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# IMPLANTS in IRRADIATED TISSUES


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# IMPLANTS IN IRRADIATED TISSUES

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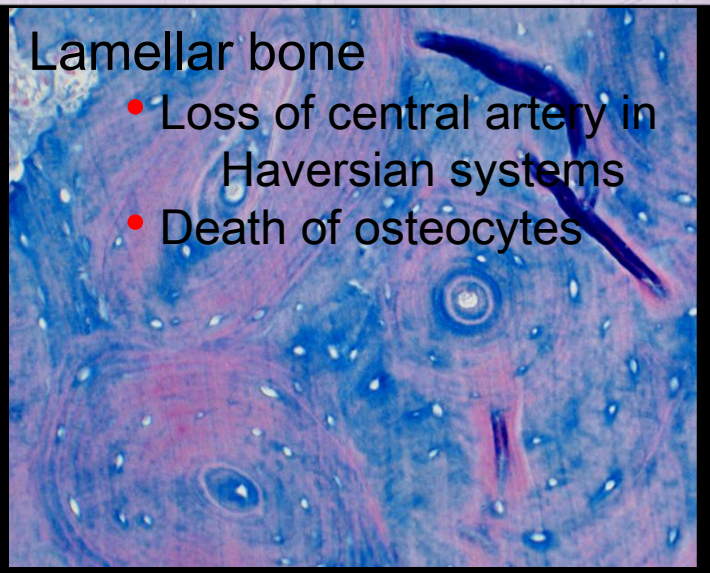
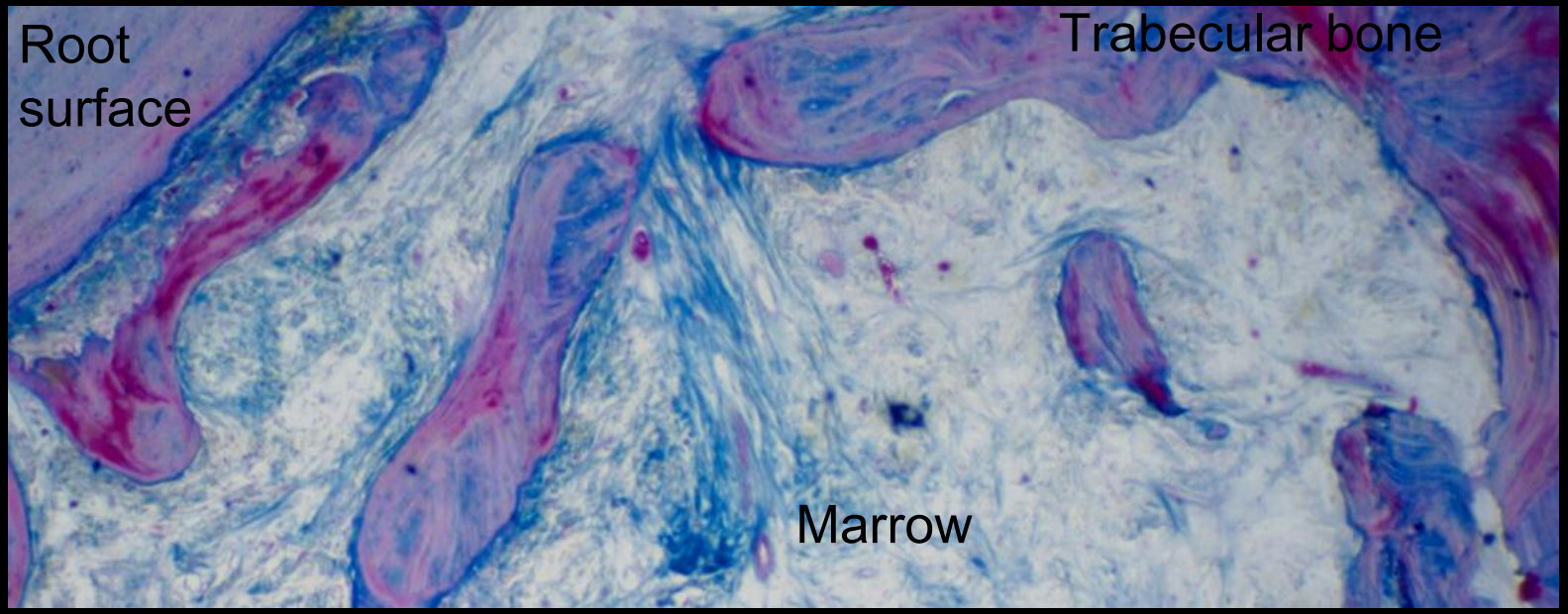
- Radiation effects & impact on osseointegration
- Modes of radiation & chemoradiation
- Clinical studies & patient selection
- Animal studies
- Human data
- Osteoradionecrosis
- HBO
- Timing of implant placement
- Irradiation of existing implants

## Radiation effects

- Reduced vasculature
- Loss of osteoprogenitor cells
- Fatty & fibrous degeneration
- Periosteum- accellular
- Loss of vasculature

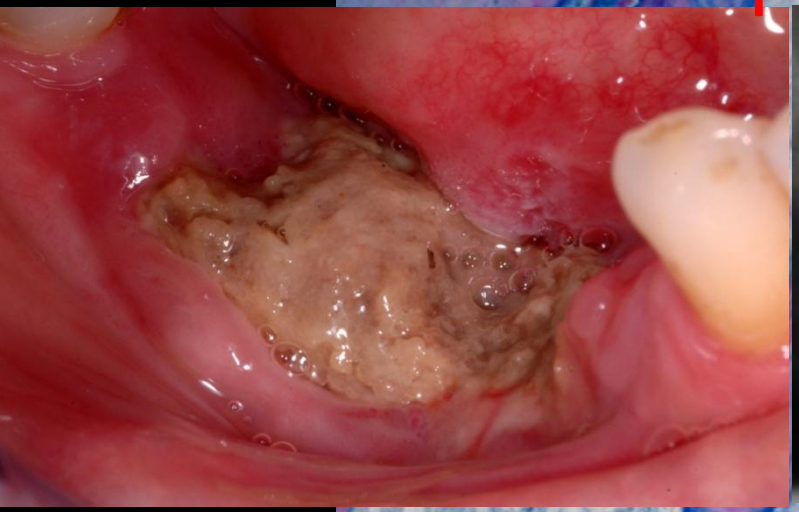


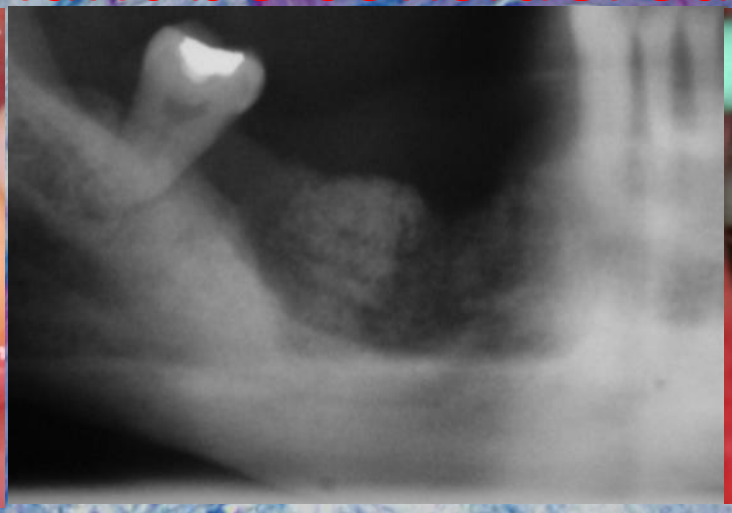



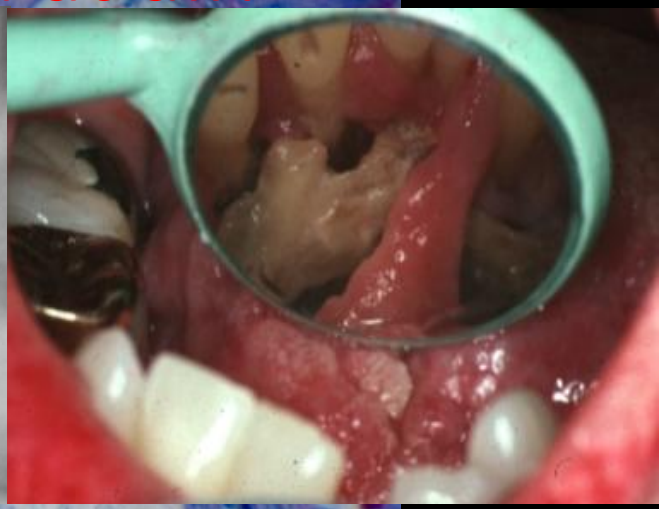
## Why are these changes important?

- Implant anchorage (mechanical vs biologic)
- Response to infection (compromised)
- Remodeling apparatus (not fully functional)
- Response to occlusal forces (compromised)
- Osteolytic

Shall implant be considered at all?







# CHANGING METHODS OF RADIATION DELIVERY

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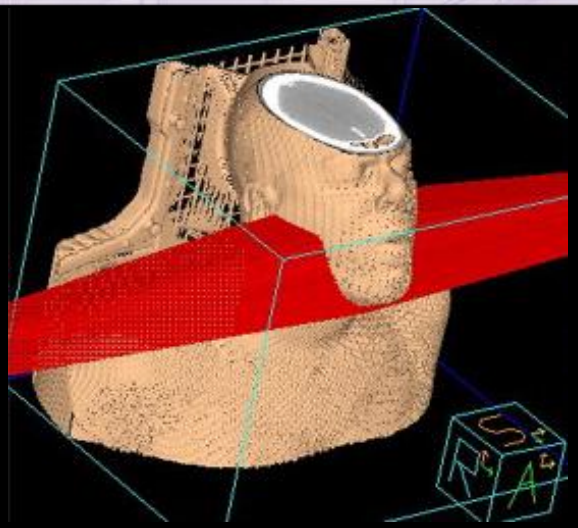
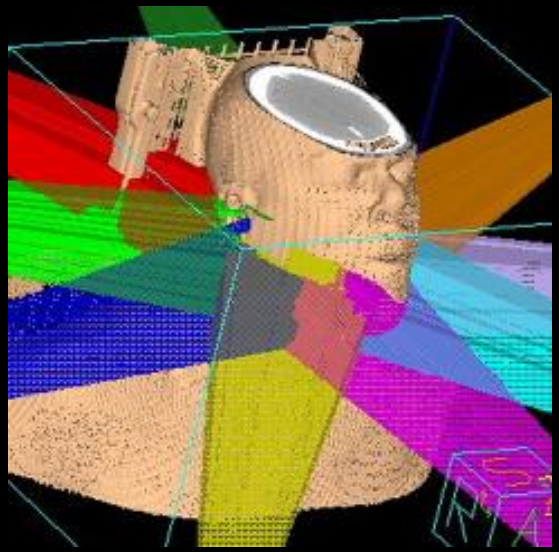
## Conventional radiation therapy (CRT)

- 200 cGy per fraction
- Total doses
  - 7000 cGy definitive dose
  - 5000-6000 cGy post op



## Intensity modulated radiation therapy (IMRT)



multiple radiation beams (non-uniform intensities)

highly conformal doses to targets

limiting dose normal tissue structures.

# RADIATION DELIVERY FACTORS

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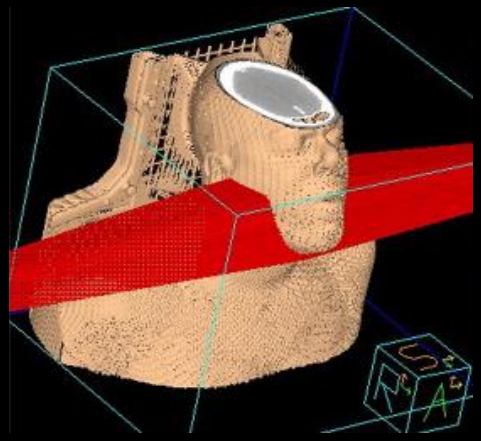
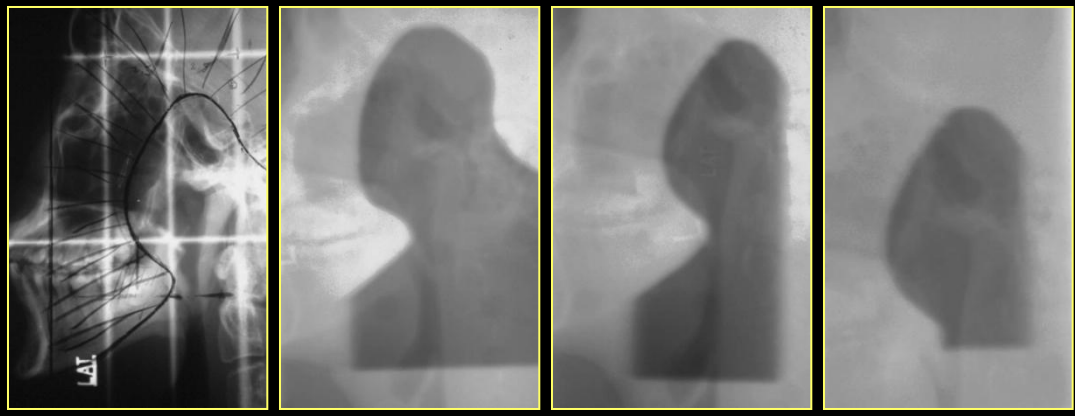
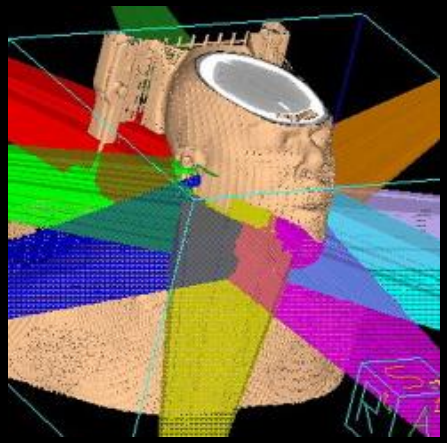
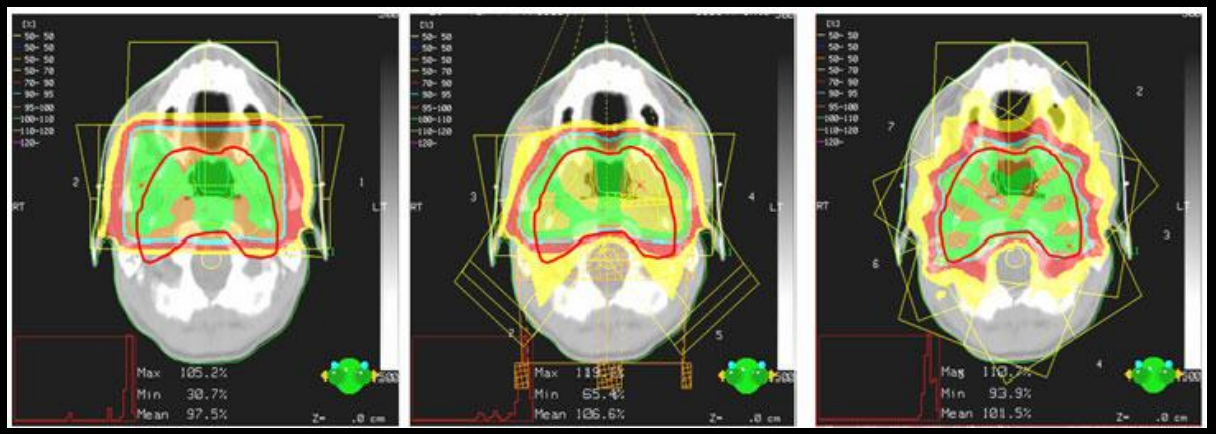
## Conventional radiation therapy





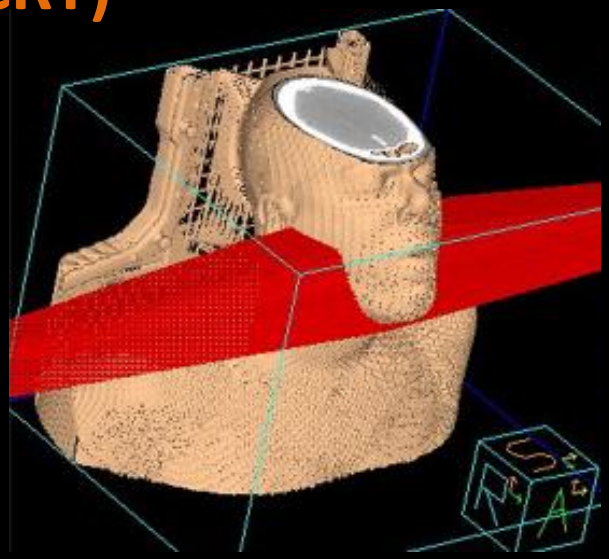

## IMRT



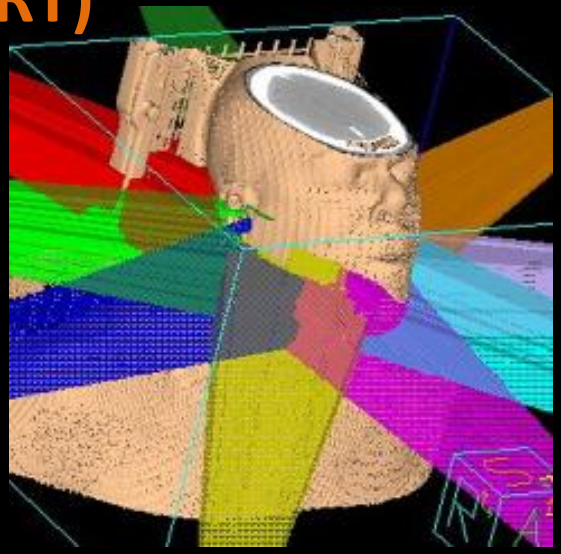



3 fields 5 fields 7 fields

(CRT)



(IMRT)



## Chemoradiation

- Combine with CRT or IMRT
- Concommitant chemoradiation is theoretically equivalent to an additional 1000 cGy (Kashibhatla, 2006).

## Consequences (particlularly with CRT):

More short & long term side effects (mucositis, trismus, osteoradionecrosis

# IMRT DOSIMETRY DIAGRAMS

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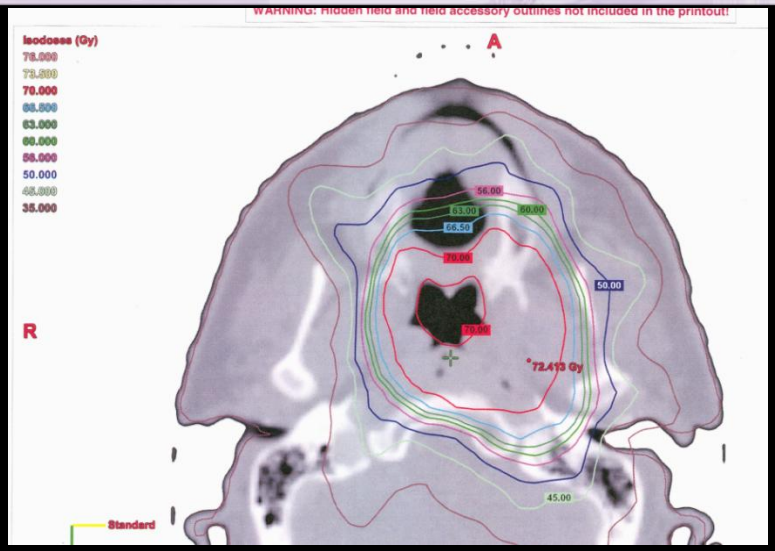


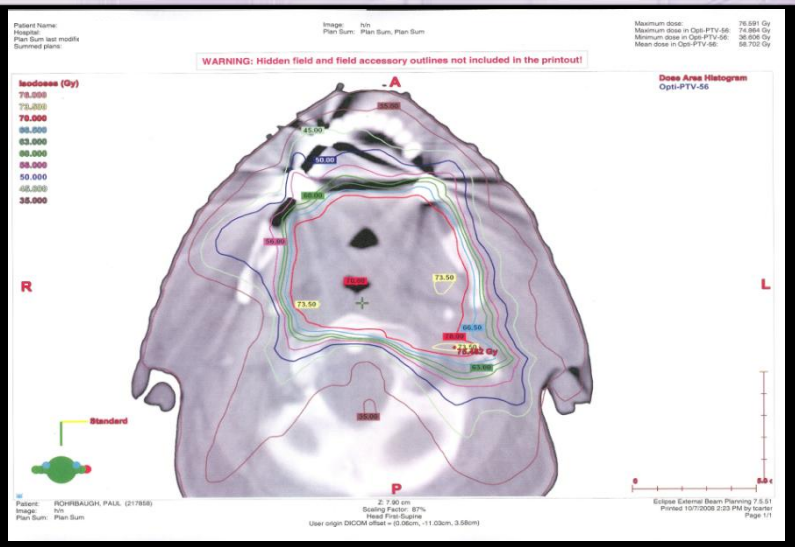


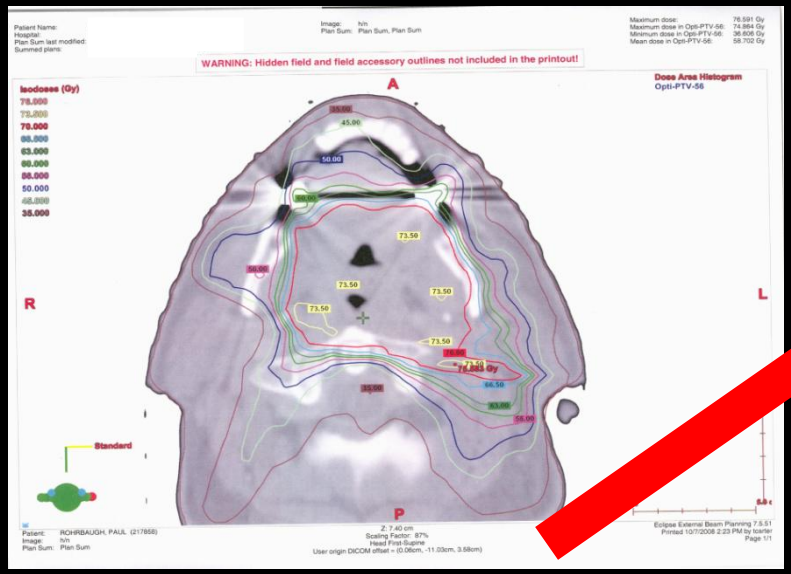


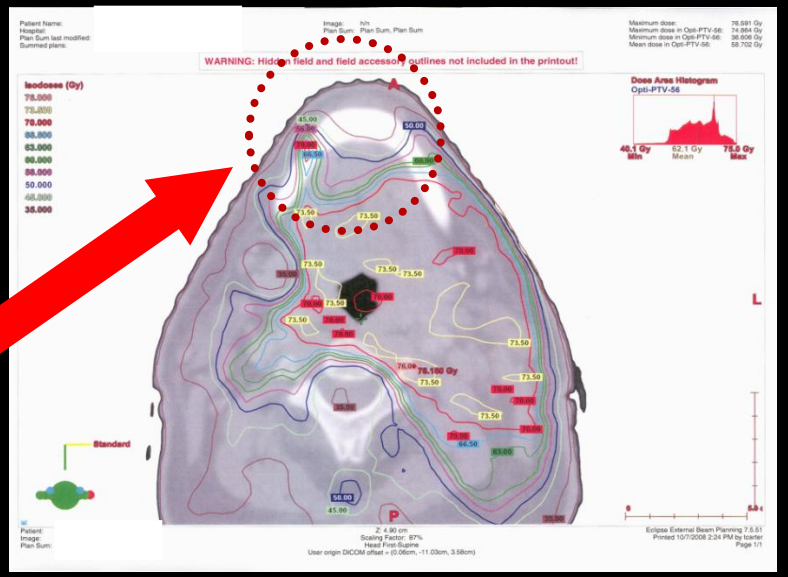


Note the hot spot on anterior mandible (oval)

# IRRADIATION OF EXISTING IMPLANTS- BACKSCATTER

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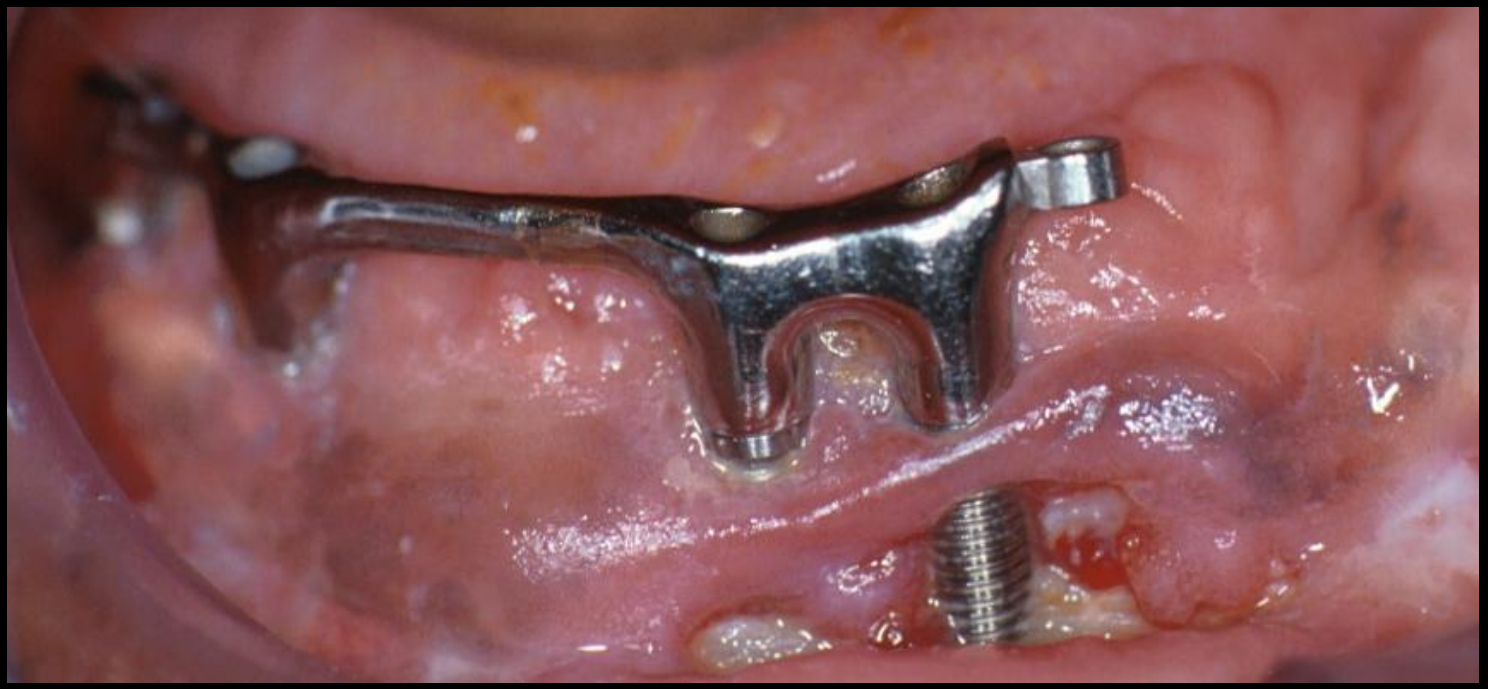

Implants were placed simultaneous with tumor resection & reconstruction of this large mandibular defect with a fibula free flap.  (6000 cGy post-op)

## Cumulative radiation effect (Fowler & Stern, 1963; Ellis, 1968)

These indices represent an attempt to account for variables of radiation delivery to indicate more accurately the true biologic response.

# IMPLANTS IN IRRADIATED TISSUES

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## Issues to consider

- Potential benefit to the patient
  - What are the objectives & wishes of the patient
  - Risk – reward ratio
- Risk of osteoradionecrosis
  - Morbidity
- Short term success rates
- Long term success rates

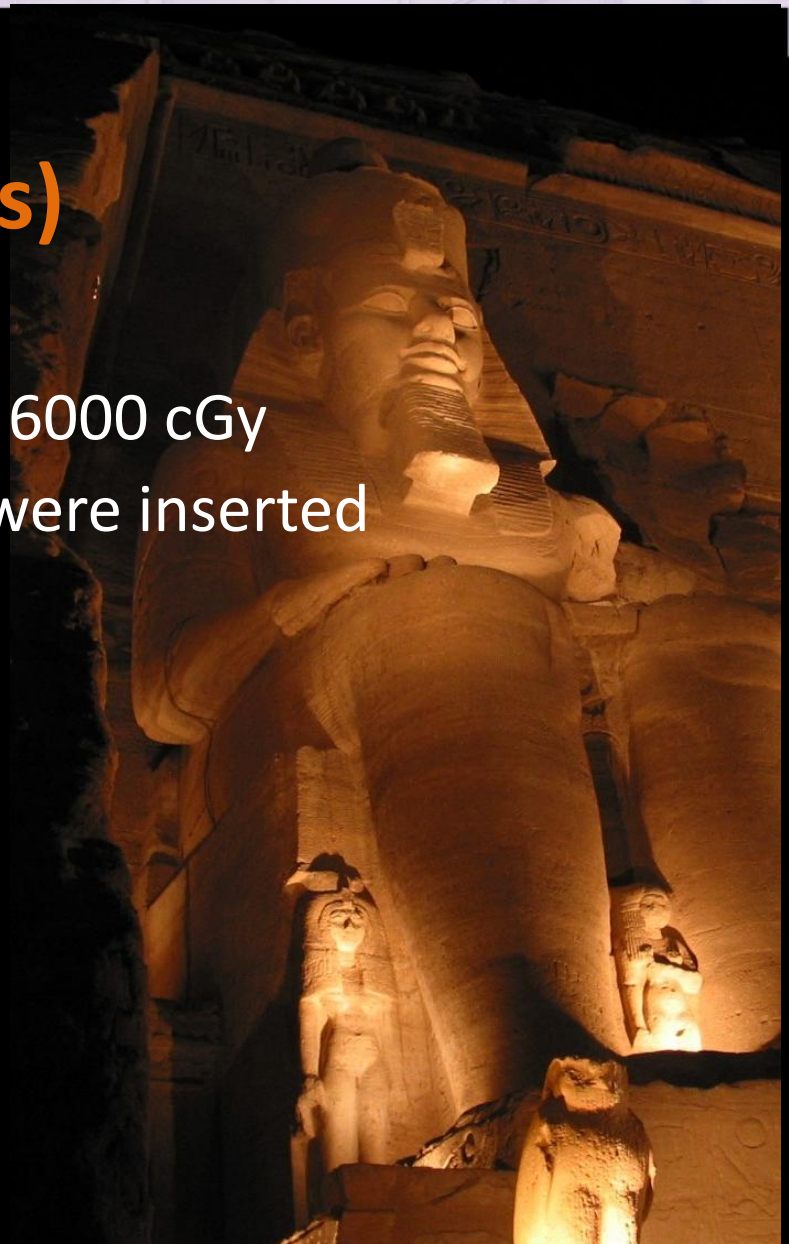
## Biologic viability (animal studies)

- Hum and Larsen, (1990
- Weinlander et al, (2006)
- Nishimura et al, (1994)
- Asikainen et al, (1998)
- Ohrnell et al,  (1997)
- Jacobsson et al, (1988)

# Biologic viability (animal studies)

## Asikainen, 1998

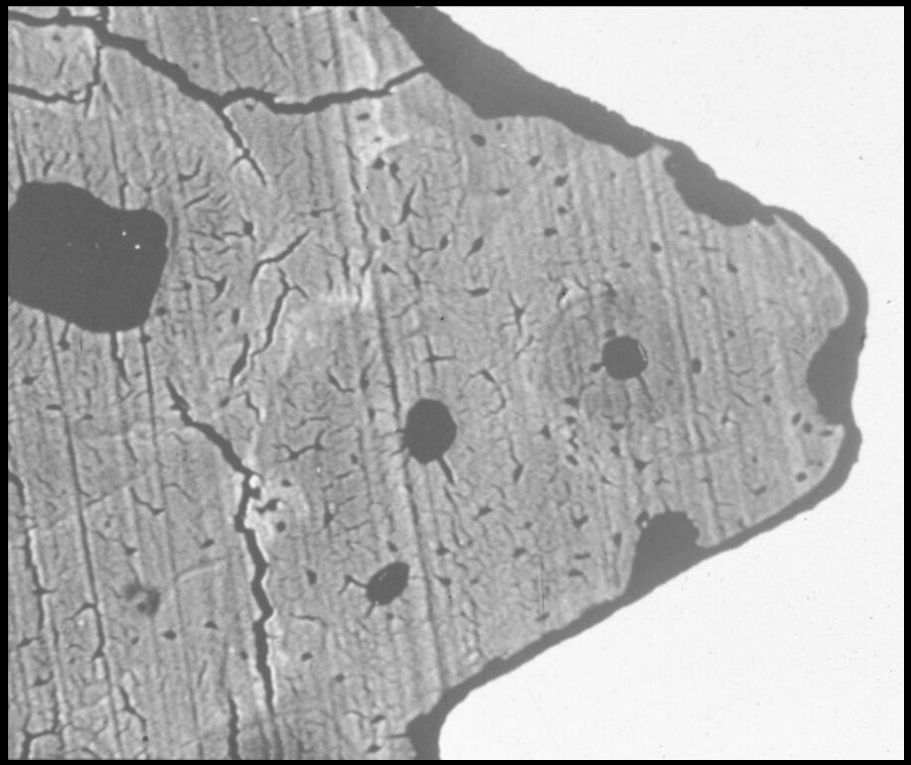
- Dogs received either 4000, 5000, or 6000 cGy
- 2/12 later TPS screw type implants were inserted
- 4/12 later the implants were loaded
- Success rates:
  - 4000 cGy group – 100%
  - 5000 cGy group – 20%
  - 6000 cGy group – 0 %



## Weinlander et al, (2006)

- Dogs (partially edentulated mandible)
- Following a healing period 3 implants were placed
- All 7 dogs: radiation tx at 3/52 post implantation,
- Dose equivalent to 5000 cGy delivered in 4 fractions during 2/52

- SEM of bone, soft tissue & implant



Histometry calculation yielded volume & boundary fractions for the implant, bone & soft tissue components

Weinlander et al, 2006

# RESULTS

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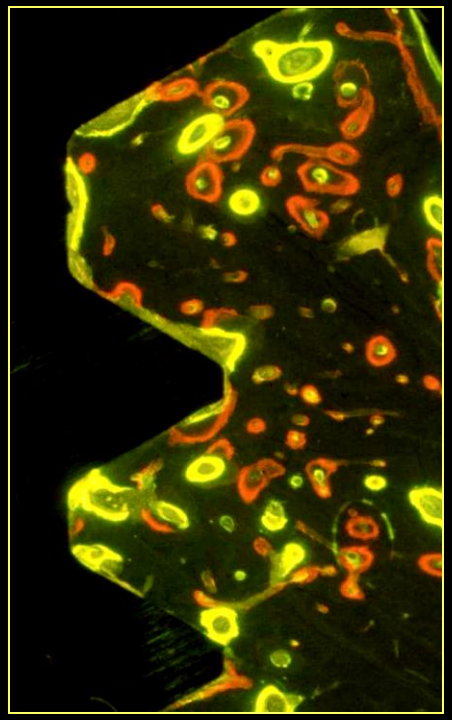
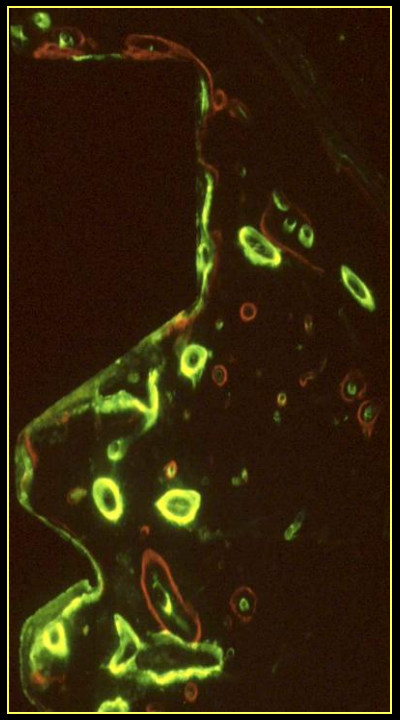
Nishimura et al, 1995

Normal



5200 cGy



5800 cGy

3/12 after implant placement the tissue samples were harvested & were evaluated with light & fluorescent microscopy (Fluorochrome labeling).

A steady decrease in biologic activity at the higher doses.

# RESULTS

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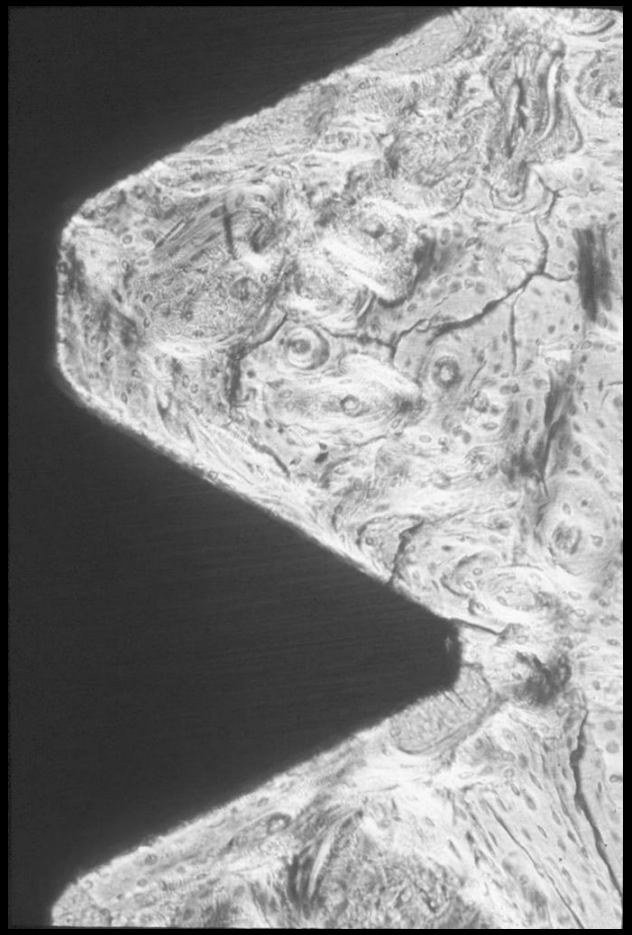
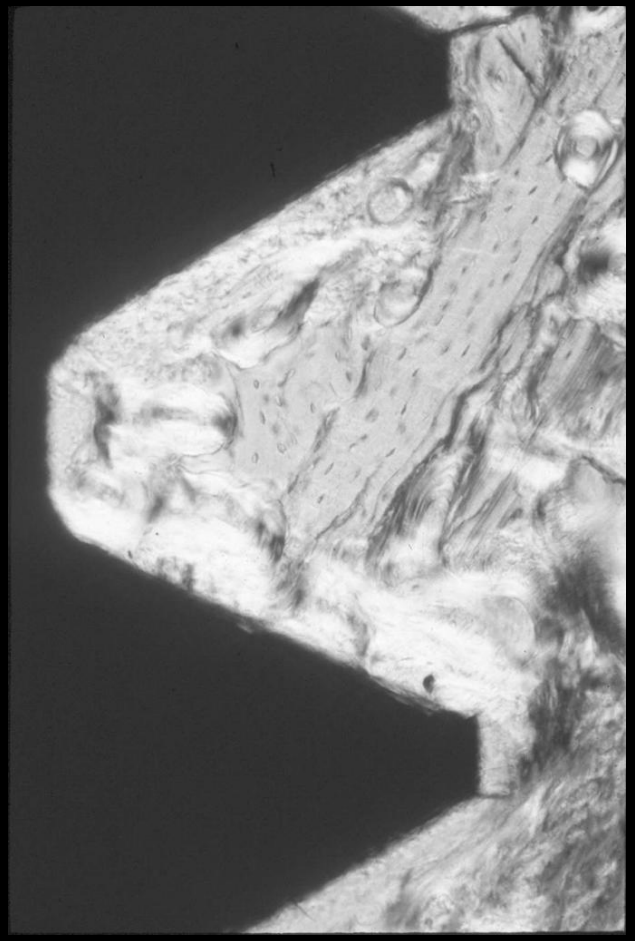
**Normal bone**



**Irradiated bone** Nishimura et al, 1995



lower doses irradiated specimens:
(more woven bone) than normal specimens

# ADDITIONAL ANIMAL STUDIES



- Jacobsson et al (1988) - Reduction in bone formation capacity, increase in bone resorption & reduction in the number of capillaries
- Ohrnell et al (1997) - Bone marrow fibrosis, bone resorption, less bone adjacent to the implants, reduction in bone remodeling capacity
- Hum & Larsen (1990) - Appositional bone index irradiated specimens < nonirradiated specimens

# SUMMARY OF TISSUE CHANGES AFFECTING OSSEOINTEGRATION BASED ON ANIMAL STUDIES



- At higher doses virtually no bone is deposited on the surface. (Anchorage is mechanical)
- At lower doses a greater component of woven bone is seen in the interface
- Death of osteocytes, loss of osteoprogenitor cells & osteoclasts compromises the remodeling of bone at the bone implant interface (alter response to load)

# SUMMARY OF TISSUE CHANGES AFFECTING OSSEOINTEGRATION BASED ON ANIMAL STUDIES



- Poor blood supply in the marrow predisposes to infection, implant loss
- Mandible: doses above 6500 cGy may lead to osteoradionecrosis.
- At lower doses, radiation induced tissue effects significantly reduced the bone appositional index (compromise load bearing)

# Disclaimer

- No animal model truly reflects human biology. Lower form vertebrates (more tissue & vascular tolerant of radiation damage than humans)

- Using the mathematical biologic equivalent of human doses in a single administration or using fewer fractions with large doses, serves a mathematical purpose only (does not guarantee biologically equivalent outcomes)

- Animal studies have yet to be reported assessing the impact of chemoradiation on osseointegration.

# SUMMARY OF TISSUE CHANGES AFFECTING OSSEOINTEGRATION BASED ON ANIMAL STUDIES



## Based on these data, reasonable to assume that:

1. Load carrying capabilities of osseointegrated implants in irradiated bone < nonirradiated bone.

2. Success rates of osseointegrated implants in irradiated bone < nonirradiated bone.

Higher dose = lower success rates.

3. Mandible at higher doses (>6500 cGy with conventional fractionation) osteoradionecrosis risks become significant.

4. Because of compromise of the remodeling apparatus of bone, late failures should be expected

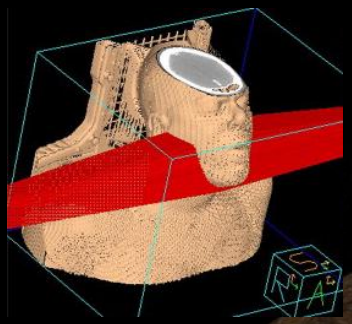
# HUMAN STUDIES



- Yerit et al, 2006
- Roumanas et al, 1997 (Maxilla)
- Roumanas et al, 2002 (Craniofacial sites)
- Nimi et al, 1998 (Maxilla)
- Esser et al, 1997 (Mandible, maxilla)
- Granstrom et al, 1994 (Craniofacial sites)
- Granstrom, 2005 (All sites)

## Yerit et al, 2006 (Data 1990-2003)*

- Patients – 71
- Dose 5000 cGY (Fields?)
- Number of implants - 316
- Implant survival
  - Nonirradiated – 95%
  - Irradiated sites – 72%





***HBO was not used**

# Yerit et al, 2006 (Data 1990-2003)*

Success rates – Irradiated (154 implants)

- 93% at 1 year
- 90% at 2 years
- 84% at 5 years
- 72% at 8 years followup. The survival rates for the 84 implants placed

Success rates - nonirradiated residual mandiblular (84 implants)

- 99% at one year
- 99% at 2 years
- 99% at 5 years
- 95% at 8 years followup

# IMPLANTS IN IRRADIATED MANDIBLE

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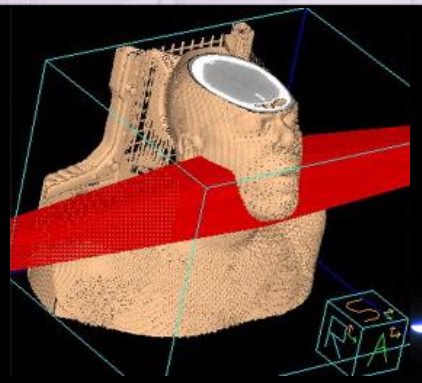

## Esser and Wagner, 1997

Post op dose (CRT) – up to 6000 cGy

Opposed mandibular fields – **Symphysis?**

Pts - 58 (from 1985-1995)

Implants placed – 221

Implants lost – 32

- Before loading - 18
- After loading -17

Success rate 84.2%

## Granstrom, 2005

63% survival rate for 15 implants placed in the mandible

***HBO was not used**

# IMPLANTS IN IRRADIATED MANDIBLE

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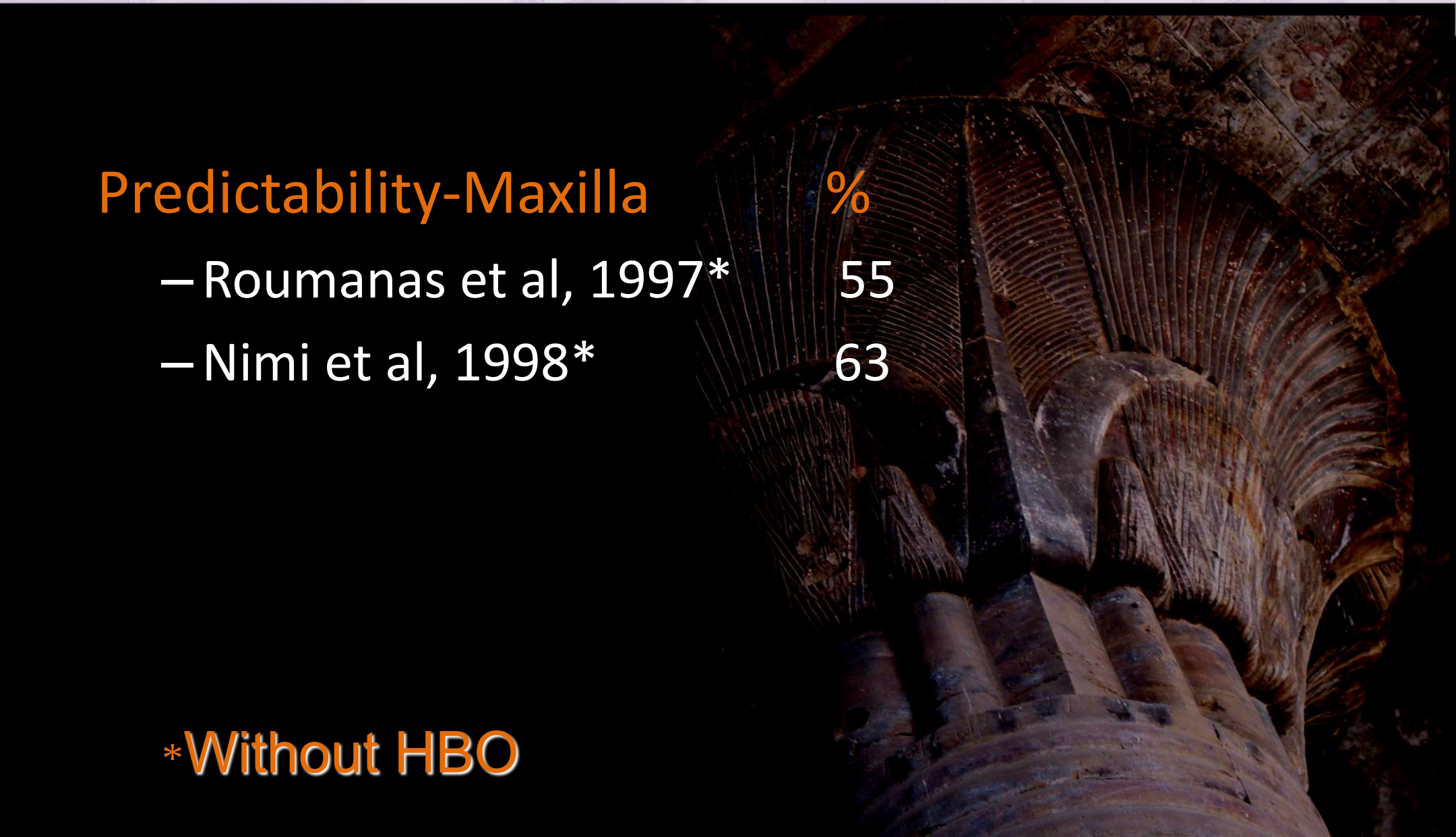
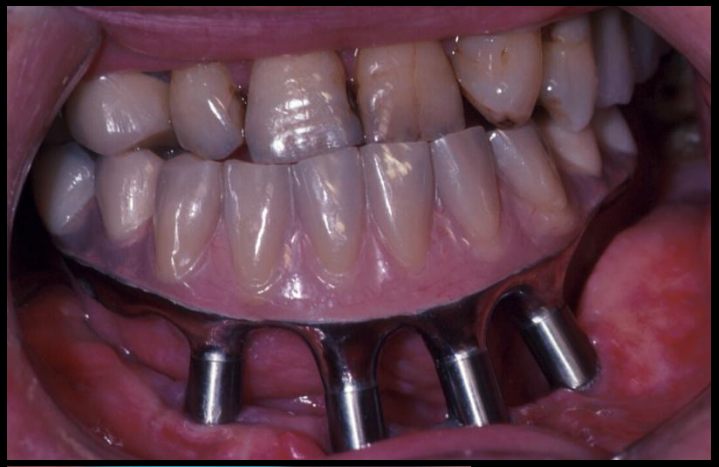


## Predictability-Maxilla %

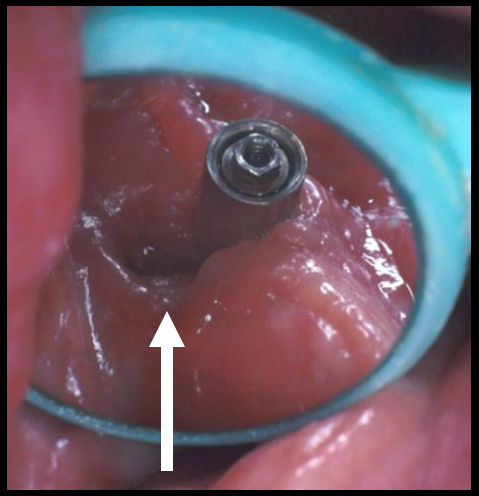
- Roumanas et al, 1997* 55
- Nimi et al, 1998* 63

*Without HBO

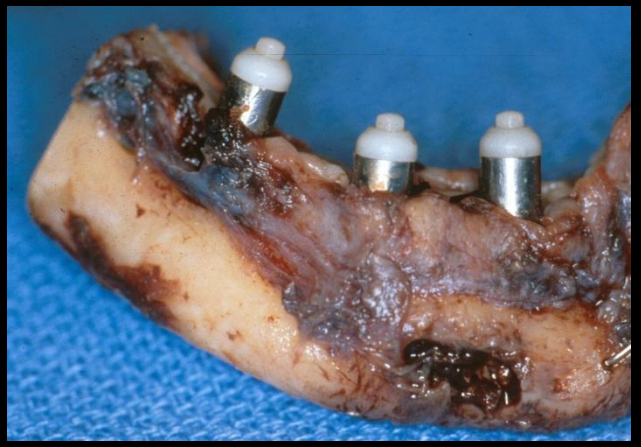
# Osteoradionecrosis



Patient received 6600 cGy (SCC) of the lateral tongue. Implants were placed 3 years post Tx.



36 months after implant placement the patient developed an infection with the left implant.



Eventually, the patient developed an osteoradionecrosis, a pathologic fracture of the mandible & subsequently the mandible was resected.

# Predictability – Mandible

## Role of hyperbaric oxygen

- Data unclear

- Appears to help (Granstrom et al 1993, 2005)

- Success rates appear to be higher & the risk of osteoradionecrosis risk may be reduced (depends on dose to the implant sites)

- 63% survival rate for 15 implants placed in the mandible
- 100% survival rate for 30 implants placed in the mandible with pre-op HBO

# IMPACT OF HBO



## Granstrom 2005 -- All sites – 25 years

| | Implants placed | Implants lost | ORN |
|---|---|---|---|
| Without HBO | 291 | 117 | 5 |
| With HBO | 340 | 29 | 0 |

Does HBO following high doses of RT lead to biologic anchorage Vs mechanical anchorage?

# IMPACT OF HBO

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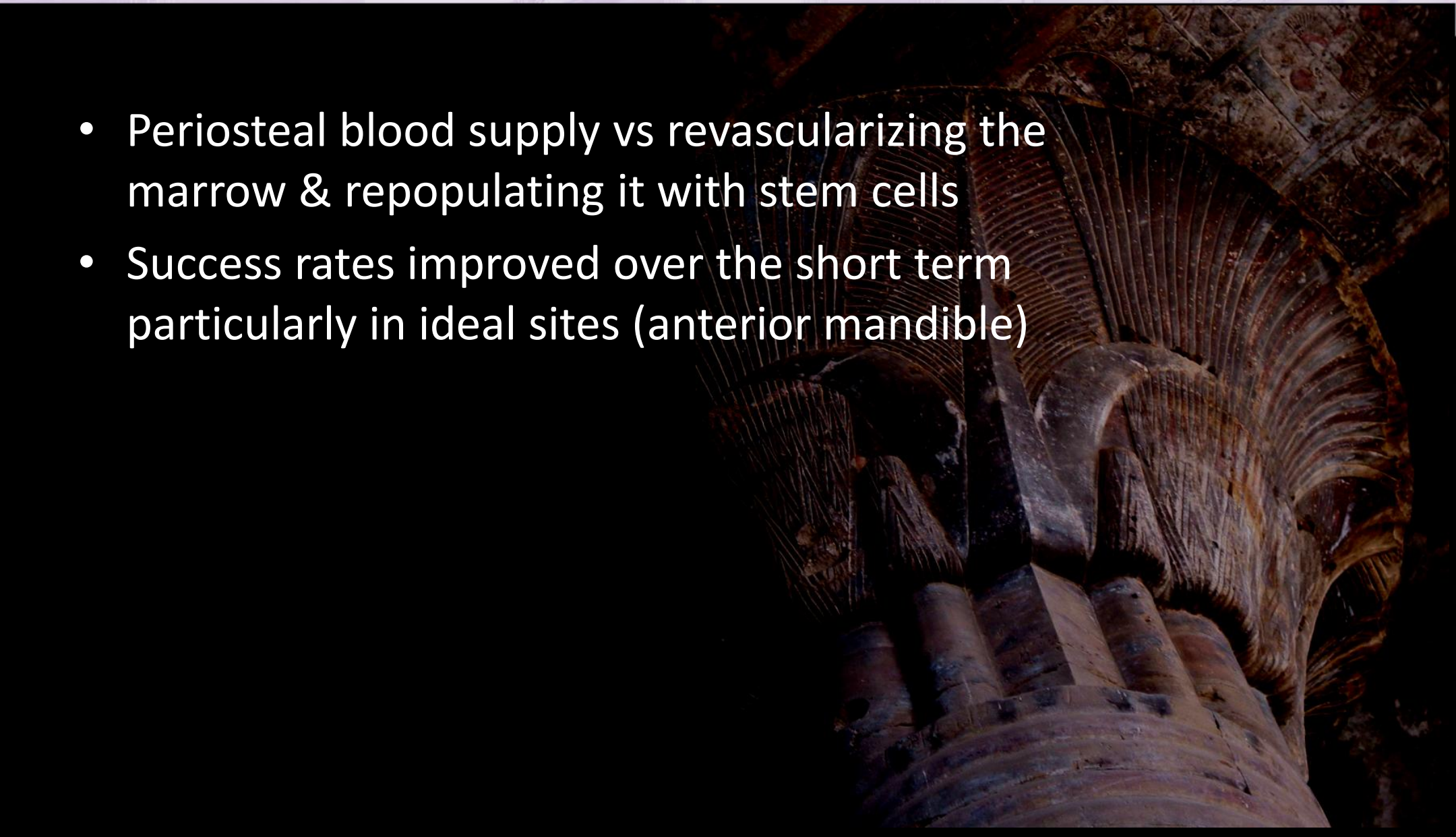
- Periosteal blood supply vs revascularizing the marrow & repopulating it with stem cells
- Success rates improved over the short term particularly in ideal sites (anterior mandible)



## Impact of time – After cancerocial doses of radiation do the tissues recover ?

- At cancericidal doses the irradiated tissues do not recover. With time the irradiated tissues continue to deteriorate & become less vascular, more fibrotic etc.

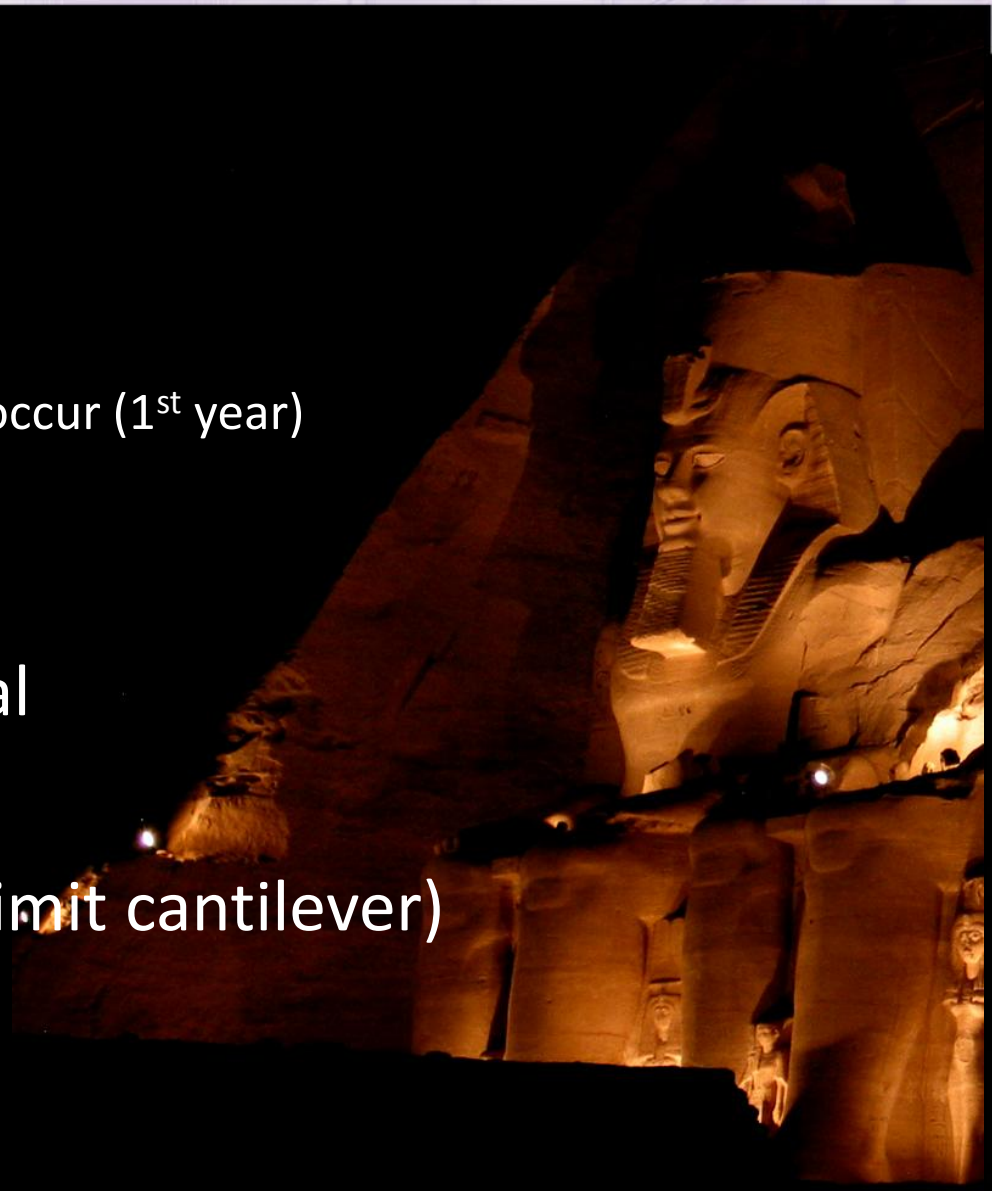
- **The longer the time from radiotherapy the poorer the results (Granstrom, 2005)**

## Recomendations

- Patient selection
  - Edentulous patients
  - Risk - reward
  - Tumor status – 80% of recurrences occur (1st year)
  - Check the dosimetry
- Longer implants
- More implants than the usual
- Favorable engineering

(Splinting, Rigid frameworks, Limit cantilever)

- HBO



# IMPLANTS IN IRRADIATED MANDIBLE



- Dosage < 5500 cGy
  - Implants can be inserted with little or no risk of osteoradionecrosis
  - **Success rates will be probably be lower than normal**
- Dosage ~ 5500-6500 cGy
  - Decision makers (patient factors) e.g. :
    fractionation, tissue responses, clinical findings, dental history etc..
    **Success rates not well documented**
- Dossge > 6500 cGy
  - The risk of osteoradionecrosis becomes significant & implants should not placed unless HBO is given.
    - In such patients the success rates have been in the 70-80% range (possible osteoradionecrosis)

## Clinically significant ("newer implants") in the irradiated patient?

- Probably not.

- The major problem in the irradiated patient is loss of vasculature & with it the loss of osteoprogenitor cells (stem cells) in the marrow.

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