



Effects and side-effects of radiation therapy in cancer treatment

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Epidemiology

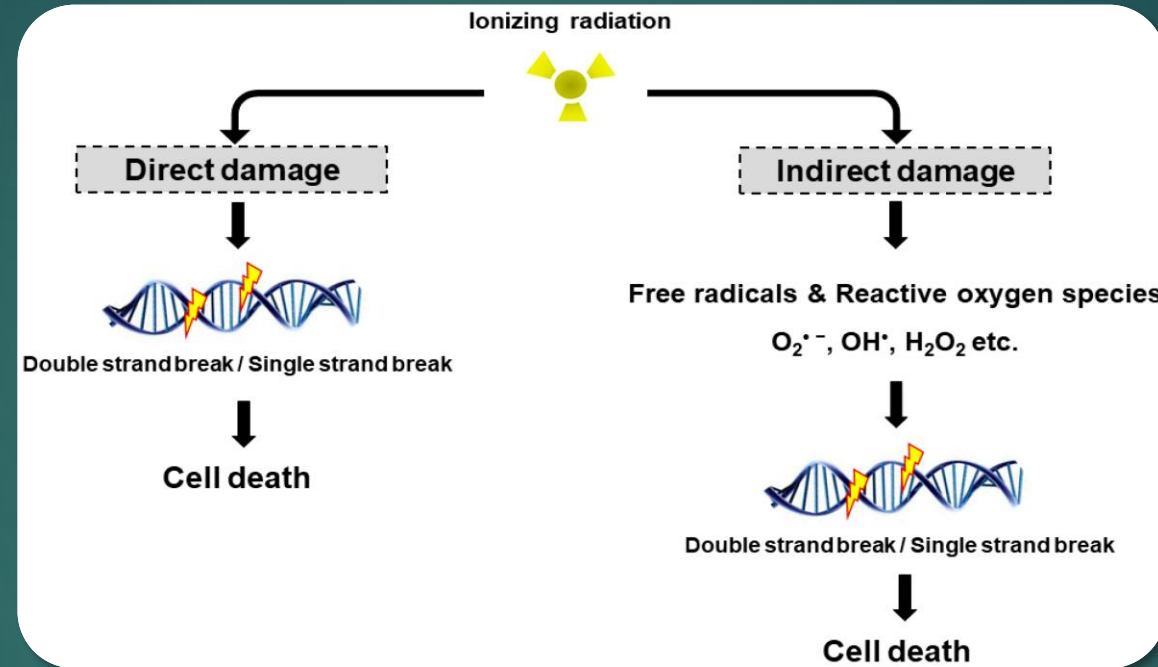


- International Agency for Research on Cancer (IARC) data:
 - 12,7 million new cases
 - ~ 8 million deaths per year
 - 63% of deaths in developing/undeveloped countries

Radiotherapy effects

direct

double-stranded breaks of nuclear deoxyribose nucleic acid (DNA)



indirect

via free-radical intermediaries formed from the radiolysis of cellular water

Radiation also affects

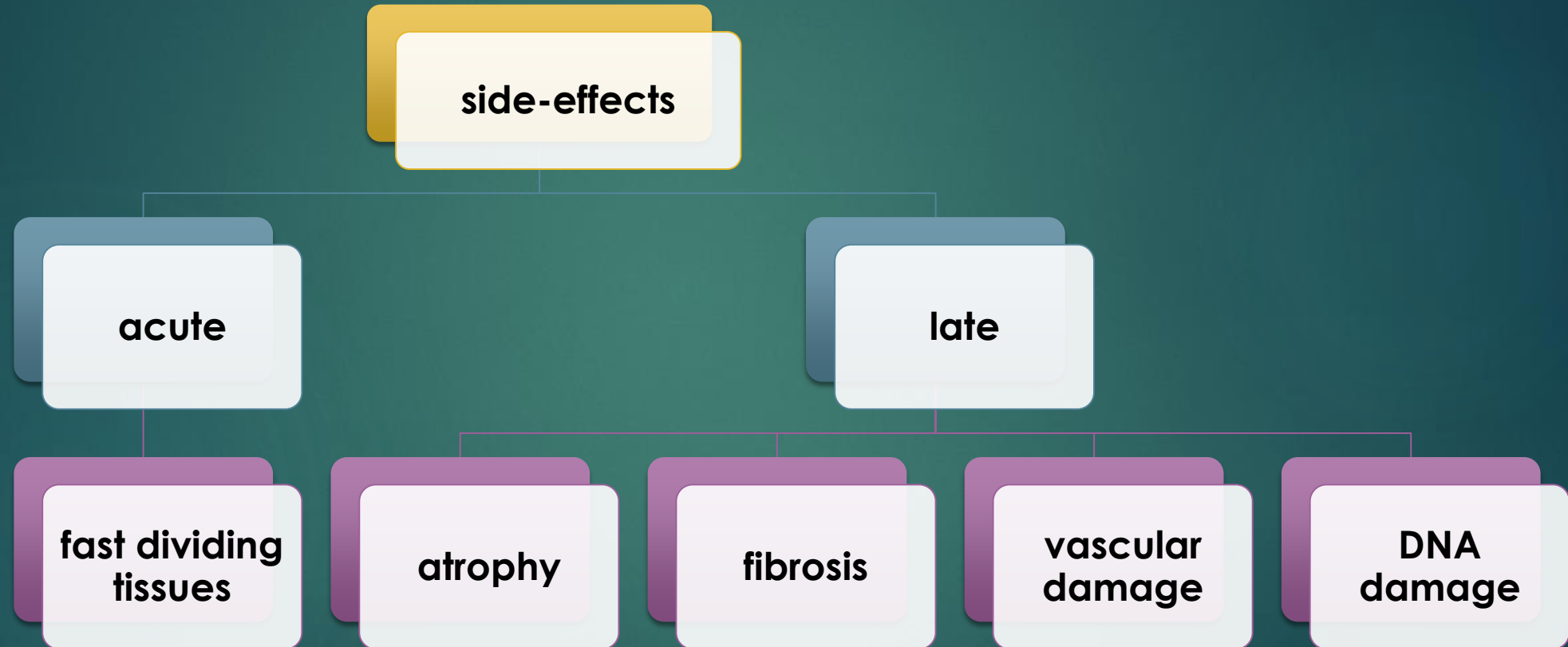
- processes of the cell cycle, apoptosis induction, G1/S cell cycle arrest, mitosis inhibition
- changes in the microenvironment through inflammatory cytokines, fibrotic cytokines, influx of inflammatory cells and the induction of reparative processes

Radiotherapy effects

- main radiotherapy goal: delivery of the tumoricidal irradiation dose and sparing of the surrounding normal tissues (Organs At Risk)
- Gain in therapeutic ratio, the balance between cure and toxicity of treatment
 - RT techniques
 - changes in fractionation regimes
 - prostate (60Gy/20 vs 74Gy/37)
 - head & neck
 - different concomitant HT medicaments
- improved cure rates, long - term toxicity become increasingly important



Radiotherapy side-effects



Radiotherapy side-effects: depression and fatigue

- for many patients one of the most unpleasant and most dominant symptoms during RT
- irradiation of oro/nasopharyngs, brain, breast, lungs
- tumor induced cytokine release, hormonal changes, stress, sleep disorders, volume of tissue receive high doses, reparation of normal tissues damaged by radiotherapy
- 80% patients feel fatigue during RT
- 30% patients feel fatigue as a chronic symptom

Therapy

- selective serotonin take-up inhibitors
- occupational therapy
- sleep regulation

Radiotherapy side-effects: neurologic

- important side-effect, leads to significant reduction in quality of life
- accidental whole body dose of 10Gy – cerebrovascular Sy. - death
- **acute/subacute** – somnolence Sy. – transitional demyelization and edema
- **late** – white matter damage leads to cognitive decline
 - 24Gy to whole brain in children leads to IQ degradation
- **late** – Willis ring vessels atherosclerosis, increased risk of CVI
- **very rare** – radionecrosis, radiation myelopathy

- Therapy:
 - corticosteroids, hyperbaric oxygen therapy
 - radiation neuropathy (sacral and brachial plexus):
Duloxetine, anticonvulsive medicaments, tricyclic antidepressives

Radiotherapy side-effects: hematologic

- mostly as acute side-effects, as a consequence of stem cells damage
- in patients with pelvis irradiation
- radiotherapy technique implemented has a huge influence
 - V10, V20, V40 IMRT vs 3D CRT
 - RT-HT vs RT alone
- leukopenia with neutropenia – enlarged risk of secondary infection
- rarely thrombocytopenia

Therapy:

- poly-vitamin therapy
- high-grade leukopenia - white blood cells growth factor, antibiotics, substitutional therapy

Radiotherapy side-effects: cardiac

- mainly in patients with mediastinum irradiation (Hodgkin lymphoma), younger patients – impact of radiotherapy technique used
- ischemic disease, cardiomyopathy, arrhythmia, pericarditis – main morbidity
- acute myocardial infarction – main mortality
- radiation pericarditis
 - acute, nonsteroidal anti-inflammatory
 - late, latency of 10 years, pericardium effusion rich with proteins – heart tamponade and pericardium fibrosis

☐ Therapy: usual cardiology therapy according to symptoms

Radiotherapy side-effects: respiratory

- radiation pneumonitis and pulmonary fibrosis depends on RT technique used
- past 43% - now 5-15% in patients breast, mediastinum, lung
- pathology – chronic inflammation – pneumonitis/alveolitis – fibrosis - atelectasis
- usually starts after several months and can significantly reduce QOL
- Most studies NSCLC have validated V20 and mean lung dose (MLD) as the most frequently correlated parameters
- combined dose to the heart and lungs might have a synergistic effect on the risk of developing RP
- clear benefit of IMRT over 3D CRT, especially in large tumors over 460ml
- Proton RT no benefit

- Therapy: corticosteroid therapy, symptomatic, O₂
- Trenal for prevention
- Amifostine
- Celecoxib

Radiotherapy side-effects: urogenital

- mainly lower urinary tract after pelvic irradiation ~ acute/chronic, hemorrhagic cystitis, degradation of the bladder volume
- G3/4 late toxicity ~ VV fistula, urethral strictures connected with BRT – 3D BRT
- radiation nephropathy – rare, can be seen in patients treated with TBI
- male erectile dysfunction to impotence – prostate radiotherapy, connected with high BRT doses to seminal vesicles
 - 12 months – 38%
 - 24 months – 59%
- women sexual dysfunction – gynecology radiotherapy,
- decrease in sexual activities, dyspareunia, moderately decreased vagina also connected with high BRT doses to cervical and vaginal mucosa

Radiotherapy side-effects: gastrointestinal

- acute - very often
- 90% change in bowel function, 50% moderate, 15-20% significant impact on QOL caused by bowel toxicity
- typically after 6-12 months, IMRT reduces incidence by 40% compared to the conventional treatment
- G3/G4 toxicity: strictures, perforations, fistulas highly correlated with BRT delivered dose
- 3D BRT vs 2D BRT reduces G3/G4 side-effects 8-12% to 3-5%
- risk factors: previous abdominal/pelvic surgery or inflammatory disease, diabetes, arterial hypertension, smoking

Radiotherapy side-effects: secondary malignancies

- minimal latency period is 5 years, the risk rises and the peak is achieved after 30 years of radiotherapy treatment
- higher risk for patients treated before 30 years of life
- gynecology tumor irradiation:
 - increased risk for bladder, rectum, surrounding soft tissues
 - moderately increased risk of acute leukemia
 - decreased risk for breast, brain and melanoma – ovarian ablation
- is radiotherapy or genetic responsible for secondary tumors - still without a definitive answer

Vielen Dank für Ihre Aufmerksamkeit