

- 166 -

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: Holmium-166  
holmium-166-chitosan  
가

: Absorbable gelatin sponge holmium-166-chitosan  
50  $\mu$  calibrator  
1.5 mCi Wistar  
holmium-166-chitosan 가 gelatin sponge  
2, 4, 6  
: 2 gelatin sponge  
holmium-166

3.3 mm holmi-  
um-166  
2.9 mm . 4  
가 3.3  
mm 가 가 3.3 mm  
. 6 가, .

: Holmium-166-chitosan 가 gelatin sponge  
가 . 가  
3 mm 가

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:  
215-4

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holmium-166

가

가  
holmium-166

(external beam

irradiation)

가

가

1.

(vital organ),

가

gelatin sponge Johnson & Johnson  
Medical SPONGOSTAN, Standard

2

(radiation induced secondary malignancy)

(biodegradable

(tumor mass)

material)

microinvasion

2. Holmium-166

1). Absorbable gelatin sponge 7×7×5  
mm

가

2). Holmium 166-chitosan 240  
mCi/4 ml activity 50  
μ 3.0 mCi

가

3). Pippeting 50 μ gelatin sponge  
6 well

cell culture plate

가

4). 24 holmium-166-chitosan  
4 mm

1.7 mCi

10%

Victoreen

Model 34-

056 dose calibrator

1.5 mCi

holmium-166

chemical synovectomy

<sup>10,12)</sup>

3.

Monte Carlo  
using EGS4)

(Monte Carlo simulation  
가(dosimetry)

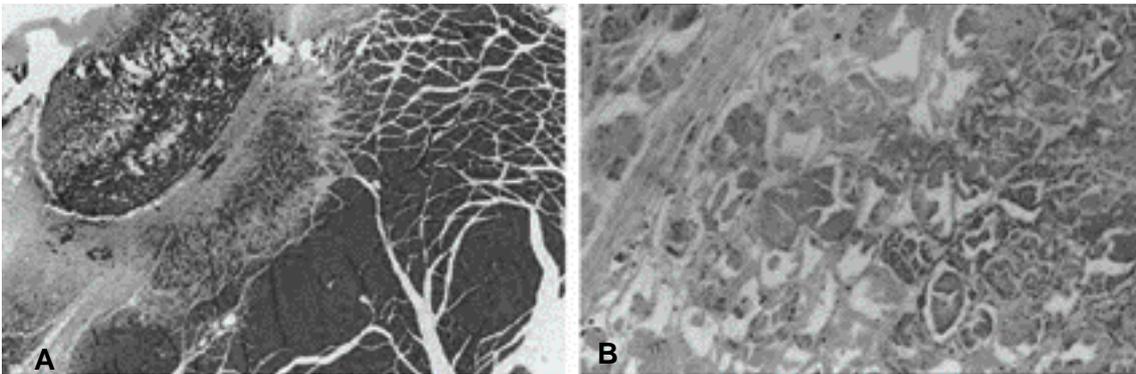
1-4,9,13,15)

330 Gy, 3 mm, 5 mm, 22 Gy, (control) 1 33

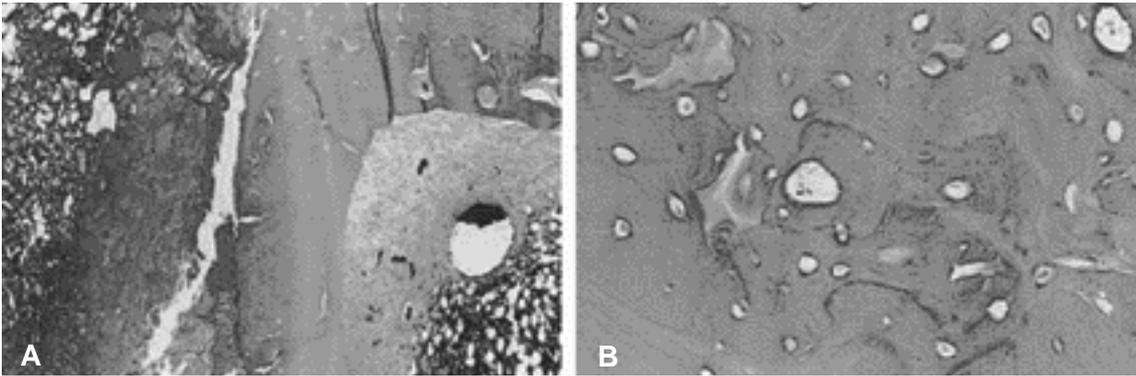
4. holmium-166 gelatin sponge 1. 2

300 g Wistar  
 2 cm 가  
 가 holmium-166 gelatin sponge  
 um-166-chitisan 가 gelatin sponge  
 sponge 가 (deep side) 가 gelatin sponge  
 가 (fibrosis)  
 가  
 gelatin sponge holmium-166  
 gelatin sponge

5. holmium-166  
 가  
 gelatin sponge  
 가 holmium-166  
 (coagulation necrosis)  
 (degenerating myocyte)  
 , 4 , 6 , 10 (regenerating myocyte), (inter-  
 , 가 gelatin sponge muscular edema),



**Fig. 1. A)** At 2 weeks, muscles contacted to the holmium-166 attached gelatin sponge (left) showed tissue necrosis(right) in low power view( × 40, H&E stain).  
**B)** At 2 weeks, muscle group showed fragmentation and destruction of muscle fibers, absence of nucleus of muscle cells( × 400, H&E stain).



**Fig. 2.** **A)** At 2 weeks, bone group showed gelatin sponge (left), cortex necrosis, and bone marrow fibrosis (right) ( $\times 40$ , H&E stain).  
**B)** At 2 weeks, in bone group cortical bone showed absence of osteocytes in the lacuna (empty lacuna), in high power field ( $\times 400$ , H&E stain).

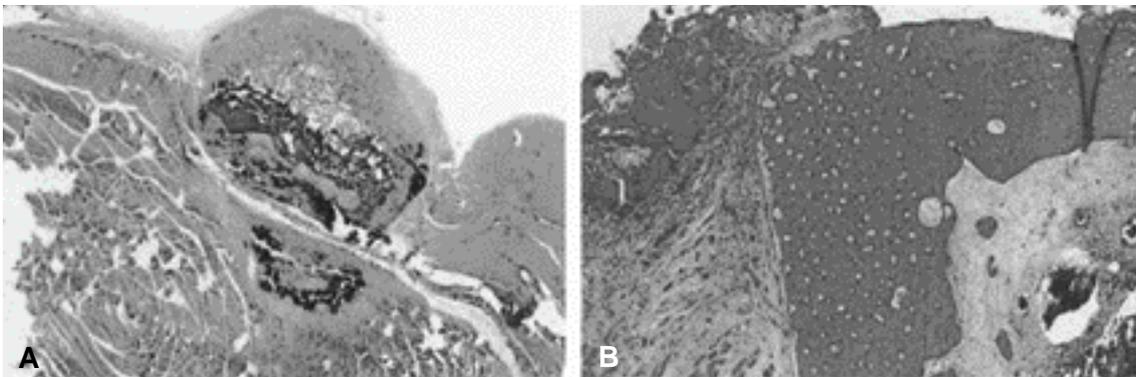
**Table 1.** Groups at 2 weeks after materials insertion

	Histology	Necrosis depth	Gelatin sponge
Control	inflammatory cells, fibrosis	0.0 mm	inflammatory cells, absorption
Muscle	inflammatory cells, coagulation necrosis, degenerating myocytes, intermuscular edema, regenerating myocytes	3.3 mm	inflammatory cell, fragmentation
Bone	empty lacuna (osteocyte), marrow fibrosis, inflammatory cells	2.9 mm	inflammatory cells, fragmentation

(Fig. 1). 3.3 mm , 0.5 1 mm 가 (Table 1).  
 2. 4  
 holmium-166 (lacuna) (osteocyte) (empty lacuna) 2  
 (Fig. 2). 2.9 mm (nodule formation) 가 , gelatin sponge

**Table 2.** Groups at 4 weeks after materials insertion

	Histology	Necrosis depth	Gelatin sponge
Control	none	0.0 mm	full absorption, minimal fibrosis
Muscle	coagulation necrosis, calcification, increased fibrosis (intermuscular edema) (inflammatory cells) (degenerating & regenerating myocytes)	3.4 mm	minimal inflammation, increased fibrosis
Bone	empty lacuna (osteocyte), increased marrow fibrosis, inflammatory cells	3.4 mm	minimal inflammation, increased fibrosis



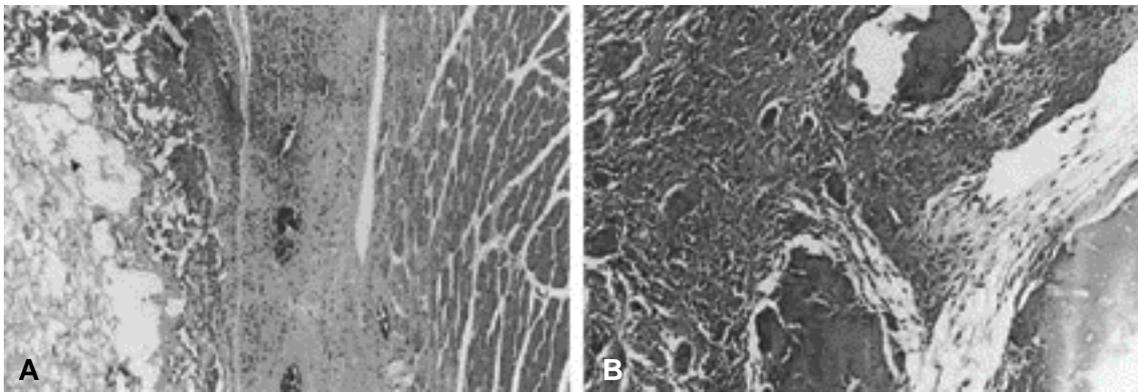
**Fig. 3. A)** At 4 weeks, muscles contacted to the holmium-166 attached gelatin sponge (upper) showed necrosis and calcification (lower) in low power view ( $\times 40$ , H&E stain).

**B)** At 4 weeks, bone group showed granulation tissue formation (left) close to the bone cortex ( $\times 40$ , H&E stain).

gelatin sponge  
(calcification) 2  
2  
holmium-166 (degenerating myocytes) (regenerating myocytes), (intermuscular edema),  
collagen material (Fig. 3A).  
holmium-166 3.3 mm  
가 2  
band가  
calcification gelatin sponge 2  
2

**Table 3.** Groups at 6 weeks after materials insertion

	Histology	Necrosis depth	Gelatin sponge
Control	none	0.0 mm	full absorption
Muscle	shrinkage, granulation tissue, no inflammation, increased fibrosis, calcification, necrosis	2.0 mm	fragmentation, granulation
Bone	empty lacuna (osteocyte), marrow fibrosis, decreased inflammation	2.5 mm	fragmentation, granulation



**Fig. 4.** **A)** At 6 weeks, muscle contacted to the holmium-166 attached gelatin sponge (left) showed fibrosis and shrinkage (right) in low power field ( $\times 40$ , H&E stain).  
**B)** At 6 weeks, bone group showed abundant granulation tissue formation (left) close to the bone cortex ( $\times 40$ , H&E stain).

(lacuna) (osteocyte)  
 (empty lacuna) (shrinkage) 가  
 (granulation tis-  
 gelatin sponge 가 sue) 4 가  
 (Fig. 3B). (Fig 4A).  
 2.0 mm .  
 3.3 mm (Table 2). gelatin sponge  
 4  
 3. 6 gelatin sponge (fragmentation)  
 (breakage)  
 gelatin sponge (Fig. 4B) 2.5 mm (Table 3).

holmium  
(cystic)

가(dosimetry)

1. Holmium-166

vessel channel

가

Holmium-166

가

가

1-4,6,11,14)

가 (solid state)

chitosan

가가

chemical synovectomy

4,9,13)

가가 가 ,

5)

Holmium-166 가 26.8

, 1.78 1.86 MeV 6.2% 80.6  
KeV

absorbable gelatin sponge

8.4 mm, 3

holmium-166-chitosan

mm

7)

Holmium-166

chitosan

가

가가

가

Holmium-166-

patch

chitosan

가

patch

3,6,8,11,14)

Holmium 166-chitosan

가

(cystic)

가

3.

gelatin sponge

2. Holmium-166 containing solid material

2

가

0.5 1

holmium-166

mm

holmium

gelatin

sponge

가  
 patch  
 Gelatin sponge 4  
 4  
 가 ,  
 2  
 gelatin sponge 6  
 (shrinkage)  
 가 , 가  
 gelatin sponge가  
 (fragmen  
 tation)가  
 Holmium 166-chitosan  
 가 gelatin sponge  
 collagen material  
 collagen material  
 가  
 가 (predictable)  
 가 (reproducible)  
 3 mm  
 가

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**Abstract**

**Histological Changes in the Normal Tissues of Rat after Local Application of the Holmium-166-Chitosan Complex attached to Biodegradable Solid Material**

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**Purpose:** The aim of this study was to find out a clinically applicable method to insert a biodegradable solid material containing holmium-166-chitosan complex into the surgical field, and to evaluate the histological changes in the normal tissues after  $\beta$ -ray irradiation from holmium-166 according to the dose, period and type of tissues.

**Materials and Methods:** 3.0 mCi, 50  $\mu$  of the liquid state  $^{166}\text{Ho}$ -chitosan complex was attached to the absorbable gelatin sponge. The radiation activity measured by dose calibrator was 1.5 mCi. These  $^{166}\text{Ho}$ -chitosan complex containing absorbable gelatin sponges were inserted into the thigh muscles and over the femur bones of the Wistar rats. The cases were evaluated at 2 weeks after insertion, and 4, 6 weeks with respect to the histological changes of the soft tissues and bone, the depth of the tissue necrosis, and the changes of the  $^{166}\text{Ho}$ -chitosan complex containing absorbable gelatin sponges.

**Results:** At 2 weeks, the muscles showed coagulation necrosis, degenerating myocytes, regenerating myocytes, intermuscular edema, and inflammatory cells. The necrosis depth was 3.3 mm. In the bones, there was no osteocyte in the lacuna of cortex (empty lacuna), marrow fibrosis, inflammation. The necrosis depth was 2.9 mm. At 4 weeks, in the muscle, calcification and increased fibrosis with necrosis depth by 3.3 mm were the additional findings. In the bone, marrow fibrosis with necrosis depth by 3.3 mm were detected. At 6 weeks, soft tissue shrinkage, increased fibrosis and granulation tissue formation, and nearly resolving inflammatory reaction were the findings.

**Conclusion:** The local application of the  $^{166}\text{Ho}$ -chitosan complex attached to biodegradable gelatin material with surgery in the laboratory animals resulted in no mortality and morbidity, and satisfactory tissue necrosis. Holmium-166 can be applied to the treatment of the malignant tumor patients.

**Key Words:** Holmium-166, Gelatin, Histological change

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