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Iodine-131 for therapy of thyroid diseases. Physical and biological basis

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Abstract

Iodine-131 is successfully used in the treatment of hyperthyroidism and differentiated thyroid cancer. Thyroid is the critical organ for iodine. Iodine is taken up by the thyroid follicular cells. Radioactive isotope iodine-131 simultaneously emits two types of radiation: radiation beta minus (β-) used for the treatment and gamma (γ) used for diagnosis. Due to the penetration of beta particles in tissue, damaging effect of β-radiation is restricted to thyroid cells. In this article, characteristic of iodine-131, mechanism of action and mechanism of tissue damage is presented. HIGH energy γ-ray emission, contributes to the dose of both: patient's body and the personnel. In accordance with the principles of radiation protection, reducing exposure to ionizing radiation should be achieved by: use of proper shieldings, organization of work, appropriate distance from the radiation source and reducing the time of exposure. Treatment with I-131, depending on medical indications, may be carried out on stationary or outpatient basis. All activities conducted in the exposure to radiation must comply with the principles of radiation protection, in accordance with the applicable regulations, that are also presented in this article.

KEY words: iodine-131, radioiodine therapy, radiation protection

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I-131 — physical and biological basis for therapy

Iodine-131 is successfully used in the treatment of hyperthyroidism and differentiated thyroid cancer. Advantages of iodine include: good tolerability, ease of application, safety and efficacy of therapy. Currently, iodine-131 is available as sodium iodide in gelatine capsules and drinking solution for oral application as well as in intravenous injections. Thyroid is the critical organ for iodine. Iodine is taken up by the thyroid follicular cells. Retention of iodine in the cells depends on the metabolic activity of the cells. It is assumed that 30 % of iodine is trapped by the thyroid, and 70% directly excreted in the urine [1, 2].

Radioactive isotope iodine-131 simultaneously emits two types of radiation: radiation beta minus (β^-) used for the treatment and gamma (γ) used for diagnosis (Table. 1). Physical half-life (T_f) I-131 is 8.04 day. With regard to living organisms it should be taken into account that the biological half-life (T_b) of iodine in the thyroid gland is about 120 days. Thus, according to the formula:

$$T_e = \frac{T_f \cdot T_b}{T_f + T_b}$$

effective half-life (T_e) of iodine in the living body is about 7.6 day (Table 1) [3, 4].

Table 1. Physical properties of iodine-131 [2]

Type of radiation emitted	Energy	Percentage
Beta minus (electrons)	248 keV	2.1
	334 keV	7.4
	606 keV	89.3
	812 keV	0.7
Gamma	723 keV	1.8
	637 keV	7.3
	364 keV	81.2
	284 keV	6.1
	80 keV	2.6

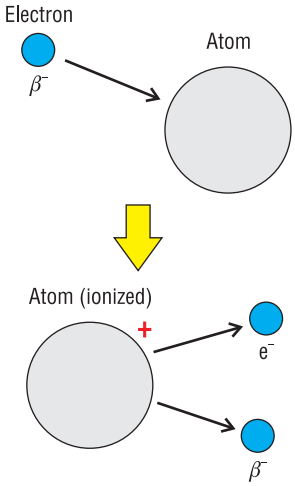

Figure 1. Atom ionization by the electron β^-

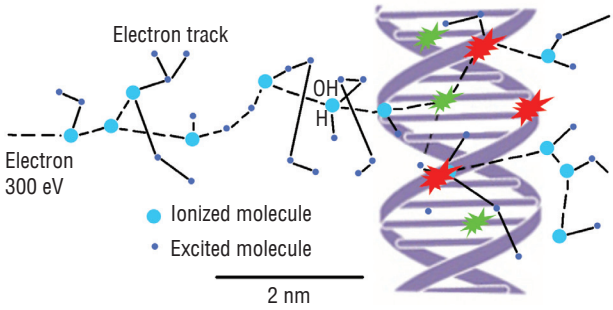

Figure 2. Trace of the electron in the matter, damage to DNA

The electrons are carriers of β^- radiation. Electrons store their energy in form of kinetic energy that determines their speed. While passing through matter, electrons interact with it thanks to its electric charge. The β^- electrons interact with electrons and atomic nuclei of the matter (Figure 1). β^- radiation interaction with nuclei of the matter leads to the conversion of the electron energy into X-ray energy. This phenomenon is called deceleration of the electrons (bremsstrahlung). Significant deceleration radiation is characteristic for the matter of high atomic number (Z), i.e. for heavy materials such as lead, uranium, tungsten, and for large nuclei. β^- radiation interaction with matter of low atomic number (human tissue) is essential for the radionuclide therapy. In this case, the most important is the interaction between β-ray electrons and atomic electrons of the matter. If an electron of β^- radiation is near an electron of the matter, then they will repel each other, because both have the same charge. In many cases, the repelling force is significant to drive the electron out of its shell in the atom, and thus ionize the atom.

In materials of low atomic number, electrons of β^- radiation lose about 33 keV of their energy to cause a single ionization. Typical β^- electron with energy of several hundred keV, therefore, can cause multiple ionizations before it loses all its energy. Energy of β^- electrons is transferred to the ionization as well as excitation of atoms of the matter (Figure 2).

The penetration of electrons in a tissue depends on the electron energy and density of the tissue, so it is characteristic of each radioactive isotope. For I-131, penetration of electrons in soft tissue is about 1 mm (Figure 3). This means that the energy of the electron radiation is absorbed very close to the source of radiation.

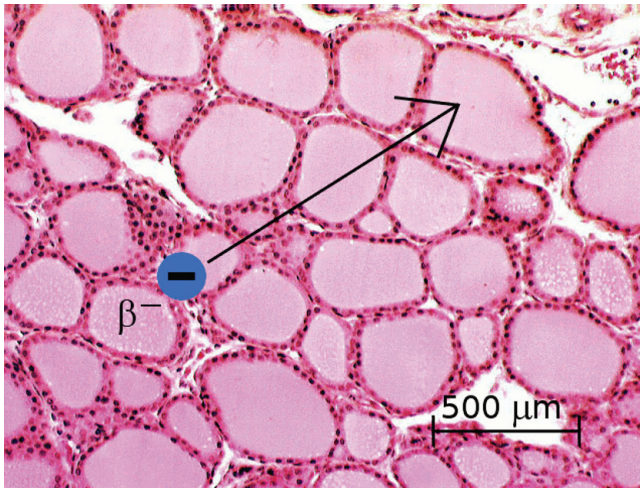

Figure 3. Penetration of the electron β^- in the thyroid [5]

Table 2. LET for different electron energy [4]

Electron energy (keV)	LET (keV/µm)
1000	0.2
100	0.3
10	2.2
1	12

The linear energy transfer (LET) is a measure of the energy transferred to material as an ionizing particle travels through it. LET in soft tissue for several different electron energy is given in the table below [2, 4]. Thus, for electrons emitted by I-131 LET is approximately 0.25 keV/µm (Table 2).

The effectiveness of the biological damage caused by corpuscular radiation is dependent on the value of LET. Radiation with high LET deposits more energy in tissue than needed to induce biological effects [4].

Due to the penetration of beta particles in tissue, damaging effect of β-radiation is restricted to thyroid cells. Adjacent cells are not exposed to significant radiation. The normal biodistribution of iodine include: salivary glands, stomach, intestines, urinary tract including the bladder (Figure 4). Therefore they receive relatively high dose during therapy. High energy γ-ray emission, also contributes to the dose to the entire body as well as exposure to personnel [2].

Interaction of ionizing radiation with living matter takes place in three successive phases (Table 3):

— physical phase — radiation causes ionization or excitation of cells, which in turn leads to breaking of chemical bonds. As a result, free radicals are formed that further ionize the cell, or a direct damage to proteins, DNA and other components of the cell occurs;
— chemical phase — free radicals and other products of the radiation react with cell components;
— biological phase — the cells have their own mechanisms to control and repair DNA. Biological phase begins with the enzymatic reactions, which aim to repair chemical damage

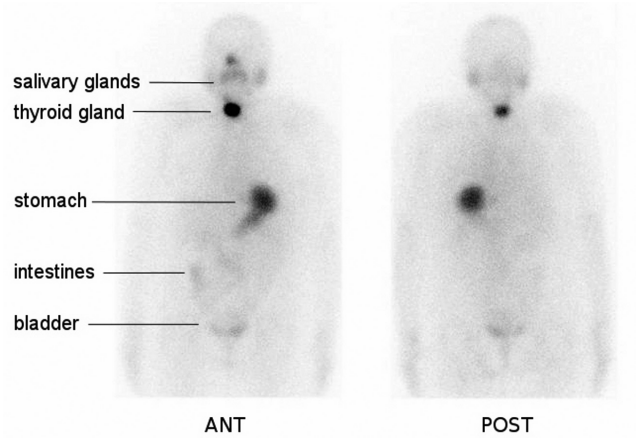

Figure 4. Physiological uptake of I-131

Table 3. Phases of ionizing radiation with matter

Interaction phase	Duration
Physical: ionization and excitation, the formation of free radicals	10^{-13}– 10^{-11} s
Chemical interaction between the product of physical and physico-chemical phases, and other components of the cell	10^{-3} s
Biological: change of the biological properties	Days, years

in the cell. These reactions may last seconds, days or weeks. Damage that is impossible to repair or is improperly repaired causes the cell death [1, 6].

Ionization and excitation of cells under the influence of radiation leads to the lethal or non-lethal effects. Cell death is usually caused by the fact that a double strand of DNA damage is repaired incorrectly or is not repaired at all. As a result of changes in the DNA chain, while trying to activate mitosis, so-called reproductive cell death occurs. Many healthy as well as malignant cells undergo radiation-induced apoptosis. Apoptosis is a natural, programmed cell death [1]. Non-lethal effects include: genetic damage (mutations), impaired function of enzymes that normally do not lead to cell death.

Biological effects of exposure to radiation can also be divided into the effects of stochastic and non-stochastic (deterministic) (Table. 4) [1, 7, 8].

According to the ICRP 53 report "Radiation dose to patients from radiopharmaceuticals", dose for an adult (> 20 years) subjected to treatment with I-131 (sodium iodide) is 18.4 mSv/MBq, which corresponds to the effective dose value of 10.4 mSv/MBq. In the case of 131I-MIBG therapy the values are 0.15 mSv/MBq and 0.21 mSv/MBq respectively [9, 10].

Guidelines for safe radionuclide therapy using I-131

In accordance with the principles of radiation protection, reducing exposure to ionizing radiation should be achieved by:

— use of proper shieldings. A shield should be adapted to the type of radiation. Due to the deceleration radiation, the best shield for beta radiation is double-layered shield, the first layer of light material (small Z number, such as plexiglass), the second material with a high atomic number, such as lead. The best shields against photon radiation (X and gamma) are materials with large Z number. When designing the covers, it should be remembered that the patient who undergoes radioiodine therapy is a source of photon radiation, because the β^- radiation used for therapy is entirely absorbed by the human body;

— organization of work at an appropriate distance from the radiation source, because the dose decreases with the square of the distance (the farther the safer)

— reducing the time of exposure to radiation since dose increases in direct proportion to exposure time.

Treatment with I-131, depending on medical indications, may be carried out on stationary or outpatient basis. In Poland, for the outpatient treatment with open sources of iodine-131, the applied activity may not exceed 800 MBq (in accordance with the applicable regulation [7]).

It is very important to minimize the exposure of young children, pregnant women and women in the reproductive age. Different cells have different sensitivity to radiation. Cells are most radiosensitive during division (high mitotic activity) and differentiation. This makes irradiation particularly dangerous for pregnant women and young children. Therefore, it is so important to protect these groups of patients. In the radionuclide therapy facility this is realized by complying with the following principles:

— no access to the facility for children under the age of 10, unless they are patients;

Table 4. Biological effects of radiation exposure [1]

Characteristics	Stochastic effects	Non-stochastic effects
Dependence on the dose absorbed	The frequency and probability of occurrence proportional to the dose	The severity of symptoms proportional to the dose
Examples	Genetic mutations, cancer	Marrow suppression, immune suppression, temporary or permanent sterility, cataract, death
Threshold dose	No	Yes
Whole body threshold dose	–	0,5 Gy
Other conditions	Effects may occur, but do not have to occur; the occurrence is described by probability distribution	After crossing the threshold dose effects are always present
Occurrence	Can occur in people exposed to radiation and offspring of these people	Occur only in individuals exposed to radiation

Table 5. Exposure of personnel

Doses	Effective dose	Equivalent dose to hands
According to the literature	0,001–0,008 mSv/GBq	0,1–0,2 mSv/GBq
According to our measurements	0,005–0,009 mSv/GBq	0,1–0,5m Sv/GBq
Dose limit	20 mSv/year	500 mSv/year
	(over the next five years globally 100 mSv)	

— during stationary treatment, a patient can be released from a hospital only after the fall in activity in the body below the 800 MBq;
— patient's housing and family condition should always be taken into account while deciding when to release him from the hospital;
— in the case of stationary therapy, medical staff's contact with the patients after administration of iodine-131 due to thyroid cancer, should be restricted to an absolute minimum, and visits to these patients should be prohibited during the 24 hours after application of the nuclide.

If therapy doses exceeds 800 MBq are applied in a hospital, special wards for patients undergoing stationary therapy should be organized. Rooms for the patient should be up to double, and the distance between the beds of patients may not be less than 1.5 m (in the absence of such a possibility a protective screen should be placed between patients). The patients' rooms should be equipped with own sanitary facilities (if it isn't possible, it is acceptable to designate and mark special facilities to be used by these patients). Sanitary facilities should be equipped with liquid soap, paper towels or hand dryers and disposable pads on the toilet seat. The patient should be advised in written how to proceed in the room [7, 8].

Patient undergoing radionuclide therapy should also receive written information about appropriate behaviour in relation to the immediate environment. Staff and patients residing in the ward should follow the instructions on reducing exposure to ionizing radiation. Information and instructions should be written in accordance with the recommendations of the committee and external audit procedures in nuclear medicine, and the recommendations of the national consultant in the field of nuclear medicine. [7, 8].

Personnel involved in the radioiodine therapy belong to the group of staff professionally exposed to ionizing radiation. All activities conducted in the exposure to radiation must comply with the principles of radiation protection. In Poland, the dose limits for workers and members of the public are included in the applicable regulation [7, 11]. The analysis of literature and our own experience, shows that in practice the doses received by staff of facilities offering radioiodine therapy are much lower than the dose limits, as shown in Table 5 [10–12].

Medical staff using open sources of iodine (I-131) for treatment, should be subject to internal control of the content of radioactive iodine in the thyroid gland. The frequency of inspection should be made dependent upon the degree of risk of internal contamination with iodine (I-131) [7].

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