Advanced 12
Medical Applications - Ⅱ -
~Regenerative Medicine~

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Nagoya University

Tissue Engineering Research In Nagoya

Tissue Engineering Triad

Scaffolds

(eg, collagen, bone mineral, synthetics)

Time

Appropriate environment

Regeneration of Tissue/organs

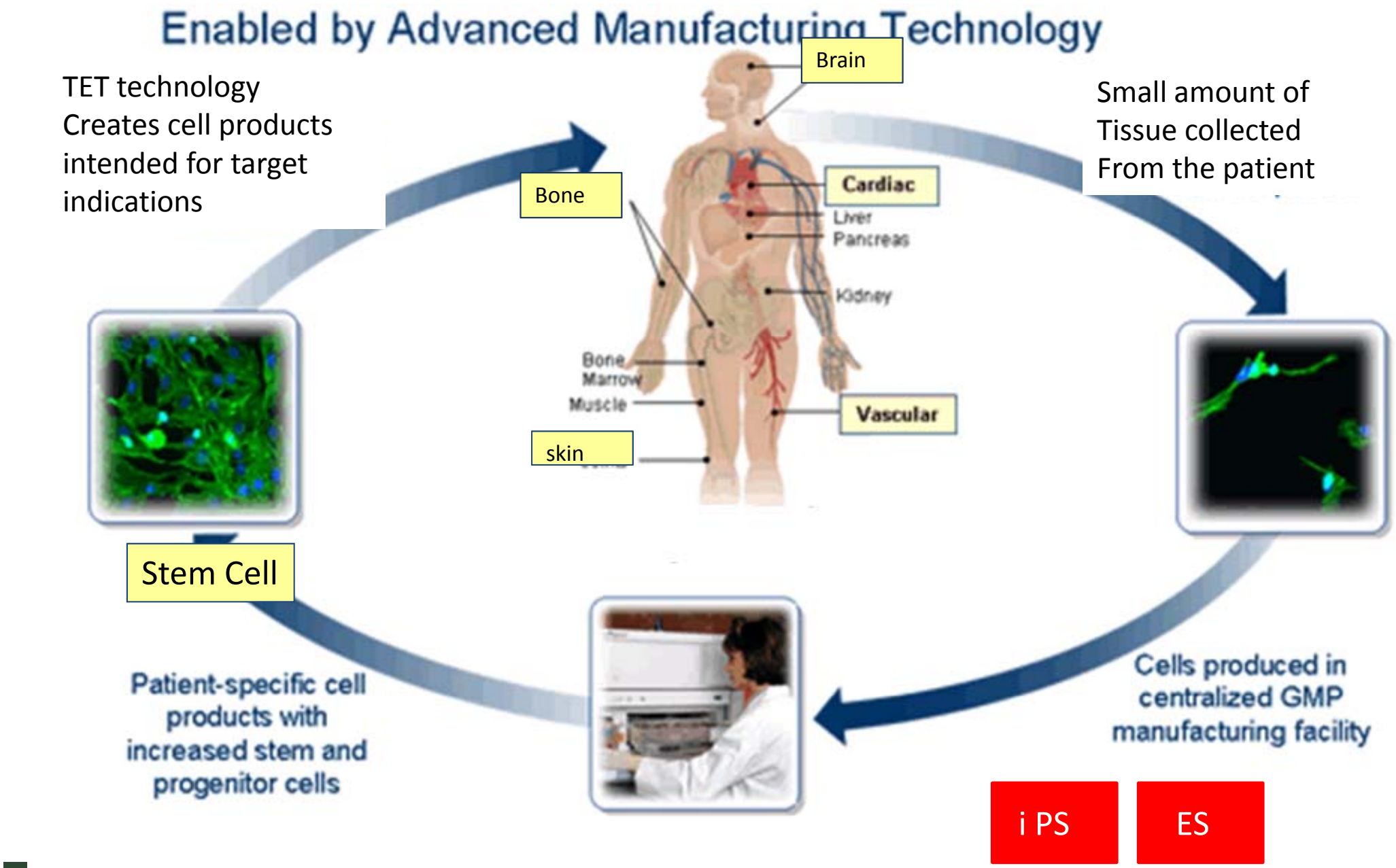
Cells

(eg, osteoblasts, fibroblasts, chondrocytes)

i PS, ES

Signaling molecules
(eg, growth factors, morphogens, adhesis)

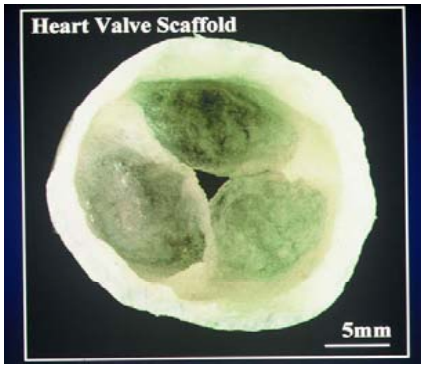
Tissue Engineering Therapy



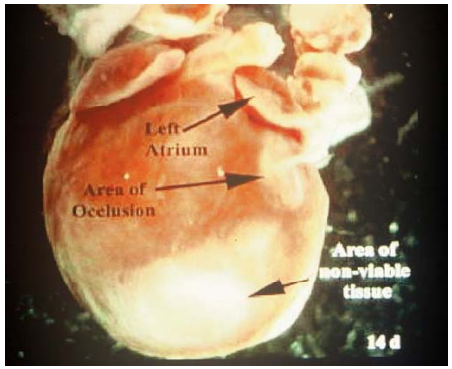
Tissue-Engineered Therapy

1. nontoxic
2. nonimmunoreactive
3. easy to manipulate
4. minimum invasive surgery
5. repeatedly use

Heart valve



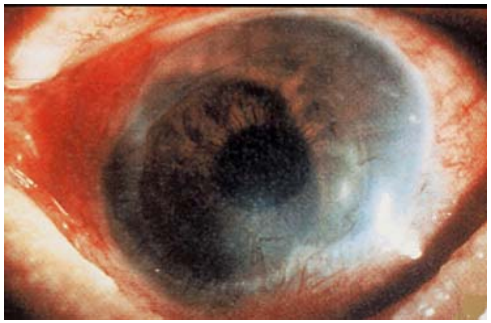
Heart



Cartilage

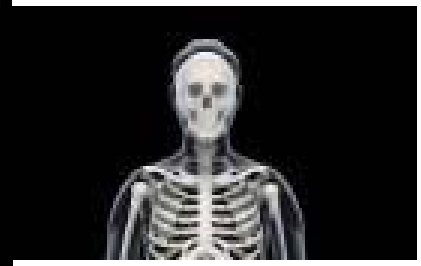
Brain

Cornea

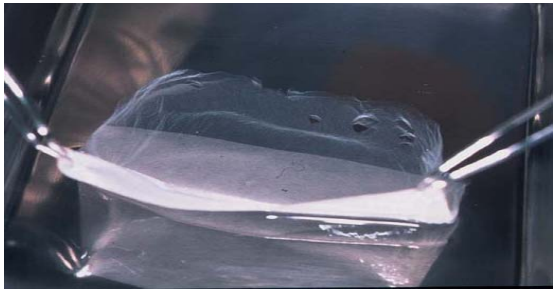


Nerve

Bone



Skin

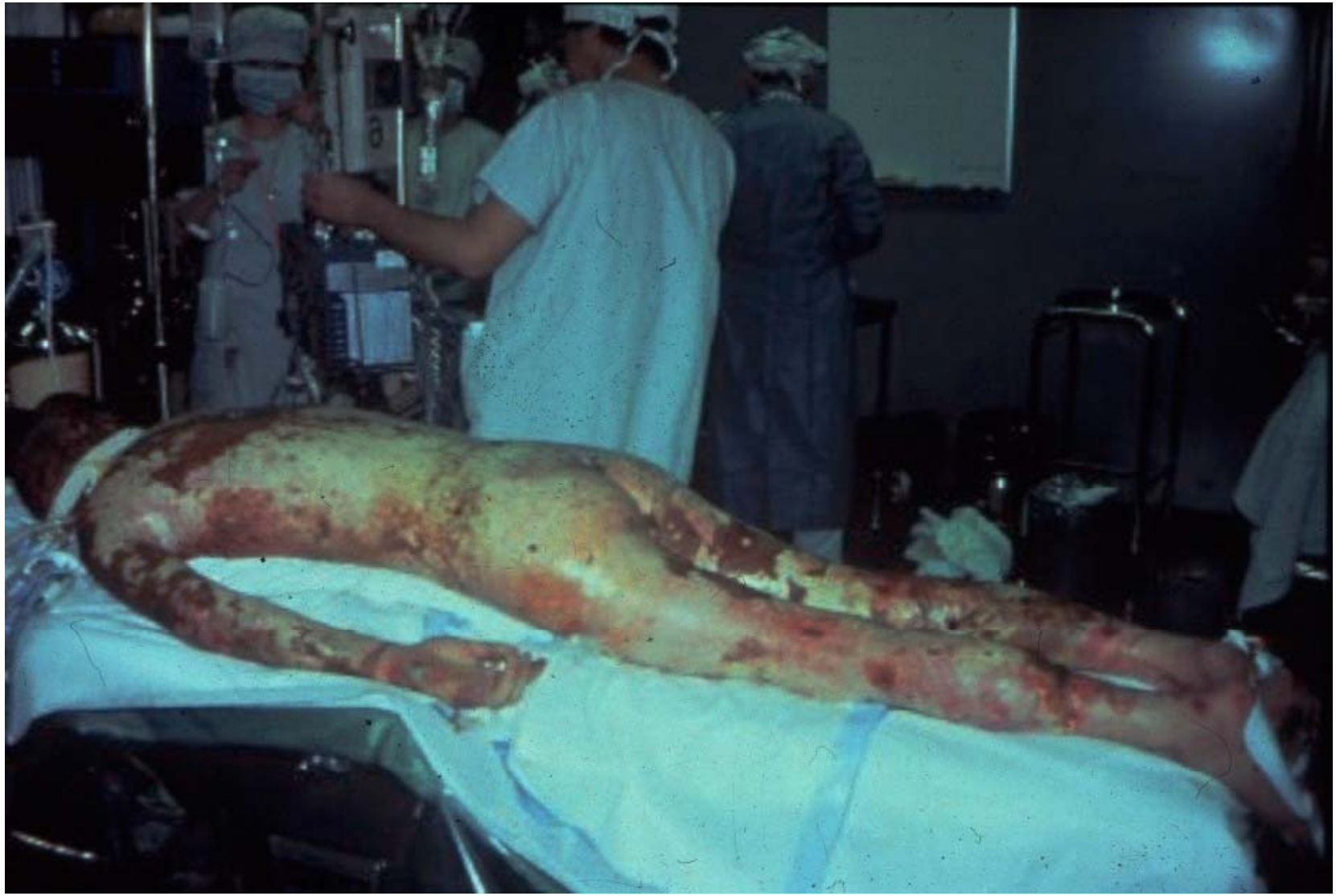


Tooth

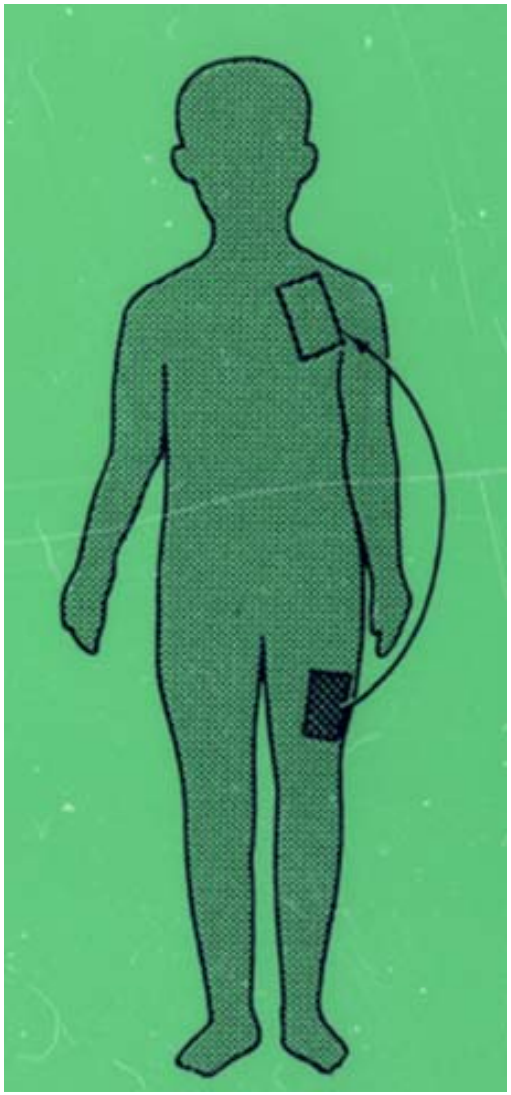
Mucosa

Skin

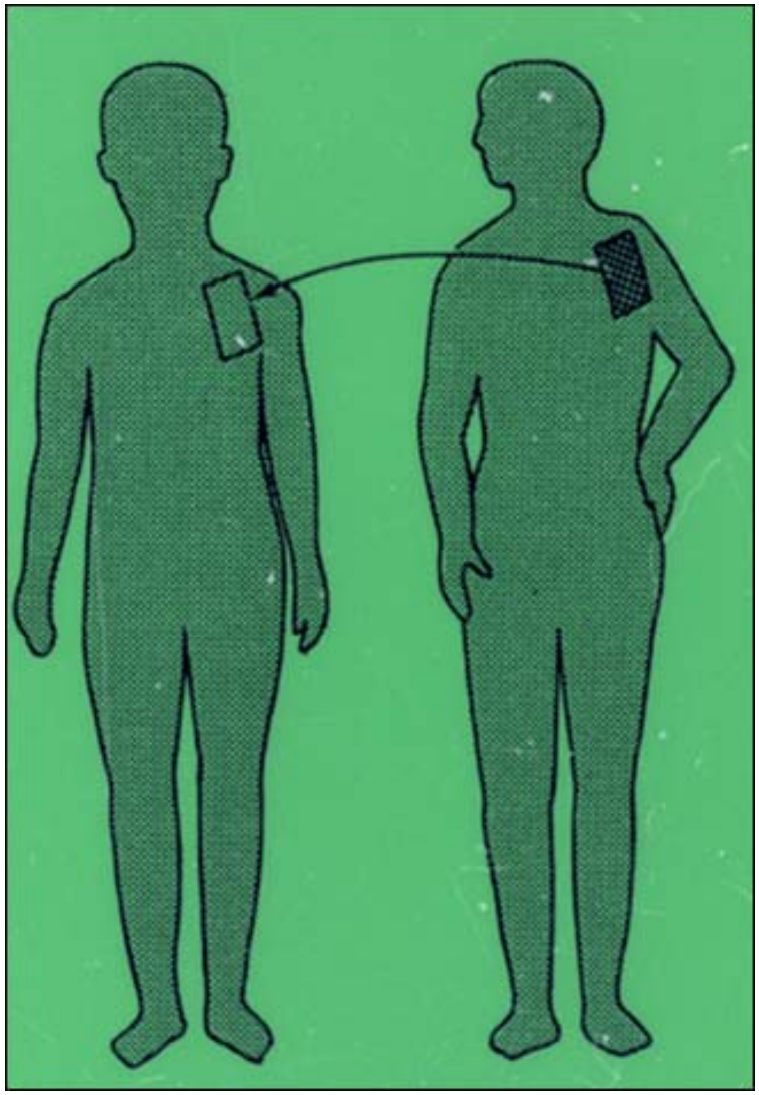
Burn



Auto and allo skin graft



Auto

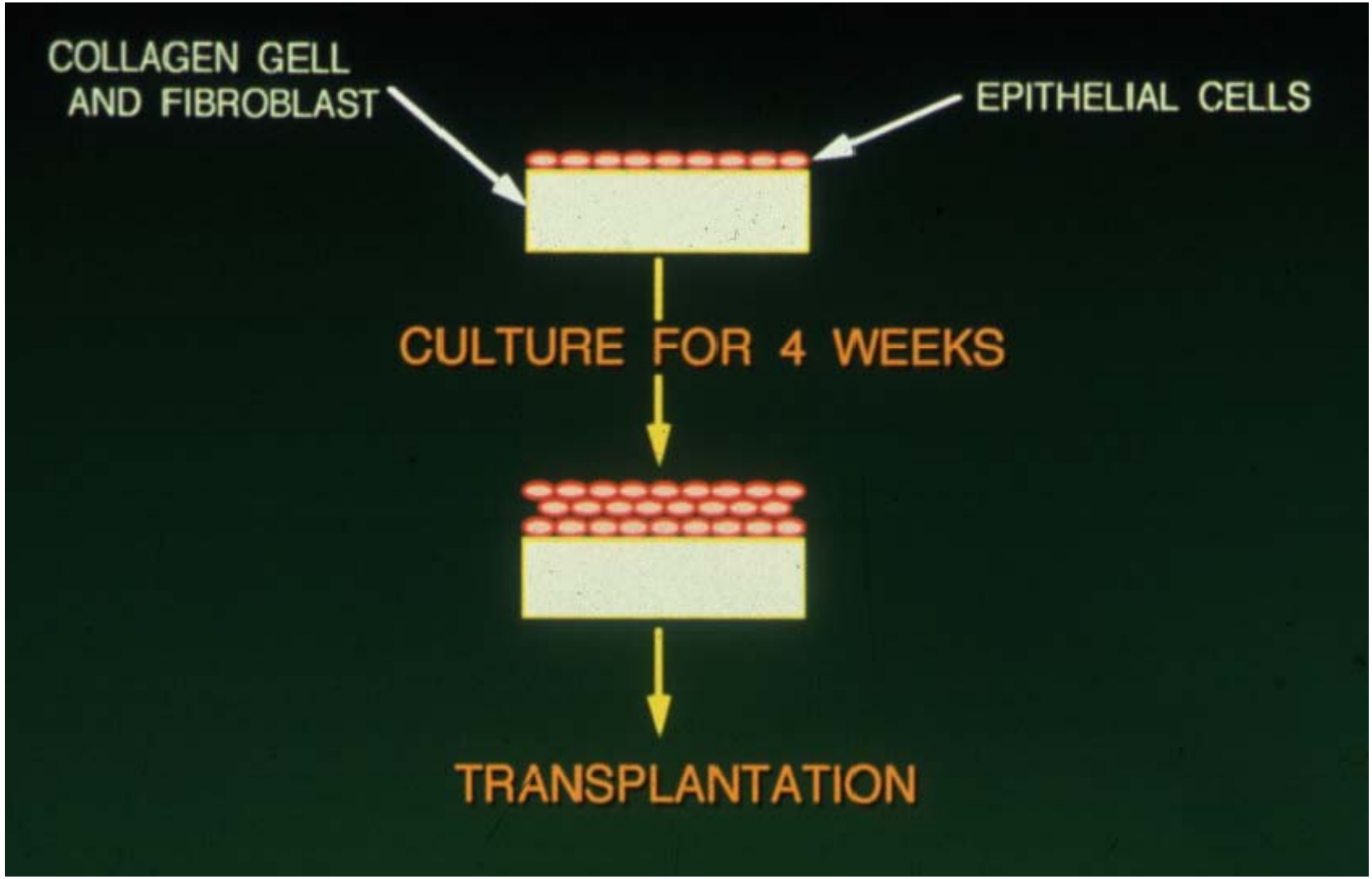


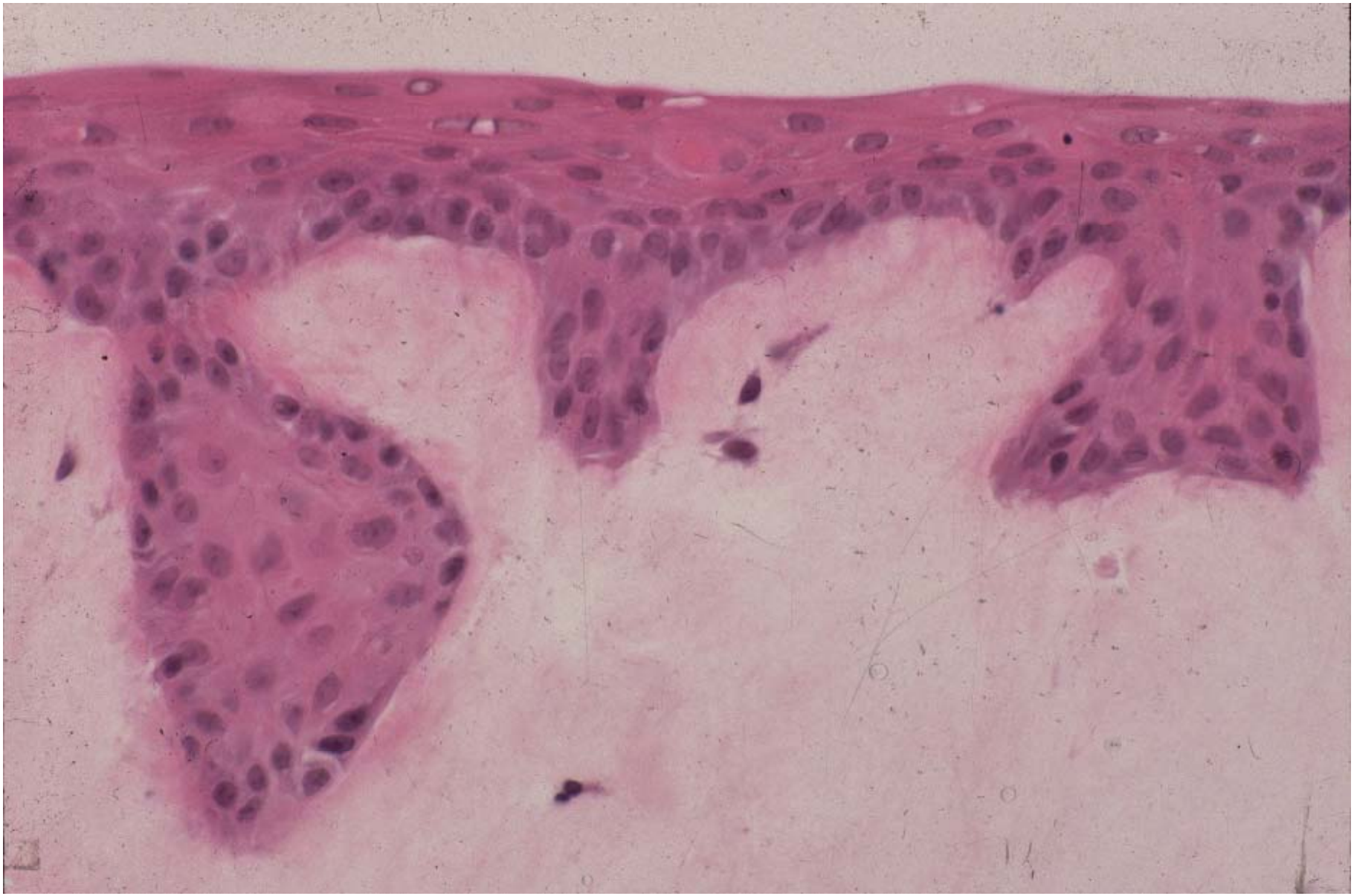
Allo

Skin Bank (allo skin)

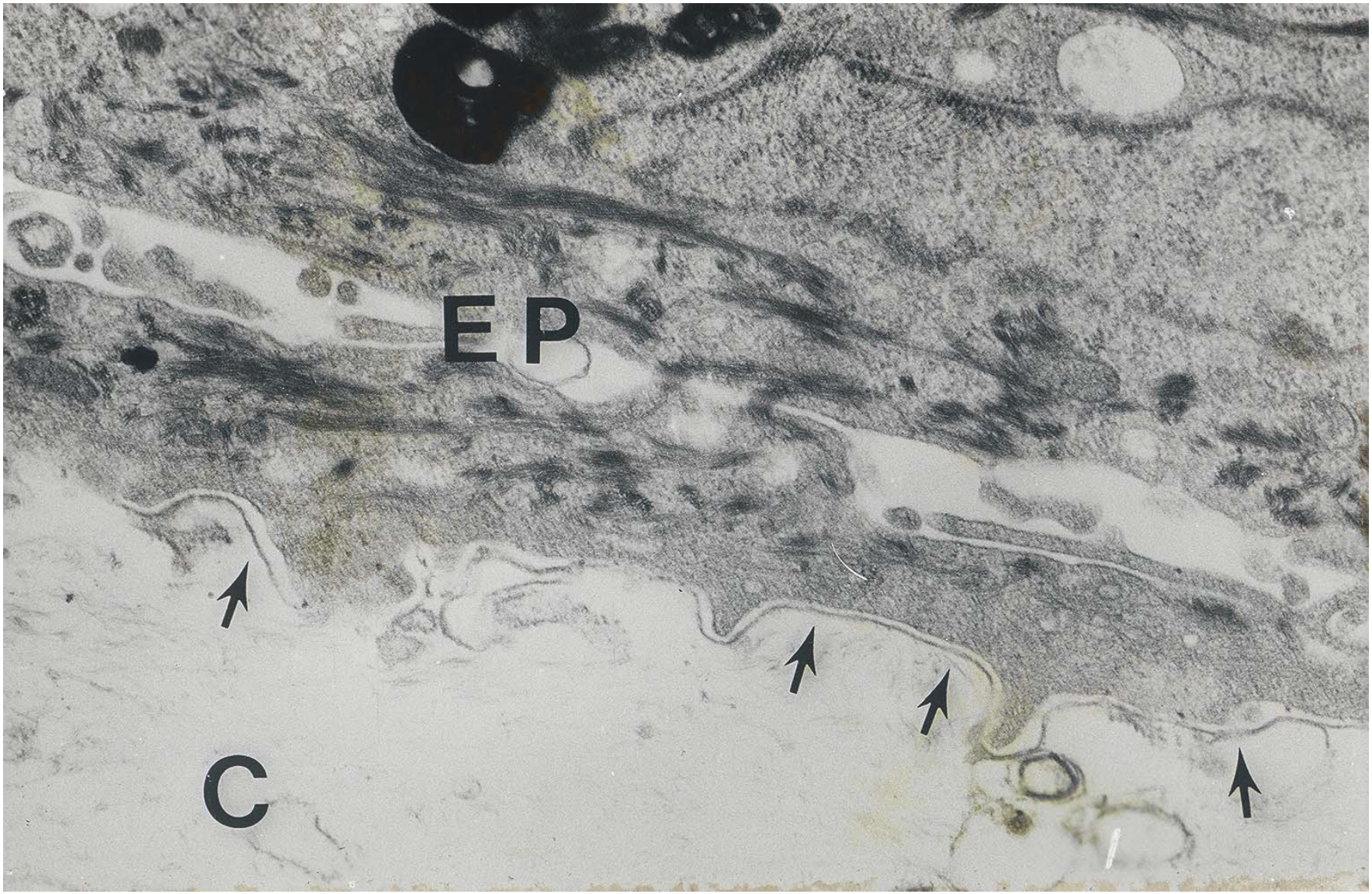
Cultured Skin

Cultured Skin



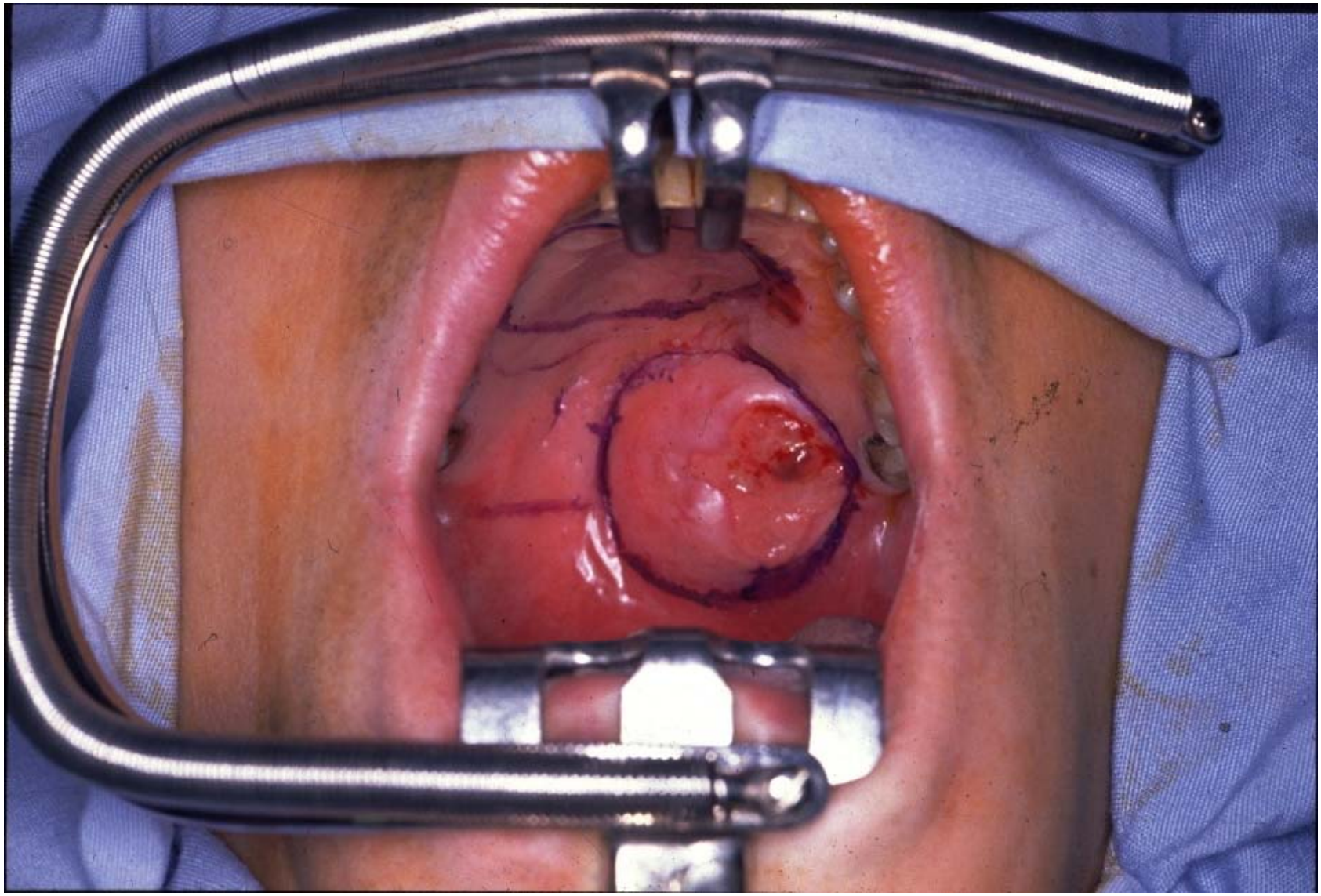


T.E Microscope

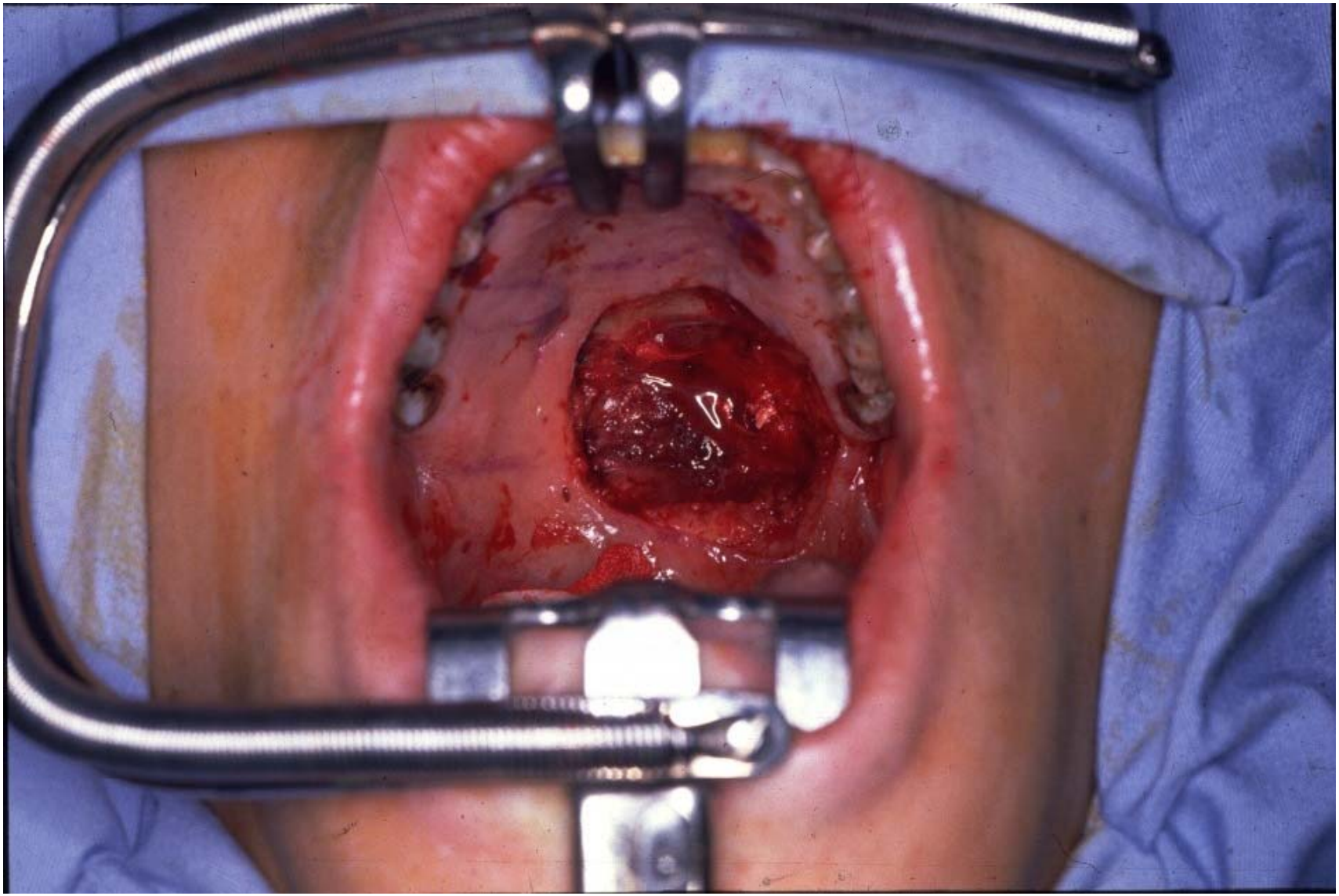


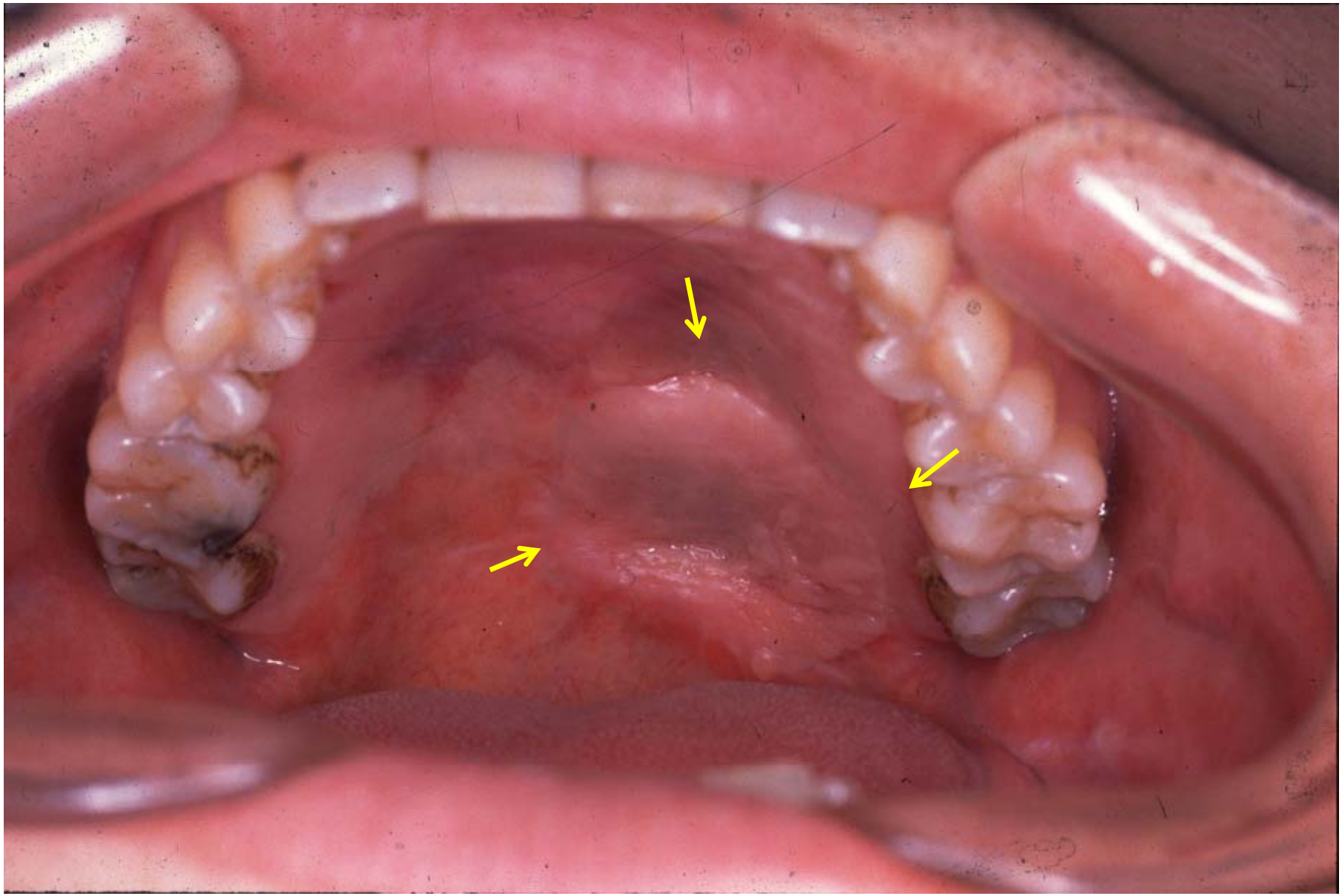
basement membrane

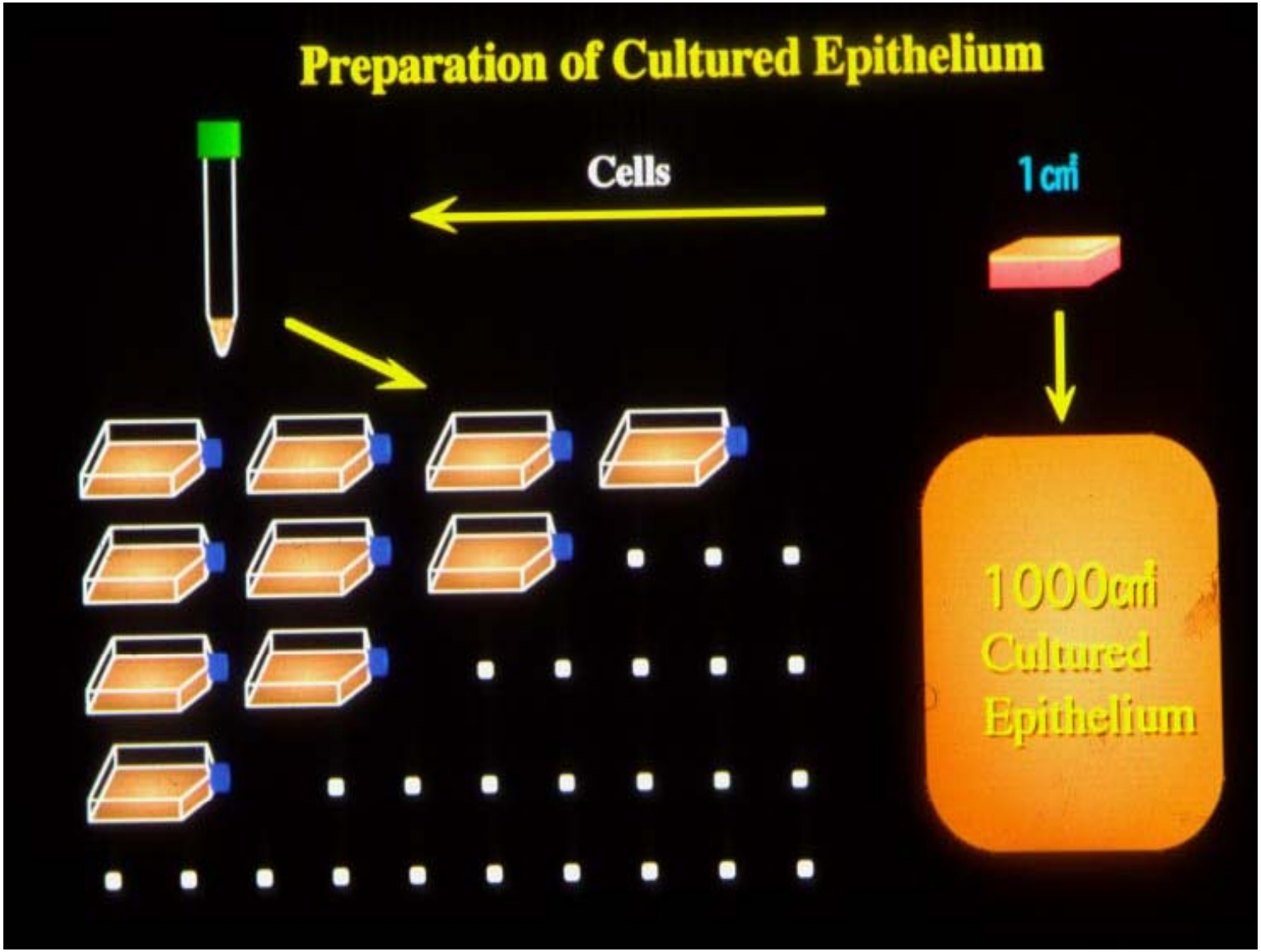
Benign Tumor in Plate



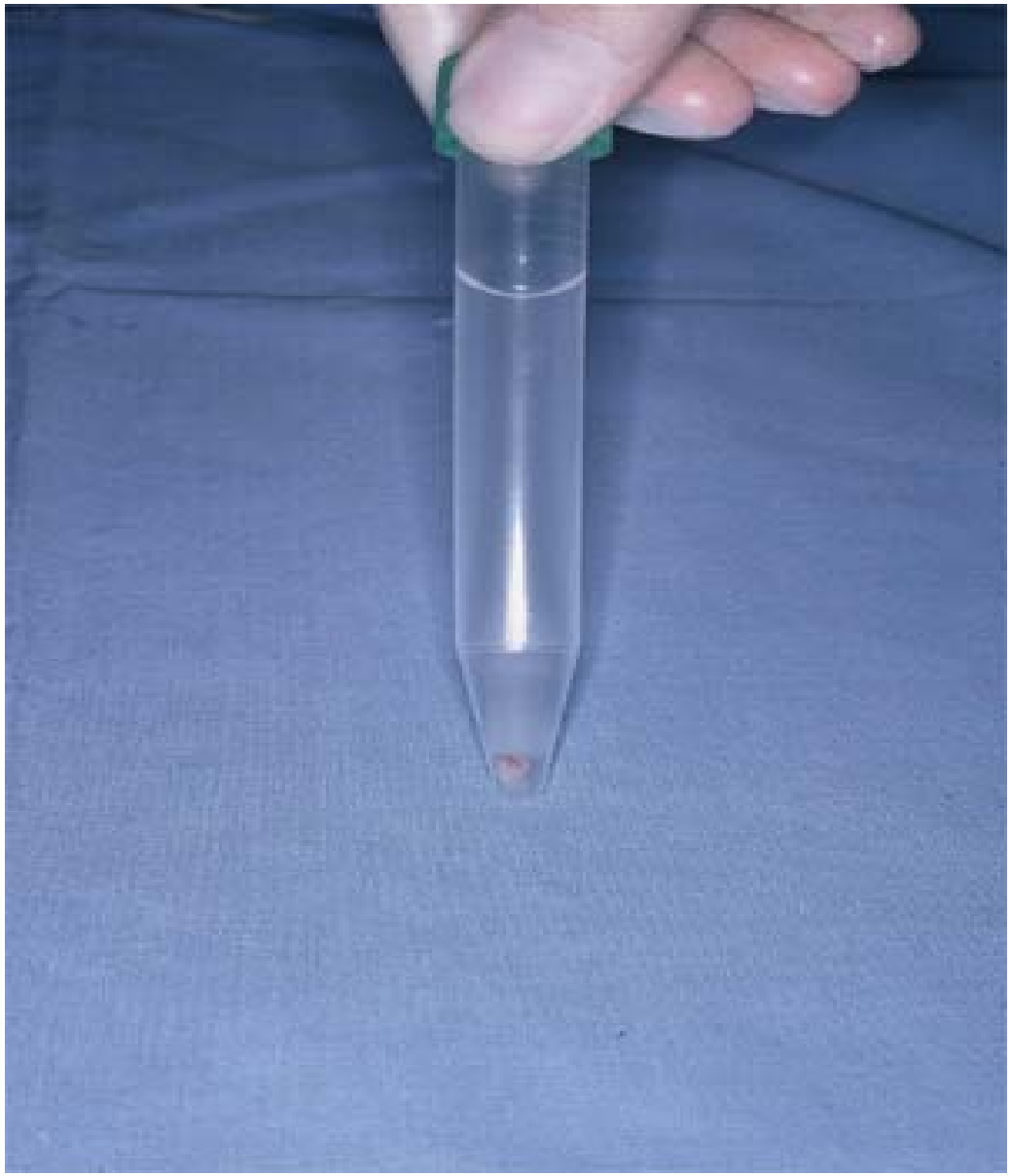
60, F

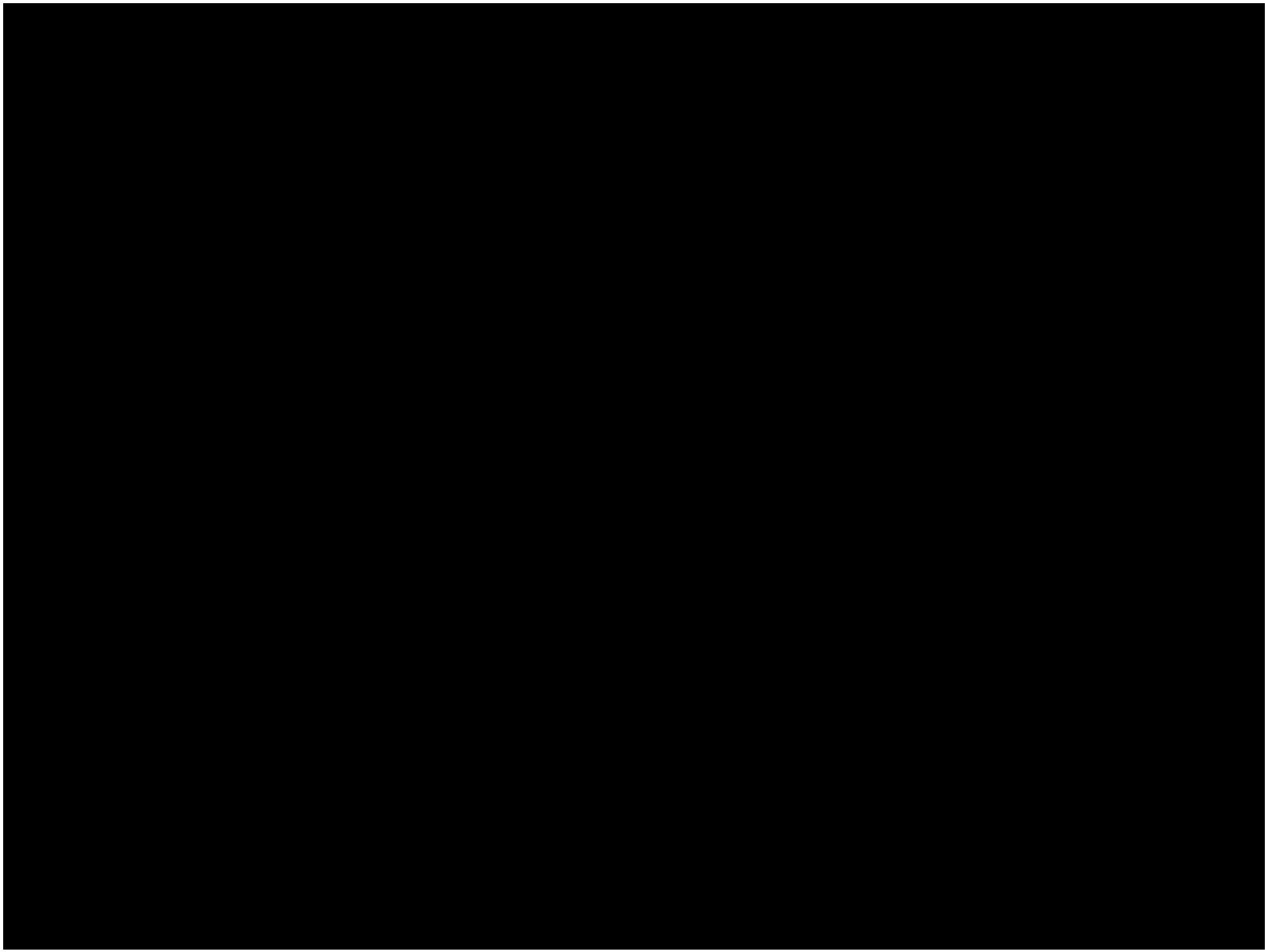





Preparation of Cultured Epithelium
Cells
1㎠
1000㎠
Cultured
Epithelium

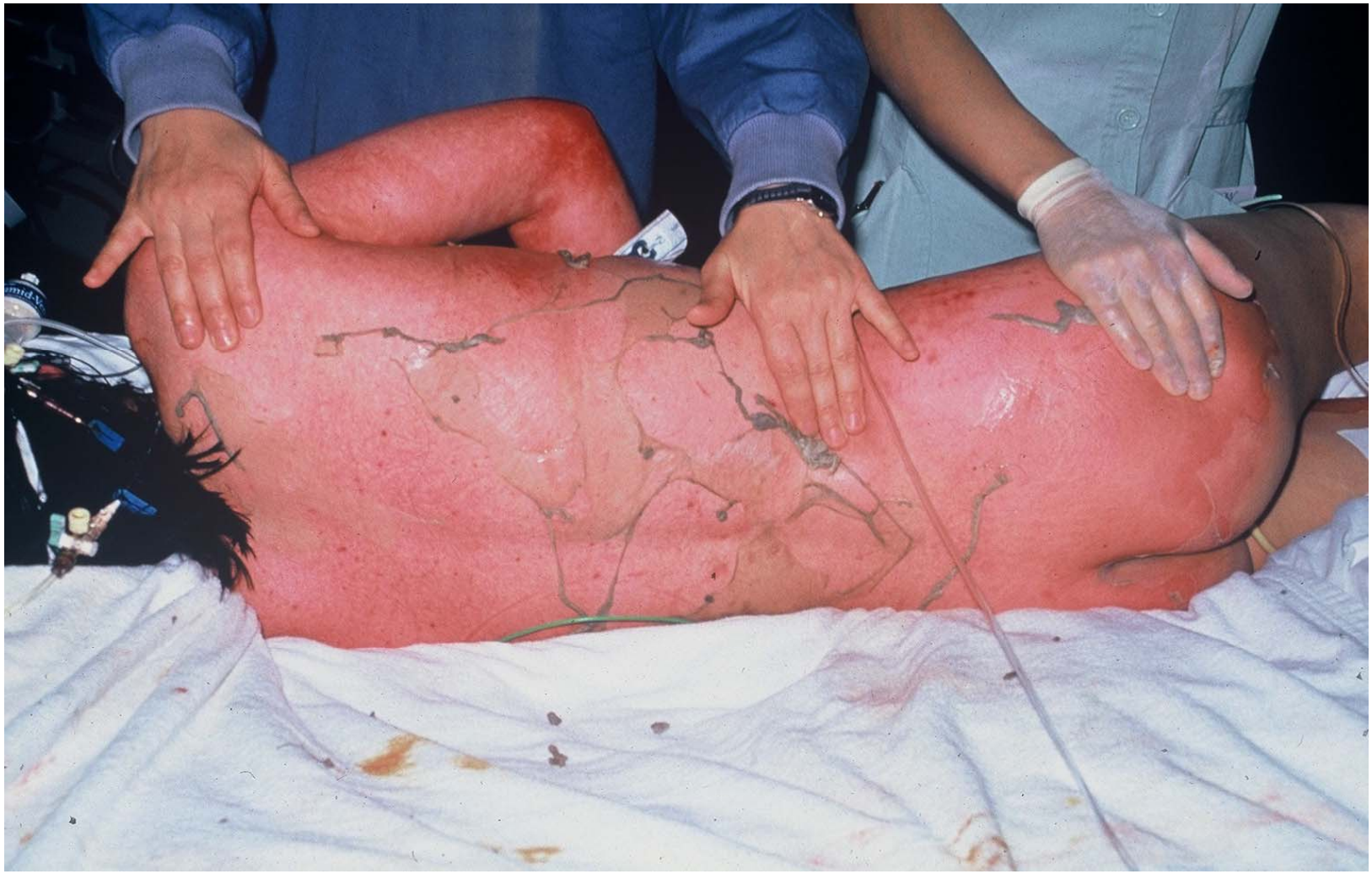
Gingival segment



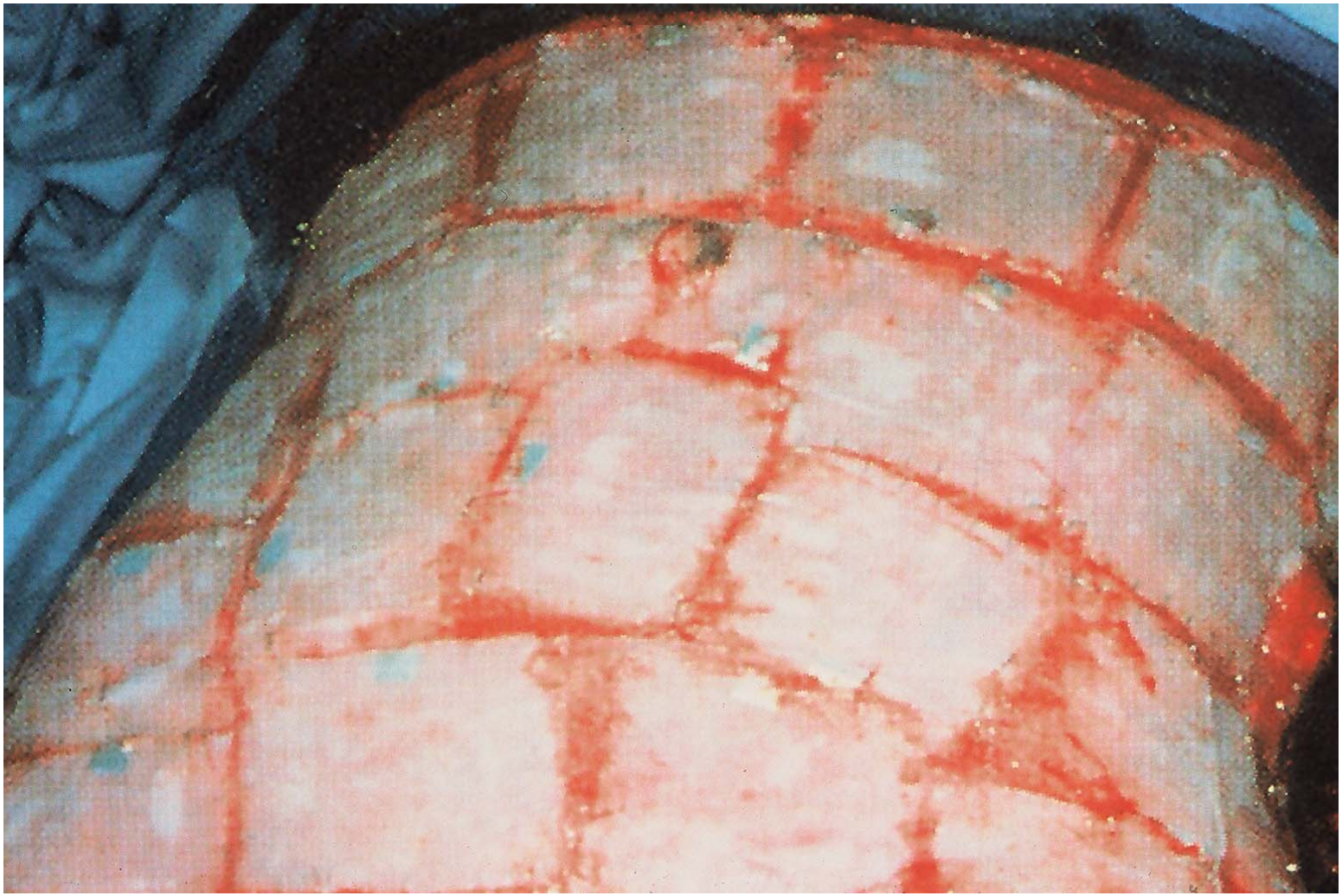


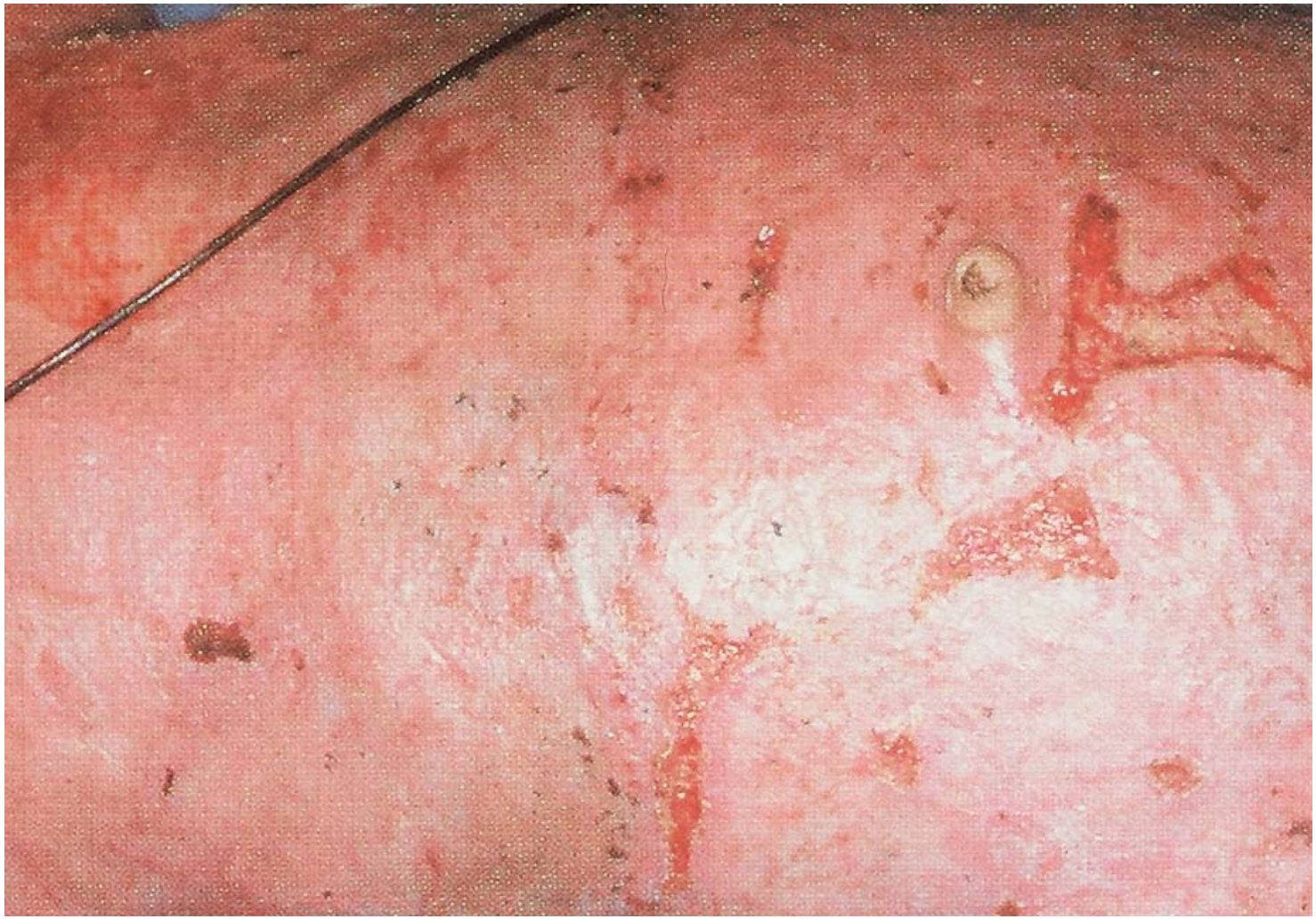
1 W

Burn



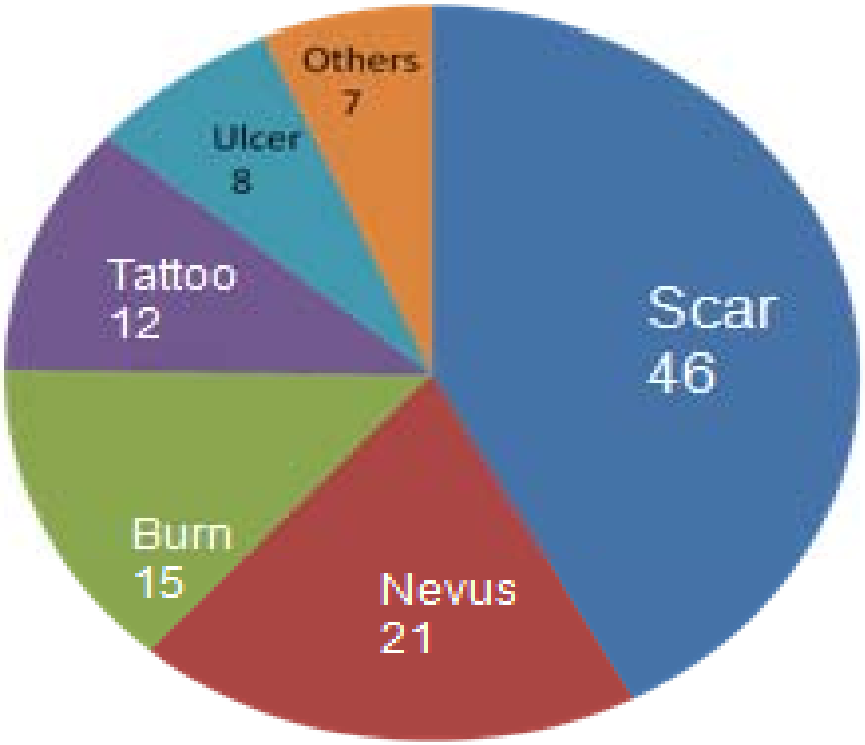
40, F



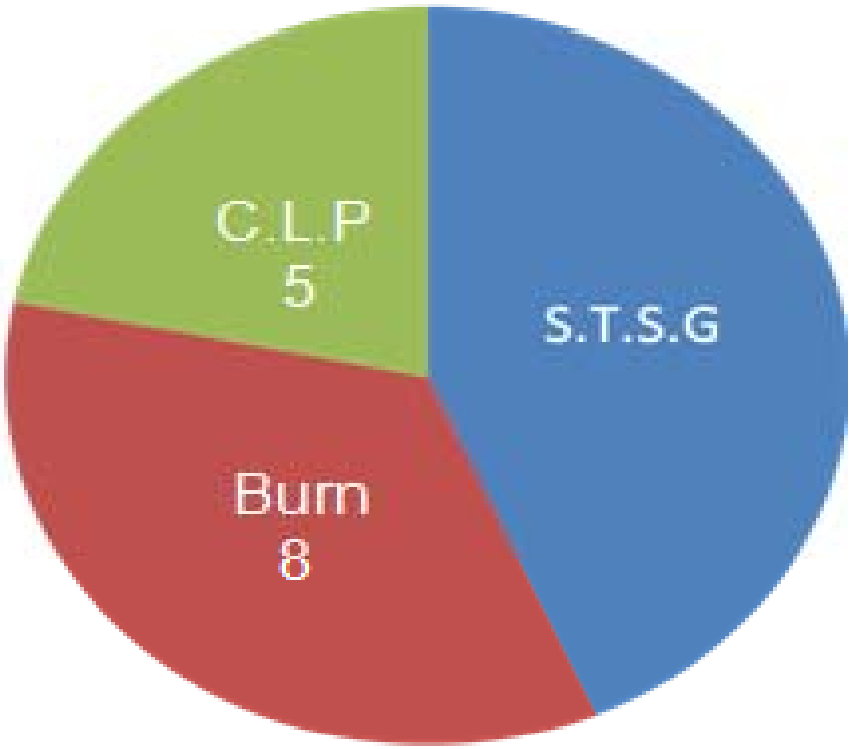


Clinical Results

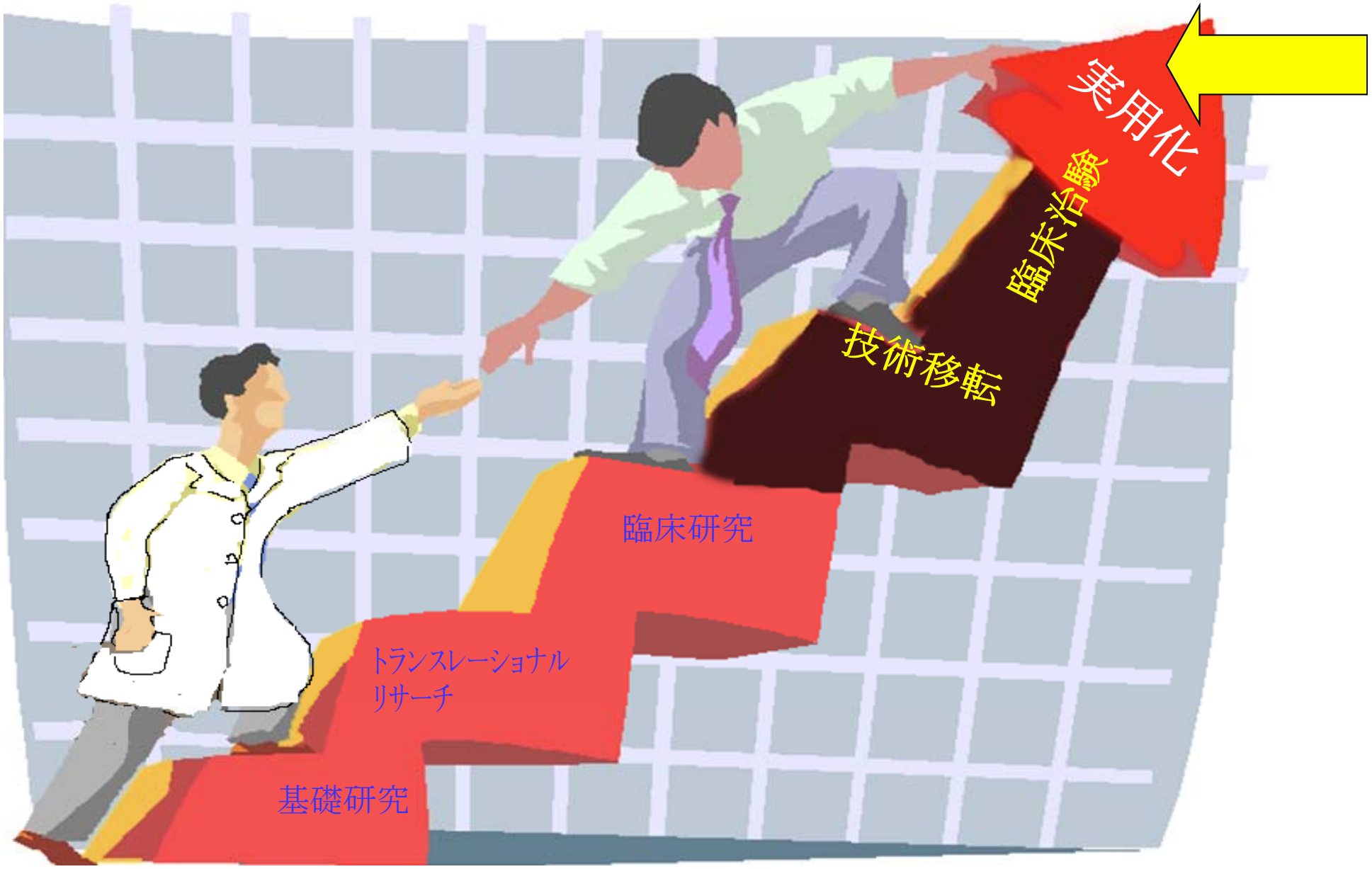
Patient treated with autograft



Patient treated with allograft



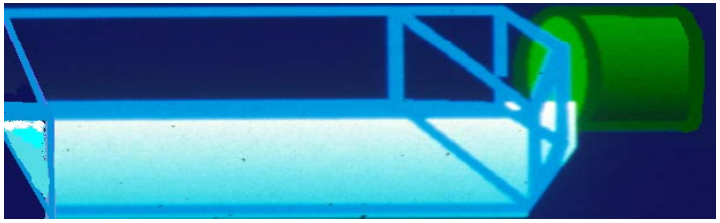
産学連携と実用化



日本初の再生医療製品　ジェイス®

（2008年承認）

The simple transplantation procedure



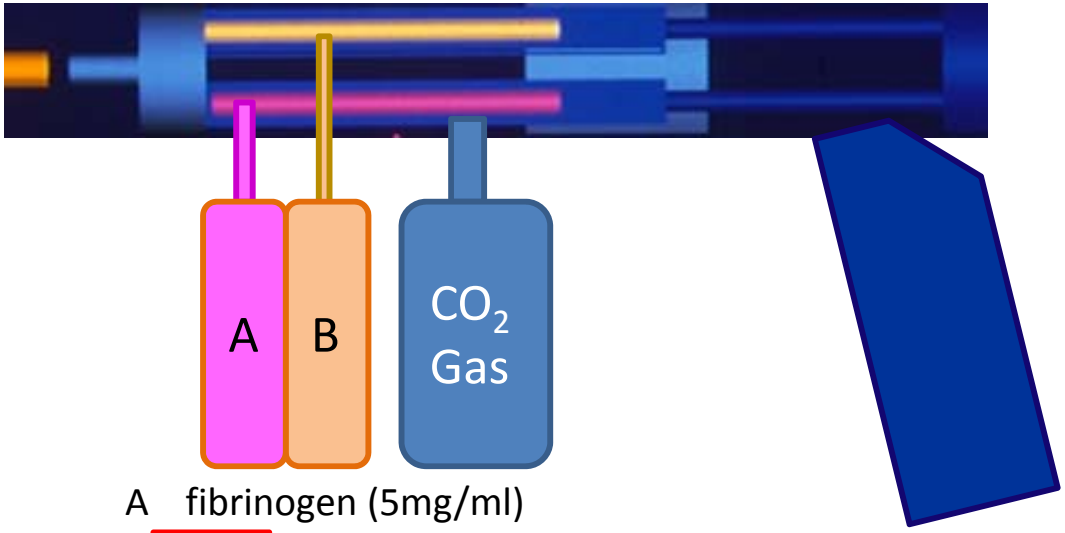
stem cells culture

Cell MSC, WJSC. DPSC, FB

Supernatant

Cell suspension

Mixed with trombin



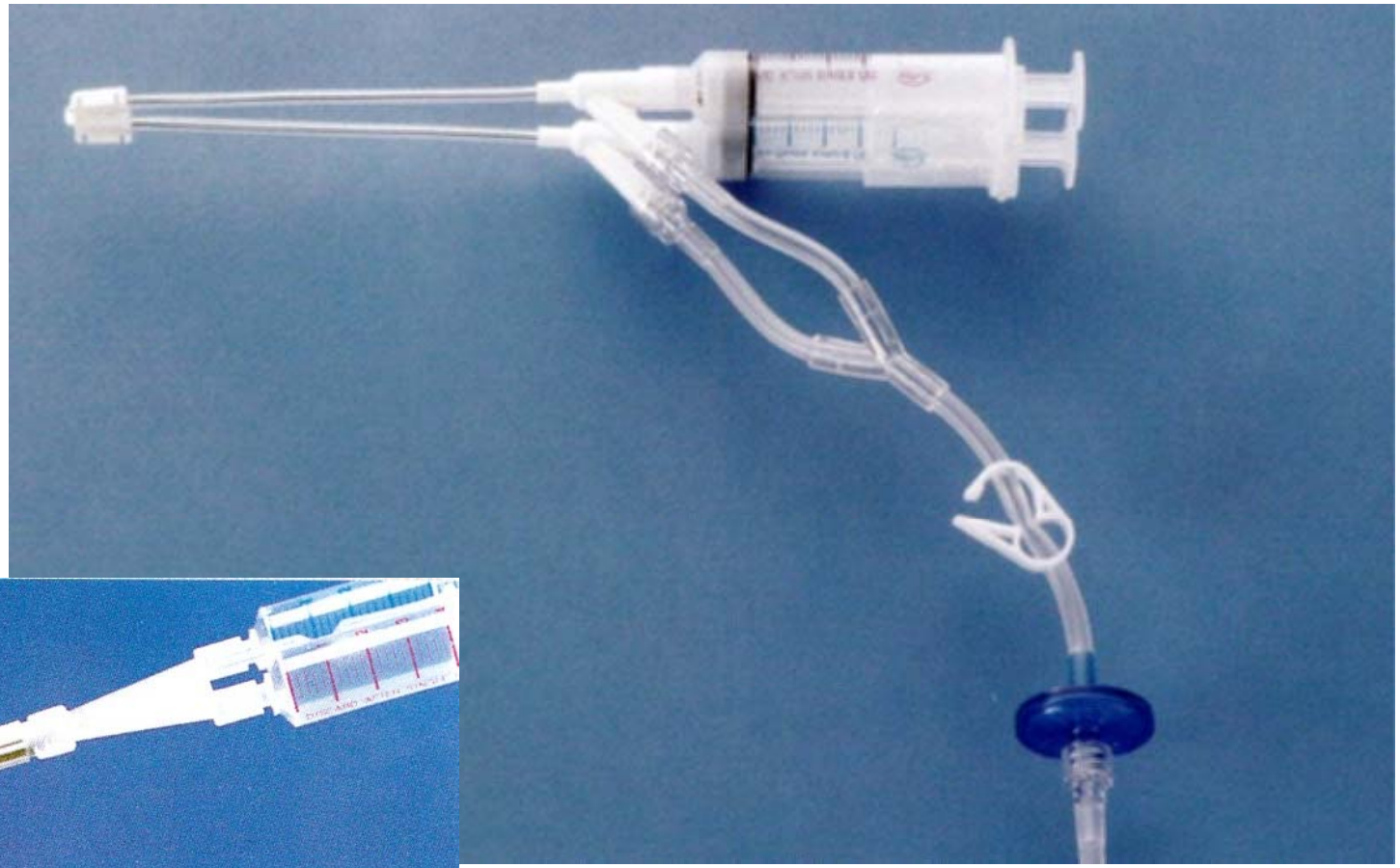
A fibrinogen (5mg/ml)

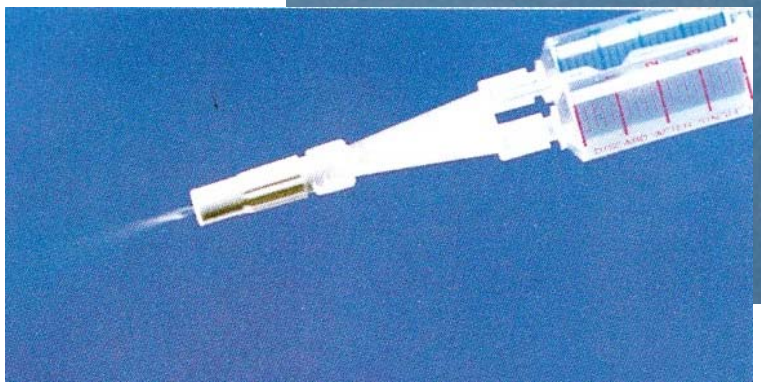
Cell

B trombin (250/mL)

Calcium chrolide ($cacl_2$, 1 mL)

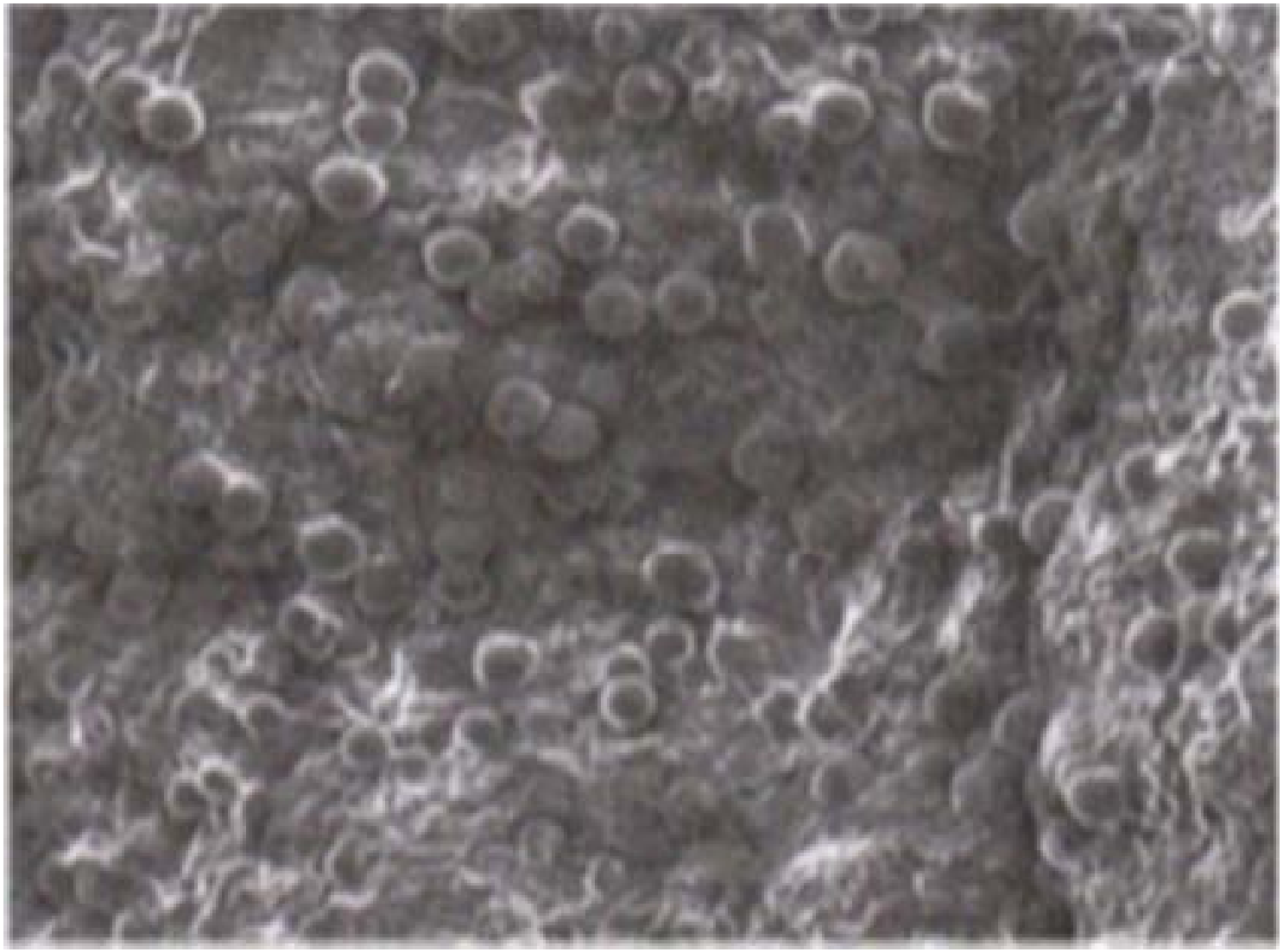
Cell Spray





↑
air

Mucosal epithelial Cell attached on the surface



The epidermal front sweeping forward

Cell Spray

70, M

Cell Spray

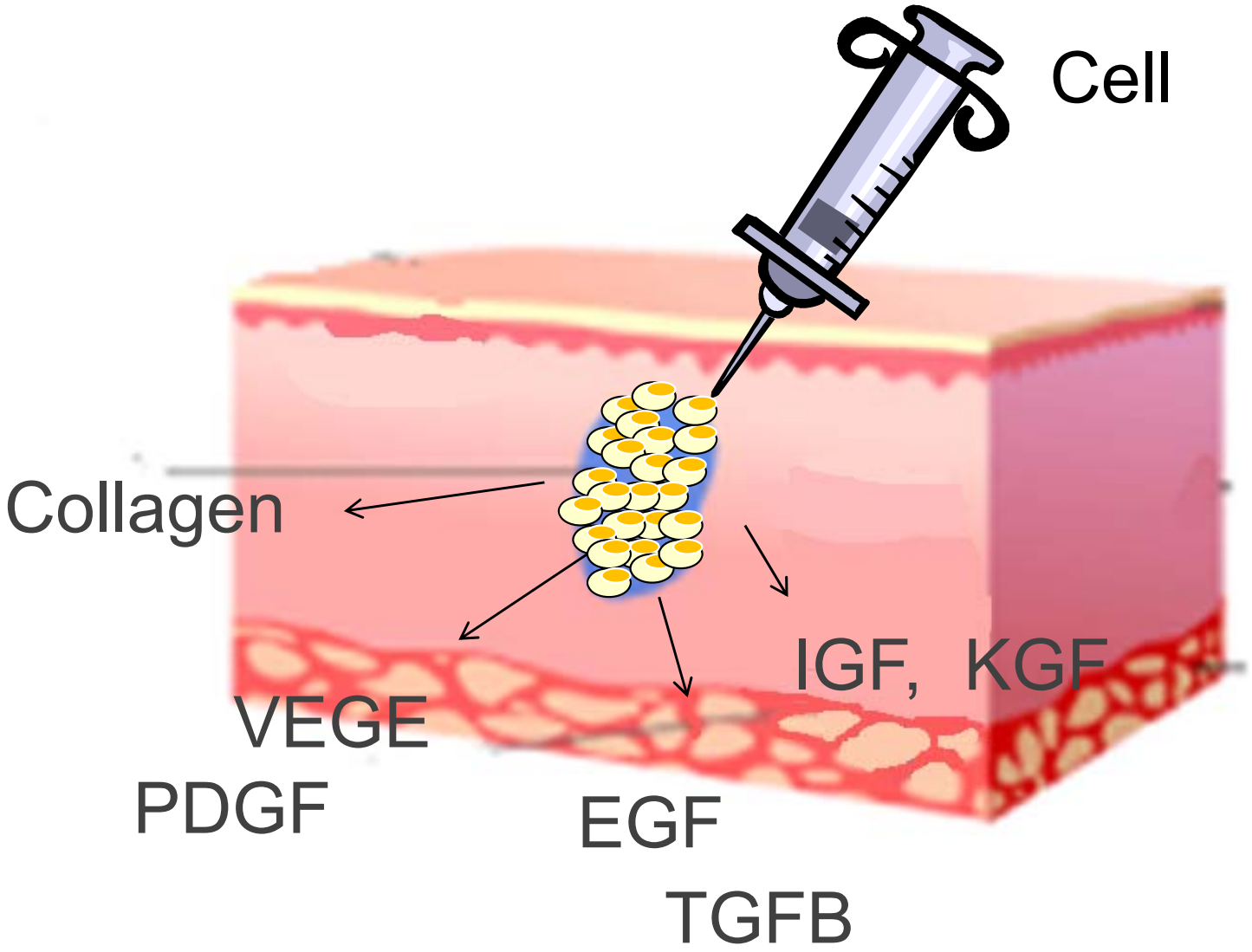
A

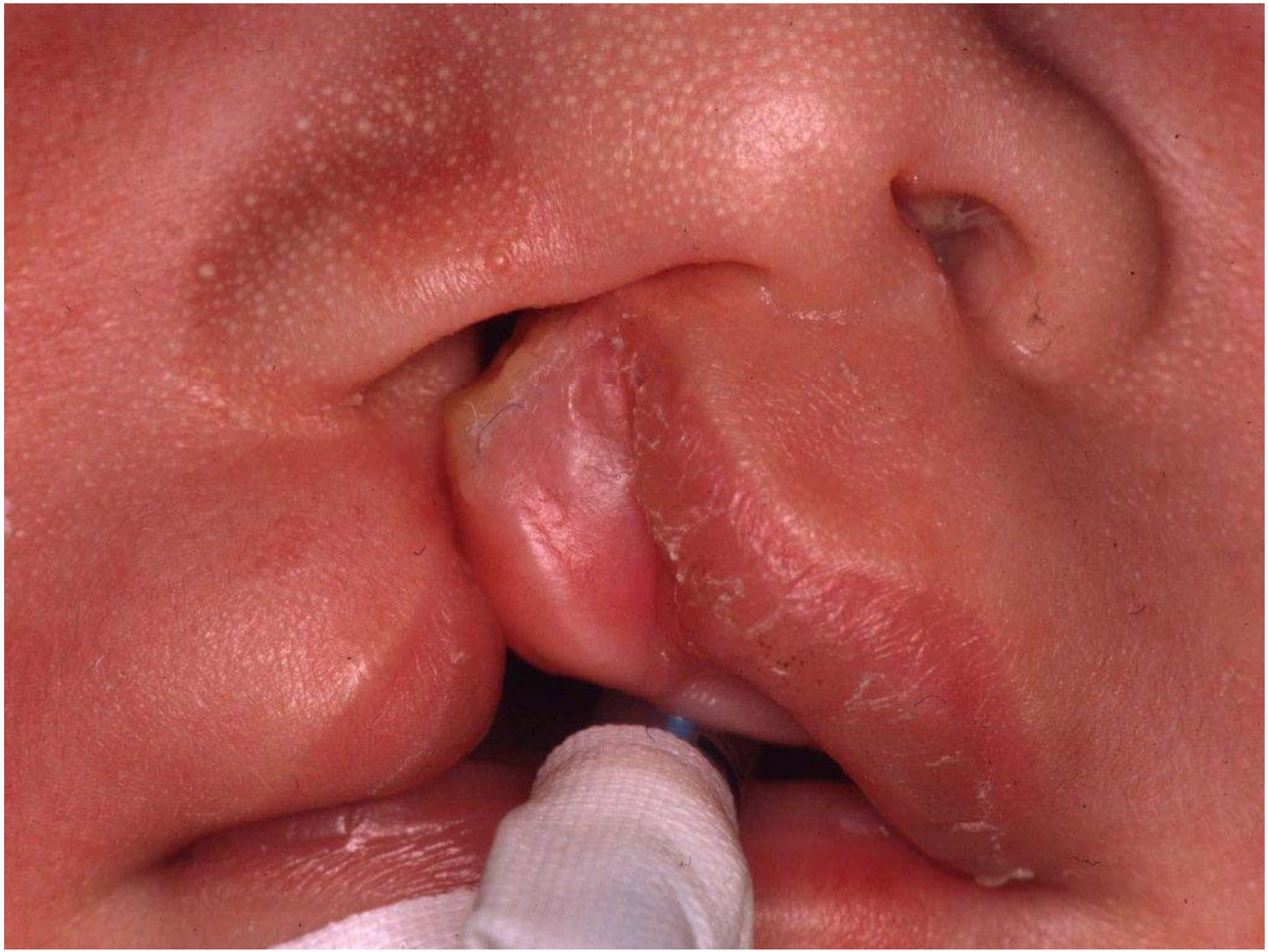
B

28, M

Scar

Mechanism for wrinkle treatment





Cheek

45, F

CAS	10.5
PSS	5.0

→

CAS	36
PSS	26

Keloid

CAS	10.5
PSS	5.0

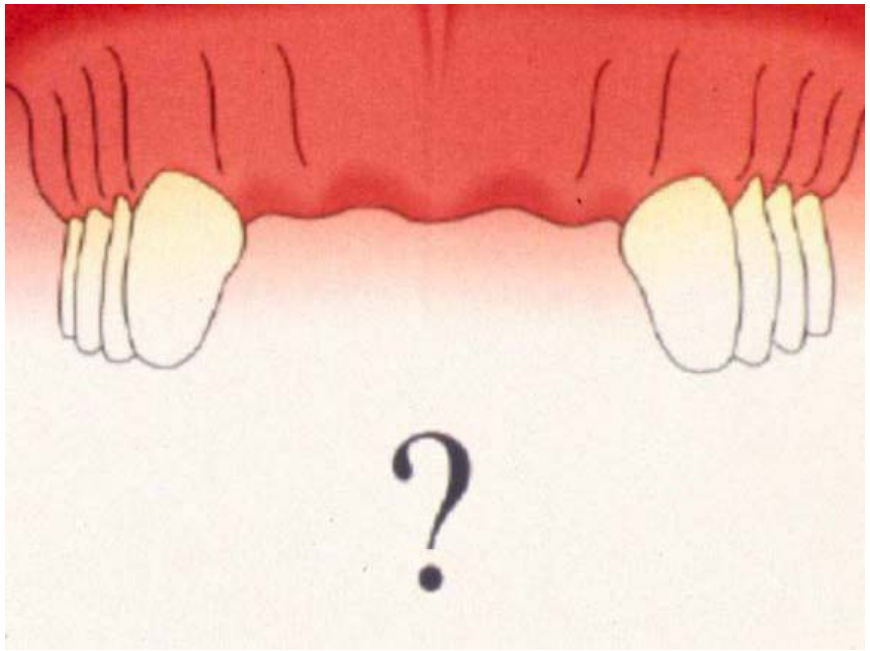
→

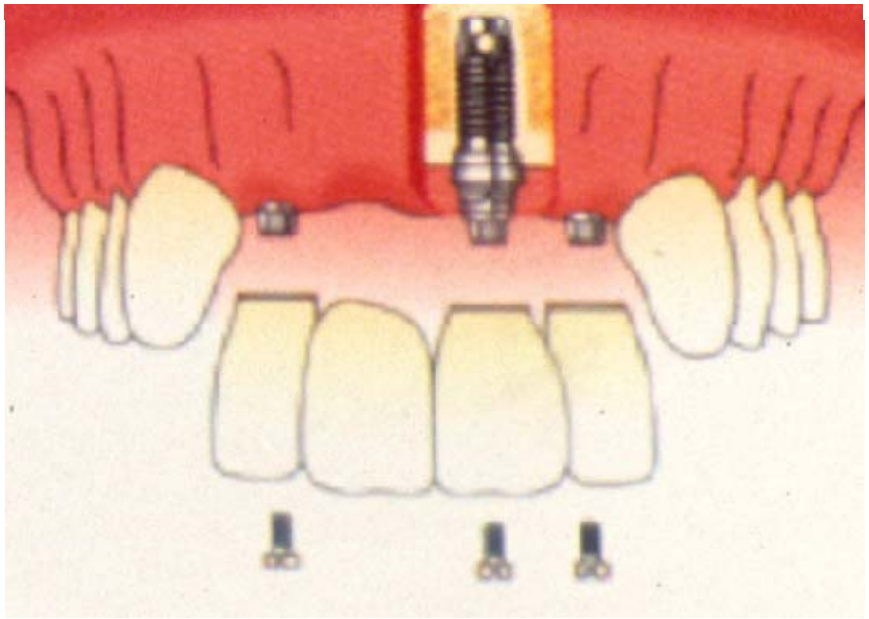
CAS	36
PSS	26

61, F

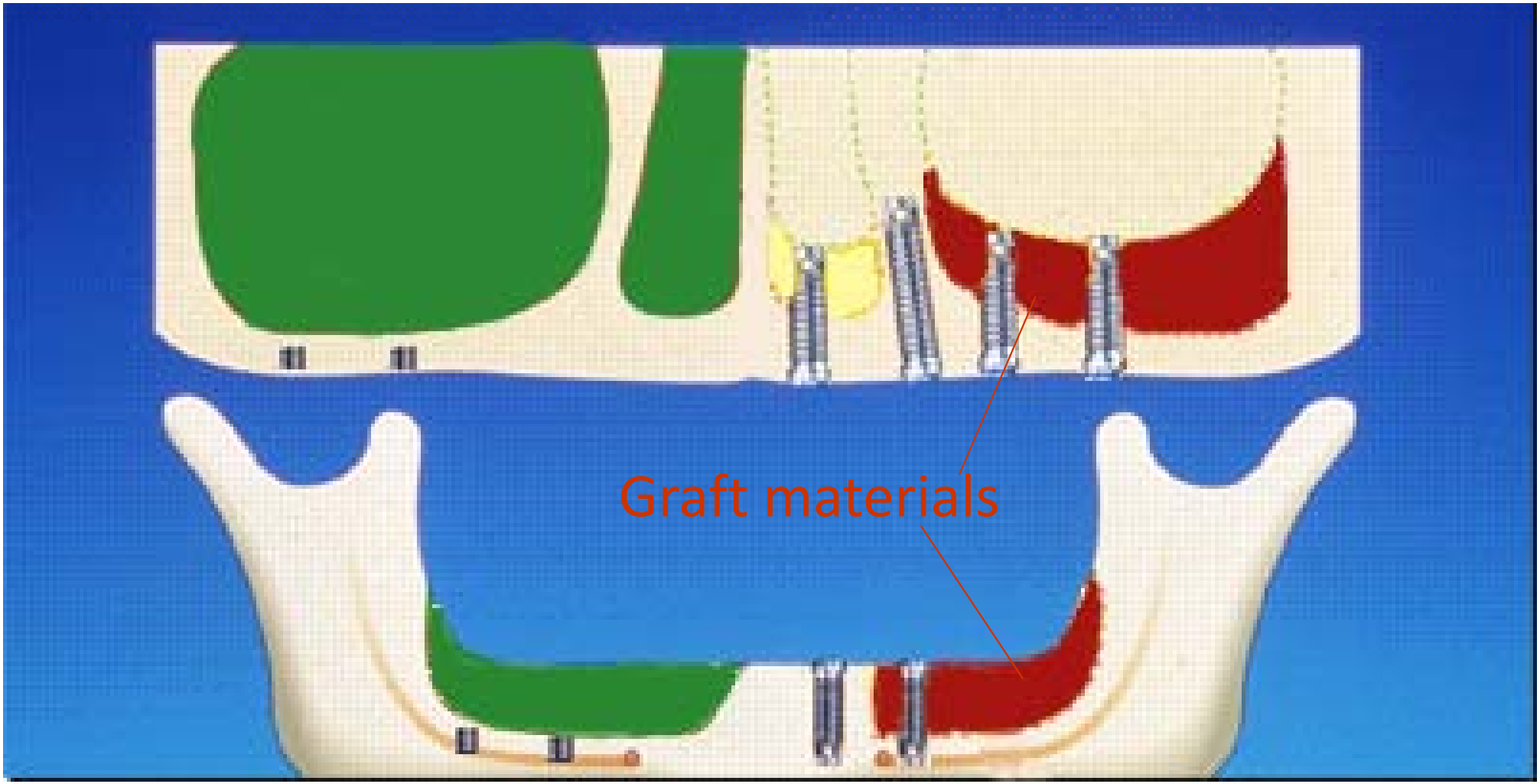
Bone

インプラント

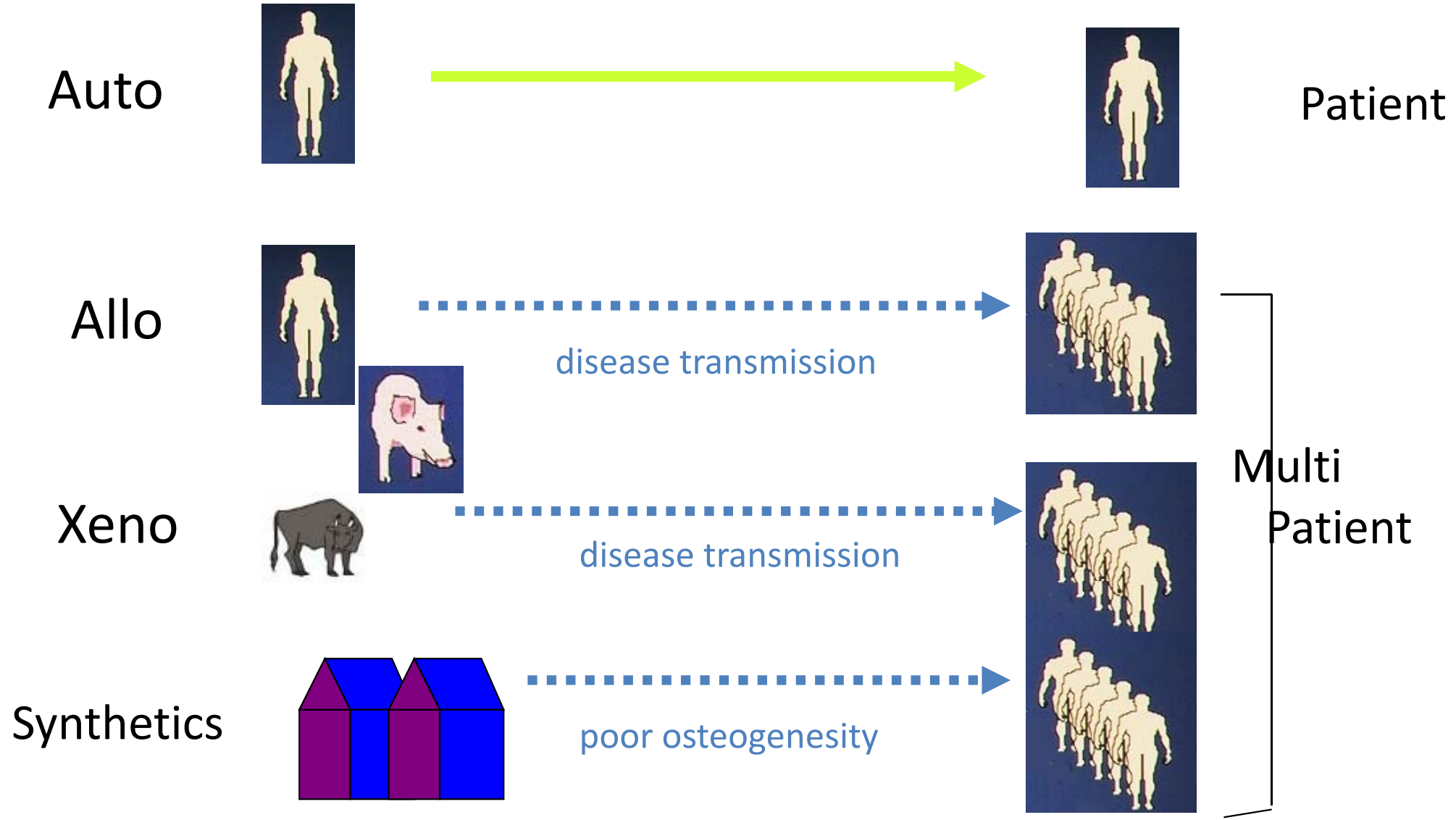




インプラントと骨再生

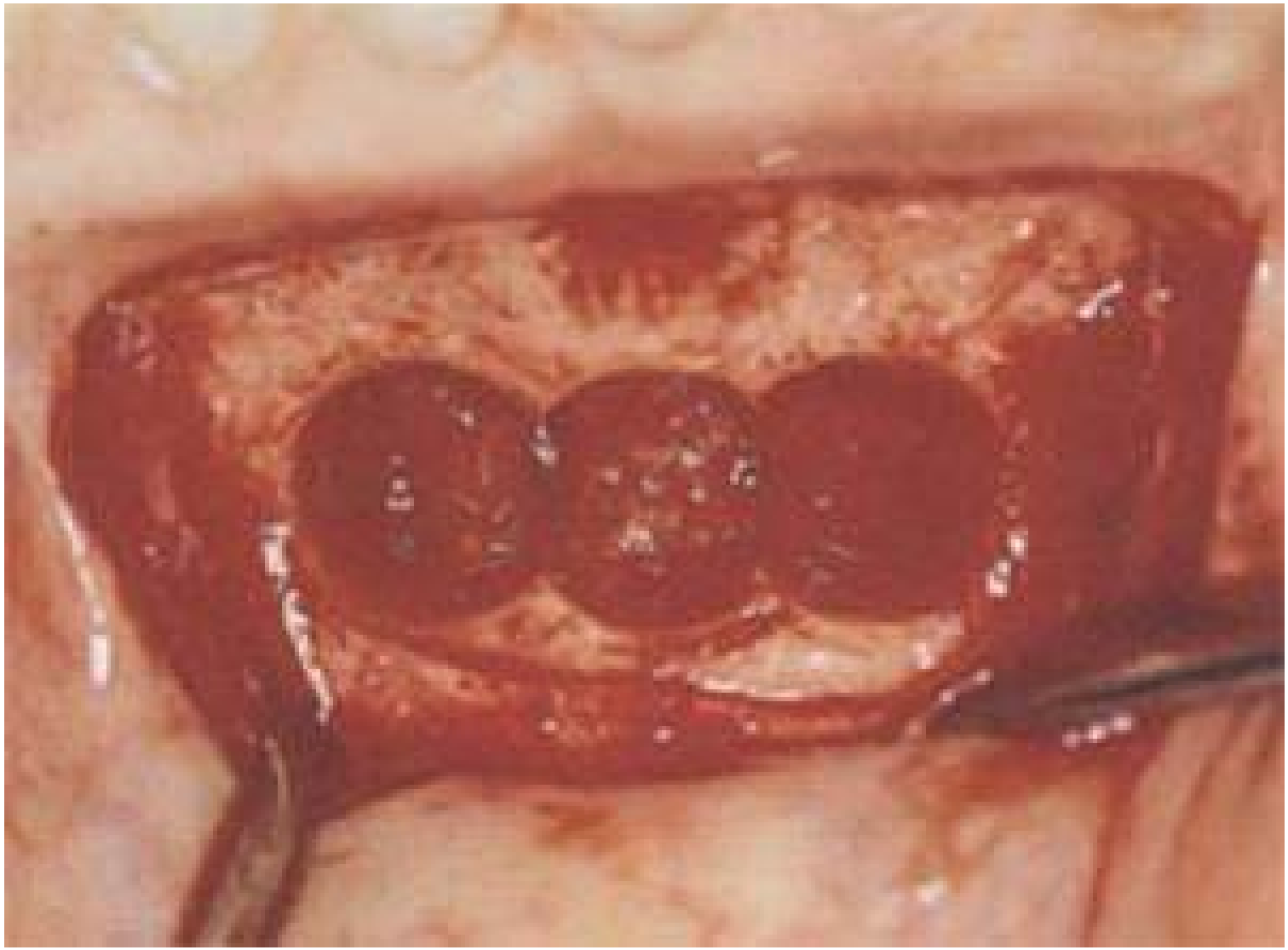


Graft Materials



Autogenous Bone Harvesting

Mental



Severe damage to donor site

Autogenous Bone Harvesting

Mental

Complications in donor site

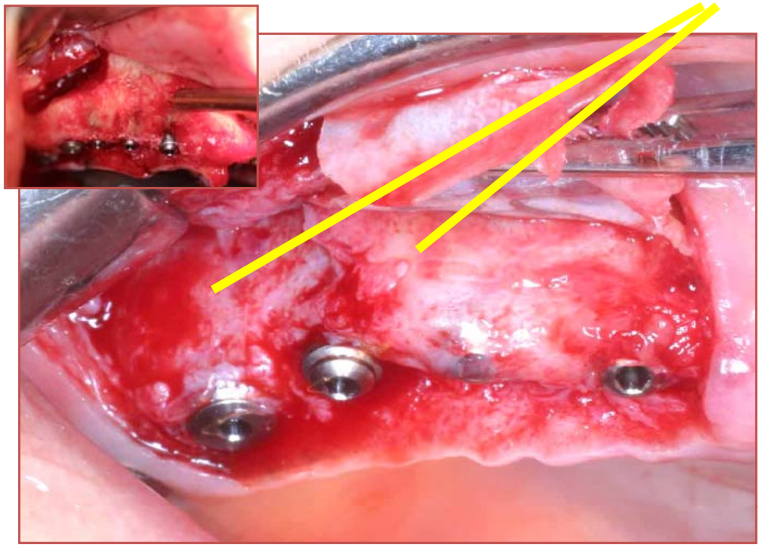
培養骨の作りかた


Implant surgery using cultured bone

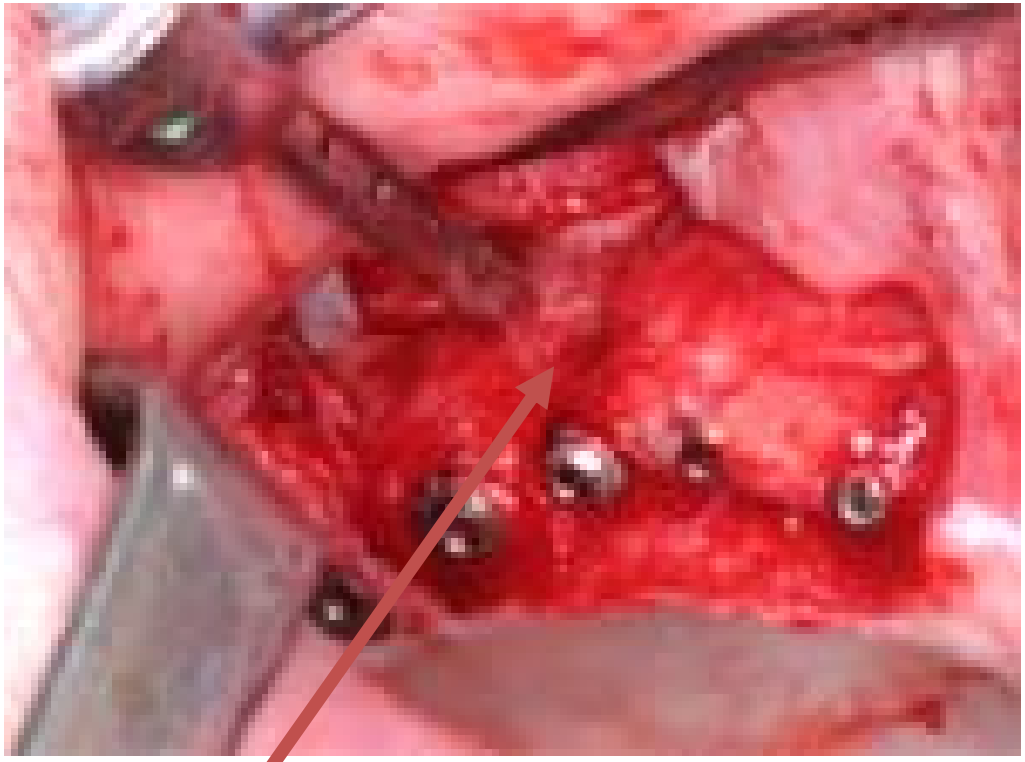
骨の再生

Case 1　61, F

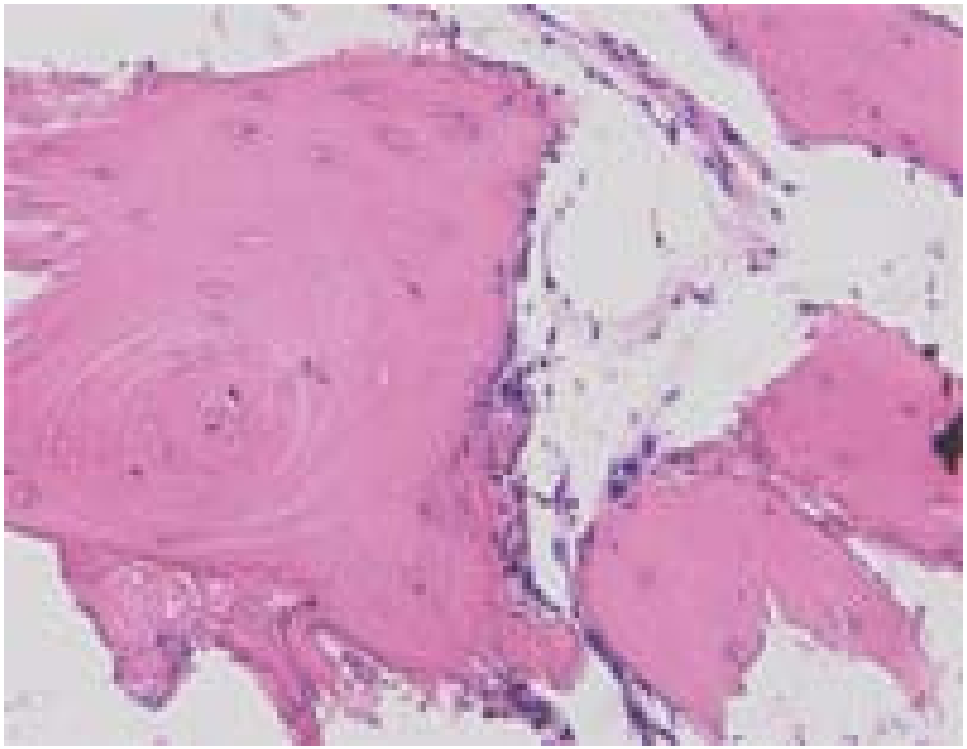
手術前



Case 1

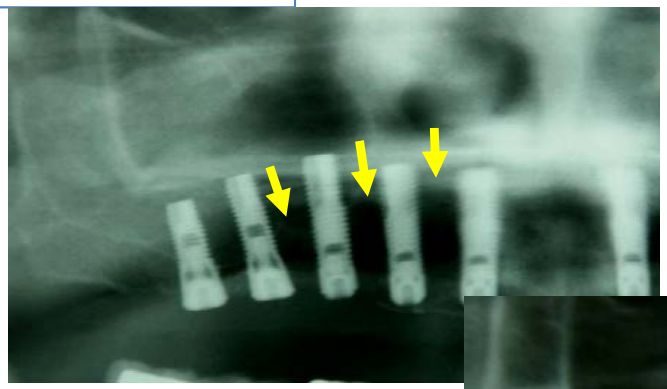


Bone biopsy

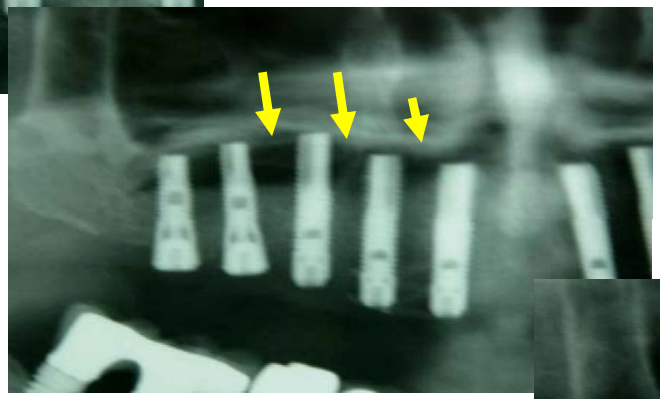


histology of new bone

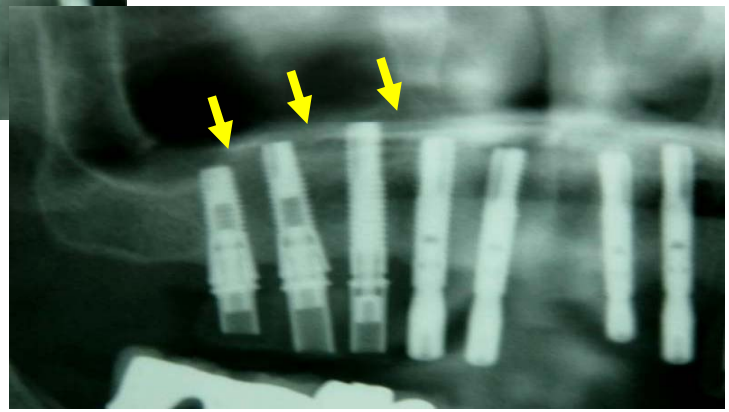
Case 1



1 w



2M



6M

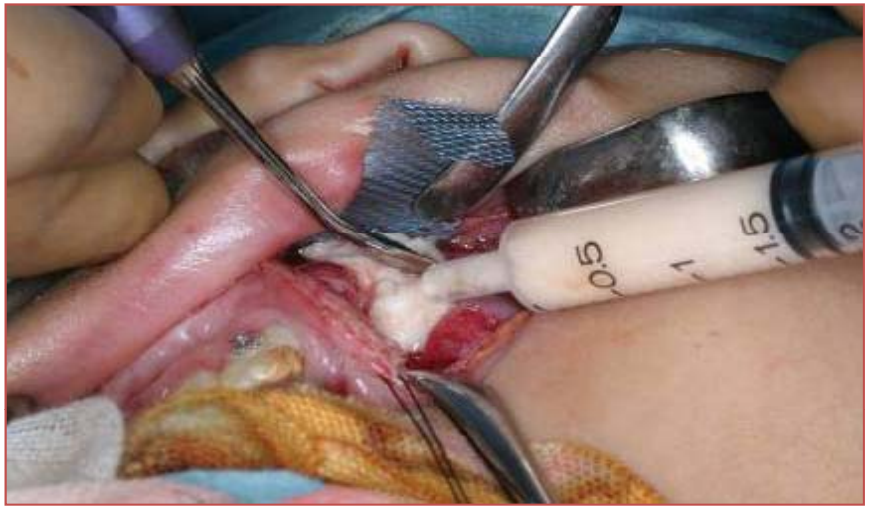
Alveolar Cleft

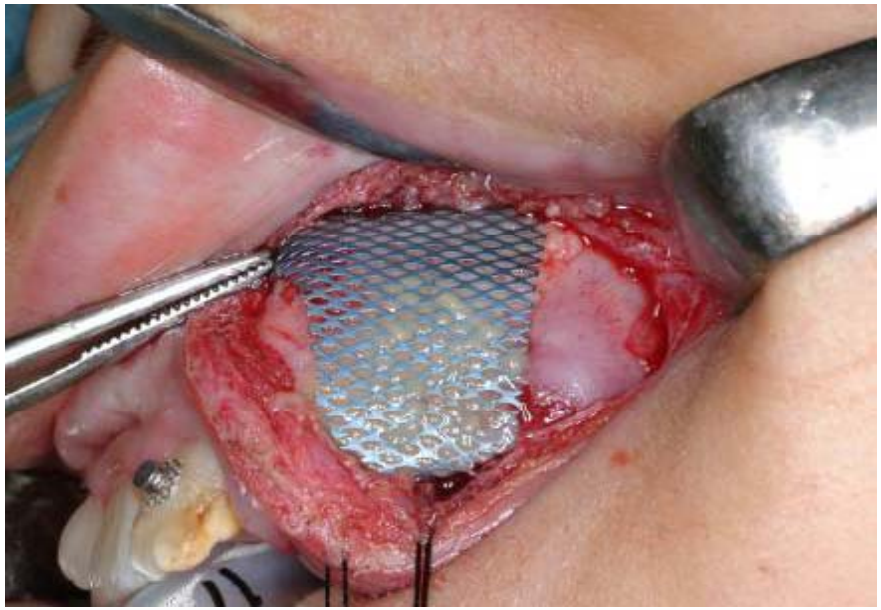
11, M

Case 2

Preoperative 3D CT

Case 3

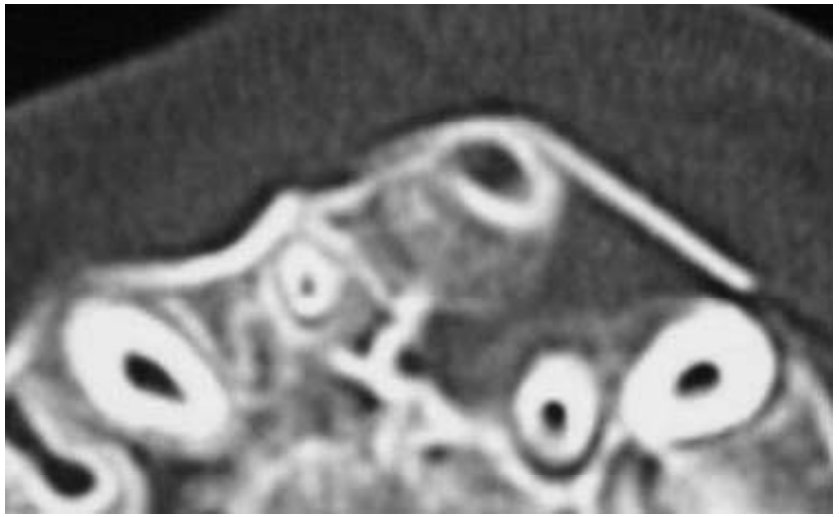




CT Images

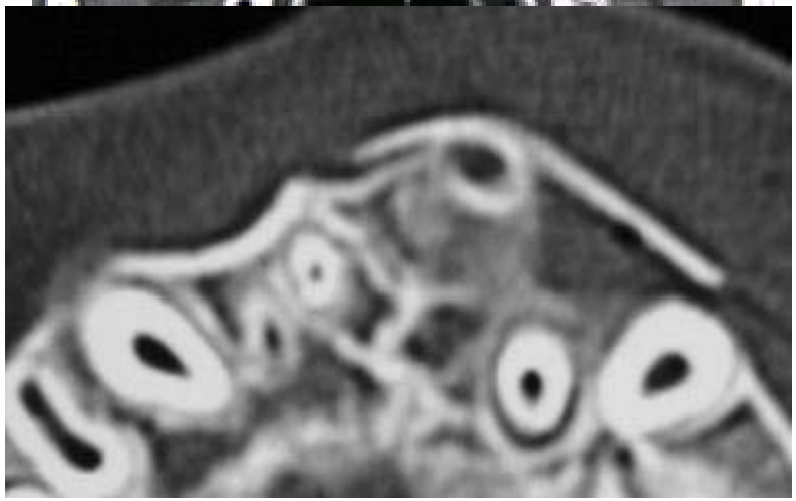
Case 4

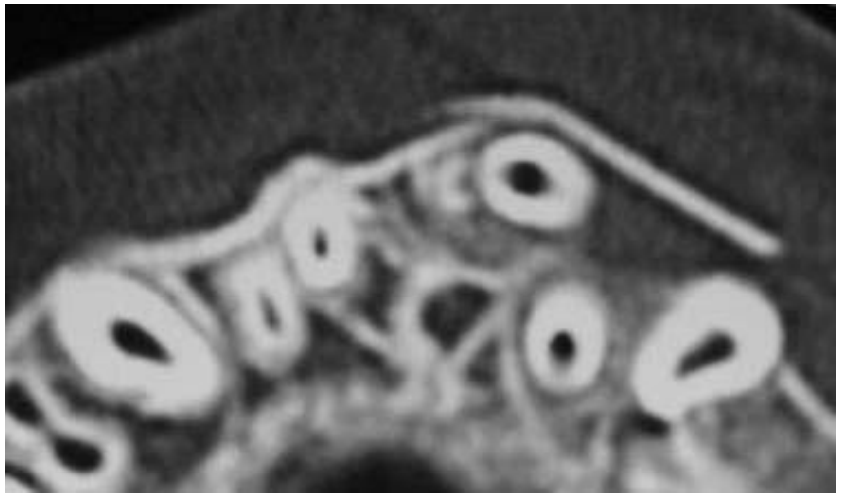
Pre-Ope



1Mx

3M





6M

Clinical Observations

Case 4

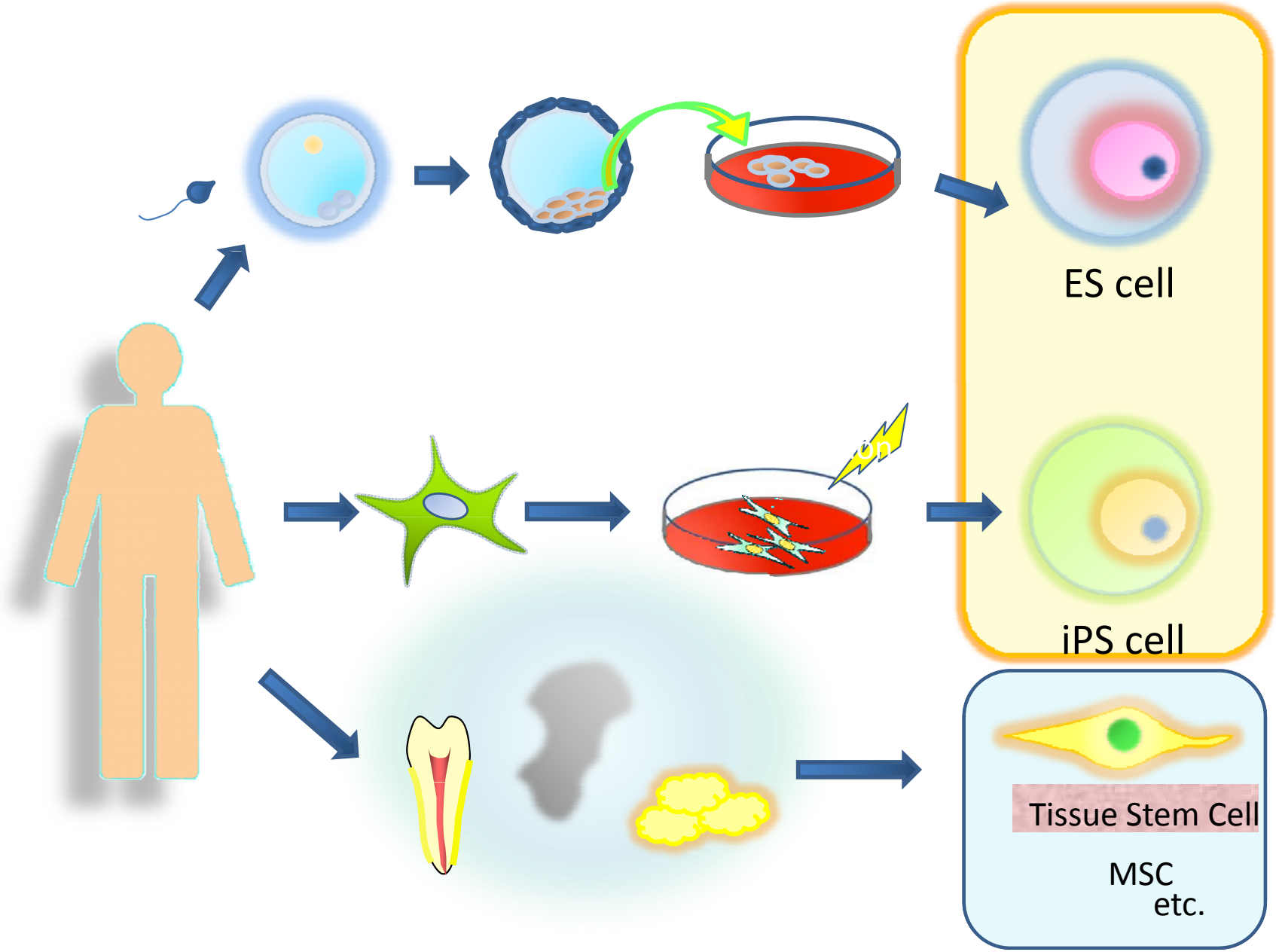
3M

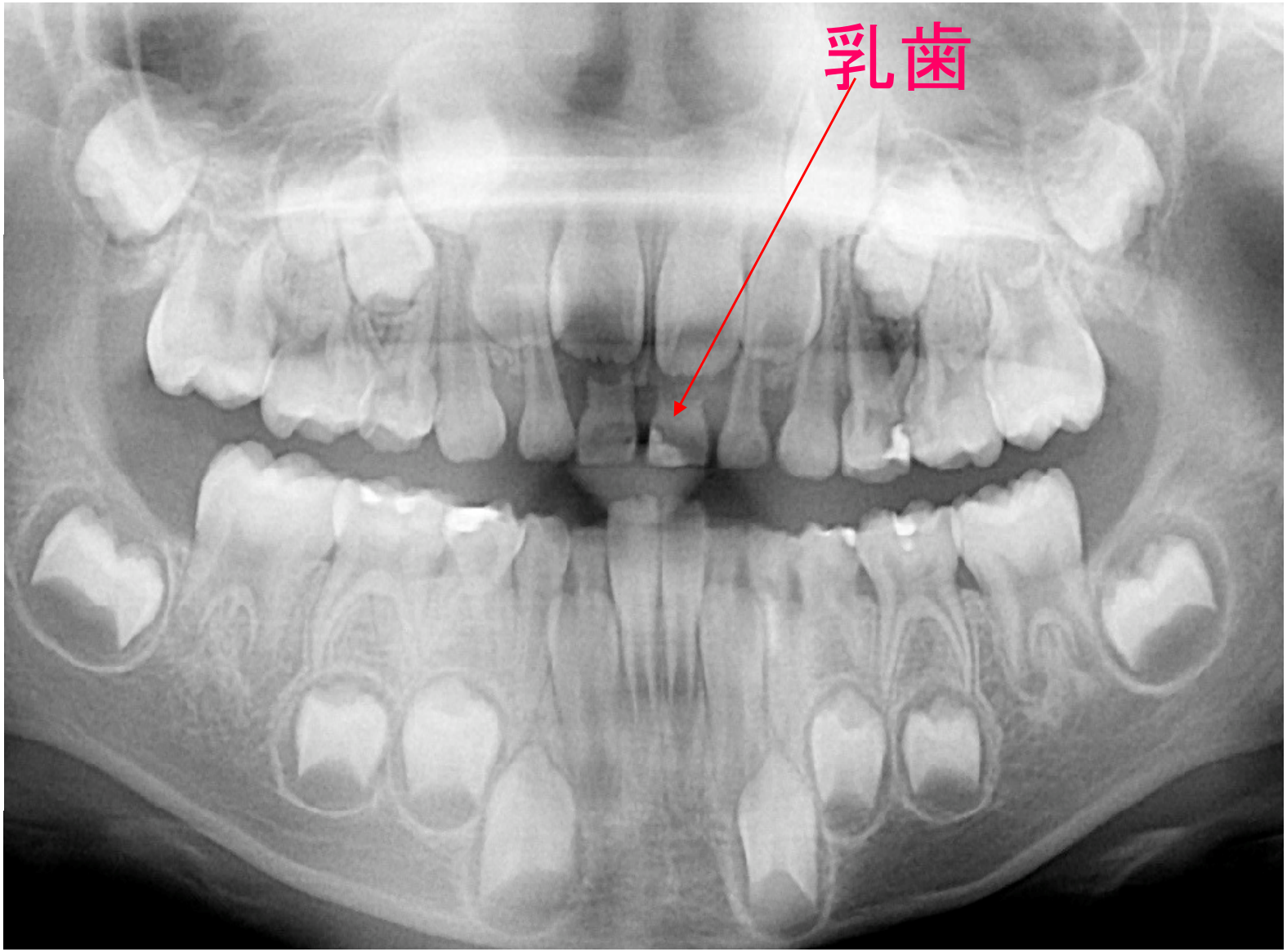
9M

24M

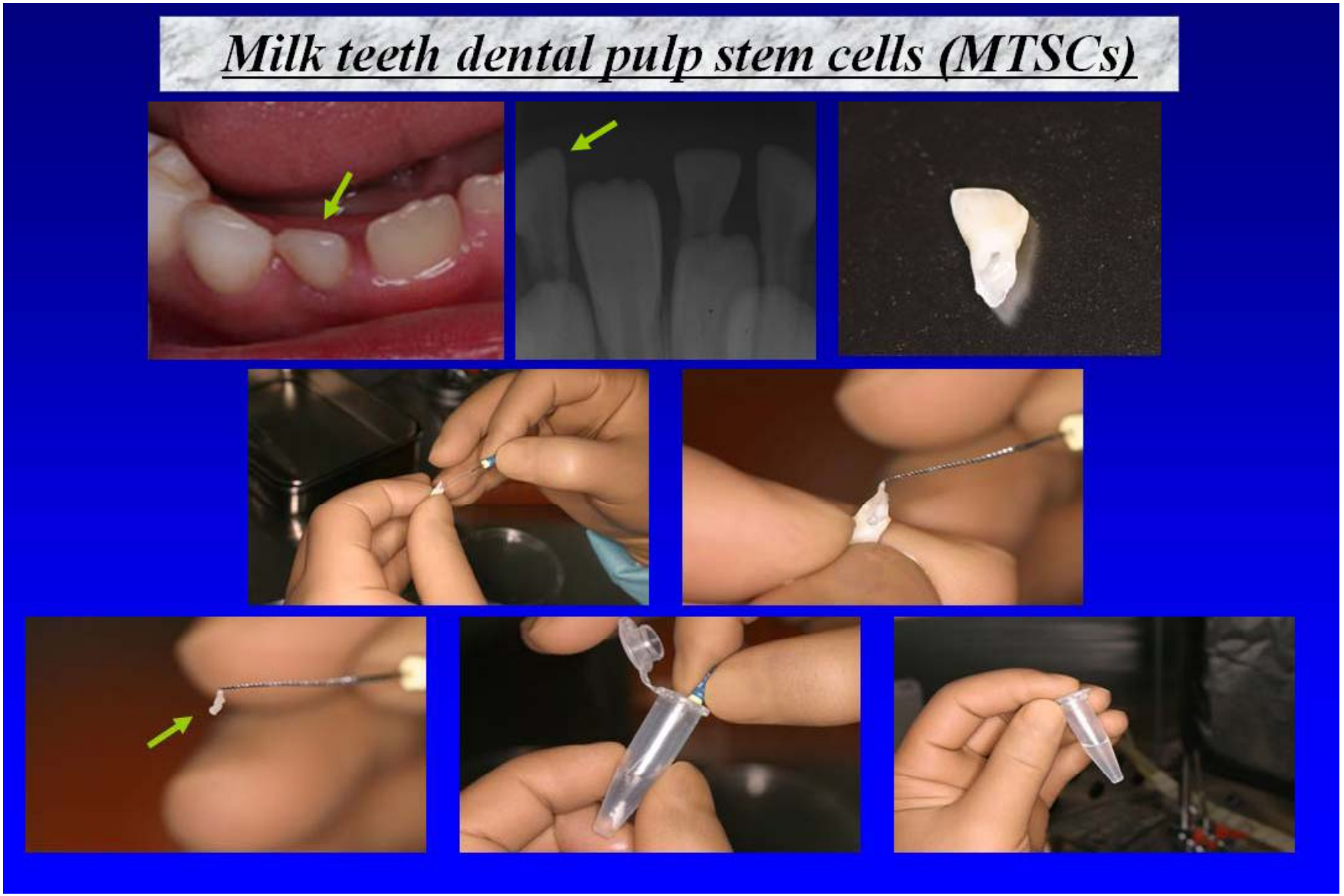
Dental Pulp Stem Cell

新しい幹細胞



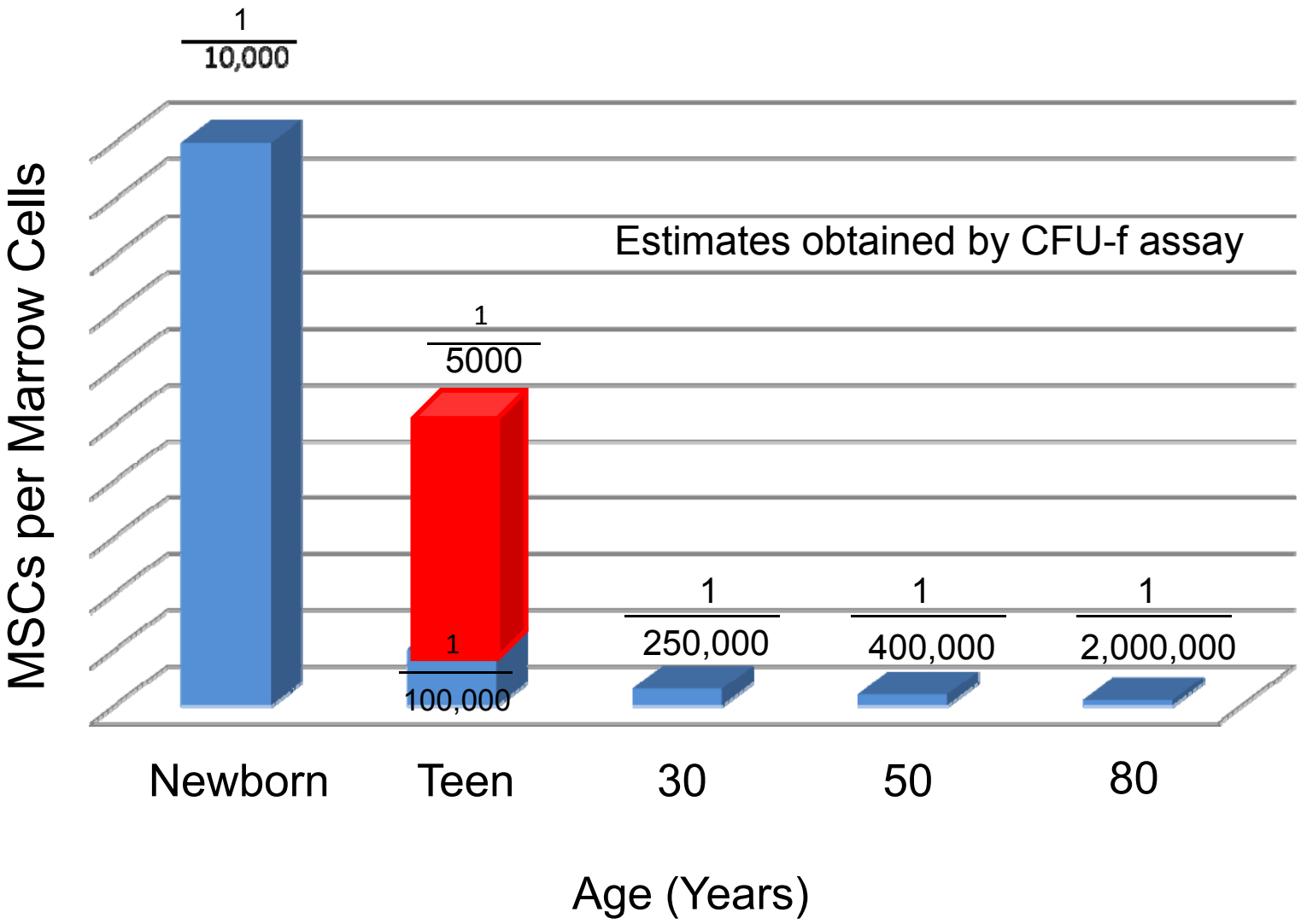

乳歯

歯髄組織の採取

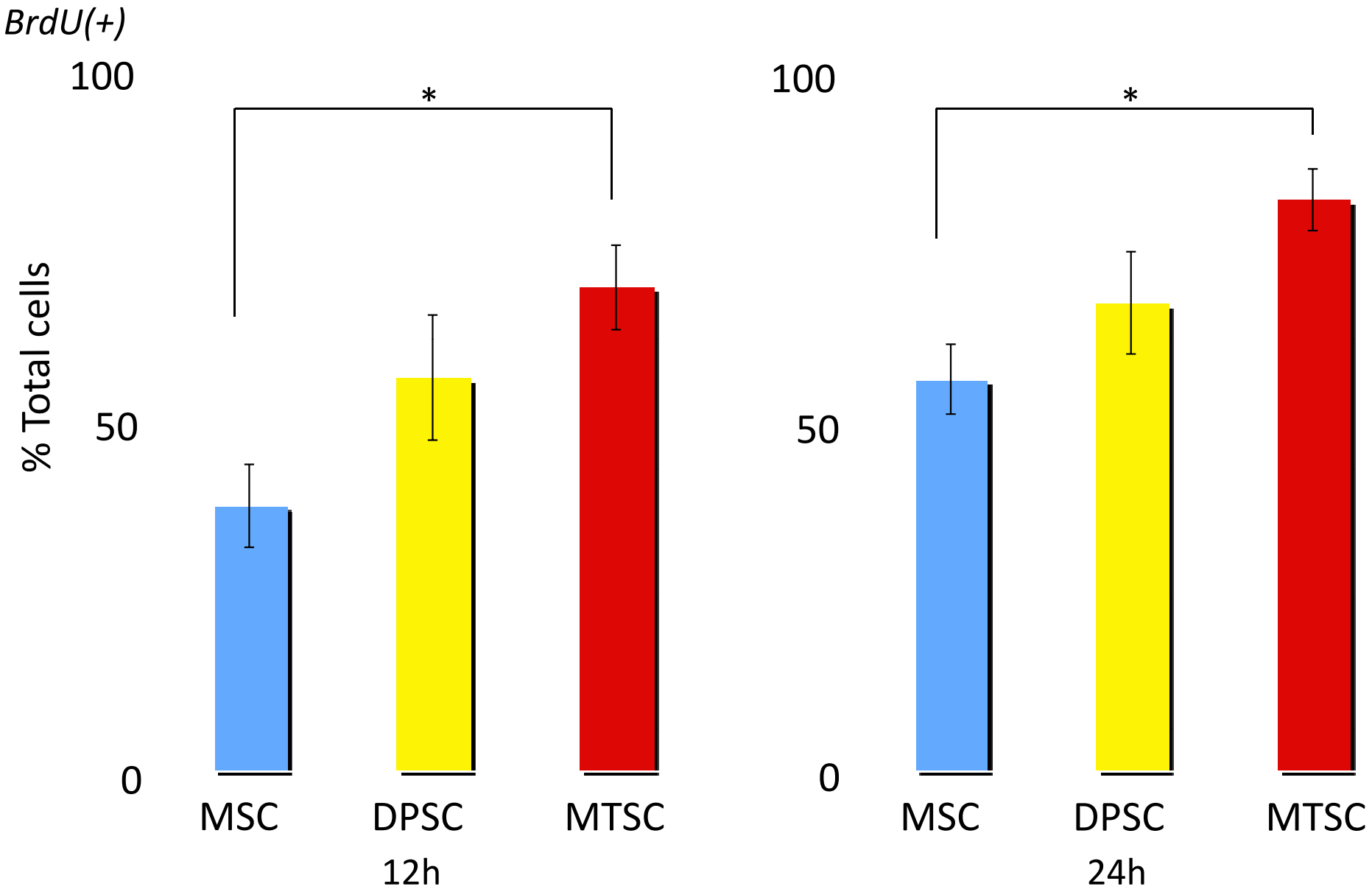


WHY DENTAL PULP TISSUE?

Comparison with Bone marrow

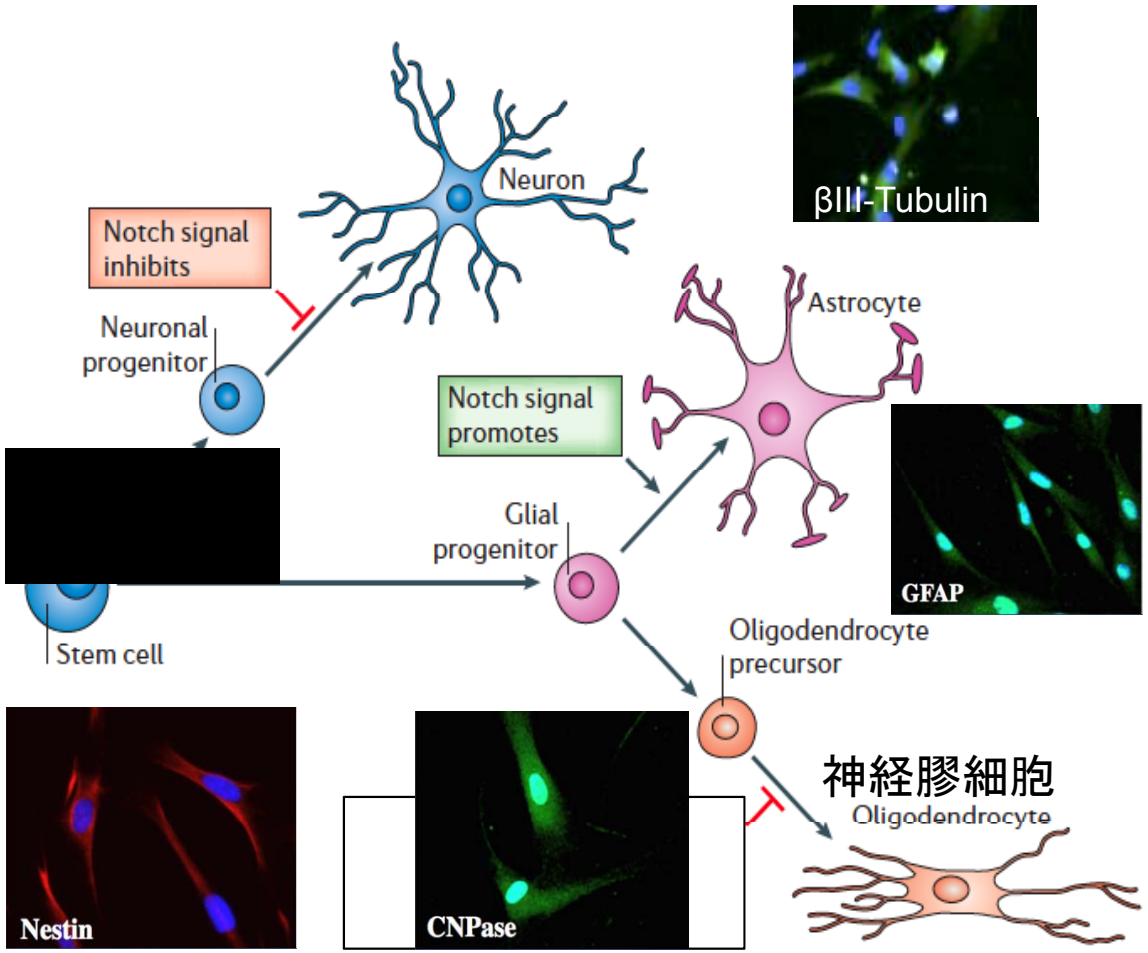


Growth Rate

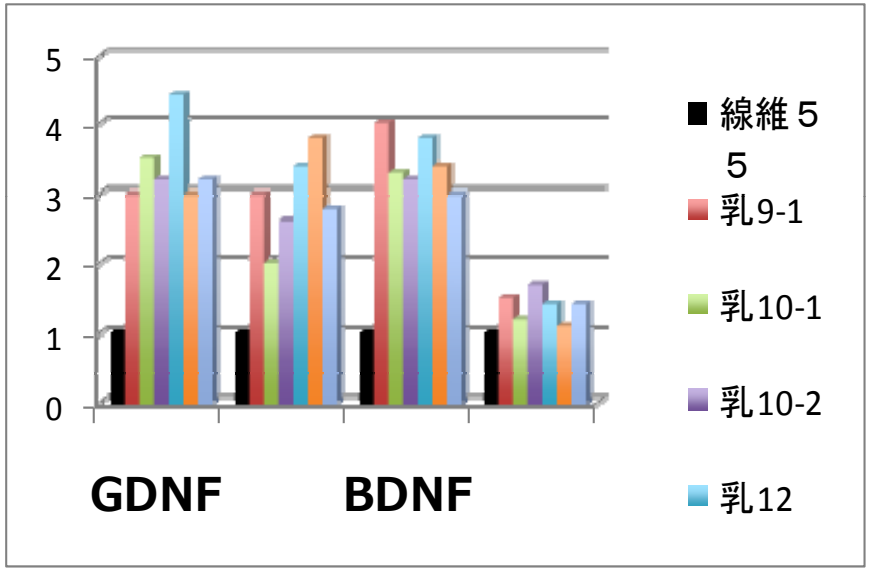

BrdU(+)
100
50
0
% Total cells
*
MSC
DPSC
MTSC
12h
100
50
0
*
MSC
DPSC
MTSC
24h

ヒト歯髄幹細胞の特徴

①神経系譜に特異的な分子マーカーを発現するユニークな細胞集団



②多数の神経栄養因子を産生する細胞集団

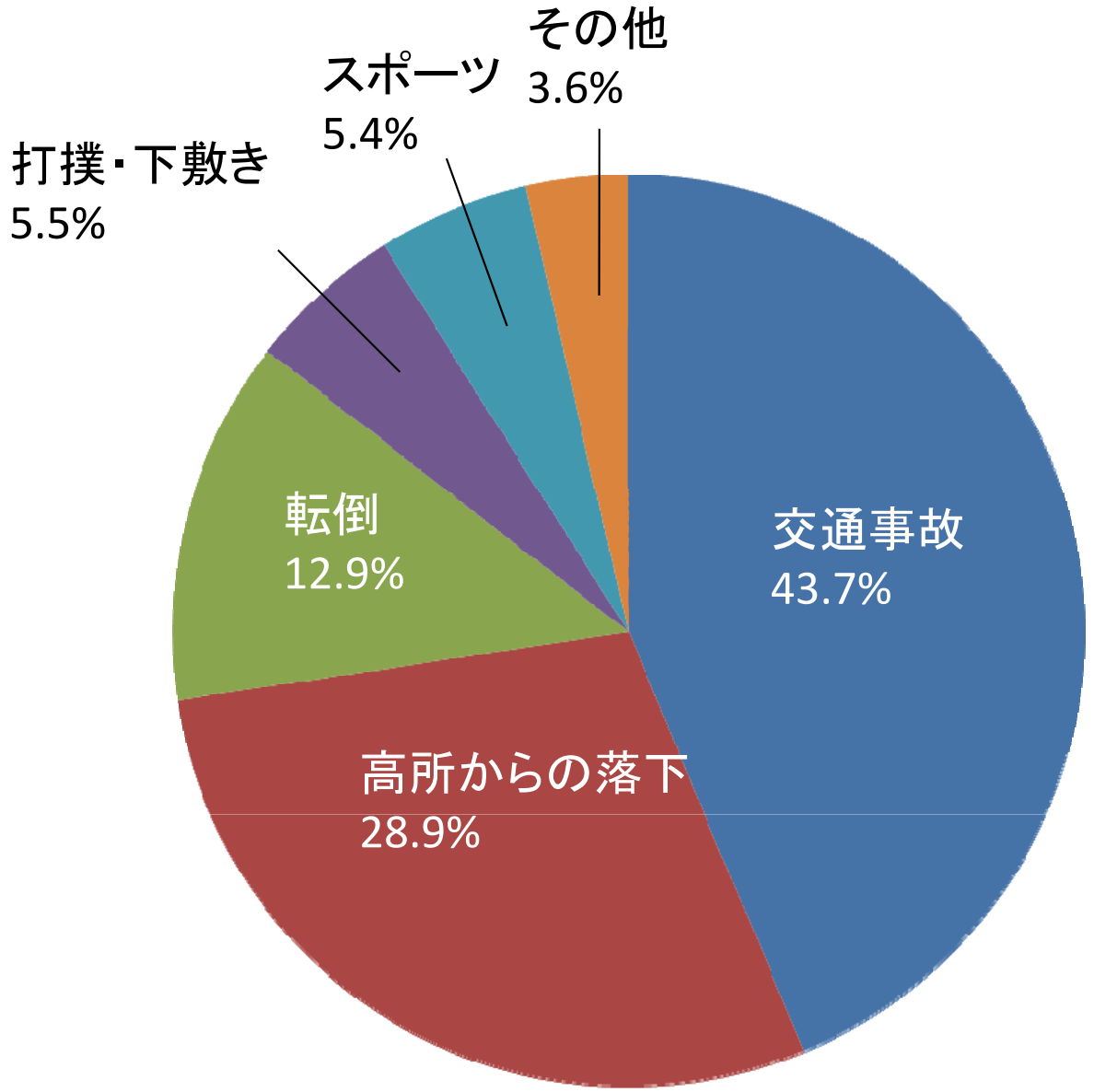


神経幹細胞に特異的な転写因子の発現

Sakai K. et al., submitted

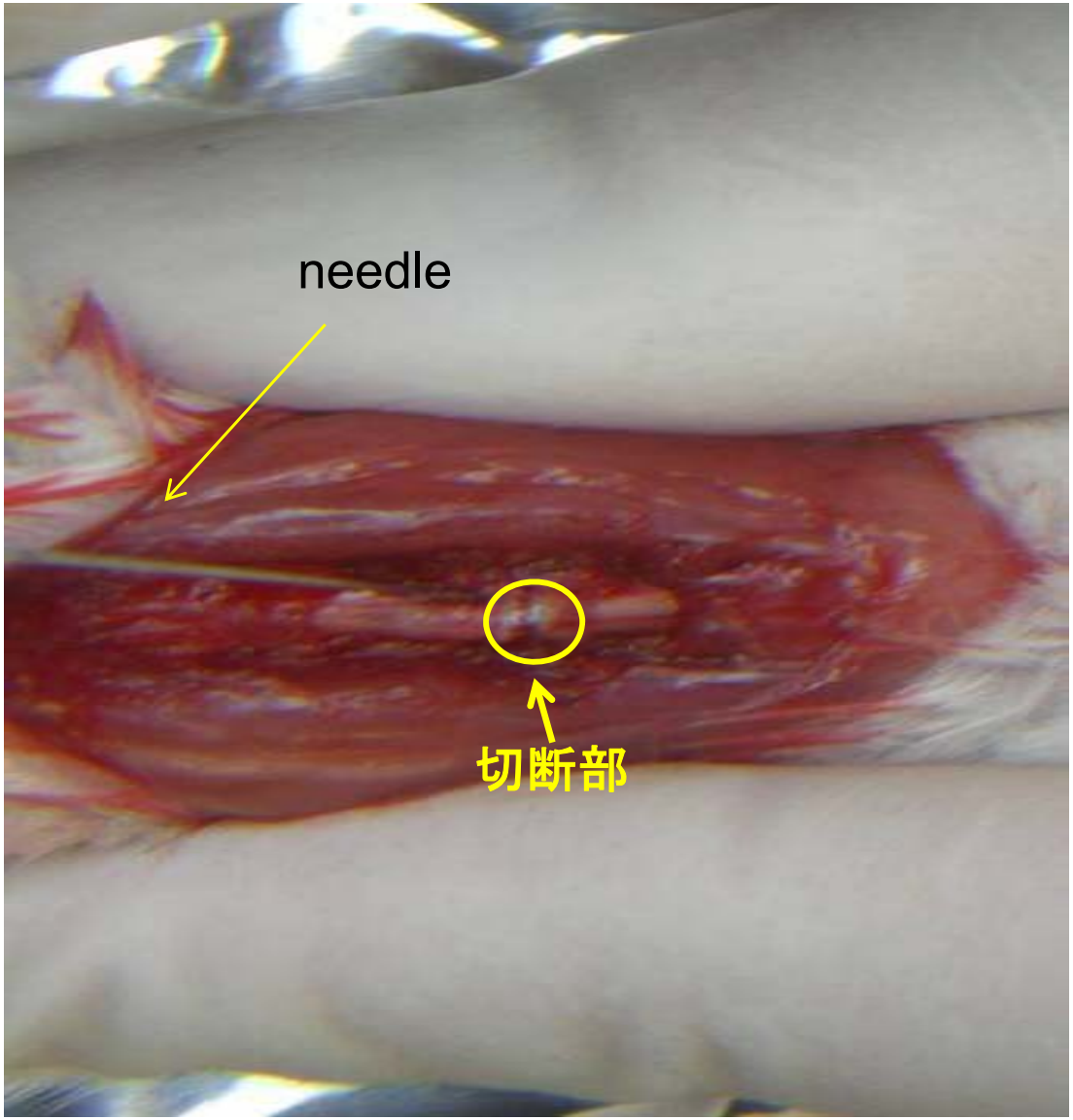
neurogenine 2, mash1 ・・・

受傷原因



・日本には10万人以上の脊損者がおり、毎年5000人以上があらたに脊髄損傷を負っている
・2005年の福知山線脱線事故による脊髄損傷者は20人以上にのぼる

ラットの脊髄切断モデル

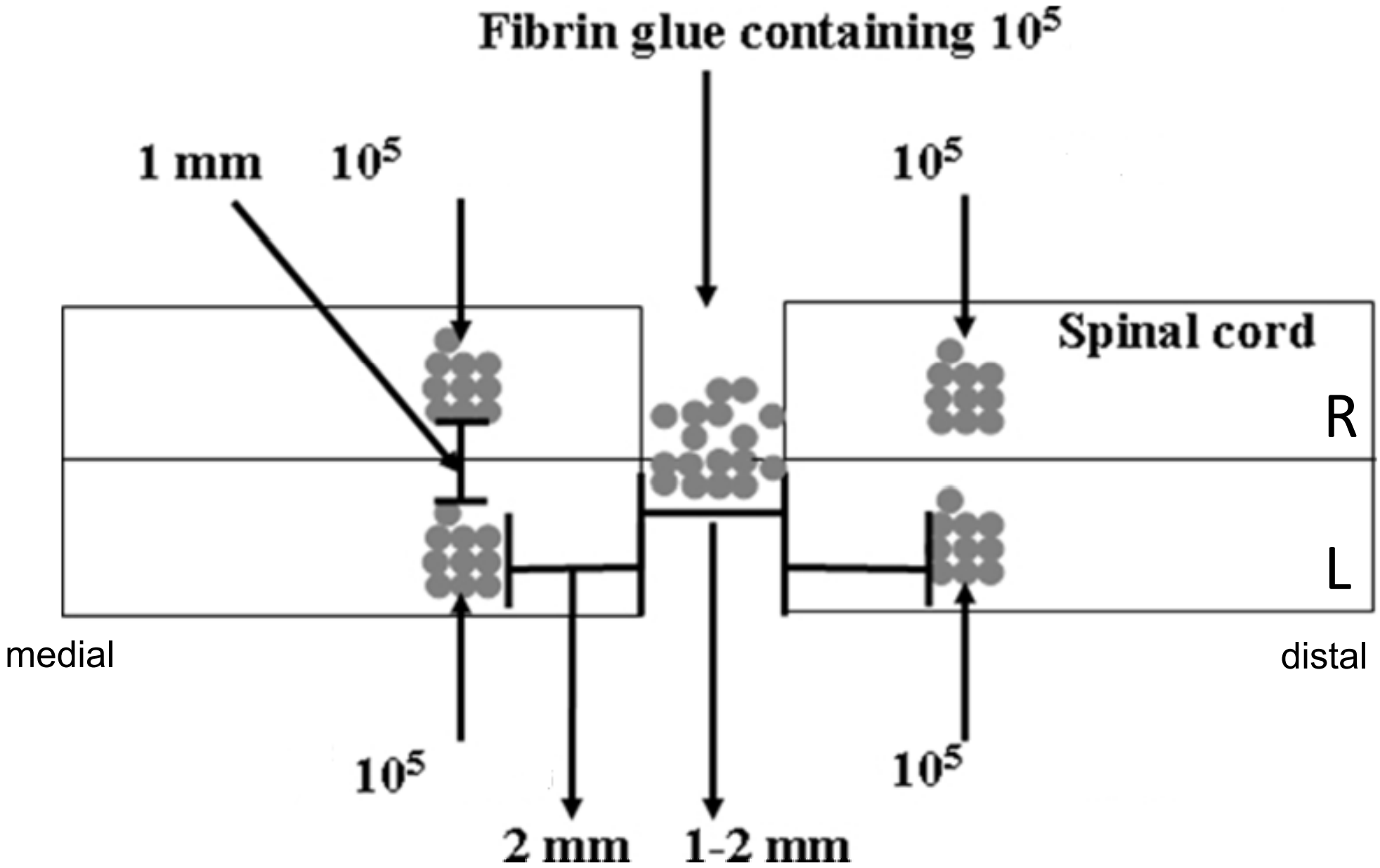


medial

distal

細胞の注入

脊髄損傷


Fibrin glue containing 10^5
1 mm
10^5
10^5
Spinal cord
R
L
medial
distal
10^5
10^5
2 mm
1-2 mm

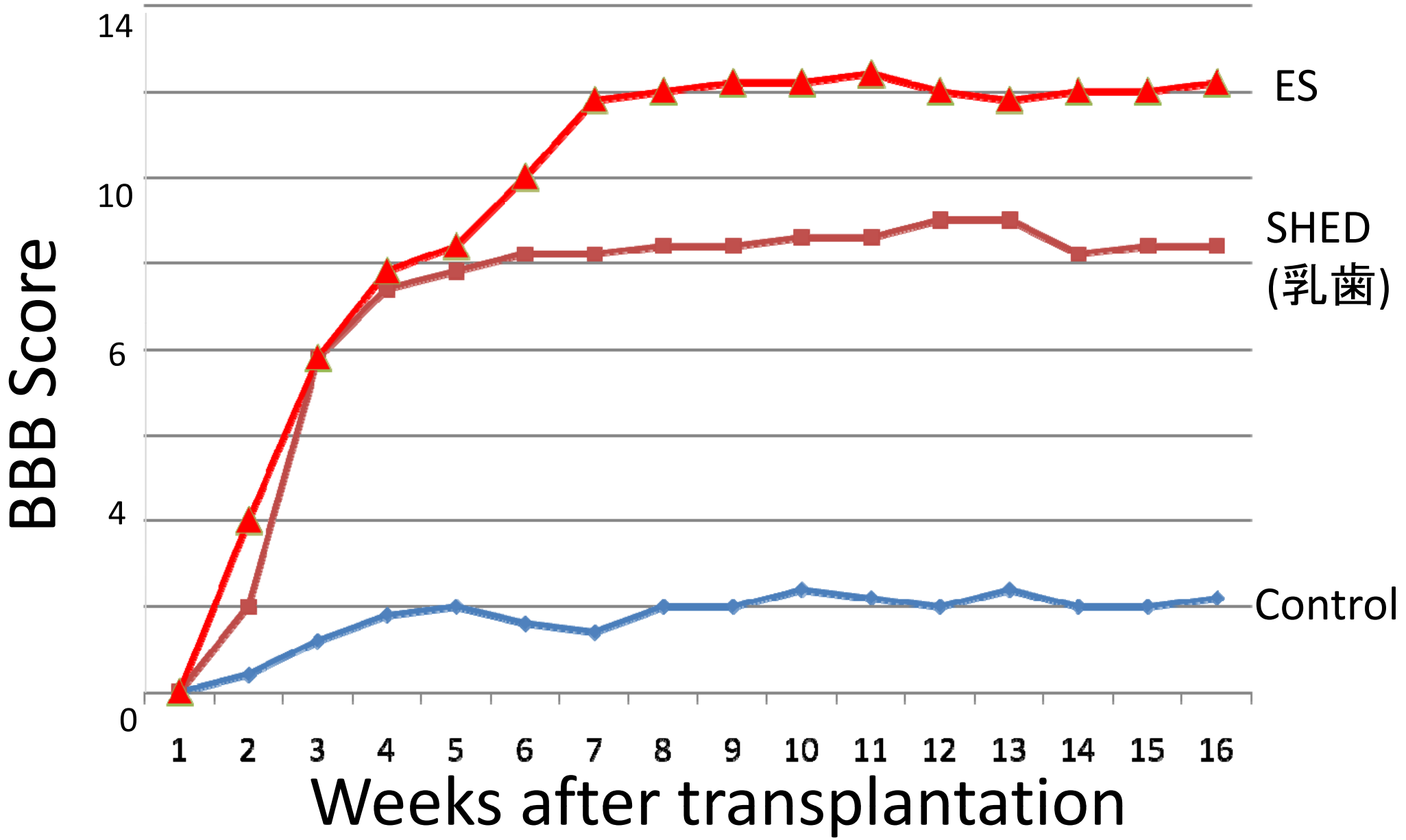
Hindlimb locomotor recovery (8 Weeks)

Control

Hindlimb locomotor recovery (8 Weeks)

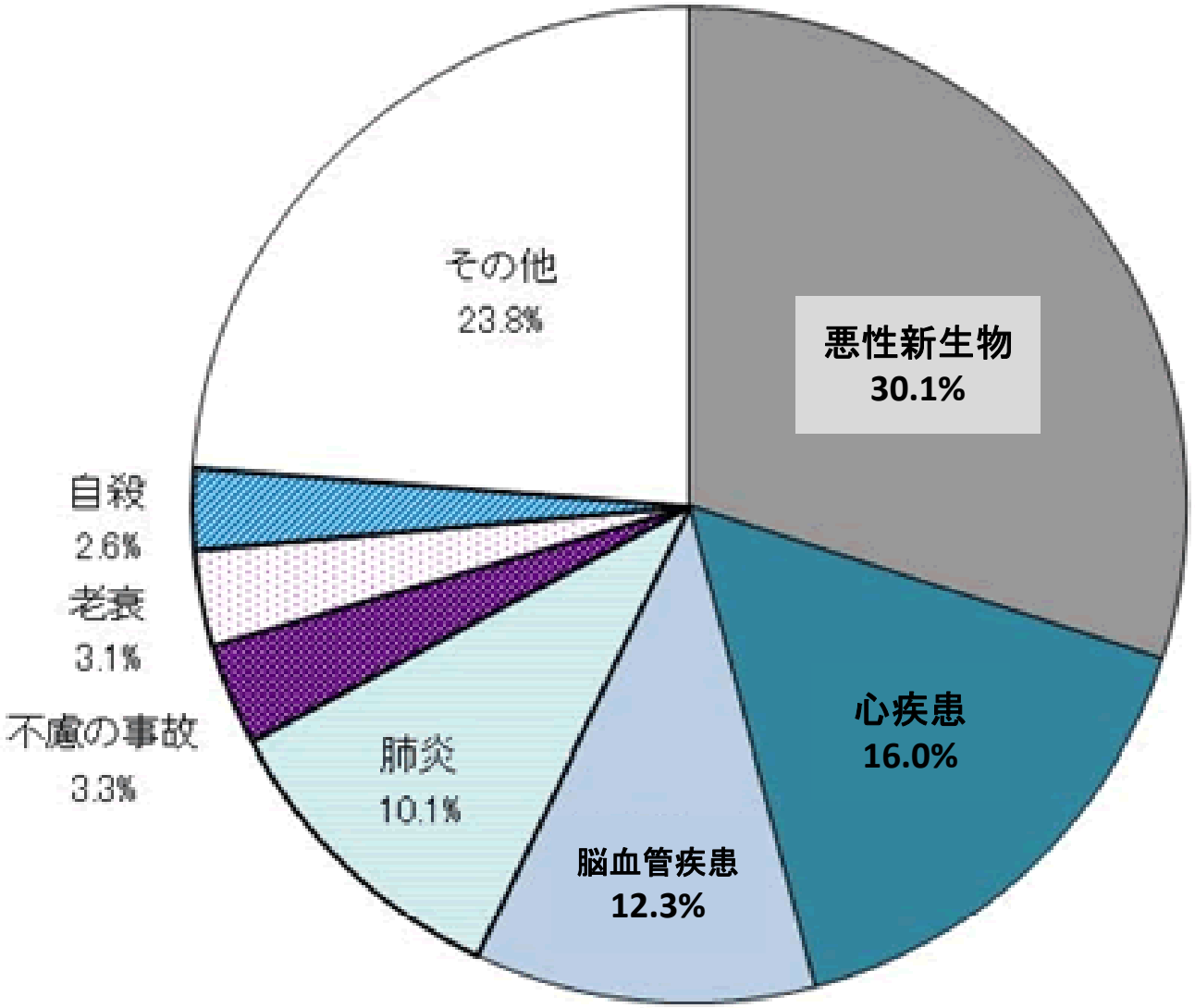
+SHED

下肢マヒの回復過程


BBB Score
14
10
6
4
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
Weeks after transplantation
ES
SHED
(乳歯)
Control

脳梗塞

主な死因別死亡数の割合



2008年厚生労働省調査

材料と方法

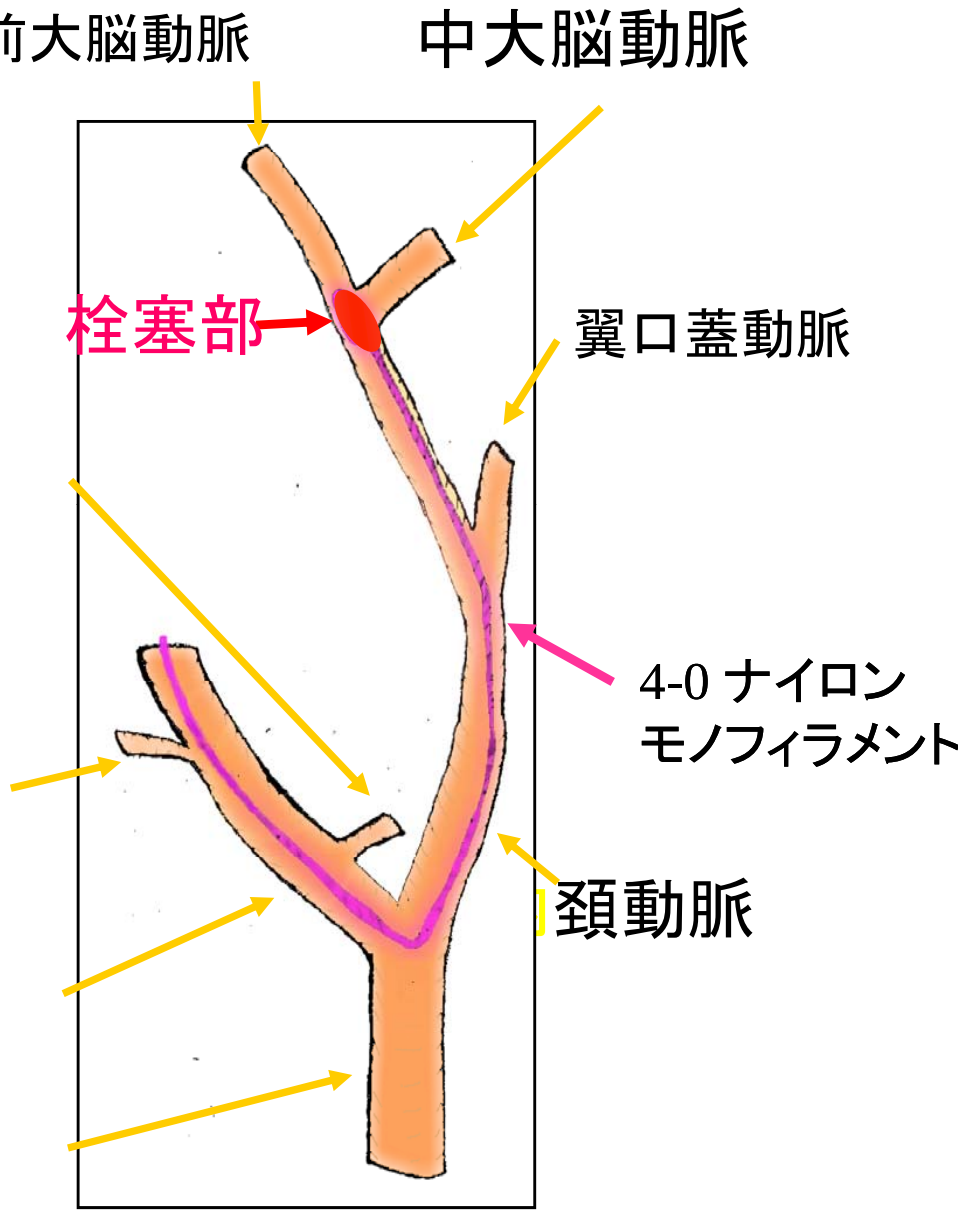
1. 脳梗塞モデルの作製

SDラット（♂）

中大脳動脈閉塞術（MCAO)

一過性閉鎖

（梗塞2時間後再開通）



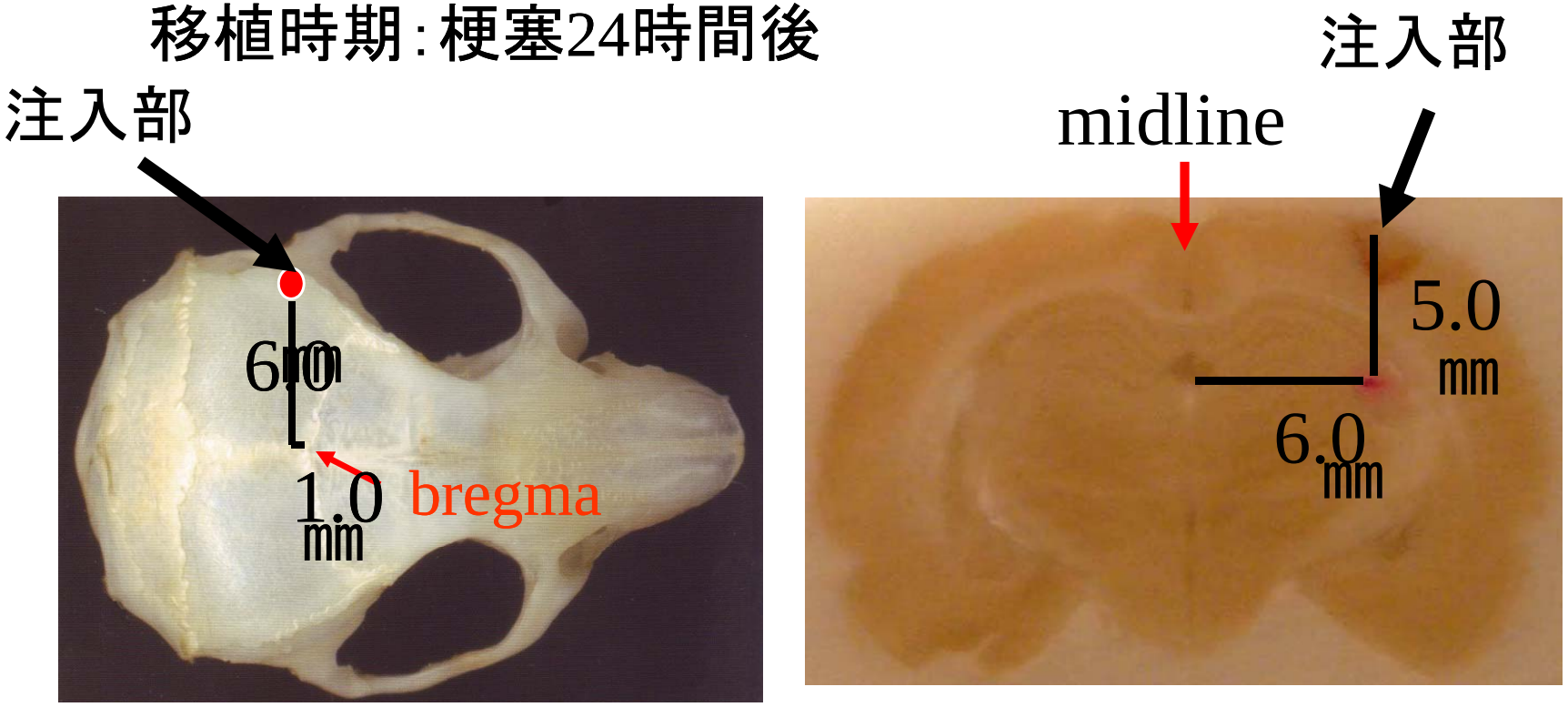
2. 細胞移植

ブタ歯髄CD31$^-$ SP細胞　5～7 代目

細胞数　1×10^6 cells

DiI染色にて移植細胞を蛍光ラベル

移植時期：梗塞24時間後



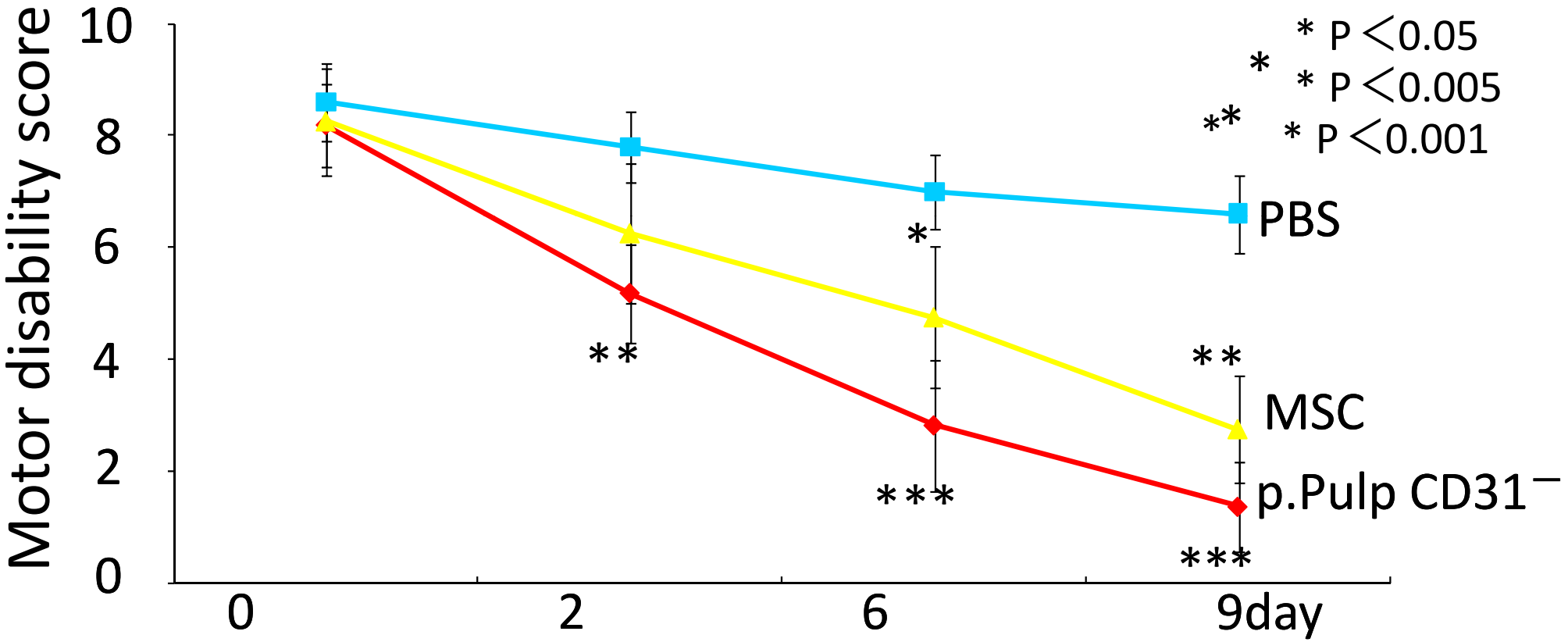
Control

PBS注入6日目

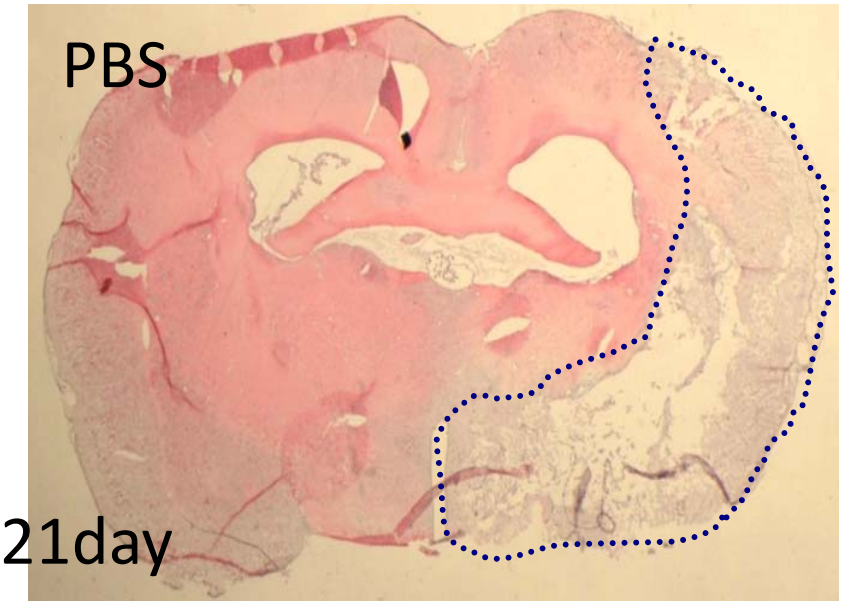
+DSPC

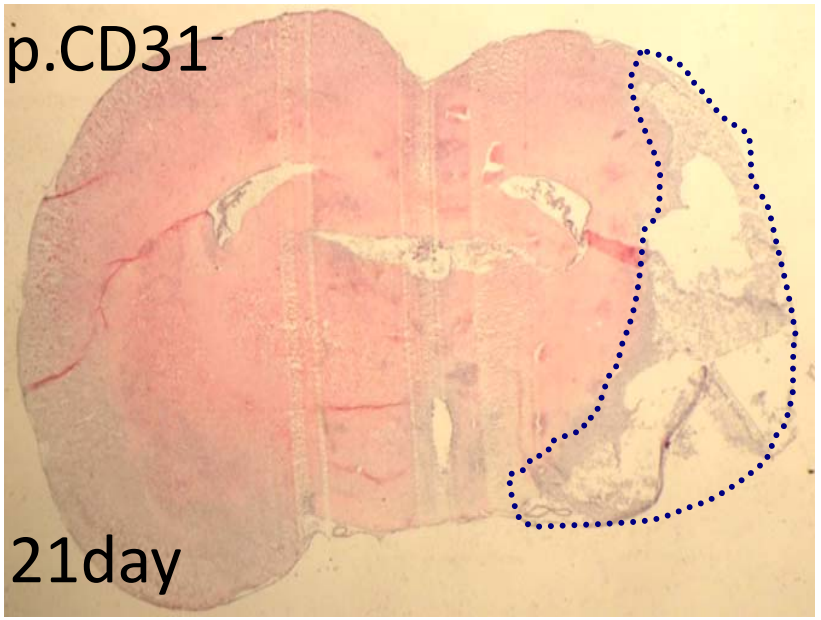
p.CD31-移植6日目

下肢マヒの回復


Motor disability score
10
8
6
4
2
0
0
2
6
9day
＊ P＜0.05
＊ P＜0.005
＊ P＜0.001
PBS
MSC
p.Pulp CD31⁻
＊
＊＊
＊＊＊

移植による梗塞体積の縮小





中枢神経再生のためのストラテジー