Radiation Therapy for Benign/Rare Conditions

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Disclosures

I have no disclosures to report.

Practice Gap

Patients with refractory symptoms and functional limitations that have not responded to conservative measures or patients deemed in-operable/non-surgical may think there are no other options.

Enhanced multidisciplinary education and collaboration offers the opportunity to provide these patients with alternative treatment options and improved outcomes.

Learning Objectives

1. Describe the basic principles of radiation physics and radiobiology relevant to benign/rare disease.
2. Explain the anti-inflammatory mechanisms and rationale for low-dose radiation therapy.
3. Identify benign/rare conditions that may benefit from radiation therapy (e.g. tumor induced osteomalacia and osteoarthritis).
4. Discuss treatment approaches and expected outcomes for selected rare/benign conditions.
5. Recognize the potential risks, benefits, and patient-selection considerations when using radiation therapy for rare/benign disease.

Expected Outcome

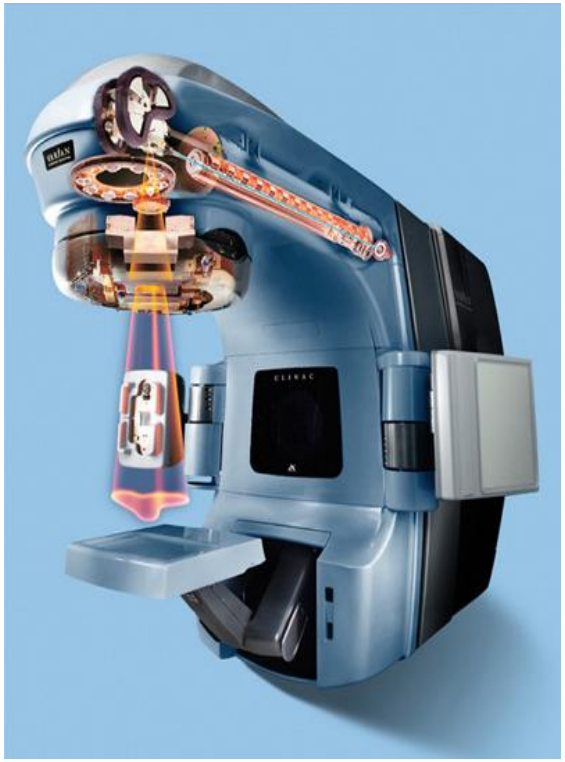
- Radiation therapy should be no longer thought of as an oncologic modality alone.
- Multidisciplinary collaboration can provide more options for patients with the end goal of improved outcomes.

2026: A Big Year for Radiation Oncology

NON-MALIGNANT DISEASE	Date Published	Publication	Narrative & Rating Table	Evidence Table	Literature Search
Low Dose Radiotherapy for the Treatment of Inflammatory Periarticular Disorders	September 2026	AJCO			
Radiotherapy for the Treatment of Peyronie Disease (Induratio Penis Plastica)	September 2026	AJCO			
Adjuvant Radiotherapy for the Prevention of Recurrent Hypertrophic Scars/Keloids	August 2026	AJCO			
Use of Radiation in the Prevention and Treatment of Heterotopic Ossification	July 2026	AJCO			
Low-Dose Radiotherapy for Treatment of Osteoarthritis	May 2026	AJCO			

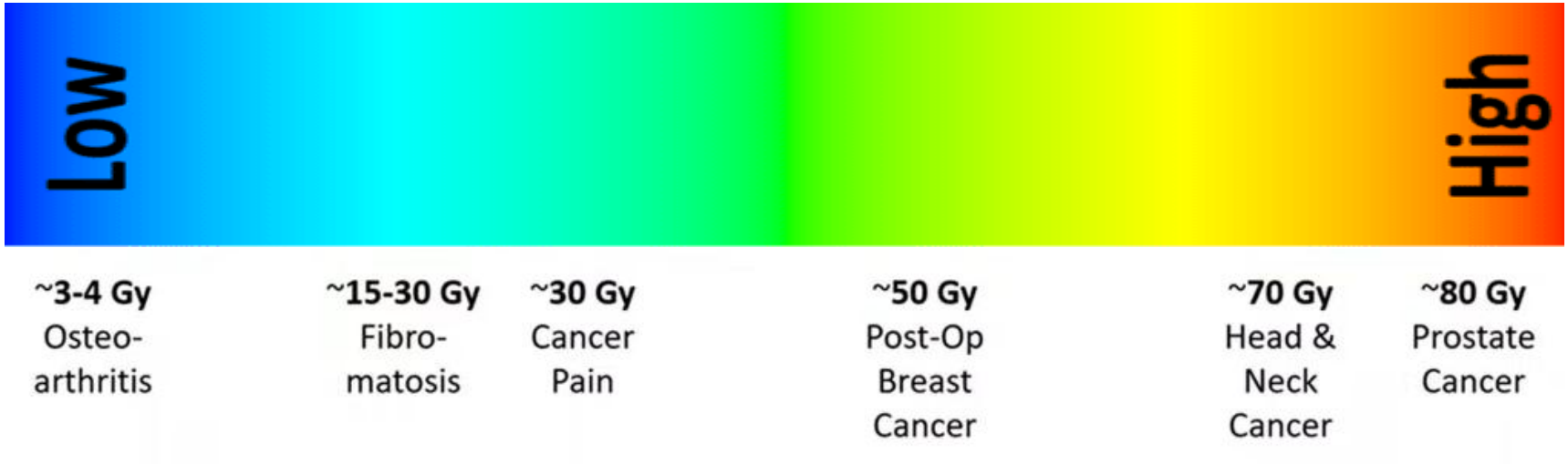
Radiation Basics – Delivery Systems

- External Beam (Majority):
  - Gamma Rays: Emitted from nucleus of atom of radioactive element (e.g. Co-60)
  - X-Rays: Produced by a linear accelerator by accelerating electrons that hit a metal target (Bremsstrahlung)
  - Electrons: Accelerated electrons from linear accelerator delivered in absence of metal target
- Brachytherapy:
  - Placement of radioactive sources within a patient (temporary or permanent)
  - Idea to deliver dose from inside out (deposit majority of dose locally)
- Radiopharmaceuticals:
  - Targeted compounds containing radioactive elements for treatment/imaging



Source: Varian Medical Systems

Radiobiology Basics I

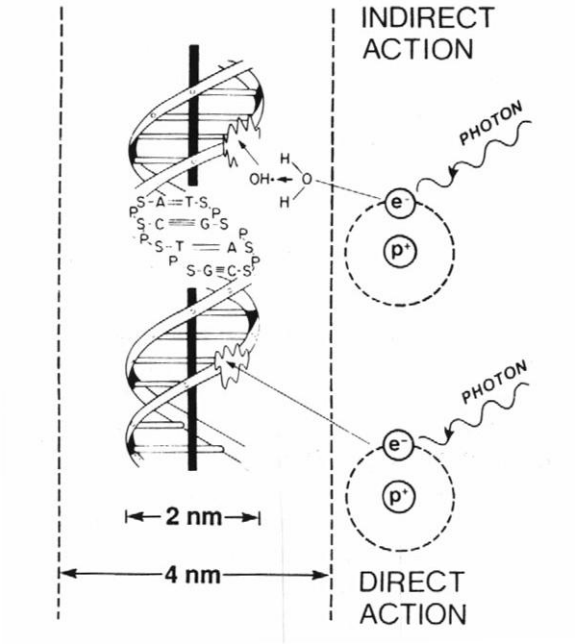


High Doses of Radiation: Cure Cancer/Ablation

Medium Doses of Radiation: Palliation of Pain

Low Doses of Radiation: Mediate inflammation & Fibromatosis

Radiobiological Basics II



- X-Rays interact in tissue, creating secondary electrons
- These electrons either:
  - Damage DNA of cells directly or,
  - Create free radicals that bind to and damage DNA
- Leads to cell death (by mitotic catastrophe)

- Both Normal & Cancer cells can be effected by radiation but cancer cells generally have an impaired repair pathway, leading to cell death

Radiobiological Basics III – 4 R's of Radiation

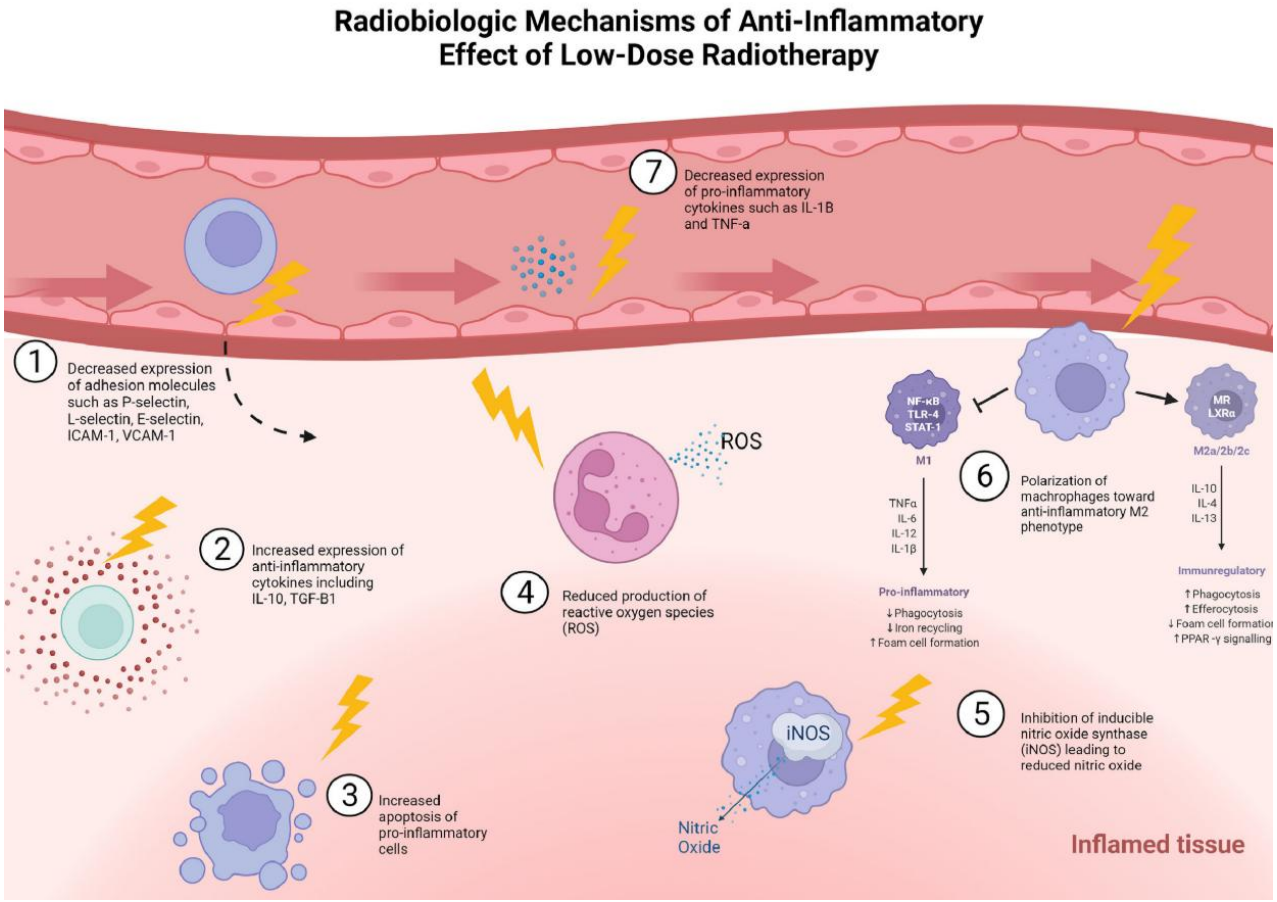
- Four major factors believed to affect tissue response to fractionated Radiation
- **Repopulation:** Regrowth of cells between Radiation Treatments

- **Redistribution:** Certain phases of cell cycle (M, G2) are more radiosensitive than others. Fractionated treatments means each cell is likely to be treated at different stages of cell cycle, ensuring irradiation during most sensitive phase

- **Repair:** Cells can repair sublethal damage between fractions

- **Reoxygenation:** Hypoxic cells can reoxygenate, making them more sensitive to radiation (more oxygen, more free radical production, more damage)

Mechanism of Anti-Inflammatory Response



Dove et al (2022): International Journal of Radiation Oncology

Radiation Therapy Overview – Patient Experience

- **Patient Consult (30mins-1hr)**
- **CT Simulation (30mins-1hr)**
  - Patient put in treatment position +/- setup marks
  - Immobilization devices & treatment aids constructed
  - Area to be treated is scanned
- **Radiation Planning (~hours-days)**
  - Target area delineated
  - Adjacent normal structures delineated
  - MD provides requested Dose & normal dose tolerances
  - Treatment fields added & Radiation shaped to treat target and minimize dose to other structures
- **Treatment Delivery (10-20mins)**
  - Patient placed in treatment position and kV images (x-rays/CBCT) taken to verify position
  - Radiation delivered: Painless experience, outpatient (unless admitted)
  - Repeated daily, q.o.d or 1-2 times a week

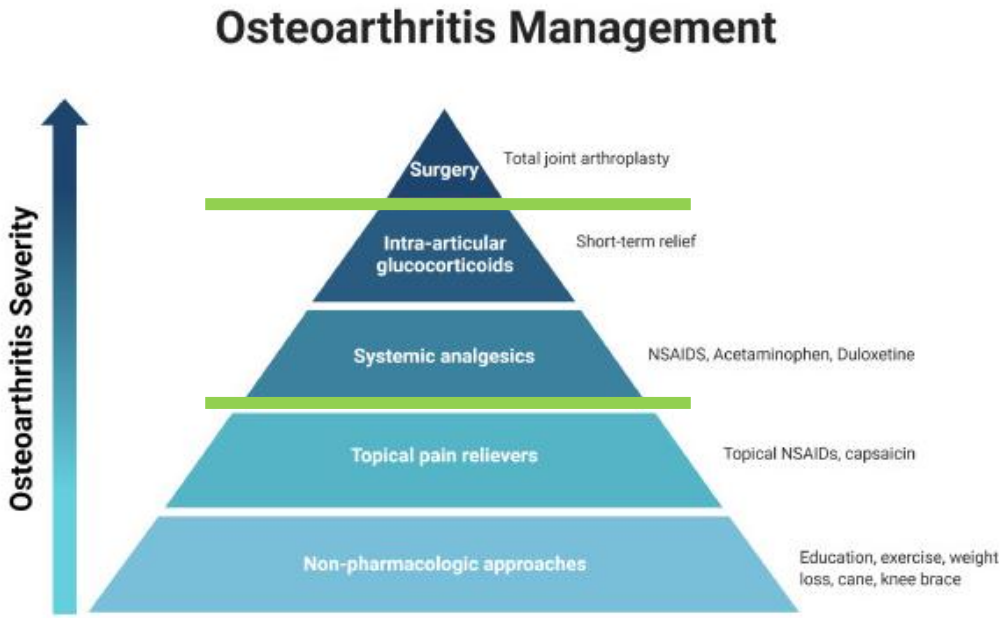
(Non-Exhaustive) List of Benign Conditions Treated with RT

- Although Radiation Therapy has historically been thought of an oncologic treatment, the paradigm is expanding. Roughly 1/3 of all RT treatments in Germany now are for ***Benign*** indications

Trigeminal Neuralgia	**Heterotopic Bone Ossification**
Acoustic Neuromas/Schwannomas	**Tumor Induced Osteomalacia**
Meningiomas	**Graves Disease**
Essential Tremors/Parkinsons	**Osteoarthritis**
Arteriovenous Malformations	**Plantar Fasciitis**
Refractory Ventricular Tachycardia	**Tendinitis**
Keloids	**Ledderhose Disease**
Paragangliomas	**Dupuytren's Contracture**

Low-Dose RT for Osteoarthritis I

- Typical uses for RT utilize levels of radiation (1.8Gy - > 30Gy/fx) for antiproliferative properties.
- Low doses (<1Gy/fx) have been shown to have strong anti-inflammatory response
- **Osteoarthritis** affects 1 in 7 US adults and often identified as **2nd most expensive** health



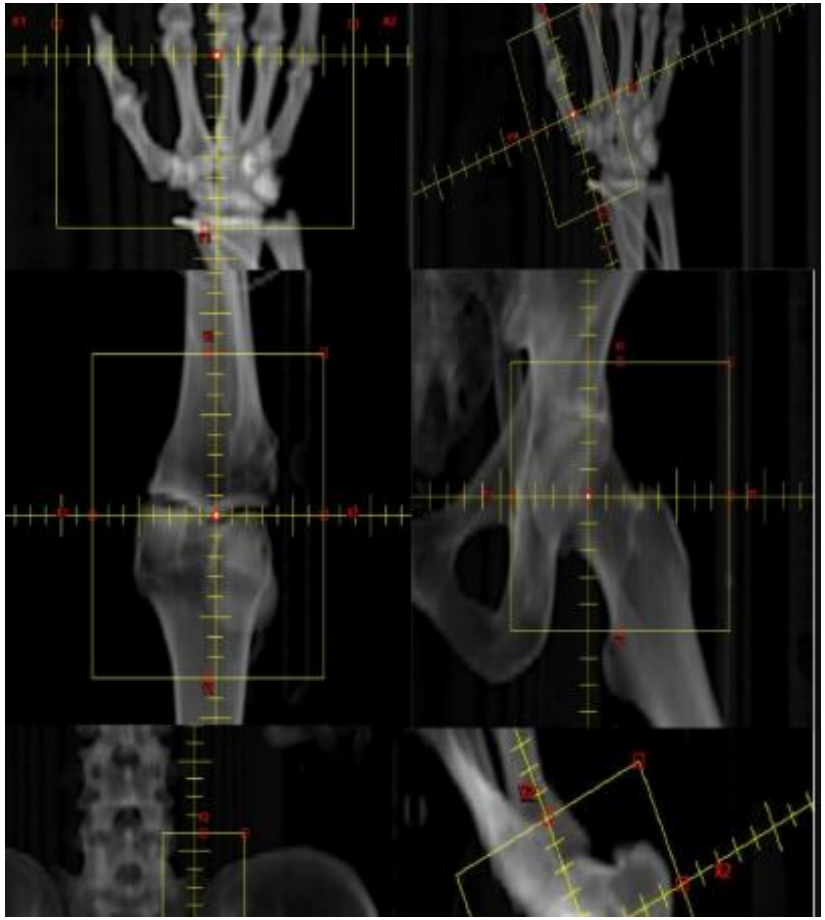
Has been treated in US previously but fell out of favor to pharmaceuticals, >85% of European physicians utilizing RT for OA (Leer et al)

GCG-BD 2018 update has shown symptomatic pain relief of 63-90% with virtually no side effects

Multiple studies suggest increased QOL and reduced progression

Low-Dose RT for Osteoarthritis II

- - Typically accepted dose fractionation is 0.5Gy for 6 fractions. 3Gy total. Delivered twice a week
- - Often treated with single or parallel opposed fields ***Simple Plans!***
- - 6MV for thinner joints (i.e. hand) +/- 5mm bolus, 10MV or higher for joints such as the hip
- - Fingernail shields often placed to protect nailbeds.
- - CT based planning allows more complex distributions if needed.
- - Target includes joint, cartilage, surrounding bursa, muscular insertion sites and surrounding soft tissue structures
- 2018 DEGRO guidelines suggest for patients > 40 years old to reduce secondary malignancy chance



Radiation for Tumor-Induced Osteomalacia I

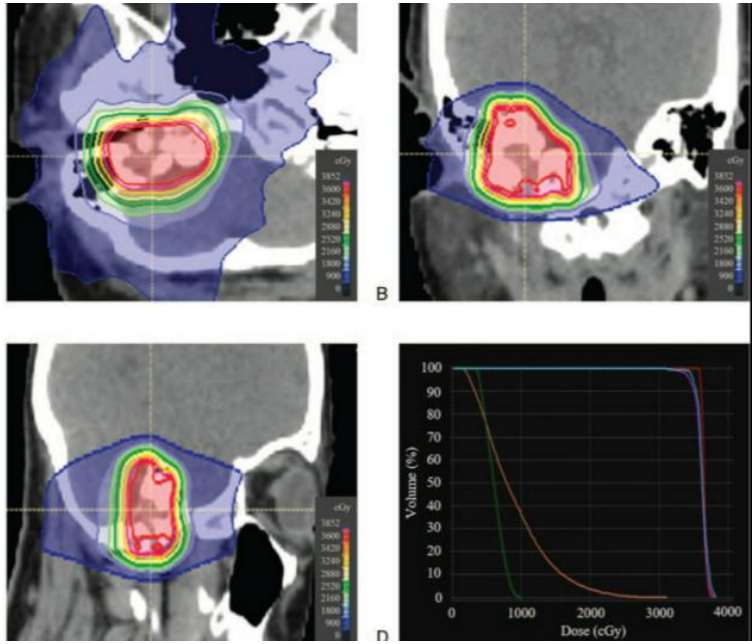
- Osteomalacia is a weakening of the bones due to low levels of vitamins/minerals including phosphorus.
- Uncontrolled FGF23 (phosphate regulating hormone) production caused by benign phosphaturic mesenchymal tumors (PMTs) that can exist in bone or connective tissue

- **Surgery** is recognized as only true definitive intervention but International Osteoporosis Foundation recognize ablative RT as an option to treat potentially unresectable PMTs to address osteomalacia.

- Limited literature, but multiple successful case studies.

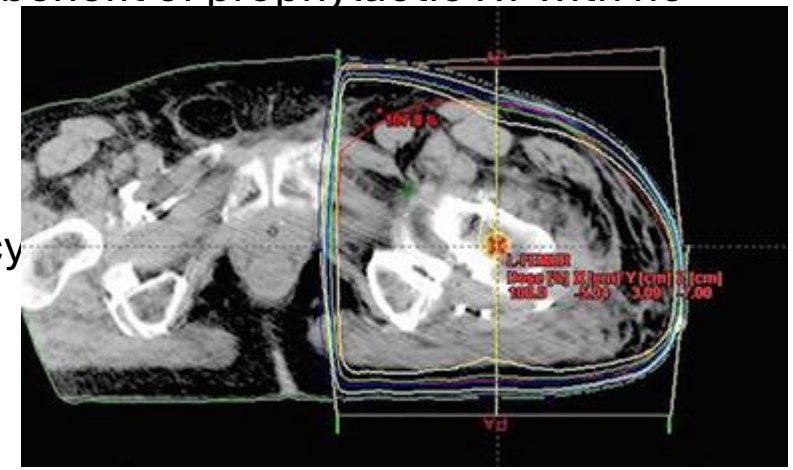
Radiation for Tumor-Induced Osteomalacia II

- Tarasova et al (2013):
  - 67 year old female treated with 60Gy over 6 weeks.
  - Lt Frontal Mass that presented as meningioma
  - CT, MRI, Osteoscan & FDG PET used to localize
  - BMD increased 50% and FGF23 decreased to normal levels after 1 year of RT
- Takaoka et al (2021):
  - Pain in Hip & Femurs, hearing loss in Rt Ear
  - Mass in middle ear discovered. 36Gy delivered in 10 fractions along with activated vitamin D
  - Lab values recovered, near-complete resolution at 5 years
- Massacessi et al (2021):
  - Rt Frontal Sinus ossifying fibromyxoid tumor recurrence
  - Multiple endoscopic resections (3) followed by 60Gy in 30 fractions to Tumor Bed
  - 5 years free from tumor relapse, TIO progression or radiation induced side effects



Radiation for Heterotopic Bone Ossification

- Single treatment of 7-10Gy as a prophylactic prevention of heterotopic bone ossification (abnormal growth in soft tissues) following Hip Arthroplasty or Trauma.
- Can be delivered either up to 24 hours before surgery, or within 72 hours of surgery.
- Bang et al (2025) performed a systematic review, published in PRO that found a **clinically, but not statistically**, significant benefit of prophylactic RT with no adverse effects
- Radiation targets mesenchymal stem cells before differentiation
- Literature suggests similar or superior efficacy to NSAIDs (although recent review claims NSAIDs > RT for high risk)



Source:Georhakopoulos et al (2020) Orthop Rev

Risks/Adverse Effects

- Radiation Induced Malignancies (stochastic), HOWEVER:
- Models suggest for 6Gy total LDRT dose to knee increases lifetime risk for induced tumor by 0.03% for 70 year old, 0.07% for 50 year old and 0.2% for treatment at 25 years old (Jansen et al, Radiation Oncology, 2005)
- Mucke et al (2020), report **no known secondary malignancy** from LDRT for OA

- Skin Erythema can occur for larger fractional doses, although very low incidence (<0.1%) for Low Dose RT.

- Radiation Therapy for malignant conditions can lead to osteoporosis & insufficiency fractures
- Radiation can decrease osteoblast function
- Incidence rate dependent on fractional dose size and patient related factors
- Plans can be optimized to reduce dose to bone matrix.

Summary

- Radiation Therapy should no longer be thought of an oncologic modality alone
- Radiation Therapy has shown to be an effective Anti-Inflammatory modality
- Opportunities exist to provide palliation and relief for a variety of Muscolskeletal conditions alongside the more established benign use cases
- Multidisciplinary collaboration and education can provide more avenues for patients and improve outcomes.
- LDRT has been shown to have minimal adverse effects, although use in patients >40 years old recommended for reduction of potential induced malignancy
    - Side effects of higher doses are well established through oncologic treatments
- USA behind Europe in utilizing RT for these conditions

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