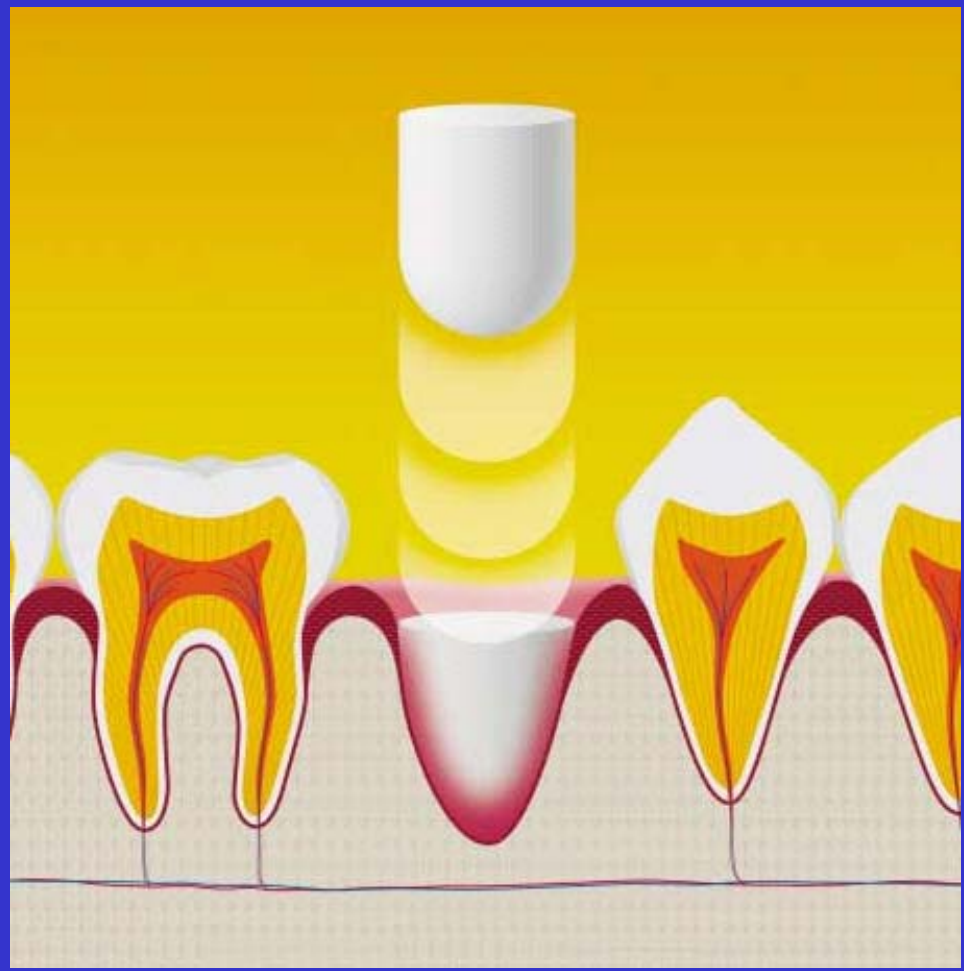
For in-house research

FOUNDATION™

Collagen-Based Bone Filling Augmentation Material
for Use in the Filling of Extraction Sockets



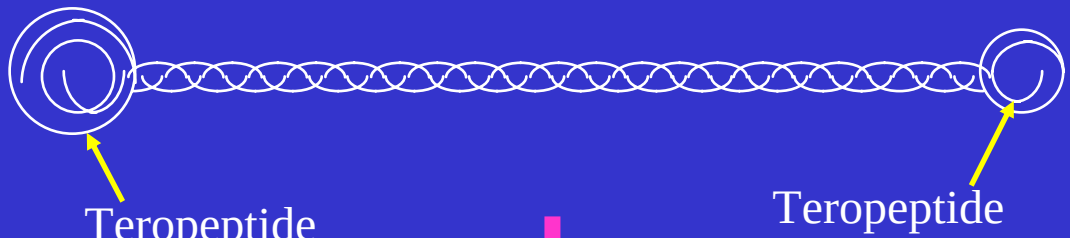
Feb. 2006

TERUMO®

Overview

* FOUNDATION is made of atelo-collagen to minimize antigenicity.
* The atelo-collagen has been cross-linked by heat treatment in order to achieve biocompatibility.
* FOUNDATION is processed in a sponge block and is then formed into a bullet shape for easy placement into the extraction socket.
* FOUNDATION consists of Fibrillar and Heat-denatured atelo-collagen. Fibrillar atelo-collagen provides the scaffolding for surrounding cells and Heat-denatured atelo-collagen stimulates infiltration of the cells into the product due to an inherent property called “chemotaxis”. This causes new bone growth cells to be drawn into the Fibrillar atelo-collagen framework at a rapid pace.
* Contents are sterile and non-pyrogenic.

Molecular Structure of Collagen



Teropeptide

(antigen in different species)

Teropeptide

Tropocollagen

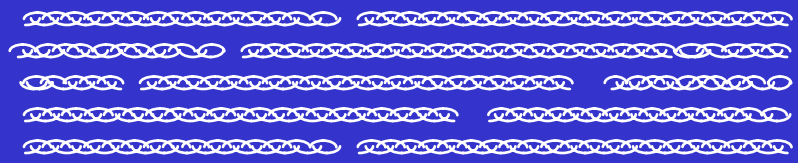
natural collagen

Protease (pepsin) treatment
to minimize antigenicity (pH 3)

Atelo-collagen

Neutralizing

Heating over 37℃/100 ° F



Fibrillar atelo-collagen

Scaffold for surrounding cells

Heat-denatured atelo-collagen

Stimulates infiltration of cells into the scaffold

FOUNDATION™

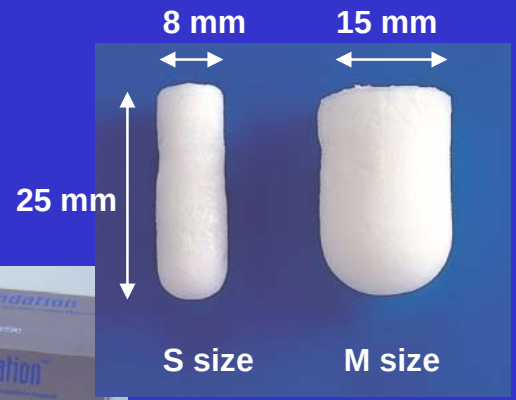
Collagen-Based Bone Filling Augmentation Material

90% Fibrillar atelo-collagen

10% Heat-denatured atelo-collagen

Cross-linked by heat

Bullet type



- Sterile and Non-pyrogenic
- Biocompatible and low antigenicity

Hypersensitivity and Safety of Collagen from Bovine skin

- **Allergic reaction**

Since FOUNDATION was launched October 1998 until March 2005, approximately 450,000 units of FOUNDATION have been sold in Japan, and only three cases of “rash” have been reported from users. Allergic reaction and hypersensitivity protocols are described in “Warnings and Precautions” in the IFU.

- **BSE (Bovine Spongiform Encephalopathy), or Mad Cow Disease**

All the bovines used for FOUNDATION are younger than 6 months old.

Only skin is extracted from the bovine body.

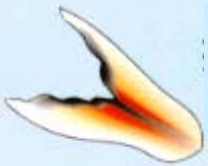
The EMEA (European Medical Examination Agency) classifies each organ into 4 risk-level of BSE infection, “High-risk”, “Middle-risk”, “Low-risk”, and “No risk”. Bovine Skin is defined as “No risk”.

The FDA also states that hide-derived bovine products present no risk for BSE.

Foundation undergoes three sterility evaluations during processing and a final dry-heat sterilization to a SAL (Sterility Assurance Level) of 10(-6) prior to packaging. This is the same SAL as sterile surgical gloves.

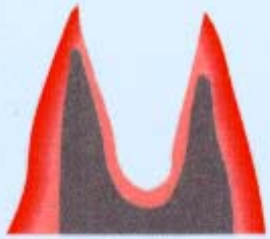
1

Tooth Extraction



2

Extraction socket is created and bone is exposed.



3

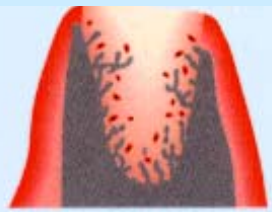
Insertion of FOUNDATION

4

The socket is filled with FOUNDATION and it also covers the extraction surface.

5

Surrounding cells and capillaries infiltrate into FOUNDATION. Peripheral gingiva extends onto it.



6

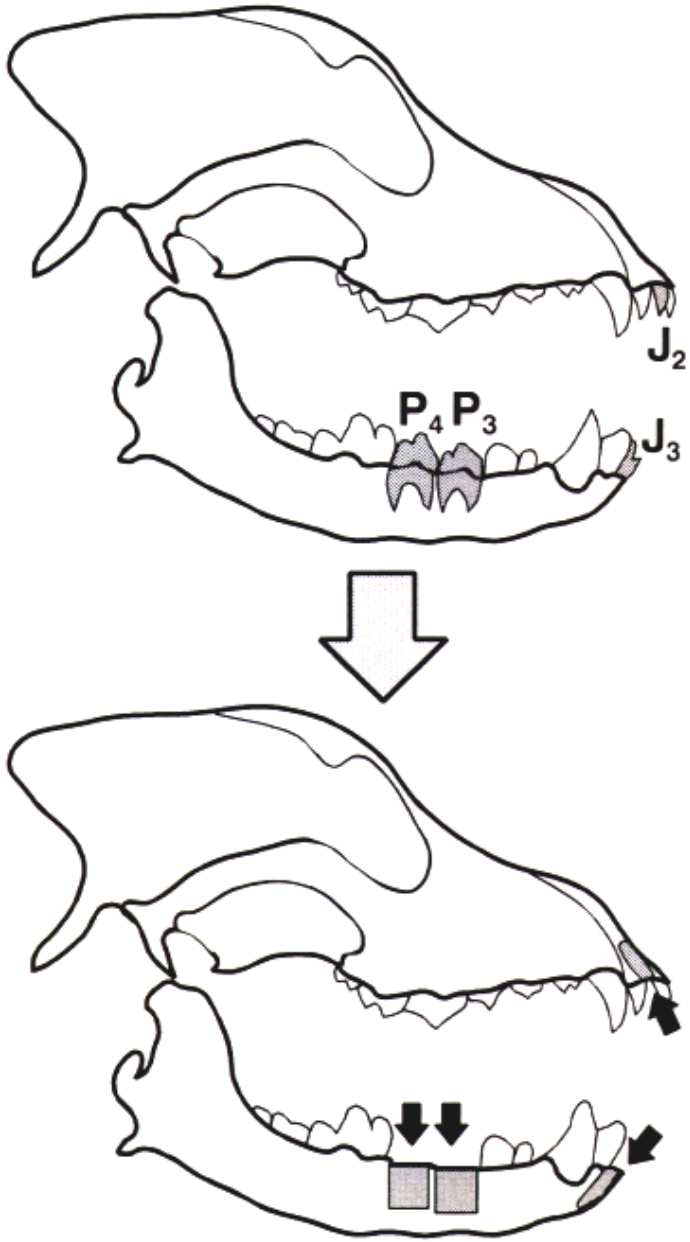
The extraction socket closes and is filled with augmented bone.

In vivo studies using beagles

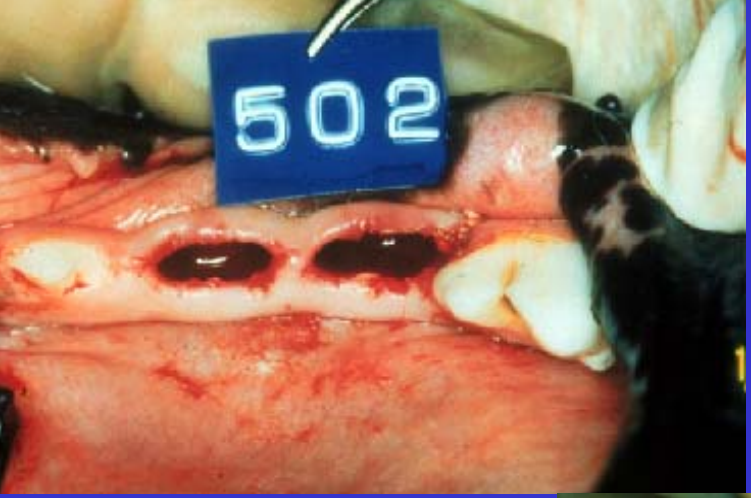
For in-house research

Premolar teeth were extracted.

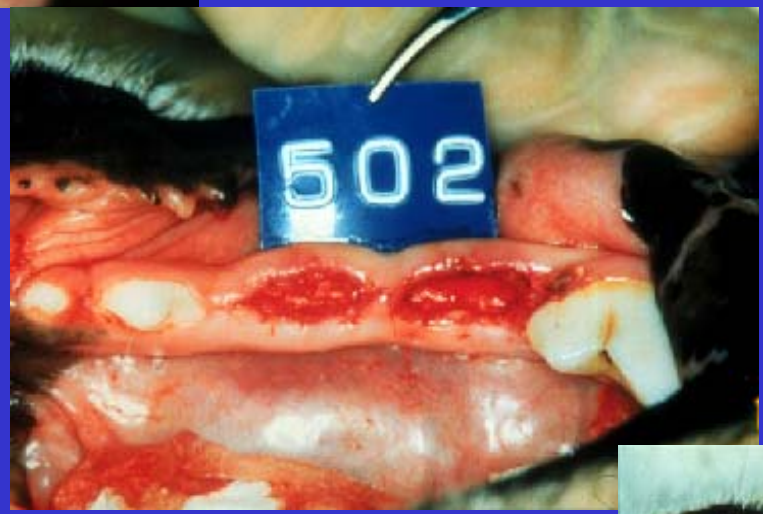
The sockets were prepared to a uniform size.



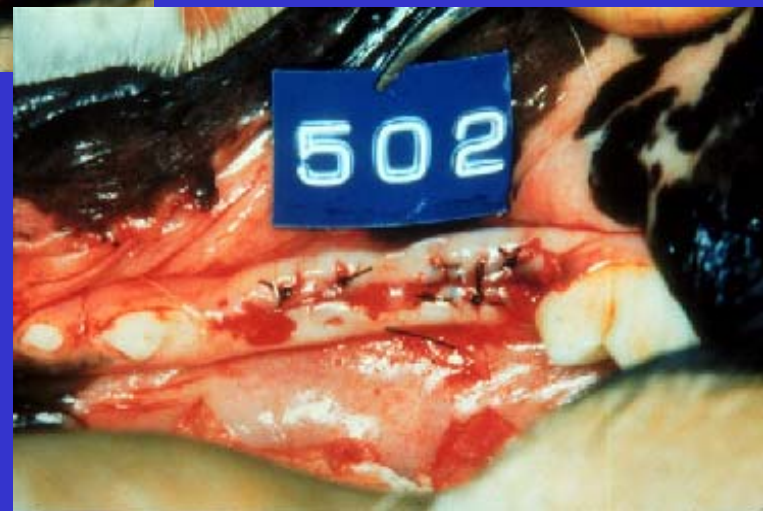
- Control
- FOUNDATION
- Helistat (Collagen hemostat)



An extraction socket was created



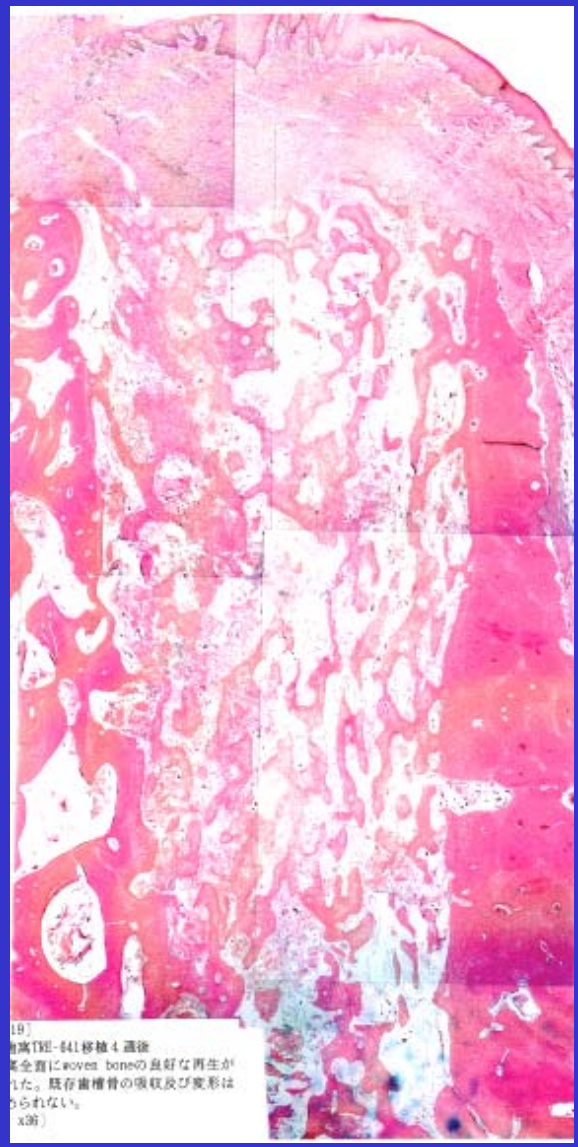
FOUNDATION was placed in the socket



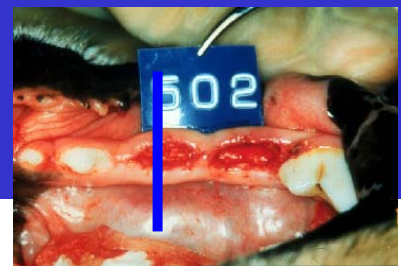
Sutures were placed

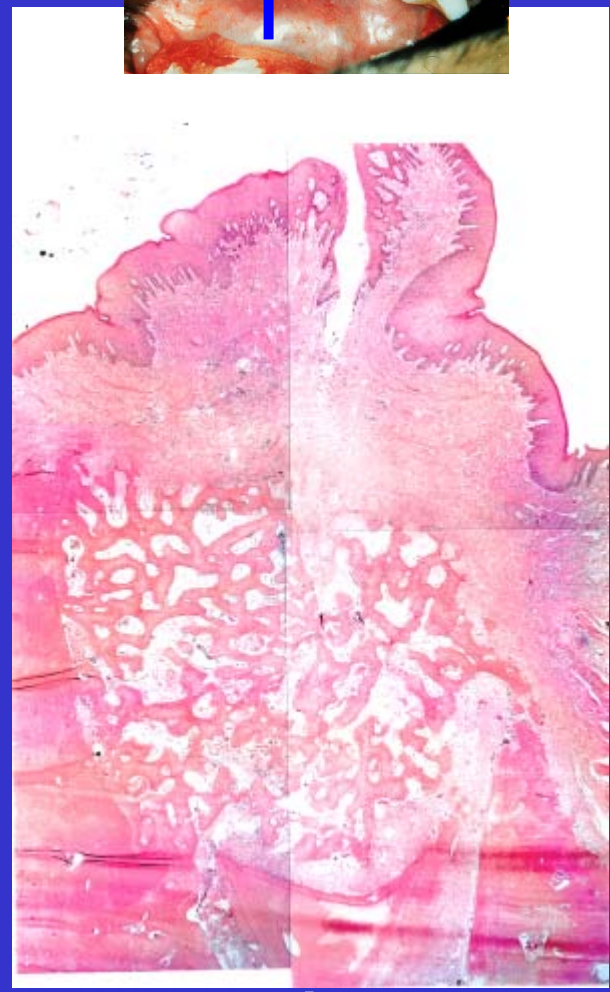
Histological sections stained with haematoxylin and eosin (4 weeks later)

Control



FOUNDATION

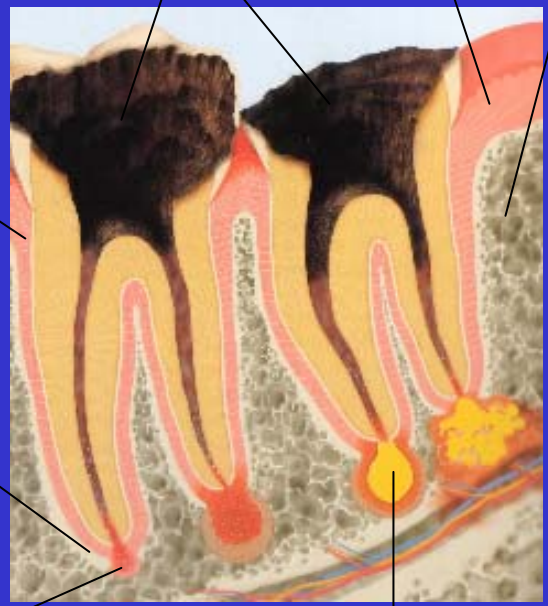




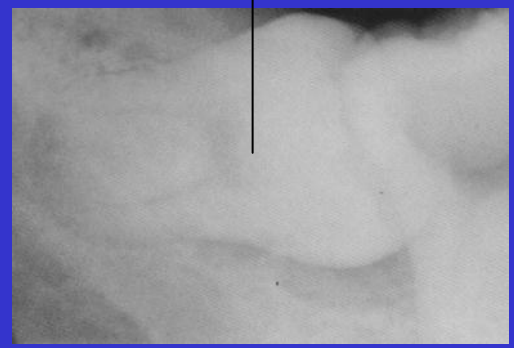
Helistat

Some Reasons for Tooth Extraction

* Carious exposure of pulp with accompanying abscess
* Advanced periodontal disease with bone loss
* Fracture due to trauma , Impacted wisdom teeth



horizontally impacted third molar
（wisdom tooth）

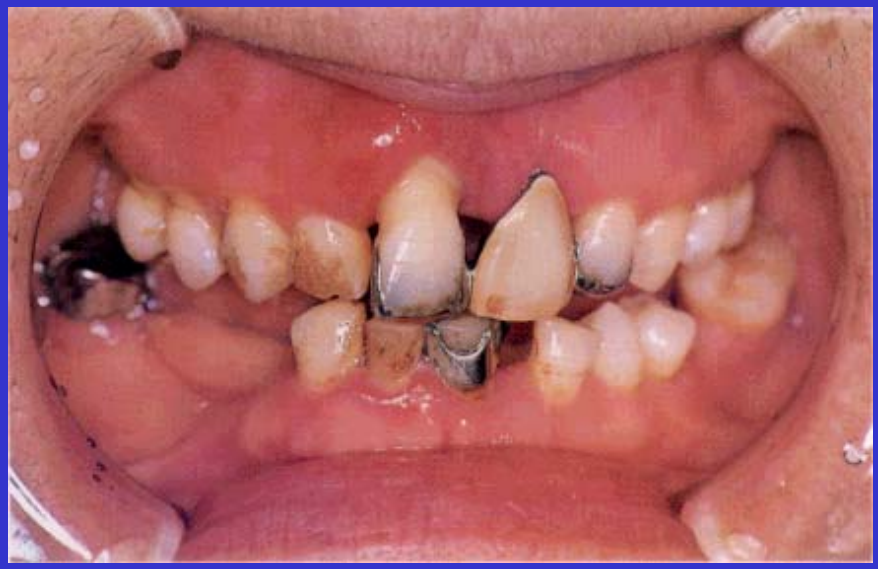


X-ray

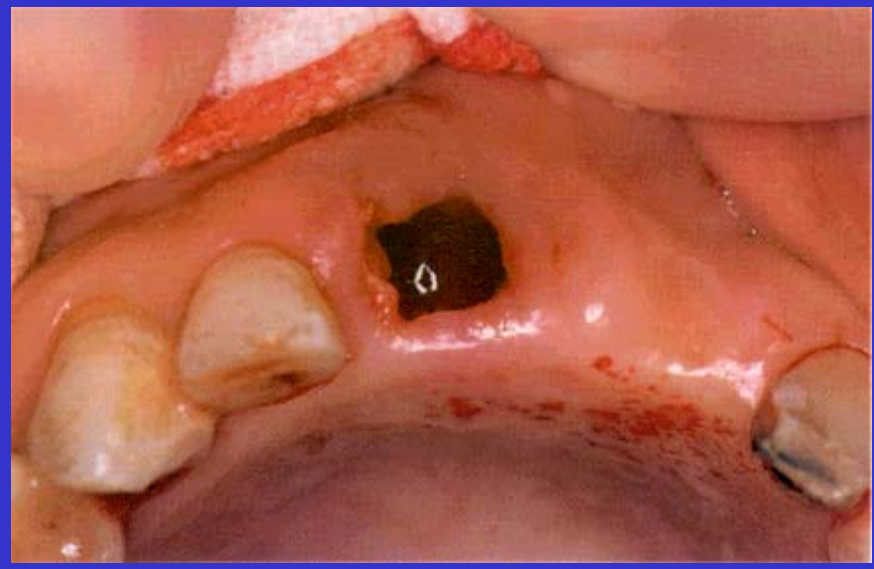
Indications for Use

The following cases demonstrate the use of Foundation in strict adherence to the FDA-approved "Indications for Use" guidelines.

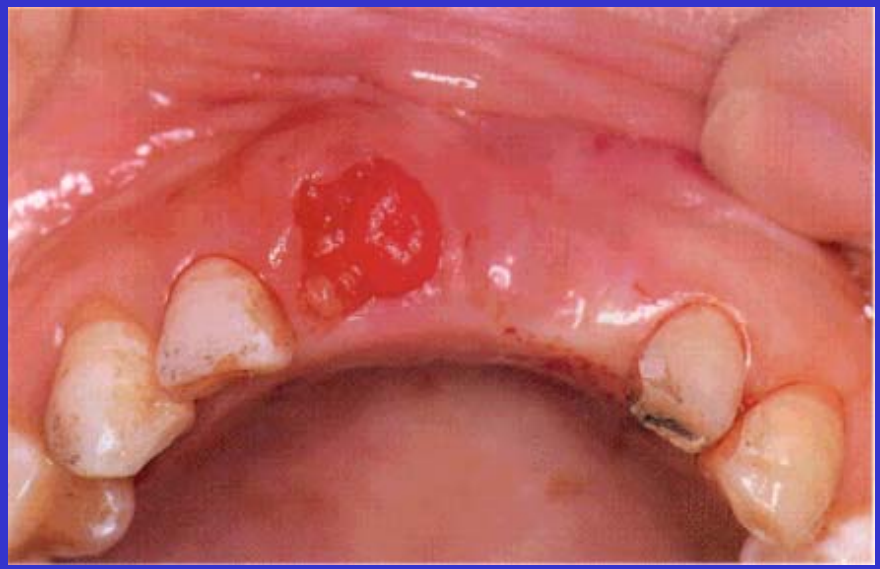
Case 1: Extraction due to advanced periodontal disease in a healthy 65 year old female



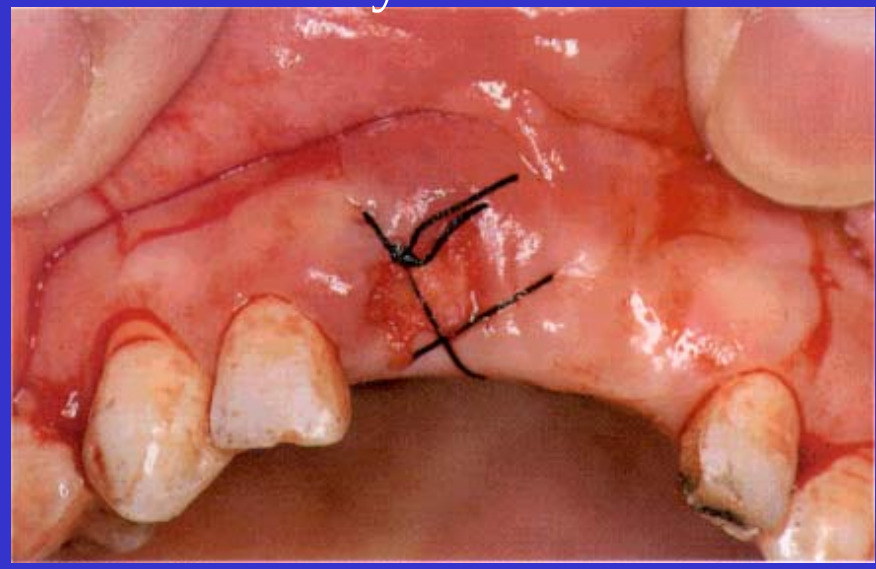
Before extraction



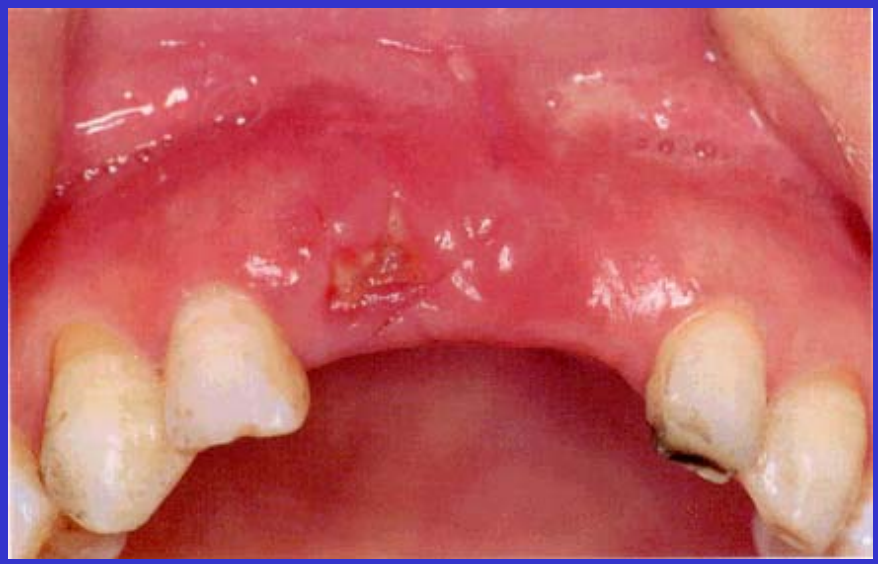
Immediately after extraction



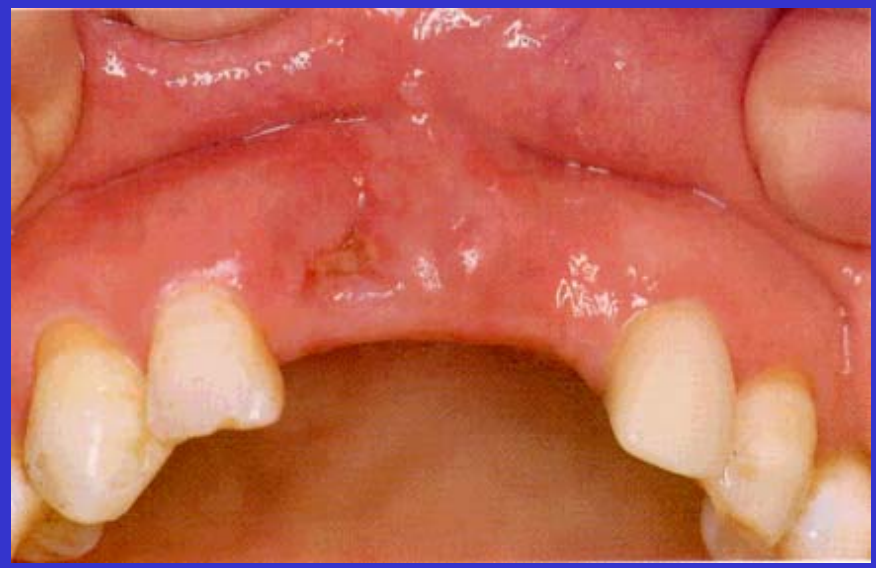
Application of FOUNDATION



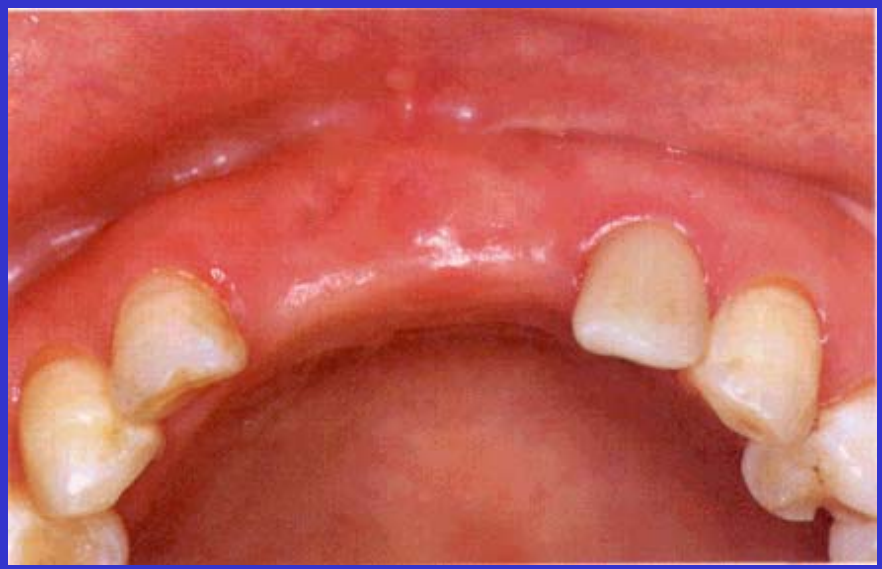
Sutured



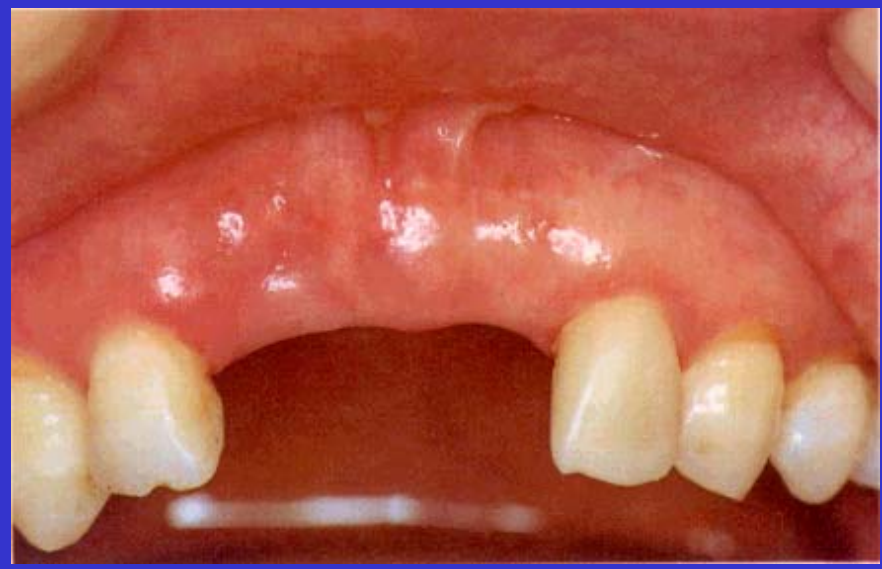
1 week later



2 weeks later

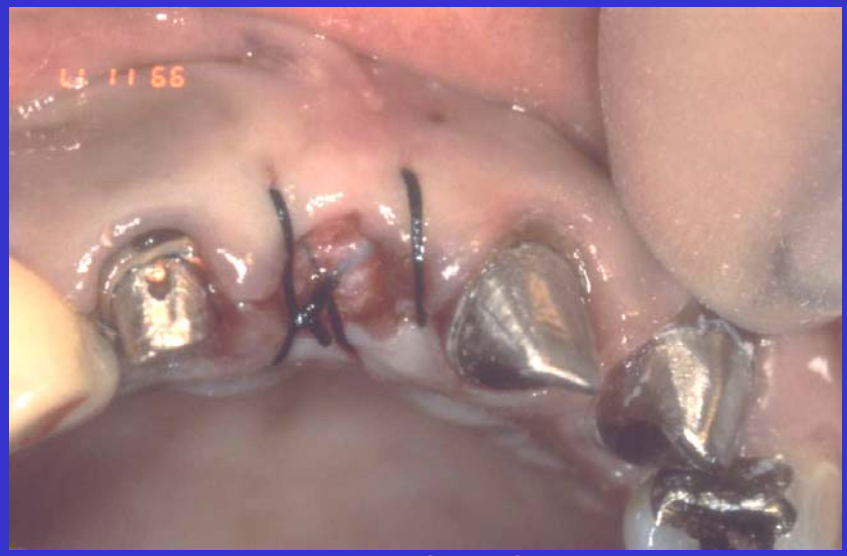


18 weeks later (from low angle)

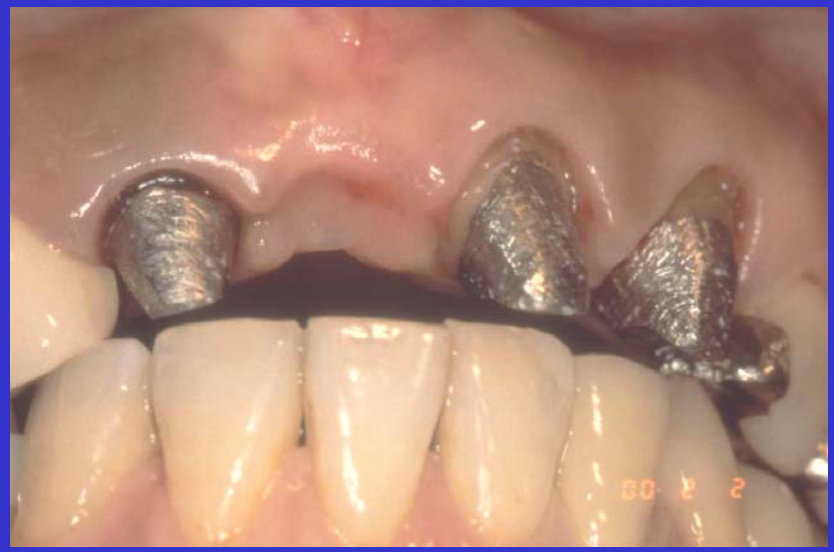


18 weeks later (front)

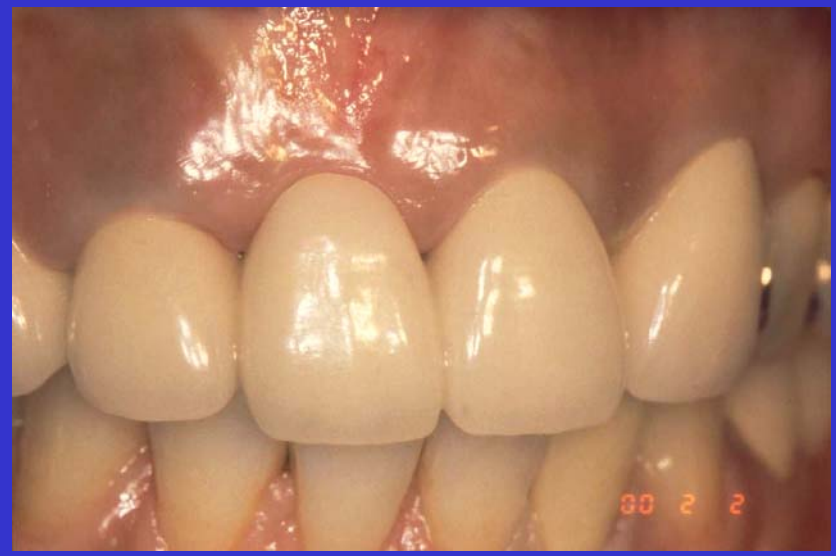
Case 2: Extraction due to fracture in a healthy 41 year old female



Immediately after filling with FOUNDATION and suturing

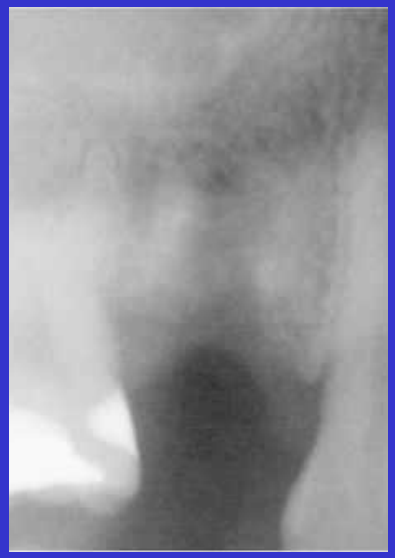


2.5 months after the filling

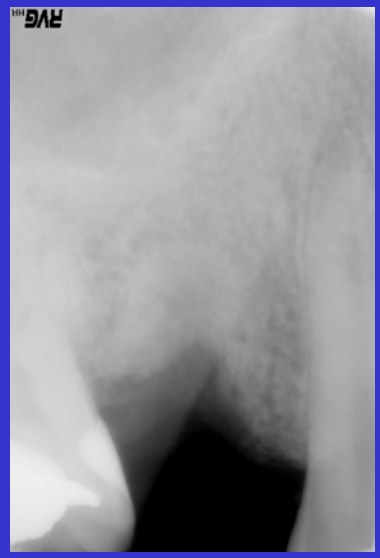


After prosthesis

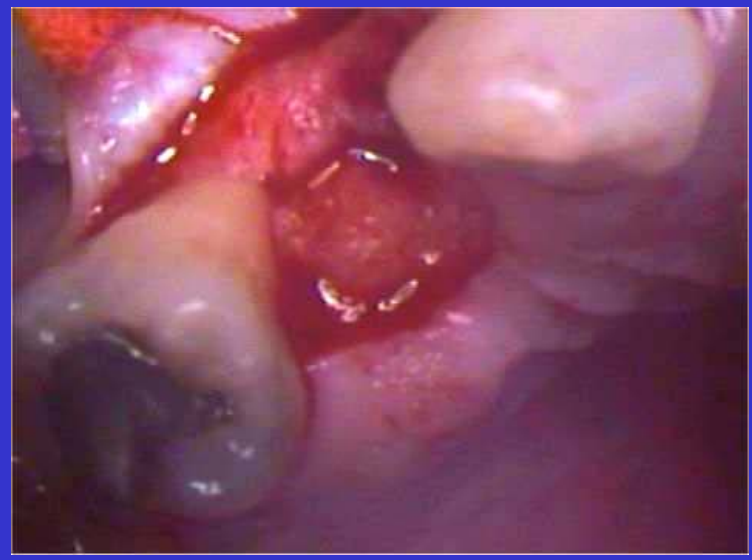
Case 3: Extraction due to fracture in a healthy 31 year old male



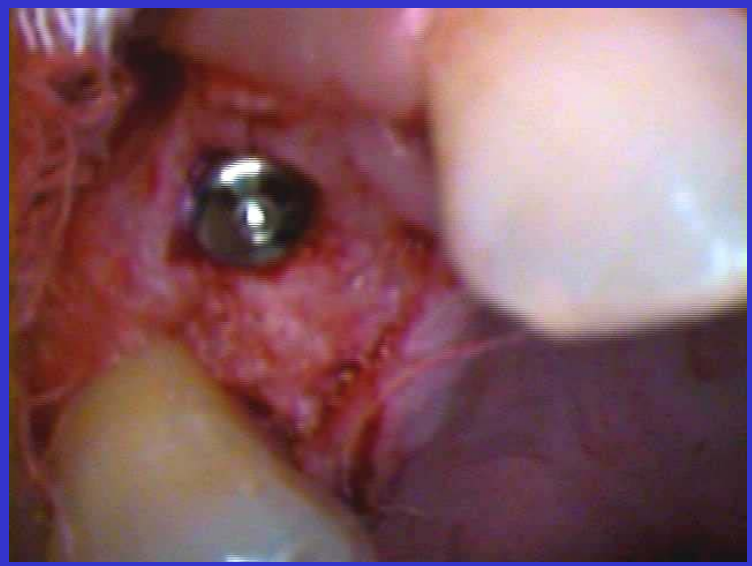
Immediately after filling with FOUNDATION



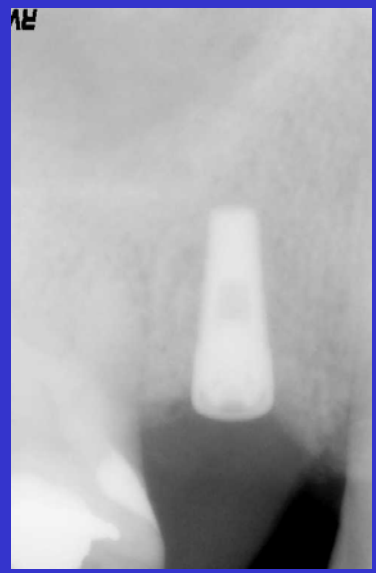
6 weeks after the filling



8 weeks after the filling

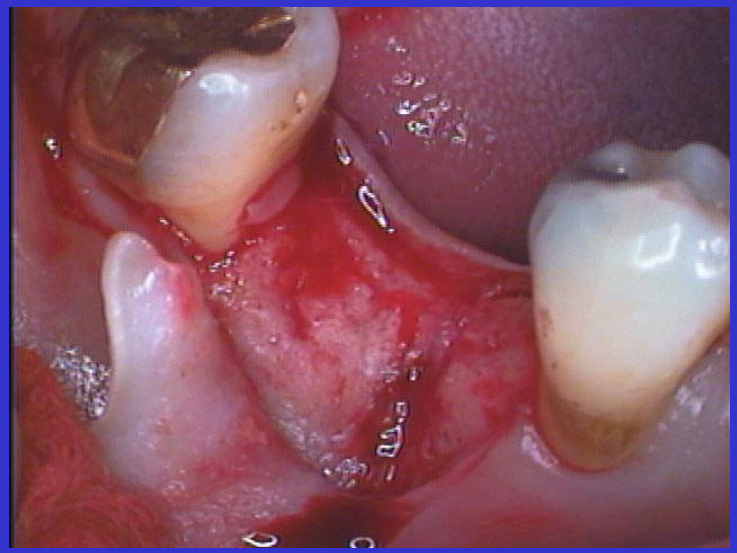


After implantation of an abutment

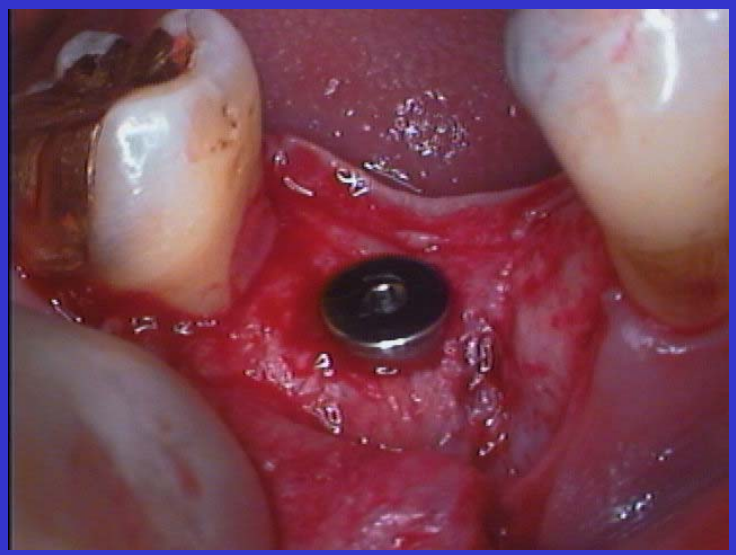


4 weeks after the implantation

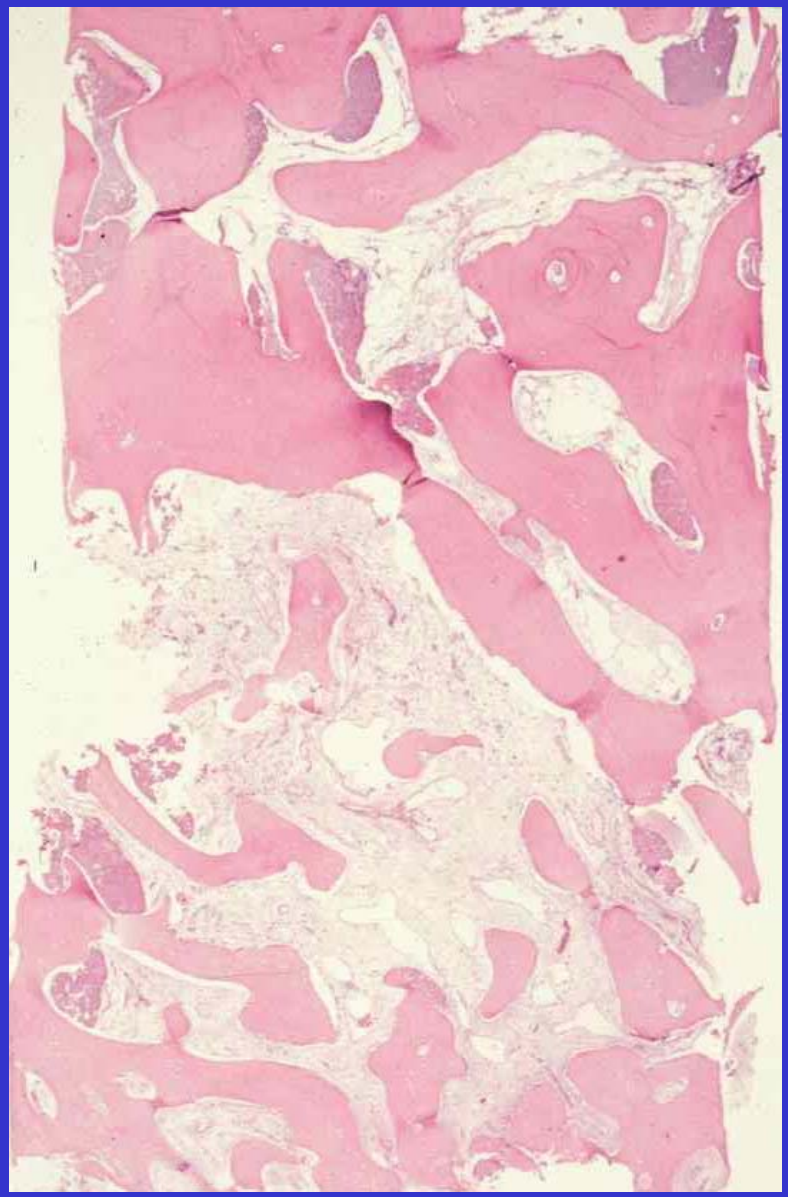
Case 4: Extraction due to tooth fracture in a healthy 58 year old female



5 months after the extraction

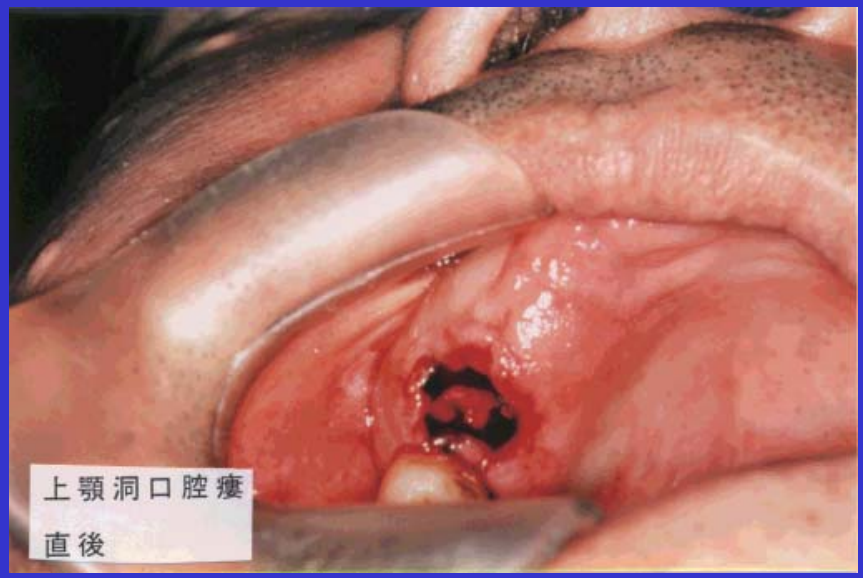


After implantation of an abutment

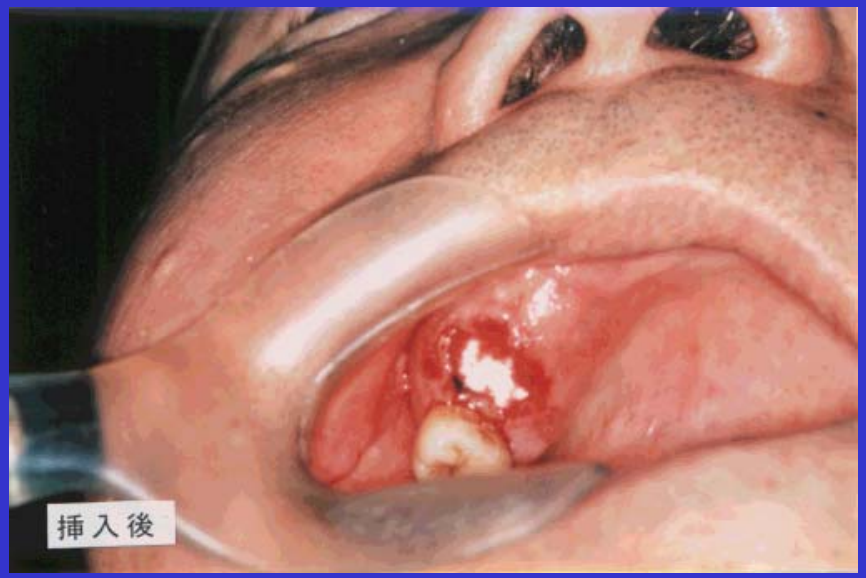


Histological section of biopsy

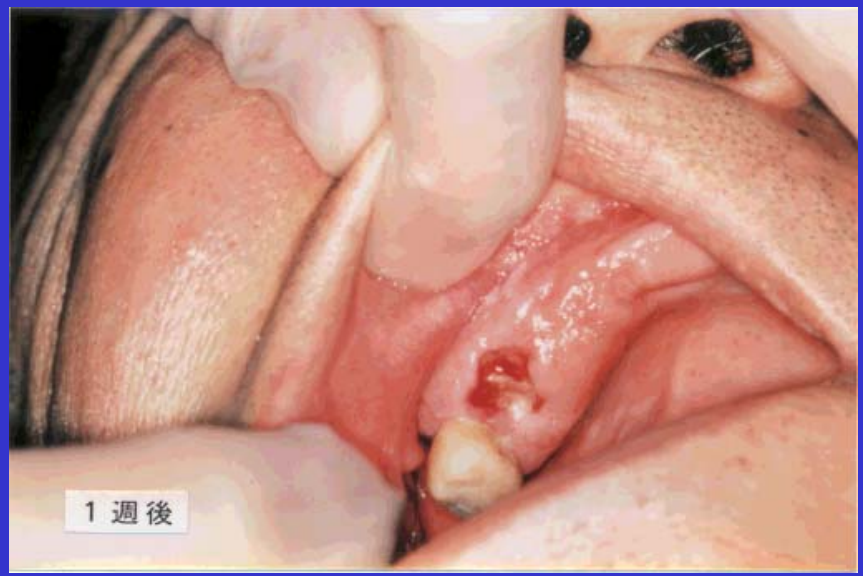
Case 5: Oroantaral fistula closure in a healthy 63 year old male



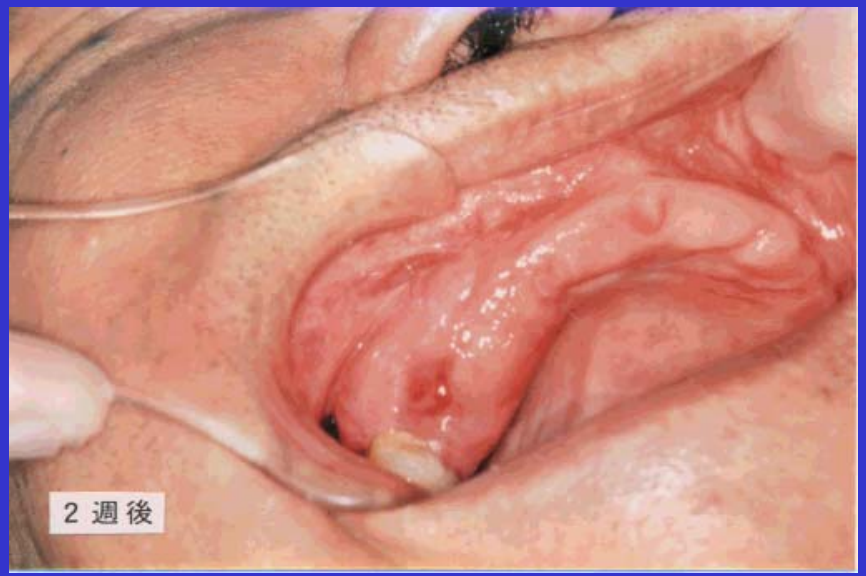
Tooth extraction



Application of FOUNDATION

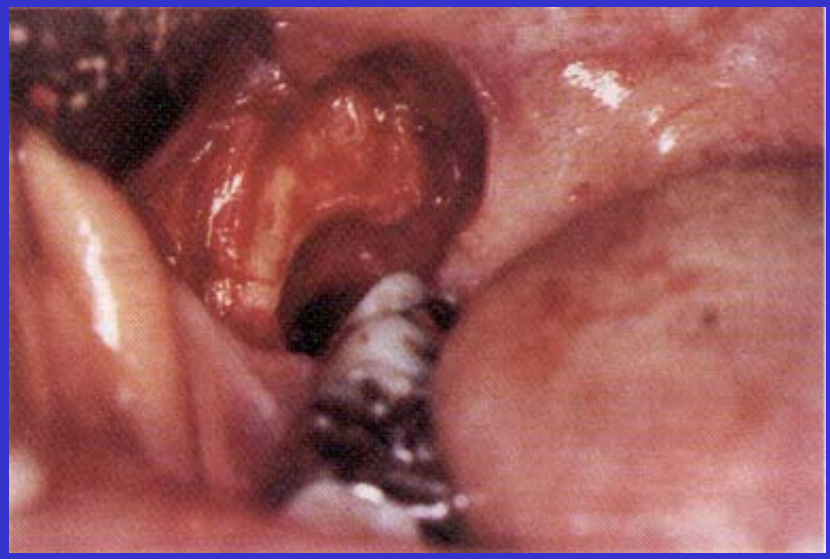


1 week later

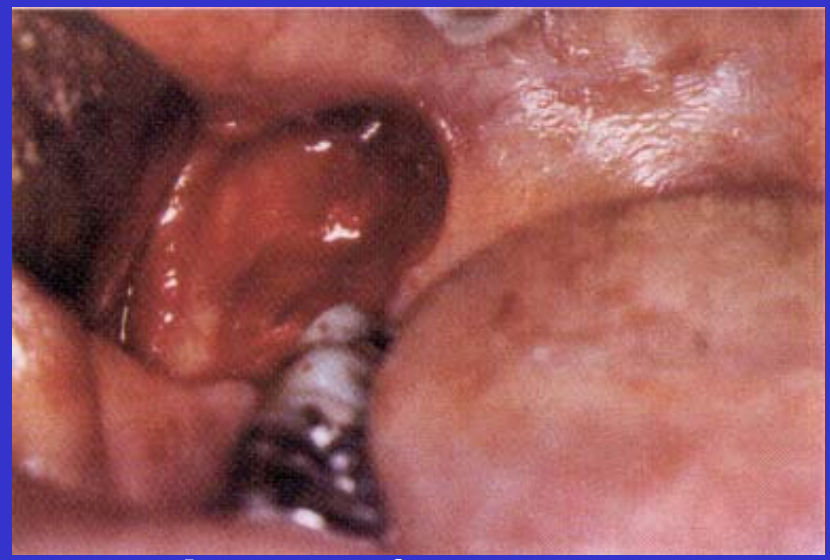


2 weeks later

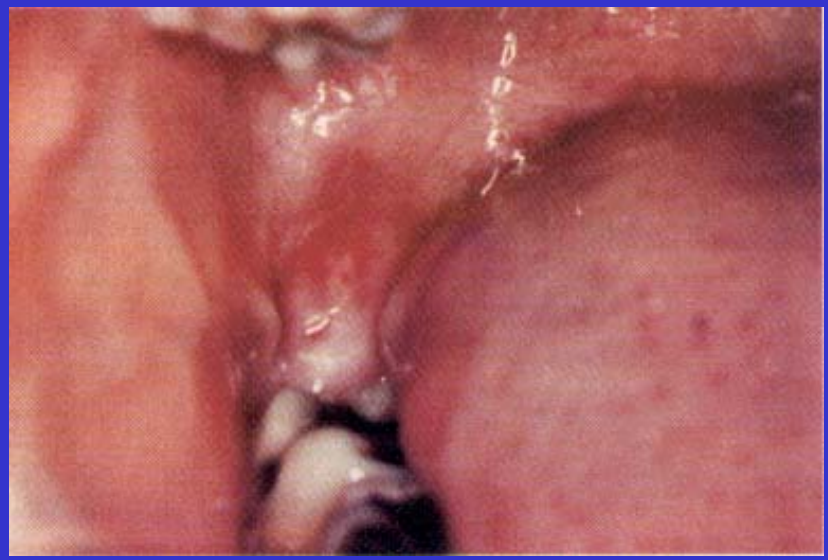
Case 6: Impacted wisdom tooth extracted in a healthy 27 year old female



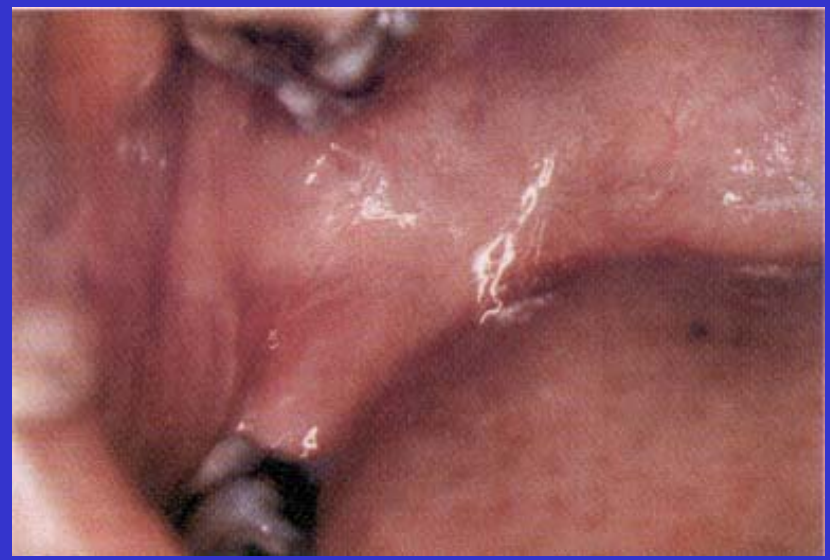
Tooth extraction



Application of FOUNDATION

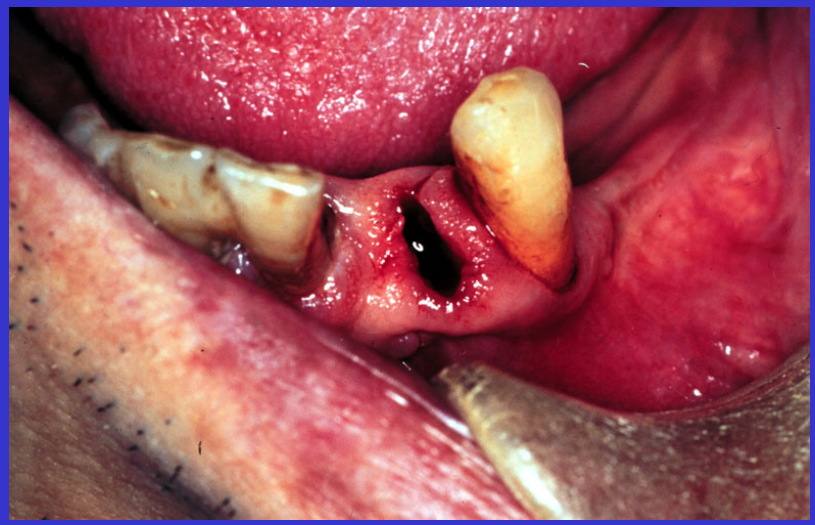


1 week later

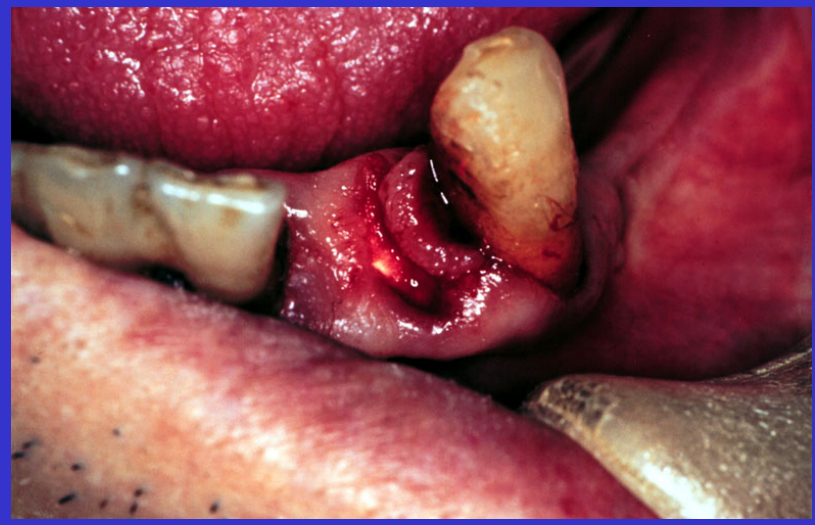


2 weeks later

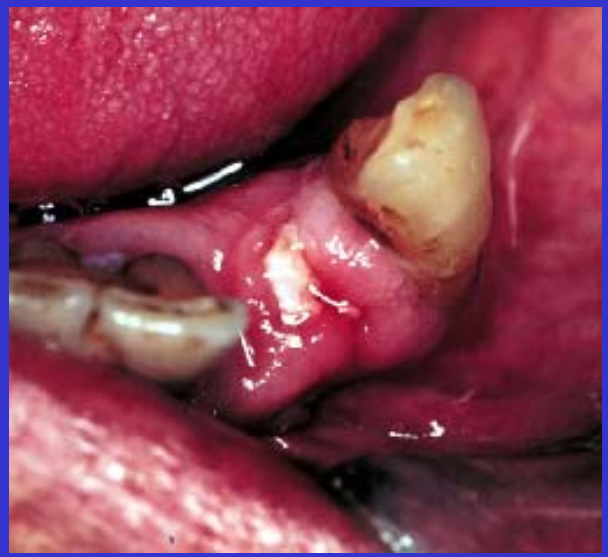
Case 7: Routine extraction in a 63 year old male diabetic



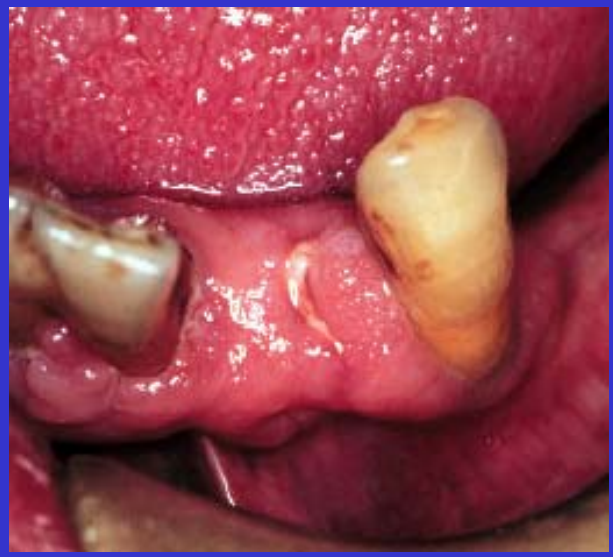
Tooth extraction



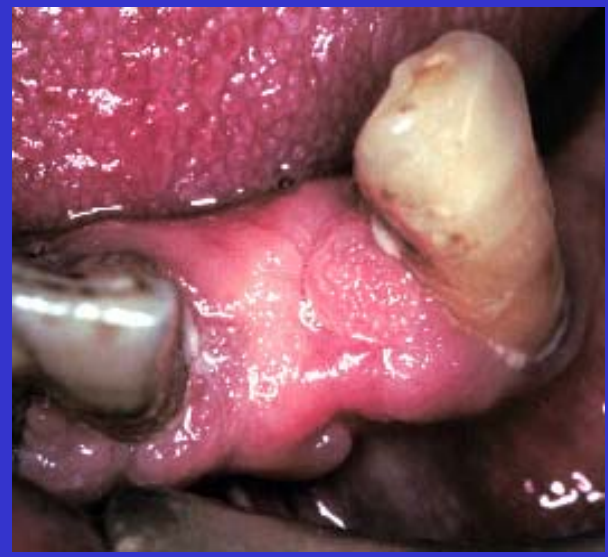
Application of FOUNDATION



3 days later

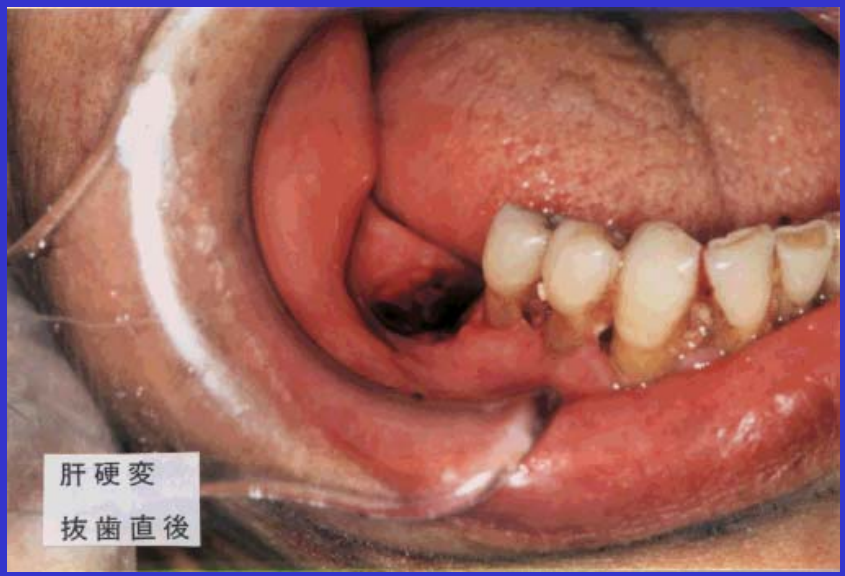


1 week later

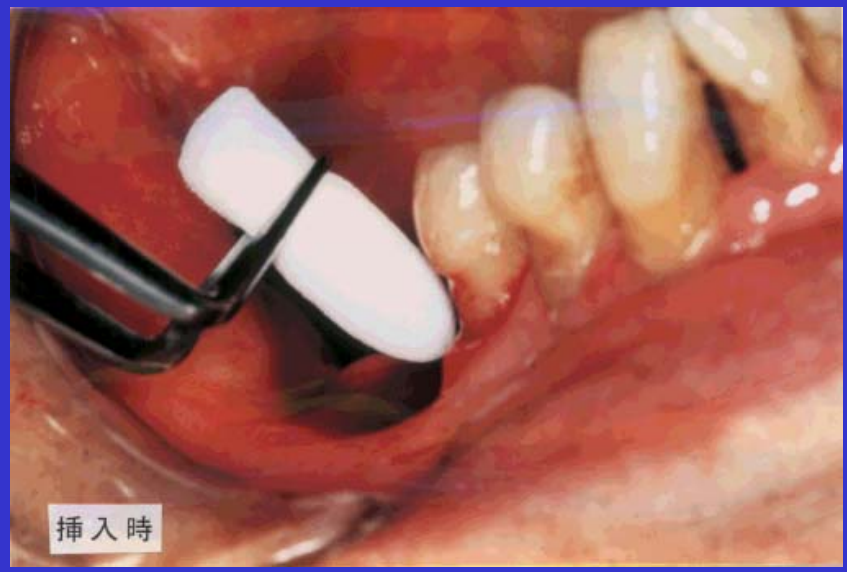


2 weeks later

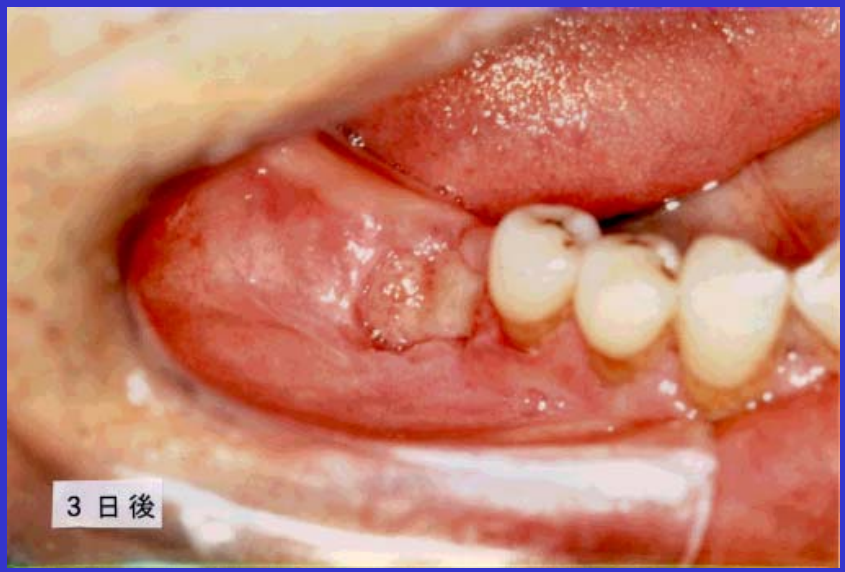
Case 8: Extraction in patient with liver cirrhosis



Tooth extraction



Application of FOUNDATION



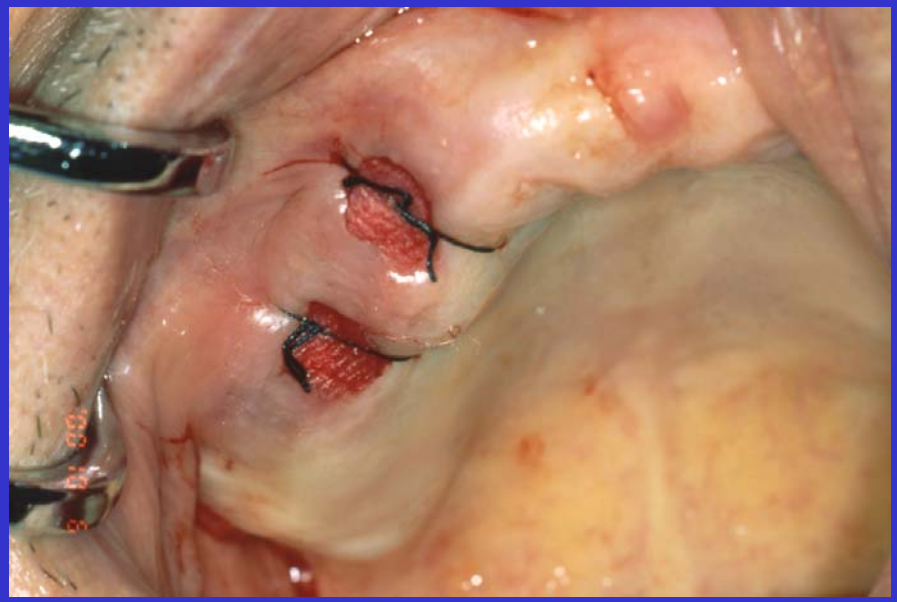
3 days later

2 weeks later

Keys to Success

1. If the extraction wound is bleeding excessively, wipe the blood off with gauze or other appropriate material otherwise FOUNDATION may shrink and dislodge from the extraction socket.
2. Secure FOUNDATION by suturing, or other means, to prevent its dislodgement from the extraction socket.
3. Where appropriate, curette the gingiva and unhealthy granulation tissue to expose bone surface. If the product is used where the gingiva has extended into the socket, in long standing oroantral fistulas, chronic inflammation, or other disease, remove the edge of gingiva from the inside of the socket to the top of the alveolar bone and curette the unhealthy granulation tissue before application of FOUNDATION. Failure to do this can result in FOUNDATION dislodging from the extraction socket and the alveolar ridge may cave in. When unhealthy granulation tissue remains in the socket filled with FOUNDATION it may cause infection and prevent new bone growth.
4. Select a slightly larger size of FOUNDATION than the socket to be filled. Remove the material from the unit package and place it in the socket using clean forceps. Do not touch the material with your hands. Applying excessive amounts of the material may cause tenderness and irritation of the socket.

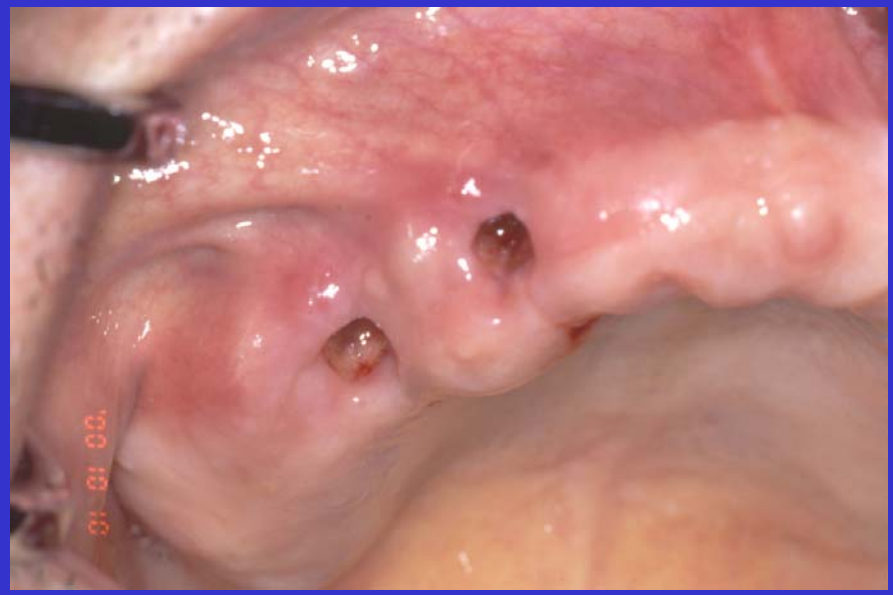
FAILURE CASE
Extraction Sockets by Marginal Periodontitis
(78 year-old male)



1

Immediately after filling with FOUNDATION and placing sutures.

The unhealthy gingiva was not removed from the inside of the sockets.



2

Four days after the fillings.

FOUNDATION fell out of the sockets despite the placement of sutures.

Dosage

Applying excessive amounts of the material may cause tenderness and irritation of the socket.
Applying excessive amounts of the material can make infiltration of cells and bone augmentation difficult due to limited opening space in the material.

Size	S	M 3.5 times of S by volume	
Anterior	1	1/4-1/2	
Posterior	2-3	1/2-1	
Horizontally impacted 3rd molar	2-4	1	

* 70-200% of FOUNDATION can be applied into socket volume