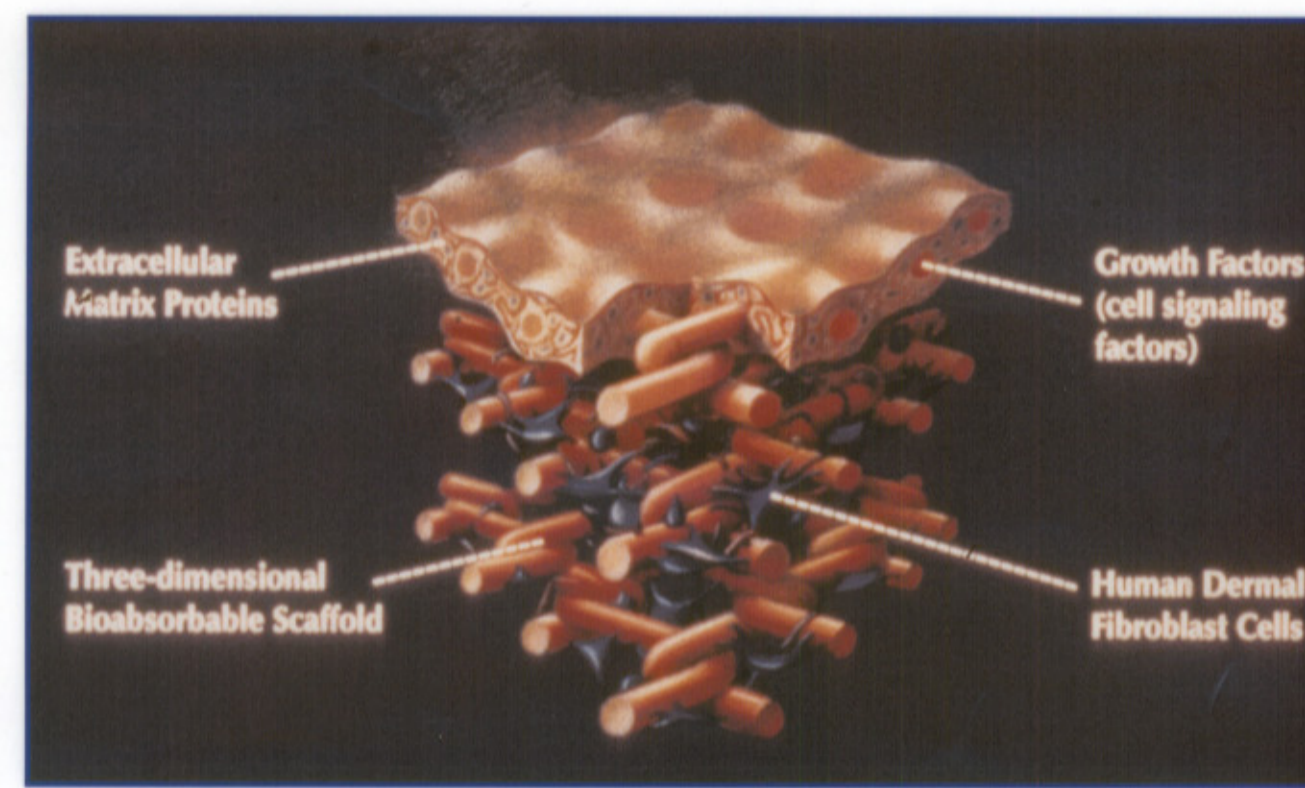


# Intra oral soft tissue regeneration with a tissue engineered metabolic active fibroblast layer

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## I. Scientific background

- Tissue engineering offers the ability to create highly tested physiological human tissue for wound coverage.
- Juvenile human fibroblasts seeded on a resorbable three dimensional vicyrl mesh and grown in a closed bio reactor system form a dermal like tissue.

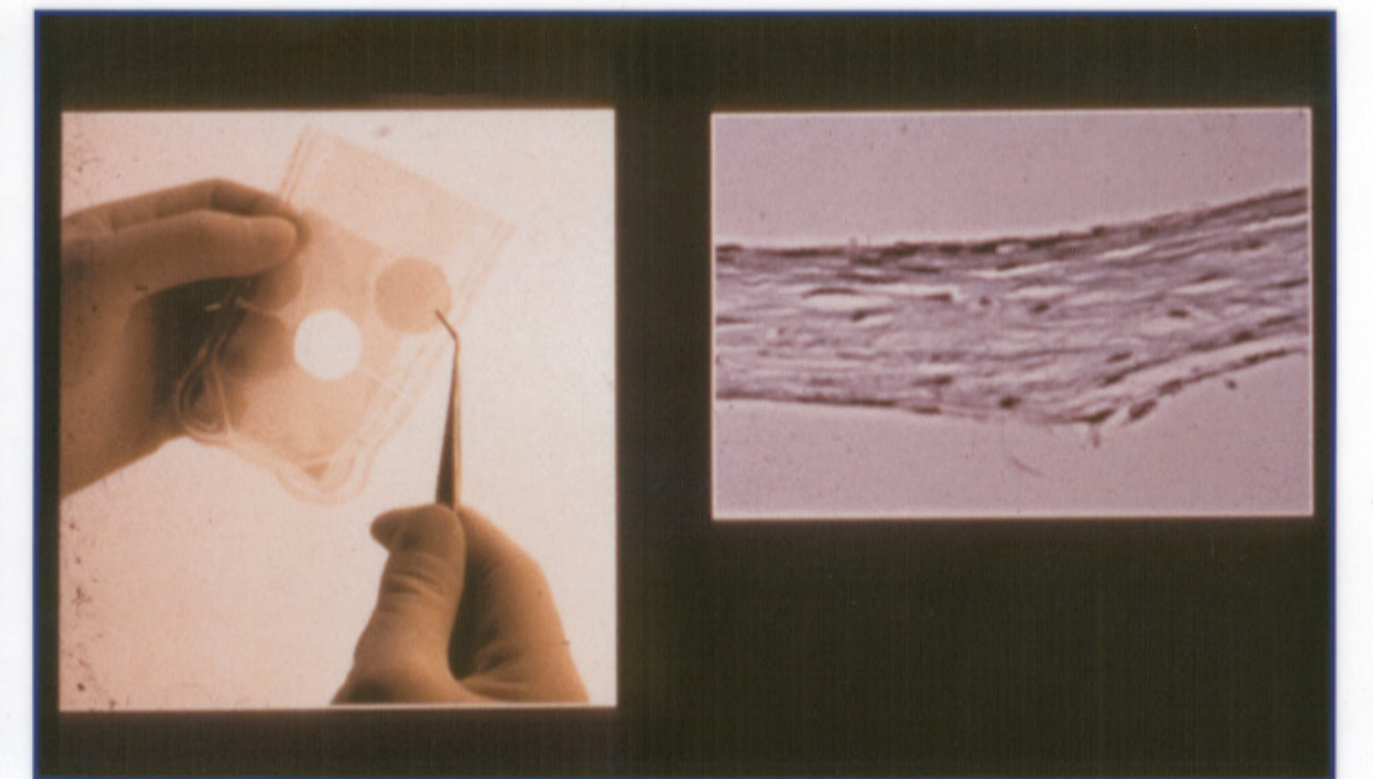


Picture 1: Tissue created by fibroblast.  
 → This tissue secrete a mixture of growth factors and matrix proteins in physiological concentration.

### Living, Bioengineered Human Dermal Replaceme

Growth Factors	Function
PDGF-A	Mitogen for fibroblasts, granulation tissue, chemotactic
VEGF	Angiogenesis
IGF	Mitogen for fibroblasts
KGF	Mitogen for keratinocytes
HBEGF	Mitogen for keratinocytes, fibroblasts
TGF- $\alpha$	Mitogen for keratinocytes, fibroblasts
TGF- $\beta$ 1	Stimulates matrix deposition
TGF- $\beta$ 3	Stimulates matrix deposition, antiscarring
SPARC	Both anti- and proangiogenic

Table 1: Growth factors secreted by the fibroblast tissue.  
 → The tissue layer can be cryo preserved at -80° Celsius and then be shipped world wide.  
 → If needed the tissue can be thawed at 37° Celsius and than implanted for wound coverage.



Picture 2: Fibroblast layer ready for implantation, histological cross section of the tissue.  
 → Implanted in the wound bed and preserved under physiological conditions the tissue regains the metabolic activity and delivering needed growth factors and matrix proteins for enhanced healing.

## II. Clinical application

### Application in tumour surgery

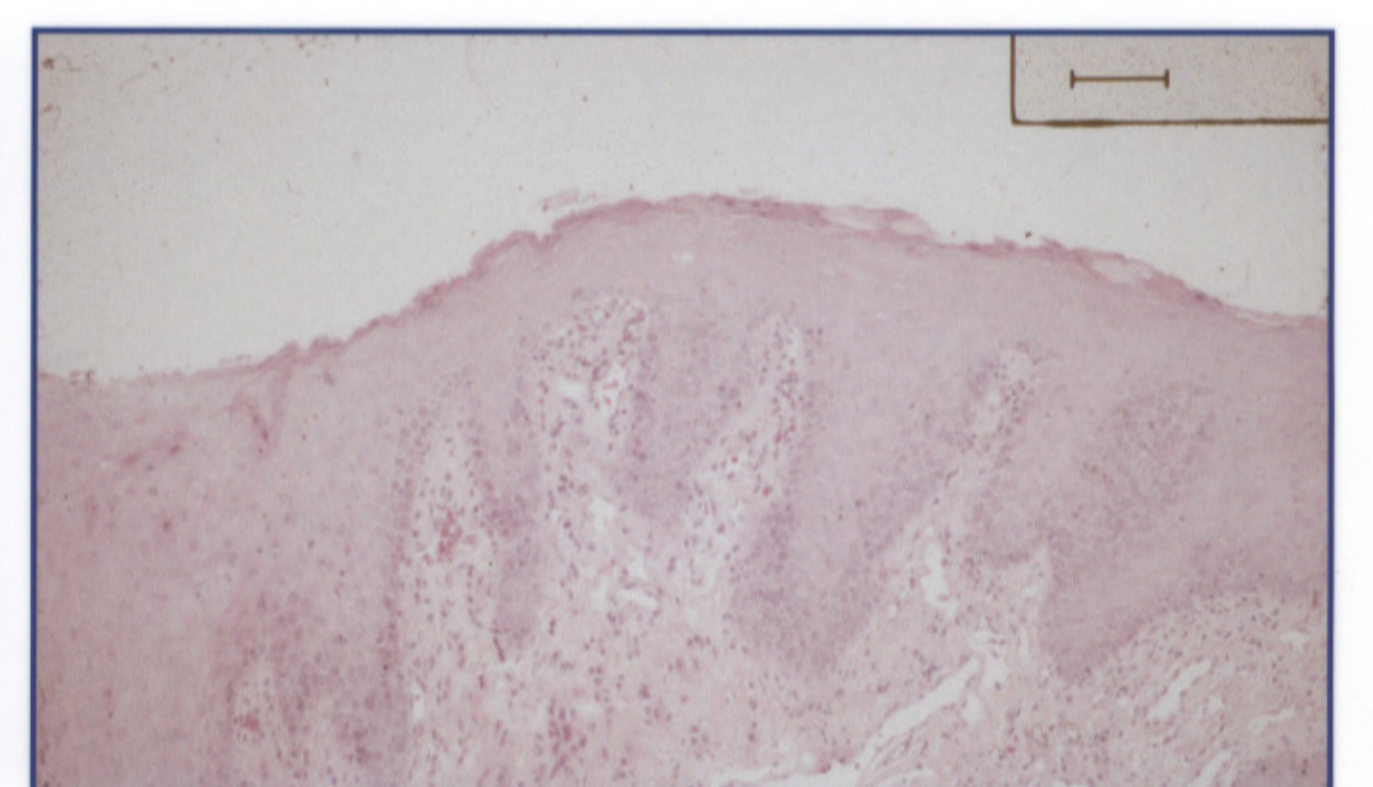
- Fibroblast layer implanted to cover a defect after resection of a squamous cell carcinoma (SCC) of the anterior floor of the mouth.
- The missing soft tissue regenerated without scar formation. (Gath HJ, Hell B, Zarrinbal R, Bier J, Raguse JD. Regeneration of intraoral defects after tumour resection with a bioengineered human dermal replacement (Dermagraft). *Plast Reconstr Surg.* 2002 Mar;109(3):889-93).
- In a pilot study we could show the reliable regeneration of soft tissue after the resection of a SCC of the buccal plane in combination with the buccal fad pad. (Raguse JD, Gath HJ. The buccal fad pad lined with a metabolic active dermal replacement (Dermagraft) for treatment of defects of the buccal plane. *Br J Plast Surg.* 2004 Dec;57(8):764-8).



Picture 3: Defect after resection of a SCC of the anterior floor of the mouth covered with the fibroblast layer. The tissue is fixed with sutures.



Picture 4: 10 days after wound coverage. Full mobility of the tongue without scar formation. Notice the newly formed frenulum.



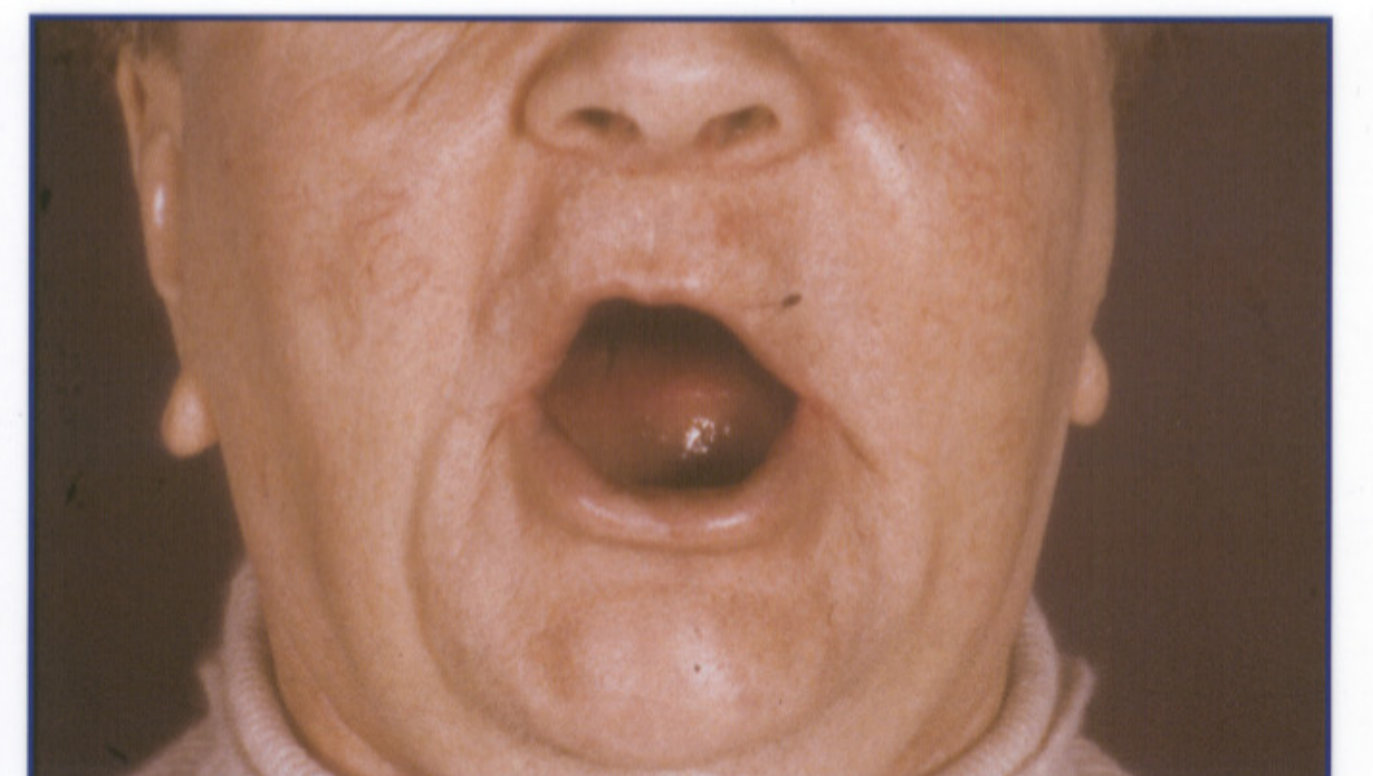
Picture 5: Histological cross section after a biopsy taken from the new formed soft tissue with now signs of scar tissue.



Picture 6: Defect after SCC resection of the buccal plane. The defect is filled with the buccal fad pad covered with the fibroblast tissue.



Picture 7: Same defect regenerated without scars.



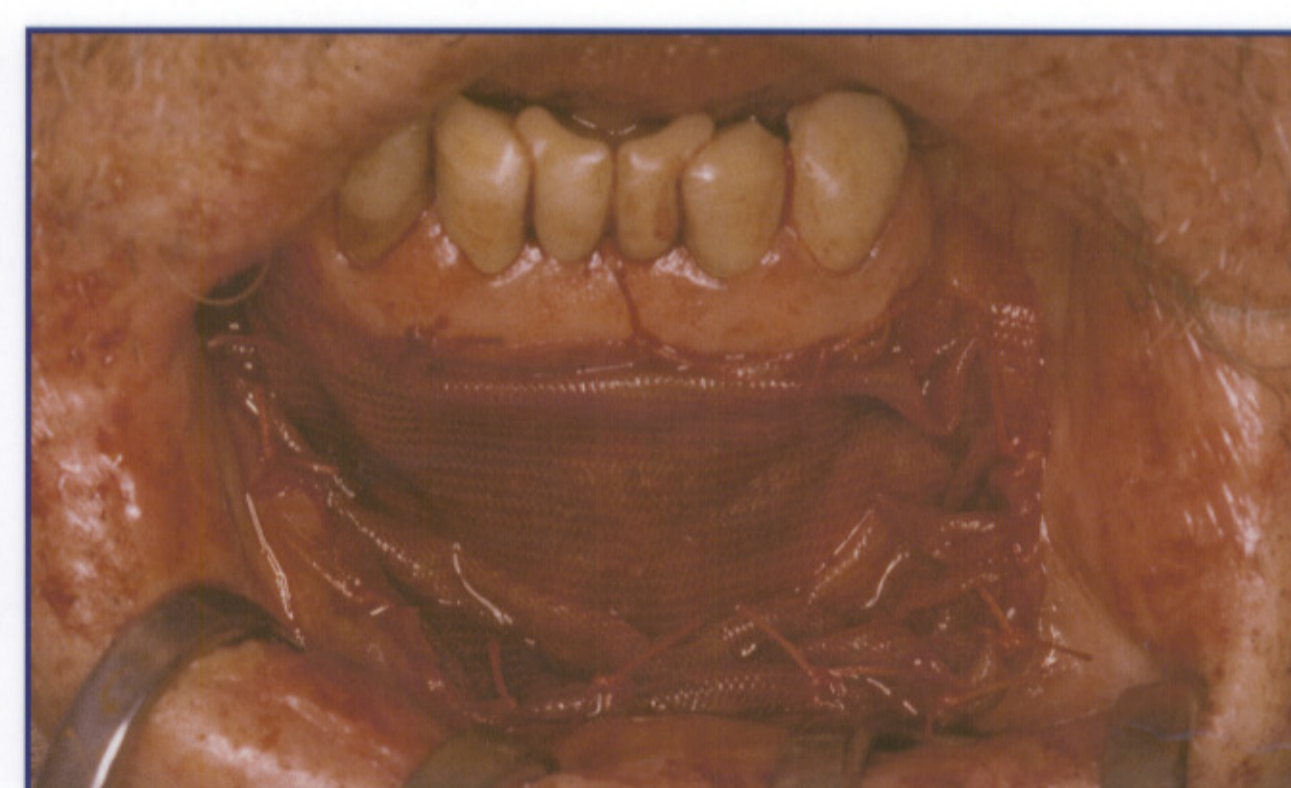
Picture 8: No impairment in function.

### Application in pre prosthetic surgery

- After being save and effective in tumour surgery the tissue was used for vestibuloplasty. (Raguse JD, Gath HJ. Metabolically active dermal replacement (Dermagraft) for vestibuloplasty. *J Oral Rehabil.* 2005 May;32(5):337-40).



Picture 9: Preoperative vestibulum.



Picture 10: Vestibuloplasty with fibroblast layer.



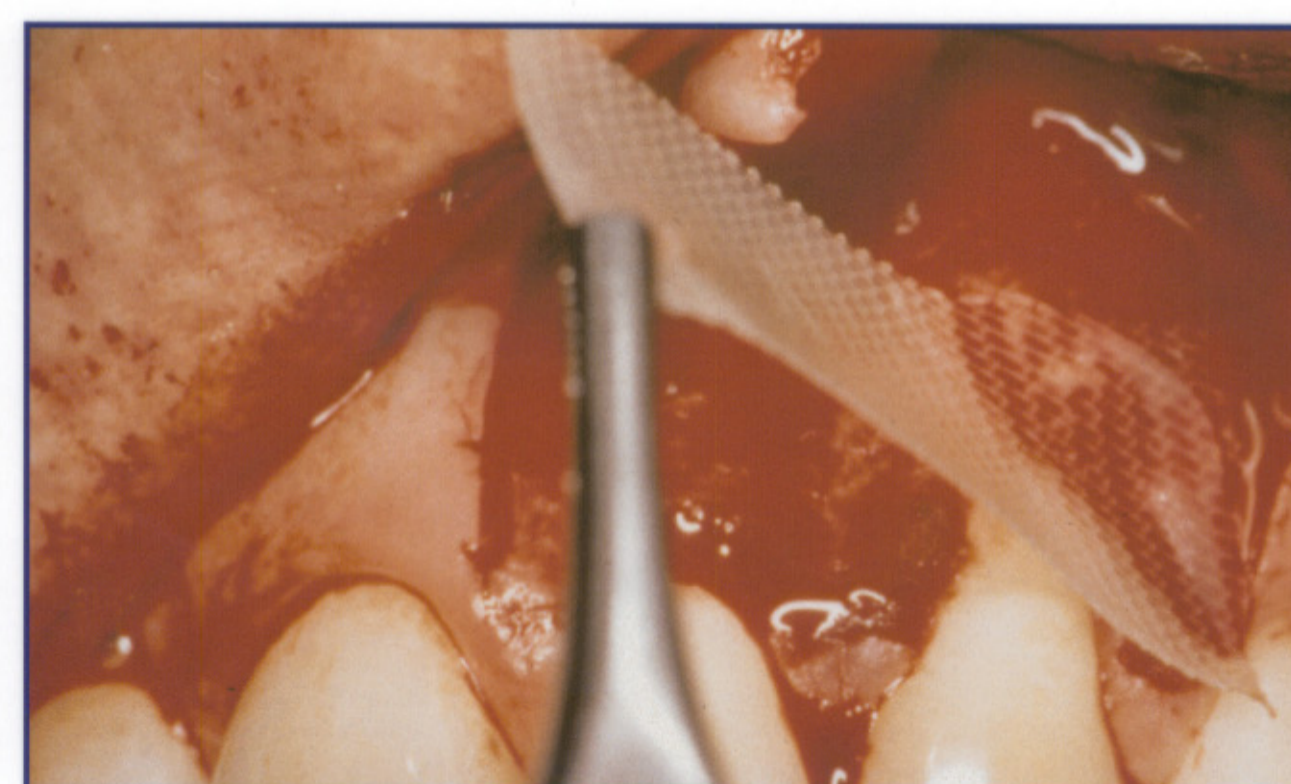
Picture 11: Postoperative vestibulum.

### Application in periodontal surgery

- The tissue was used in periodontal surgery to avoid a donor site defect. The missing tissue was regenerated under the application of the fibroblast layer.



Picture 12: Preoperative



Picture 13: Application of fibroblast layer.



Picture 14: Postoperative.

## III. Discussion

The presented fibroblast layer has several advantages:

- Metabolic active
- Ready to use
- Easy to apply
- No known side effects

- The effect to wound healing is due to its ability to secrete growth factors and matrix proteins.
- The living fibroblasts interact with the wound bed and respond by secreting growth factors in physiological amounts for a prolonged period of time. This might be of special importance in chronic wounds.
- The healing process is enhanced at several crucial steps (Table 2)
- Due to its biodegradable structure no further treatment is necessary.
- The influence of the tissue to bone formation is under investigation.

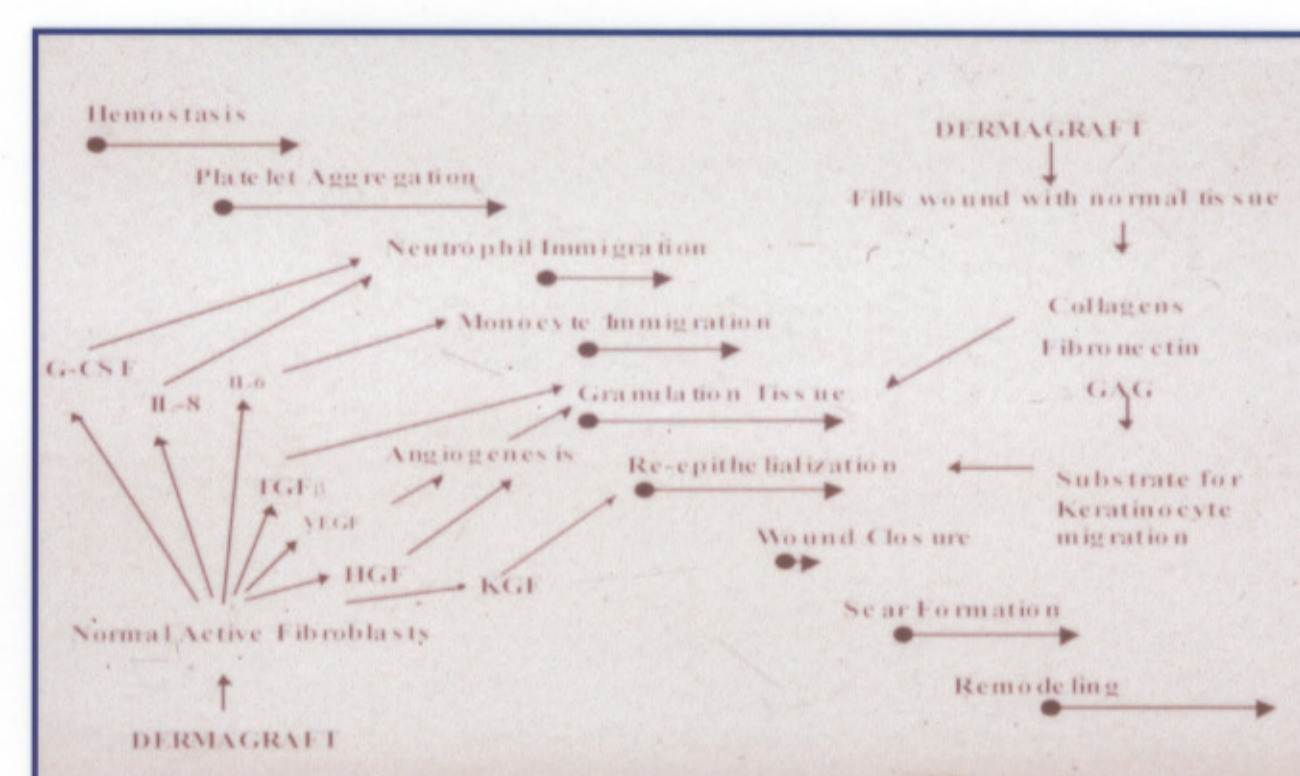


Table 2: The different steps of wound healing and the interaction with the fibroblast layer.