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COLLEGIUM MEDICUM

# Side effects of radiotherapy.

Paweł Potocki, MD

Jagiellonian University Medical College

Kraków University Hospital

Department of Clinical Oncology

*ppotocki@su.krakow.pl*

# Basics

## Techniques:

- external beam RT
- brachytherapy
- systemic isotope therapy
  - classical
  - targeted

## Radiation type:

- photons
  - **X rays**
  - gamma rays
- particles
  - **electrons**
  - nucleons (protons, fast neutrons)
  - ions (ie carbon, alpha particles)

# Theory

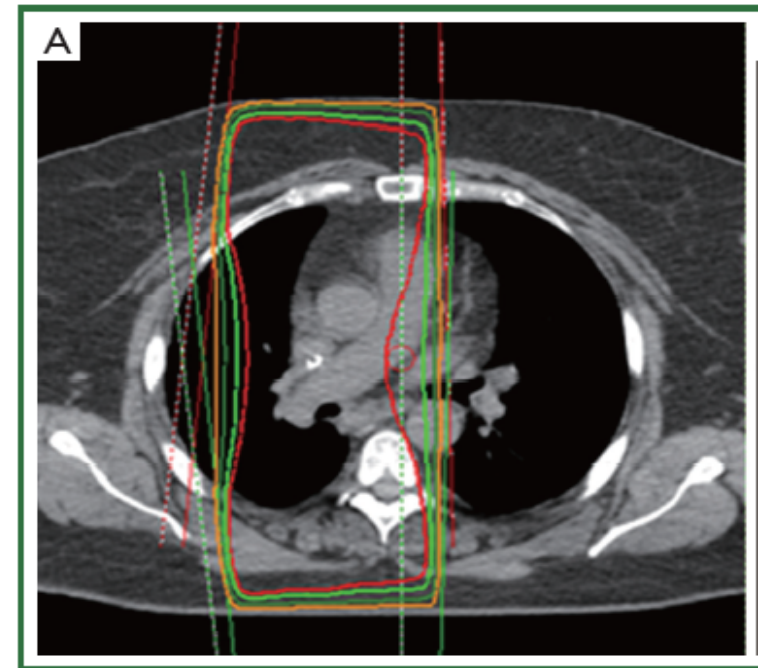
Factors contributing to RT side effects (micro):

- beam energy
- total dose deposited (early)
- fraction dose (late)
- number of ionisation events (tissue radioopacity)
- efficiency of reactive species production
  - oxygenation
  - hydration
- DNA damage (chromatine density)
- repair potential

# Theory

Factors contributing to RT side effects (macro):

- localization of target volume (superficial vs deep)
- proximity of critical (radiosensitive) organs
- dose distribution (isodose density)
- radiosensitizers
- comorbidities



# Theory

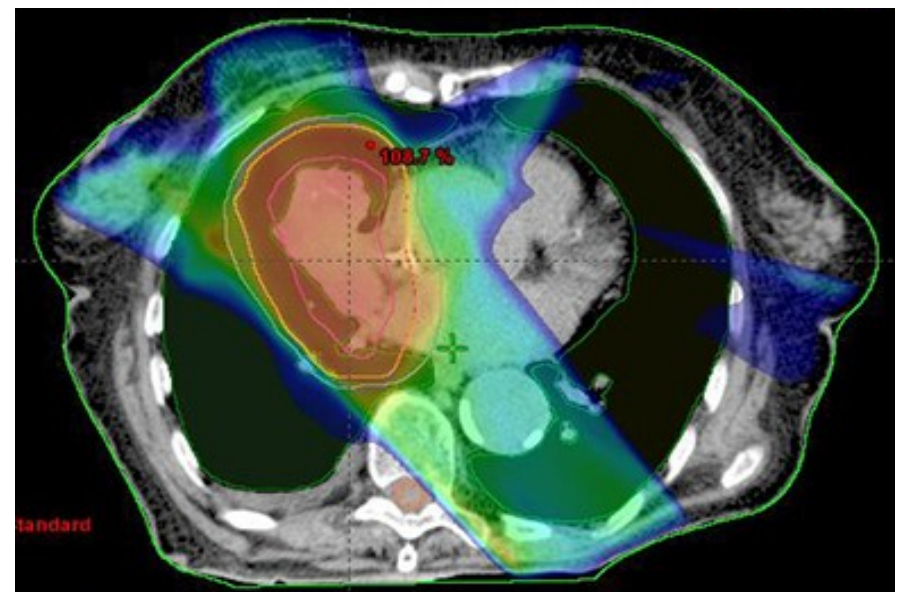
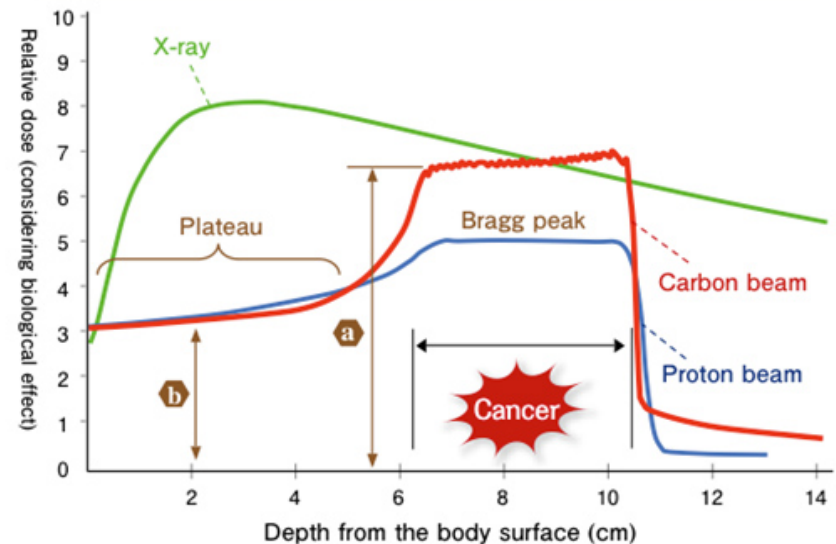
- Local treatment = localized toxicities.
- Exceptions:
  - fatigue
  - cytopenia
  - systemic consequences of RT induced organ failure

# Theory

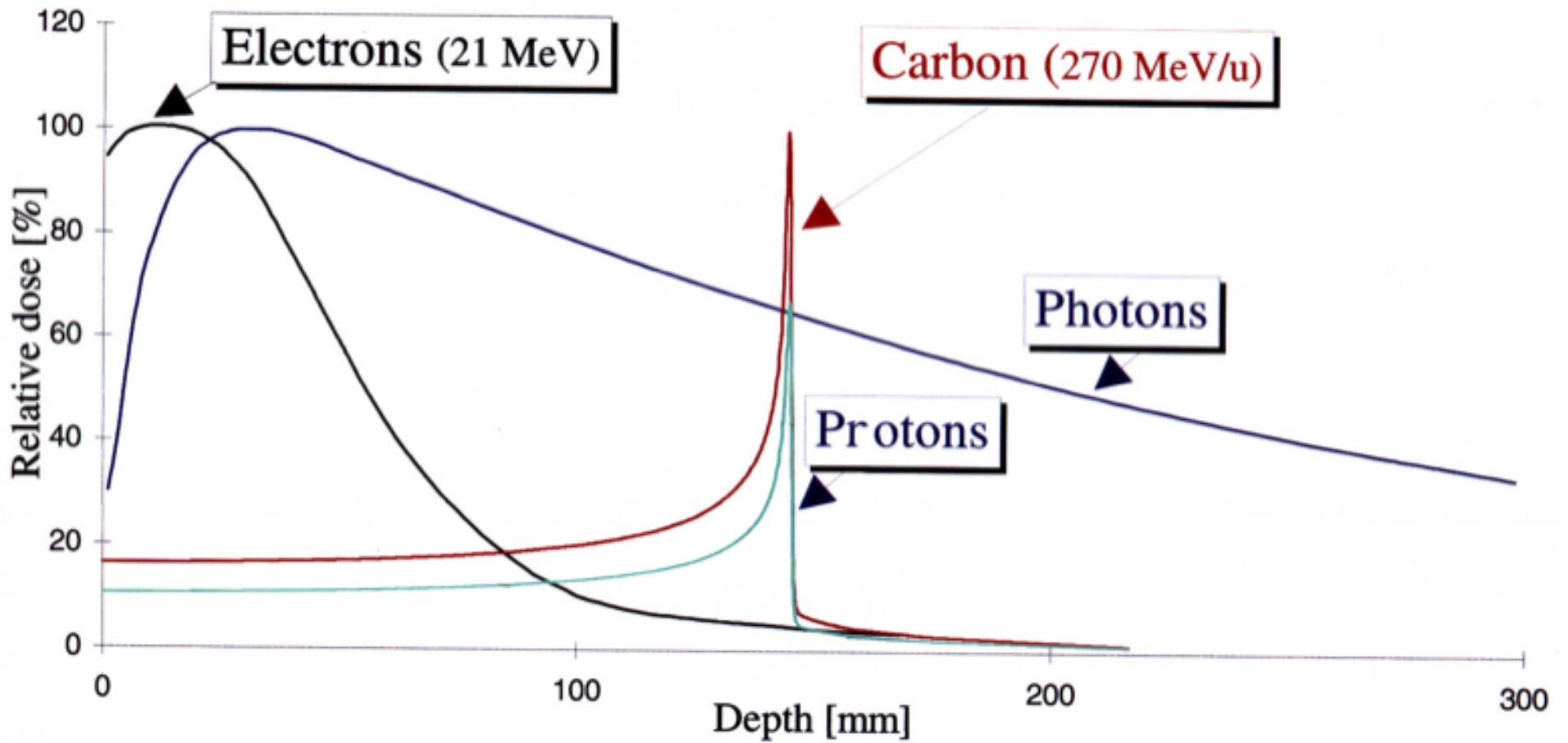
RT side effects location depend on:

- beam energy – absorption curve
  - higher energy photons deposit their energy deeper
  - at similar energies protons deposit their energy deeper than X-photons which in turn reach deeper than electrons
- beam path – amount of energy absorbed and scattered by tissues situated closer to beam source
- areas of beam intersections

When the ratios of peak to plateau (a/b) are compared while considering biological effect, the carbon beam has the largest value.



# Theory



# Radical vs palliative dosing

- Radical RT:
  - high total dose (aggressive treatment)
  - low fractional dose (to mitigate late toxicities)
  - ie. 30 daily fractions of 2Gy daily.
- Palliative RT:
  - lower total dose
  - less need for low fractional dose
  - ie. 1 fraction of 8Gy.



# Tissue dependent tolerance

## Tolerance Dose

**TD 5/5 – TD 50/5 Gy**

(at dose rate of 2Gy/fraction)

Dose at which there is a  
5 to 50% chance of cell death

### High Sensitivity

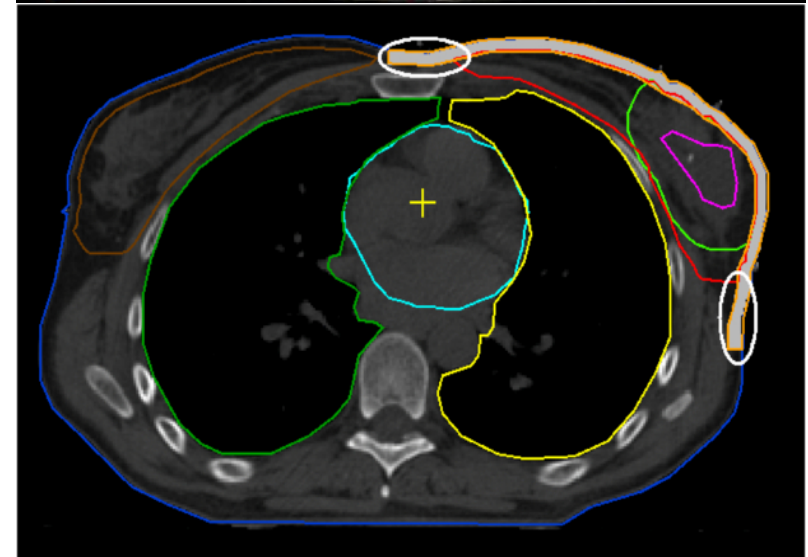
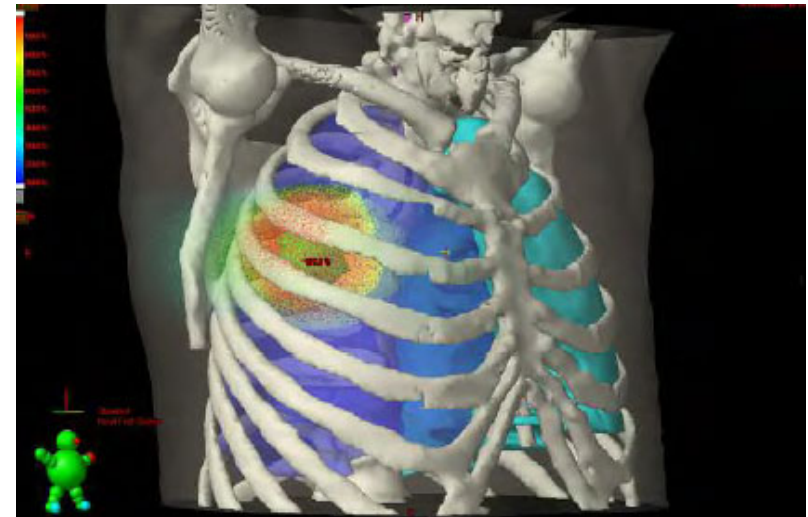
(high rate of cell division but  
stem cells present so capable of  
repair)

### Intermediate Sensitivity

### Low Sensitivity

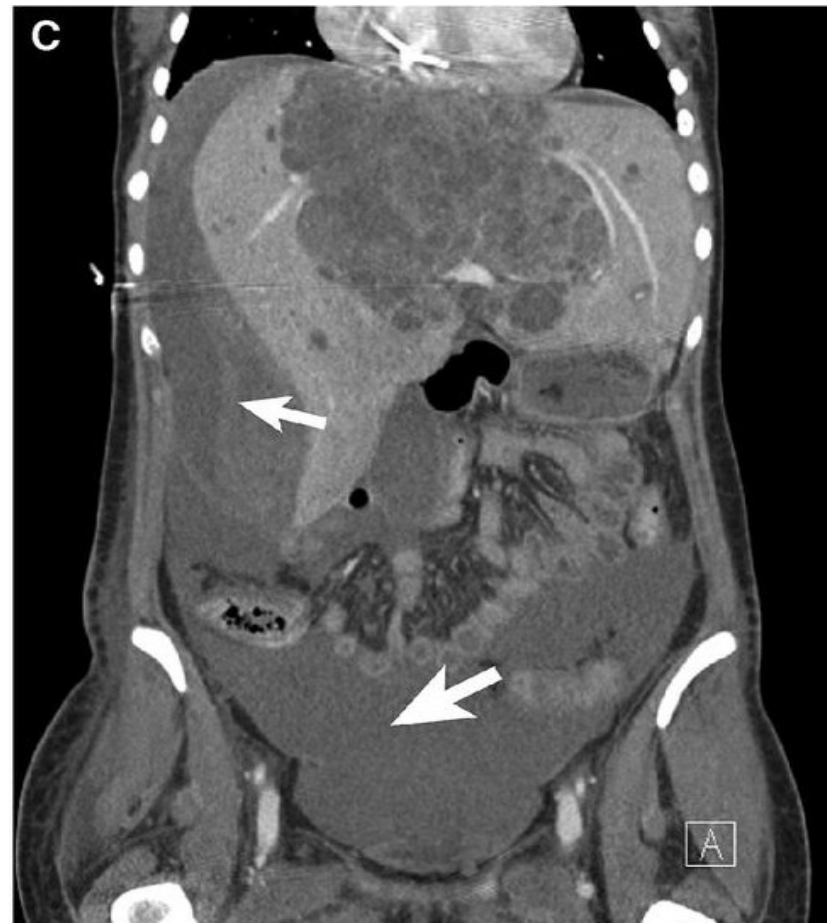
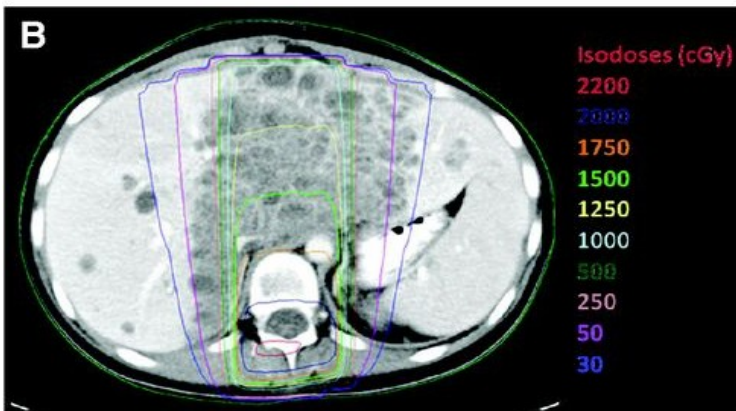
(low rate of cell division)

Testes	1 - 2
Ovary	6 - 10
Eye (lens)	6 - 12
Lung	20 - 30
Kidney	20 - 30
Skin	30 - 40
Liver	35 - 40
Thyroid	30 - 40
Heart	40 - 50
Lymphoid Tissue	40 - 50
Bone Marrow	40 - 50
Gastrointestinal	40 - 50
Peripheral nerve	65 - 75
Mucosa	65 - 75
Connective tissue	50 - 60
Brain and spinal cord	30 - 50
Bone and cartilage	> 70
Muscle	> 70



# Tissue dependent tolerance

- Exceeding the tolerance dose will result in necrosis and loss of function
- Necrosis may also occur due to antyangiogenic and metabolic effects of RT, as well as due to interactions with certain drugs.



# Radiosensitizing agents

- chemoradiotherapy application:

- lung cancer
- colon cancer
- head and neck cancer
- gastric cancer
- pancreatic cancer
- brain malignancies

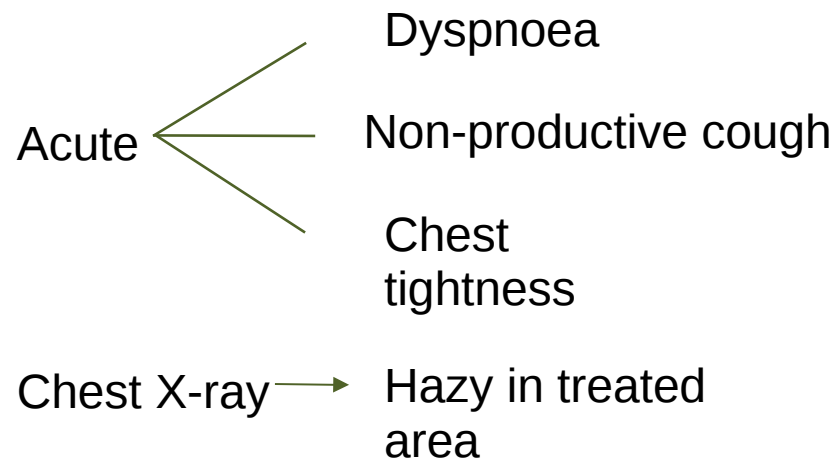
agents used:

- 5-fluorouracil, capecytabine
- cisplatin, carboplatin
- temozolomide
- mitomycin
- gemcytabine

# RT AE to Lung Tissue

- Inflammatory reaction in lung tissue (may occur up to 6 weeks after therapy)

## Radiation Pneumonitis



Treat with:

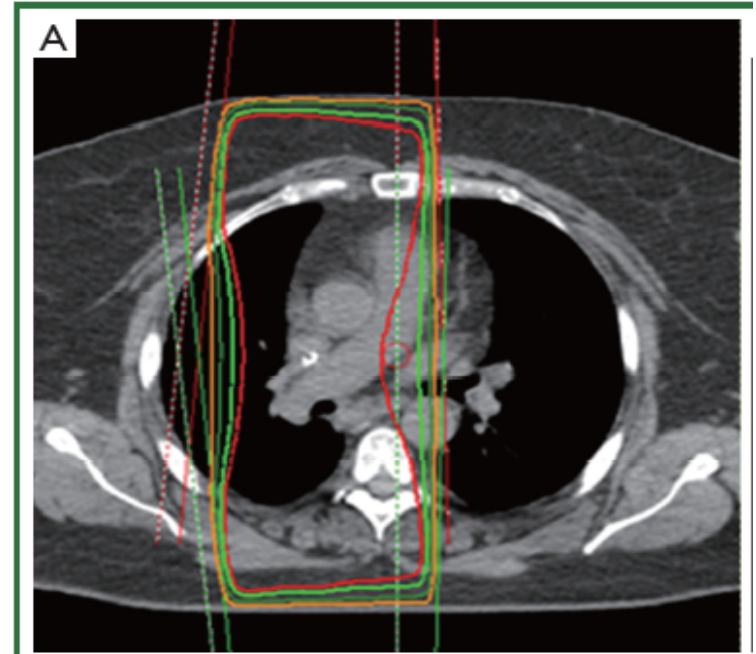
- Steroids (anti-inflammatory)
- Antibiotics (to prevent infection)

Consequence depends on volume of lung affected and region of lung

# RT AE to Lung Tissue

## **Pulmonary Fibrosis**

- Usually occurs after radiotherapy in treated volume.
- May cause long term dyspnoea.
- Degree depends on:
  - pre-existing lung disease
  - secondary infection
  - severity of pneumonitis
  - total dose and rate of radiation
- Symptoms: chronic cough, diminished respiratory reserve



# RT AE to heart

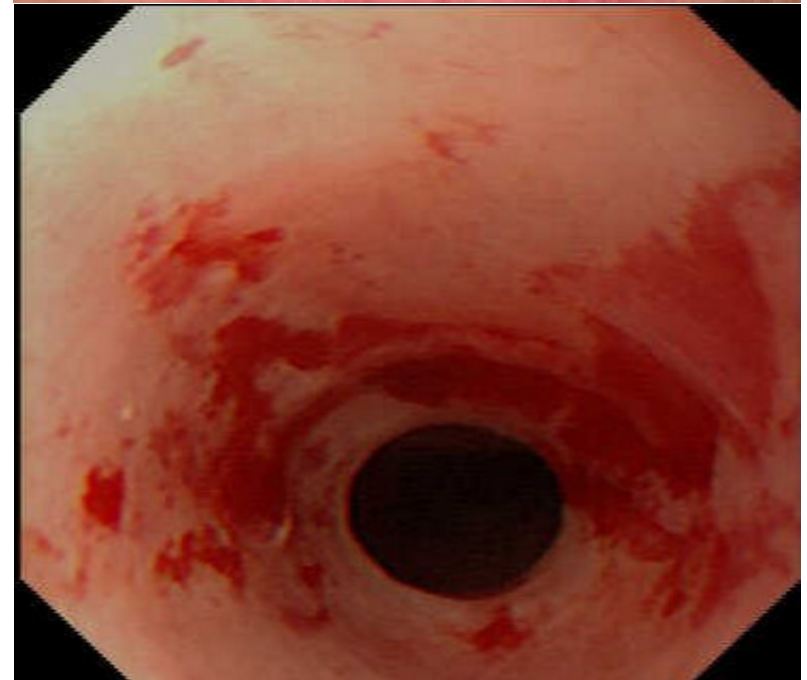
- Loss of systolic and diastolic function
- Risk factors:
  - high total dose
  - preexisting heart failure
  - Treatment with cardiotoxic agents (anthracyclins)
- Probable after:
  - lung cancer radical RT
  - breast cancer adjuvant RT
  - lymphoma consolidating RT
  - esophageal cancer radical RT

# RT AE to heart

- Prevention:
  - risk factors awareness, careful qualification
  - careful RT plan to restrict doses received by heart
  - new RT modalities (IMRT, protons, carbon ions) for optimal dose distribution
- Treatment – symptomatic

# RT AE to upper GI mucosa

- Acute radiation reaction: mucosa stem cells death
- No immediate effect
- Lesions occur through normal wear of superficial layer
- Subsequent submucosa inflammation
- Swelling, pain, infections



**GRADE 1**



**GRADE 2**



**GRADE 3**



**GRADE 4**





# RT AE to upper GI mucosa

- Symptoms:

- dysphagia,
- severe pain,
- dryness



- Treatment:

- infection prophylaxis/ treatment
- analgesics
- fluid, diet
- dryness prevention
- local anaesthetic lavage
- recombinant keratinocyte growth factor



# RT AE to Head & Neck

- Salivary glands

Radiation sensitive – possible loss of function resulting in xerostomia and chronic mucositis.

- Thyroid gland

Radiation sensitive – possible loss of function resulting in hypothyroidism.

- Eyes and optic nerves

Radiation sensitive – possible loss of function due to retinal necrosis, optic nerve necrosis or RT induced cataract.

# RT AE to skin

Usually at doses used  
in radical treatment

Natural course:

- 14 days - hair loss
- 21 days - redness and swelling, gradually progressing
- 4-5 weeks - dry desquamation, at this point - possible infections

Treatment:

- antiseptics
- soothing cream
- non-metal-containing baby powder
- cool air

# RT AE to skin

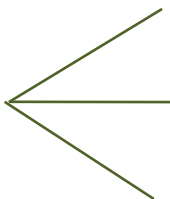
Typical resolvemement:

- 1 week – skin regeneration occurring
- 2 weeks – sweat glands regain function
- 4-5 weeks – complete recovery, possible residual hyperpigmentation
- 8-10 weeks – hair growth restarts



# RT AE to lower GI mucosa

Radiation colitis (may occur up to 6 weeks after therapy)

Acute  tenesmus, pain  
diarrhea  
mucous discharge,  
sometimes bleeding

Treat with:

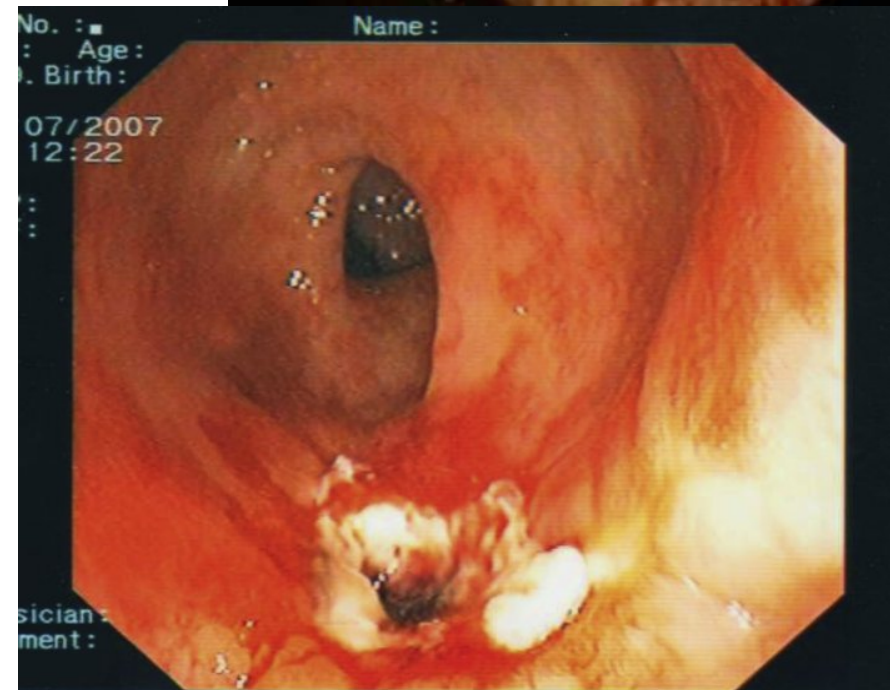
- topical steroids, mesalazine, sulfosalazine (ant inflammatory)
- loperamide
- somatostatin analogs

Possible perforation or massive bleeding

# RT AE to lower GI mucosa

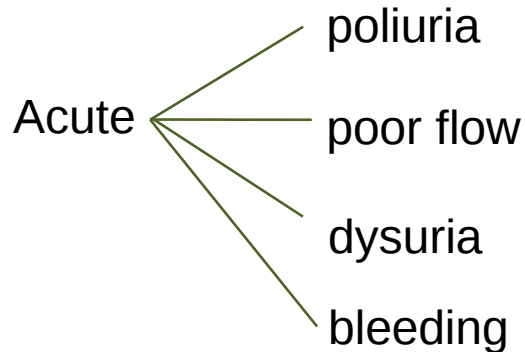
Late toxicity radiation proctitis:

- usually occurs 3-6 months after RT
- may cause long term bowel symptoms:
  - pain
  - constipation
- degree depends on:
  - volume of normal tissue
  - previous medical conditions
  - total dose and fractionation



# RT AE to urinary mucosa

- Inflammatory reaction in bladder & urethra (may occur up to 6 weeks after therapy)



- Treat with analgesics and drugs to improve flow

## Late toxicity

Usually occurs

3-6 months after RT

May cause long  
term bladder  
symptoms

Degree depends on:

- Volume of normal tissue
- Total dose and fractionation

# RT AE to bone tissue

- Osteoradionecrosis:
  - typical localizations: mandible, femur head
  - etiopathology – mainly microangiopathic
  - risk factors: high dose, risk factors for microangiopathy, preexisting osteopenia, preexisting local inflammation (ie periodontal)
  - symptoms: teeth loss, pain, necrosis of adjacent skin/mucosa often revealing the bone, fractures
  - prevention: careful RT plan
  - treatment – symptomatic, condition notoriously hard to manage.



RT AE

Questions?



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# Thank You

**Paweł Potocki, MD**

Jagiellonian University Medical College

Kraków University Hospital

Department of Clinical Oncology

*[ppotocki@su.krakow.pl](mailto:ppotocki@su.krakow.pl)*