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

IMPLANTS IN IRRADIATED TISSUES
Radiation effects

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

Lamellar bone
- Loss of central artery in Haversian systems
- Death of osteocytes

Root surface

Marrow

Trabecular bone
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?
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.
Conventional radiation therapy

IMRT

3 fields  5 fields  7 fields
Chemoradiation

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

Consequences (particularly with CRT):
More short & long term side effects (mucositis, trismus, osteoradionecrosis
Note the hot spot on anterior mandible (oval)
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.
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)
- Nishimura et al, (1994)
- Ohrnell et al, (1997)
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%

- 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
METHODS – HISTOMORPHOMETRIC CALCULATIONS

- SEM of bone, soft tissue & implant

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

Weinlander et al, 2006
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.

Nishimura et al, 1995
RESULTS

Normal bone

Irradiated bone

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

Nishimura et al, 1995
• 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.
Based on these data, reasonable to assume that:

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


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.
• 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 mandibular (84 implants)

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

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

*Without HBO
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.

Patient received 6600 cGy (SCC) of the lateral tongue. Implants were placed 3 years post Tx.
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
Does HBO following high doses of RT lead to biologic anchorage Vs mechanical anchorage?

Granstrom 2005 -- All sites – 25 years

<table>
<thead>
<tr>
<th></th>
<th>Implants placed</th>
<th>Implants lost</th>
<th>ORN</th>
</tr>
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<tbody>
<tr>
<td>Without HBO</td>
<td>291</td>
<td>117</td>
<td>5</td>
</tr>
<tr>
<td>With HBO</td>
<td>340</td>
<td>29</td>
<td>0</td>
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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 cancerocidal 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
Dosage $\leq 5500$ cGy
- Implants can be inserted with little or no risk of osteoradionecrosis
- Success rates will be probably be lower than normal

Dosage $\sim 5500-6500$ cGy
- Decision makers (patient factors) e.g.: fractionation, tissue responses, clinical findings, dental history etc..
  - Success rates not well documented

Dosage $> 6500$ 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.
• Wang RR, Pillai K, Jones PK. In vitro backscattering from implant material during radiotherapy. 1996. J Prosthet Dent. 75: 626 – 632
• Beumer J, Curtis TA, Nishimura RD. Radiation therapy of head and neck tumors In Beumer J, Curtis TA, Marunick MT, (Eds.), Maxillofacial Rehabilitation: Prosthodontic and Surgical Considerations. Tokyo, IshiyakuEuroAmerica, p. 43-111


