原文題目(出處)：	Histopathologic and hstomorphometric analysis of irradiation injury in bone and the surrounding soft tissues of the jaws. J Oral Maxillofac Surg 2016;74:190-9.
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內文：

Purpose: Surgery of irradiated tissue has an increased complication rate because of the development of hypovascular, hypocellular, and hypoxic tissue. This study was undertaken to perform histopathologic and histomorphometric analyses of irradiation tissue injury in bone and the surrounding soft tissues

Osteoradionecrosis (ORN)

- Surgery and radiation have been the standard treatment for advanced cancers of the head and neck
- Osteoradionecrosis (ORN) of the jaws is one of the most severe late complications of radiation therapy. It is defined as exposed irradiated bone tissue that fails to heal over a period of 3 months without signs of primary tumor, recurrence, or metastatic disease
- ORN was characterized by progressive obliterative endarteritis(閉塞性動脈內膜炎) and the development of hypovascular, hypocellular, and hypoxic tissues
- Micro-organisms play only a contaminating role in ORN
- A new theory was proposed by Delanian and Lefaix based on the radiation-induced fibro-atrophic process
- 3 distinct phases:

1. An initial prefibrotic phase

Characterized by changes in endothelial cells

Cytokines, released in response to injury, attract leukocytes to the site of injury that trigger an acute inflammatory response. This can lead to necrosis of microvessels, local ischemia, and tissue loss

2. Constitutive organized phase

Characterized by the radiation-induced fibro-atrophic tissue composed of fibroblasts and the extracellular matrix

3. Late fibroatrophy

Last for decades after radiotherapy and consists of poorly vascularized and cellular tissue with few fibroblasts and a dense extracellular matrix

Histopathologic

- Hyperemia(充血), endarteritis(動脈內膜炎), cellular damage, and vascular thrombosis begin soon after radiation exposure and is maintained for an additional 6 months.
- Hypovascularization and fibrosis occur 6 to 12 months after radiotherapy and represent the end stage of radiation tissue injury

Treatment

- ORN requires treatment when there is pain, impaired function, or active infection
- There are limited options for treatment of refractory and persistent cases of ORN other than complete bone surgical resection or multimodal therapy in which hyperbaric oxygen therapy (HBO) is combined with surgical resection of necrotic bone.
- No consensus exists regarding its prophylactic use, its mechanism of action, and

its effectiveness in the prevention and treatment of ORN.

- There is some evidence that HBO improves outcome to prevent the development of ORN after dental extraction in patients irradiated for head and neck tumors.
- There also is some evidence that HBO might improve outcome in irradiated patients who need resection and reconstruction surgery
- some clinical studies have suggested the use of pentoxifylline (抗凝血劑) combined with tocopherol (vitamin E) to prevent and treat ORN

Material and Methods

- Cancer Hospital Center
- 40 irradiated specimens obtained from different patients who were treated for ORN
- Fifteen nonirradiated mandibular bone and surrounding soft tissue samples obtained from different patients who were treated for head and neck tumors were used as control specimens
- The diagnostic criteria for ORN was a slow healing radiation-induced necrosis of bone with associated soft tissue necrosis for at least 3 months with the absence of local primary tumor necrosis, recurrence, or metastatic disease
- External beam radiation
  The specimens received megavoltage delivery (linear accelerator, 4 MeV). The average total dose of radiation for these specimens was 5,942 cGy (range, 5,040 to 7,040 cGy). The average dose rate per day for these specimens was 174 cGy (range, 109 to 200 cGy). The average time of specimen evaluation after completion of radiation treatment was 22.1 months (range, 2 to 108 months).

PREPARATION OF SPECIMENS AND HISTOPATHOLOGIC EXAMINATION

- Bone specimens were decalcified in a solution of 10% buffered formalin with 10% ethylenediaminetetra-acetic acid (EDTA). Five-micrometer thick sections were obtained from the original paraffin blocks and then stained with hematoxylin and eosin(HE 染色) for light microscopic histopathologic and histomorphometric observations
- Examinations were performed in a blinded manner by 2 pathologists. The amount of hyperemia, endarteritis (inflammation), thrombosis, and fat in the bone marrow cavity were categorized as abundant, moderate, rare, or none for each specimen

EVALUATION OF ENDOTHELIAL MARKER CD34 IMMUNOREACTIVITY

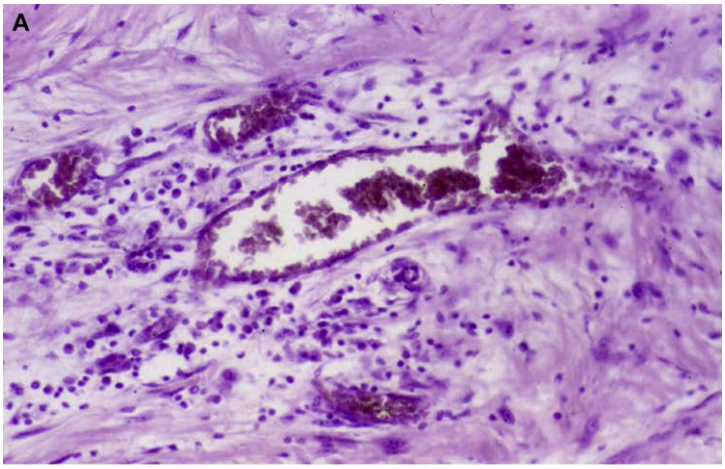
- The CD34 antigen is a sensitive marker of vascular endothelium and angiogenesis. The examination of CD34 has been reported in several physiologic and pathologic events
- Vessels were counted according to a standard in which 3 areas with dense vascularity were identified and selected in each tissue section under low-power magnification

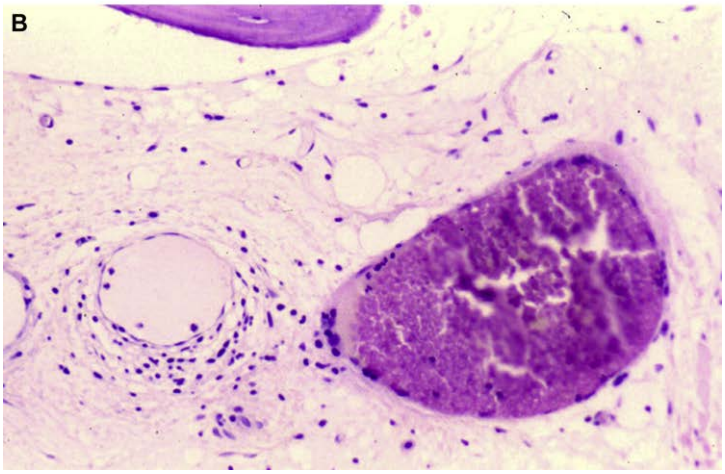
STATISTICAL ANALYSIS

All statistical analyses were performed with SPSS 10.0 for Windows (SPSS, Inc, Chicago, IL). Ninety five percent confidence intervals were calculated for specimen groups

Results

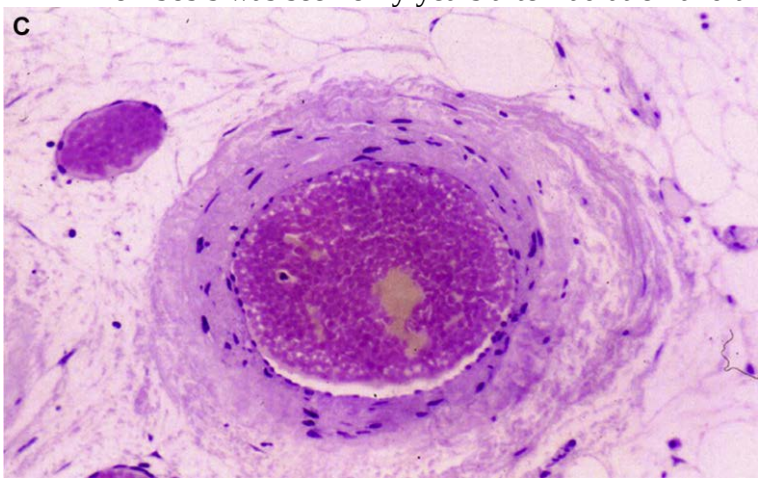
- Hyperemia and endarteritis were early effects of radiation and observed for up to 6 months after radiotherapy (Fig 1A, B)



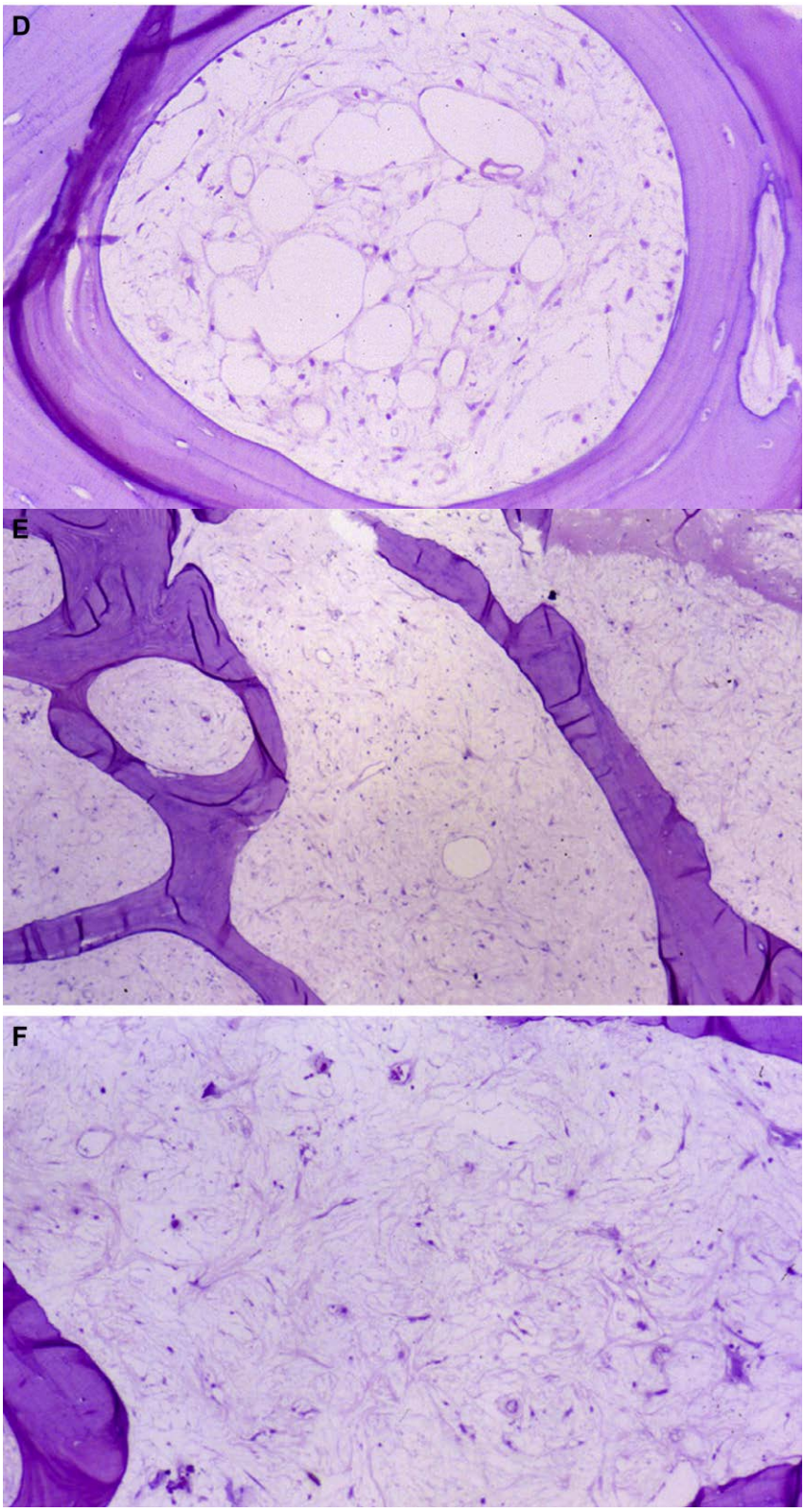


A, Early histologic effects of radiation exhibiting hyperemia and endarteritis
B, Early histologic effects of radiation exhibiting hyperemia, endarteritis, and cellular thrombosis formation. Note inflammatory cells inside the vessel lumens

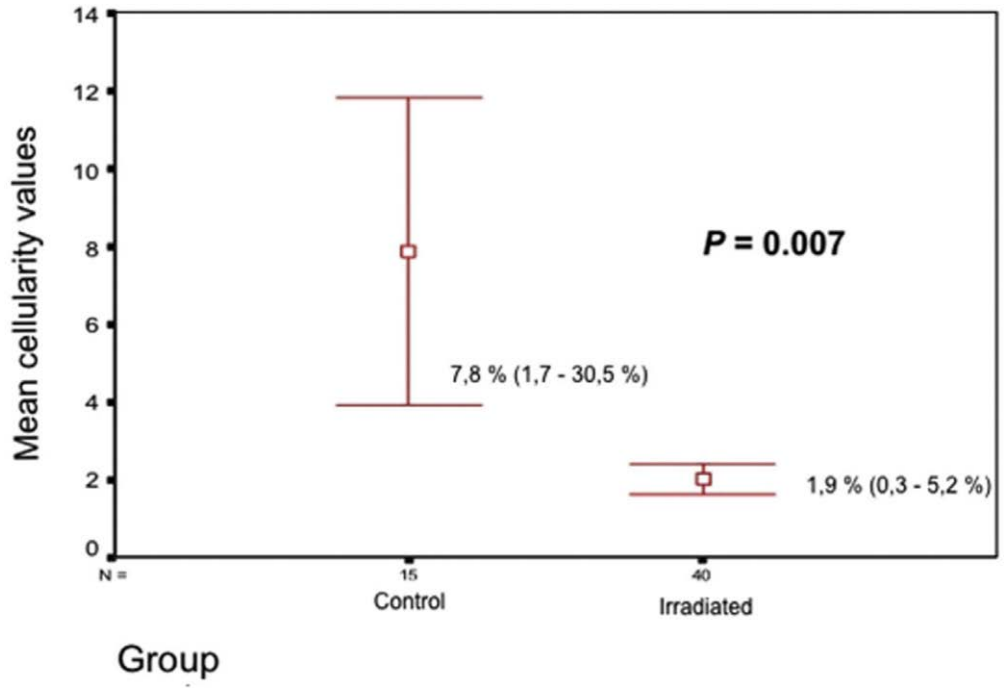
- Thrombosis was seen only years after radiation and thrombi were densely fibrous



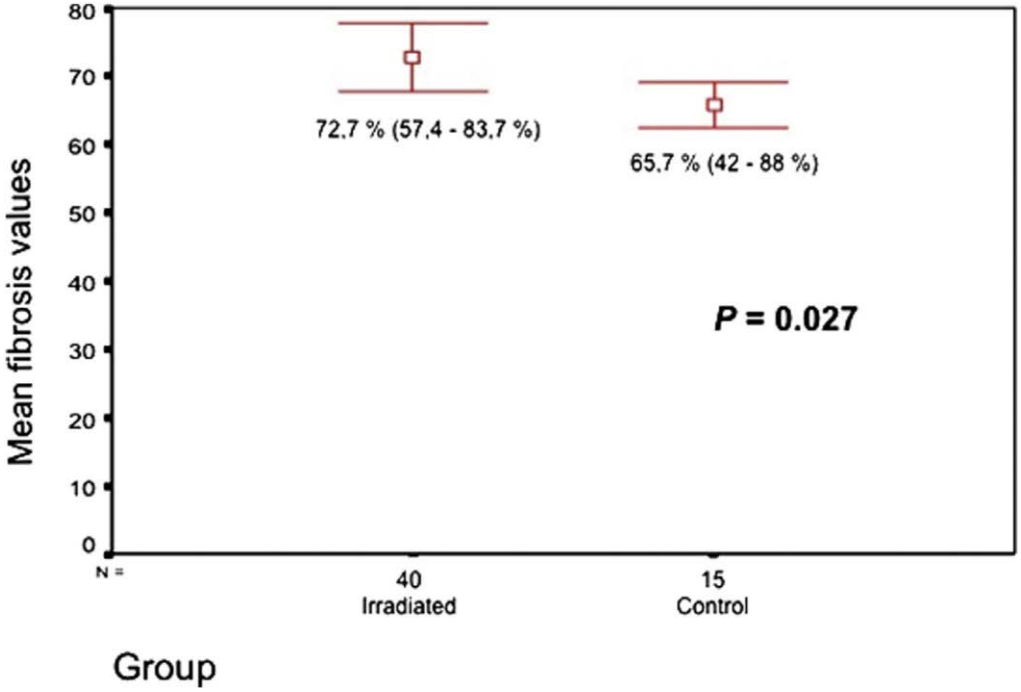
- Cell loss occurred rapidly after radiation and remained progressive through the years. Hypo-vascularization, increase of fat in the bone marrow cavity, and fibrosis progressively worsened over time after radiation and were considered the end stage of radiation tissue injury



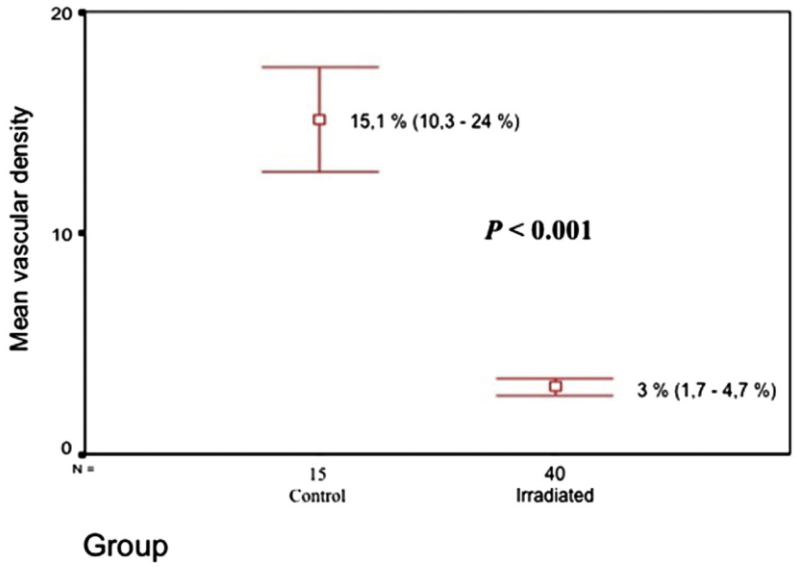
- There were significant differences between the mean cellularity values of irradiated specimens and control specimens
  Cell loss was greater in bone than in soft tissues



- There were significant differences between the mean fibrosis values of irradiated specimens and control specimens
  Fibrosis was more evident in bone than in the soft tissues



- Mean vascular density values of irradiated specimens and control specimens showed significant differences
  Six months after radiation, all specimens showed considerable hypovascularity
  However, no meaningful differences in mean vascular density values were found between those in irradiated bone and those in surrounding soft tissues



Discussion

- When considering the radiosensitivity of bone tissue, the particular physical condition must be considered Because of its high calcium content, bone can absorb 30 to 40% more radiation than the surrounding soft tissues, and this factor could account for an increase in secondary radiation produced in bone under certain conditions

  Another point related to this fact is the importance of recognizing the differences in the quality of radiation (kilovolt vs megavolt irradiation), because of the difference in absorption of radiation energy between bone and soft tissues. When using high energy photons(光子), the absorbed dose is approximately he same in bone and soft tissues
- Hypocellularity is frequently present in irradiated tissue and is often associated with a disproportionate accumulation of collagen. Marx and Tursun compared the histopathologic features of suppurative osteomyelitis(化膿性骨髓炎) of the jaws, bisphosphonate-induced osteonecrosis of the jaws, and ORN of the jaws, and all conditions evidenced the common finding of necrotic bone with empty osteocytic lacunae and Haversia and Volkmann canals, but each showed a distinctive histopathologic pattern indicating a different disease mechanism. ORN exhibited considerable marrow fibrosis, a shortage of cells, and the ghosts of old blood vessels
- A recent theory for the pathogenesis of ORN has suggested that damage to bone is caused by radiation-induced fibrosis. Thus, when ORN occurs in the jaw bone, there is a decrease in the bone matrix and its replacement with fibrous tissue

題號	題目
1	下列有關於 Osteoradionecrosis (ORN)的敘述何著為非? (A) The teeth and the periodontia should be maintained in excellent health if possible (B) The extraction of condemned teeth at least 3 to 5 days before the commencement of radiation (C) Radionuclide bone scans are helpful in determining the extent of ORN. (D) Risk factors for ORN are high age,high radiation dose, superfractionation, and the combination of tumor surgery and chemotherapy with traumatic tooth extraction

答案(B)	出處：Beumer J, Han-ison R, Sanders B, et al: Postradiation dental extractions: a review of the literature and a report of 72 episodes, Head Neck Slirg 6:581-586, 1983. The extraction of condemned teeth at least 10 to 14 days before the commencement of radiation
題號	題目
2	請問下列有關於 Osteoradionecrosis (ORN)的組織特色何者為非? (A) hypovascular (B) hypocellular (C) hyperoxic (D) hypoxic
答案(C)	出處：Marx RE, Johnson RP: Studies in the radiobiology of osteoradionecrosis and their clinical significance, Oral Slirg 64:379-390, 1987.