Therapy with radionuclides

- Aim is to achieve interaction of radiotracer and tumor cells, with minimal irradiation of surrounding tissue (absorbed dose “only” to tumor cells)

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Radionuclide therapy types

- Radionuclides in elementary form (I-131, P32; Sr 89)
- Metabolic agents: I-131- MIBG
- Antibodies
- Reducing agents
- Labeled cells
- Liposomes
- Microspheres- blockage of blood vessels
- Intracavitary application
Therapeutic radiotracers

- In-111, Y-90 i Lu-177 labeled somatosatin analogues

- In-111 (67 h, $\gamma$-173, 247 keV; Auger and conversion electron, range <1um)

- Y-90 (64h, medium $E_{\beta}$ - 900 keV, range 5,3 mm)

- Lu-177 (6,7 days; medium $E_{\beta}$ -133 keV; $\gamma$-208 keV, range < 1 mm)
Selection of radionuclide for therapeutical application

- $\alpha$ or $\beta$ emitter
- $\gamma$ emitter (detection)
- Appropriate effective time of elimination
- Increased organ accumulation, in regard to surrounding tissue
- Radionuclids that have performance of accumulation and retention in target organ
Figure 4  Liver metastases of a neuroendocrine pancreatic carcinoma (glucagonoma) before (A) and after (B-D) multiple peptide receptor radionuclide therapies using the somatostatin analog $^{90}$Y-DOTA-TATE. Whole-body scans (anterior views) using $^{99m}$Tc-EDDA-HYNIC-TOC show a continuous decrease of uptake and size of the liver lesions.
Radionuclide accumulation in tumor

It depends on:

• Blood supply

• Extravascular compartment

• Interstitial pressure and permeability
Tumor blood supply

- Decreases exponentially with mass
- Blood stasis leads to thrombosis and occlusion
- Tumor cells become hypoxic - NECROSIS
Tumor blood supply

- Decreased perfusion leads to reduced efficiency of radionuclide therapy:
  - Decreased amount of radionuclides in tumor
  - Hypoxic cells have lower requirements for metabolic substrates
  - Hypoxic cells are less sensitive to radiation
\( \alpha \) emitters:

- **Range**: 50-90 \( \mu m \) (penetration of about 10 cellular diameters), have high LET – linear energy transfer, 400x higher than \( \beta \) emitters

- **Disadvantages**: all tumor cells must be irradiated to achieve a therapeutic effect - increased absorbed dose on surrounding tissue - secondary tumor
β emitters

- Short range (<200 µm): P-33; Sn-121
- Medium range (200 µm – 1mm): I-131; Sm-153; Te-161; Re-186
- Long range (> 1mm): P-23; Sr-89; Y-90; Re-188
Auger electrons

- Radionuclides that have radioactive decay in a form of electron capture or internal conversion

- They emit X rays or Auger electrons

- Very short range (< 1 μm)

- The radioactive source must be close to the cell nucleus
Radioimmunotherapy

- Radiotracer attached to anti-tumor antibody
- All tumor cells must express target antigen, with uniform distribution
- Problems: antibodies - allergic reactions, the ratio of tumor-healthy tissue (desirable > 10:1), tumor heterogeneity, suitable for small tumors
- Problem of bone marrow irradiation!
Palliative bone therapy

- **Bone-seeking radiotracers**, β emitters
  - Sr-89 chloride ($t_{1/2}=50$ days; $\beta^- = 1.71$ MeV), Re-186 ($t_{1/2}=3.7$ days; $\beta^- = 0.98$ MeV) HEDP; Sm-153 ($t_{1/2}=1.9$ days; $\beta^- = 0.81$ MeV)-EDTMP

- Bone scintigraphy 1-2 weeks before therapy

- Evaluation of therapy success- bone scintigraphy 2-3 months after therapy

- Positive effect in 90% of patients. Duration of treatment response is about 3-4 months
• Bone metastases are most common in breast, prostate and lung cancer

• Solitary or multiple
Palliative treatment of painful bone metastases

- External irradiation – in a case of localised pain. In 80% of patients the pain is being reduced, in about 30% pain completely disappears.

- Radionuclide therapy – in a case of multiple painful metastases.
Samarium-153 lexidronam treatment of painful bone metastases
Sm-153 lexicronam

**Sm-153**
- β emitter – therapeutic application
- Range in the bone ~ 1.7 mm
- γ rays, energy of 103 keV – gama camera → visualisation of radiotracer distribution
- $t_{1/2}$ 46 hours

**lexidronam = tetraphosphate**
Mechanisam of accumulation is similar to MDP/DPD
- Urinary excretion
Sm-153 lexicronam - indications

- Pain reduction (= palliative pain relieving therapy) in a case of multiple bone metastases
Sm-153 lexidronam therapy - contraindications

- Chemotherapy or external radiotherapy over huge body surface within the last 6 weeks – bone marrow suppression
Patient preparation

- Tc-99m diphosphonate scintigraphy must be provided to confirm osteoblastic lesions.
- Level of leukocytes and trombocytes in the blood: evaluation of bone marrow function.
- Hydratation ~ 0.5 L of fluid before injection to improve renal excretion of radionuclide.
Sm-153 lexicidronam application

- 1 mCi/kg of body weight
- intravenously
Sm-153 lexidronam- therapeutic effect

- Pain reduction starts within one week
- Pain reduction in 70% of patients
- In about 30% pain completely disappears
- Therapy response duration ~ 4 months
Bone marrow suppression

- Control of leukocyte and thrombocyte levels
- Transient myelosuppression 3-4 weeks after Sm-153 lexidronam application
- Bone marrow recovery 2 weeks after
Therapy repeat

- Up to 4 applications of Sm-153 lexicronam, minimum 2 months interval between therapy
- Previously control of L and Trc
Comparison of Tc99m MDP bone scintigram before and after Sm-153 EDTMP
DOSIMETRY

• In calculation of tumor dose main limitation is maximal tolerable dose for surrounding tissue
• Dose limiting organ depends on applying modality and radiotracer characteristic (half-life, elimination, radiation)
• Bone marrow – systemic therapy
• Spinal cord – intrathecal application
• Bladder – kidney elimination
DOSIMETRY

• MIRD- Medical Internal Radiation Dose committee, American Society of Nuclear Medicine:
  - Absorbed dose calculation includes: target organ and/or tumor and its mass, dose limiting organ, average decay energy, absorbed fraction...
  - These parameters can be measured by various diagnostic tools: scintigraphy, CT, MRI...

The end!