

# **Methodological letter of Nuclear Medicine Professional College and Radiotherapy and Oncology Professional College on the treatment of bone metastases with open radioactive isotopes**

Bone metastases of tumours are relatively frequent, their frequency is approximately 65-75 percent among patients with prostate and breast cancers. The torturous pain frequently characterizing bone metastases and the resultant limitations in mobility considerably deteriorate patients' quality of life. The treatment of bone metastases is a multidisciplinary task. It is crucial not to use the available methods in an isolated manner but instead as a part of a complex treatment. Complex treatment includes the isotope therapy with high bone-affinity radiopharmaceuticals decreasing patients' pain and improving their general condition.

In agreement with Radiotherapy and Oncology Professional College, Nuclear Medicine Professional College recognizes the isotope therapy using high bone-affinity radiopharmaceuticals acceptable and implementable in the manner specified below:

Aim of treatment: delivery of therapeutic (tumor destroying) dose to the bone metastases in order to achieve the required analgesic effect.

The dose absorbed in bone metastases may vary from 10 to 140 Gy.

In the case of osteoblastic metastases, the isotope will be incorporated in the bone metastases with increased osteoblast activity, whereas in case of osteolytic lesion, the radiopharmaceutical is taken up by the new reactive bone surrounding the bone-destroying metastases, so irradiation of the metastases is indirect in this case.

Indication of therapy: Heavy, multifocal, often migrating and recurring pain that is deteriorating if workload increases, which requires the administration of strong analgesics. Isotope therapy may be applied as an alternative of strong analgesics if

- only minimal effect can be expected from bisphosphonate therapy,
- the expected lifetime of the patient is not shorter than 3 months.

Conditions of therapy:

- Bone scintigraphy examination is required prior to treatment, the optimal date of examination being 2 to 4 weeks before therapy.
- Relatively good general health status.
- Adequate laboratory test results (qualitative blood picture: thrombocyte and leukocyte numbers, renal function and if required: d-dimer or fibrin cleavage products) that are not older than one week.
- Adequate imaging examination of the painful region in order to exclude the presence of spinal compression or extensive lythic metastases

Absolute contraindication of therapy:

- Pregnancy and breast-feeding
- Leukocyte number falling under 2400 or thrombocyte number falling under 60000
- Insufficient renal function (in spite of renal function improving treatment the serum creatinin is higher than 120  $\mu\text{mol/liter}$ )

Relative contraindications of therapy:

- Suspicion of spinal compression
- Bad general health status
- Expected lifetime not exceeding two months
- Active disseminated intravascular coagulation (DIC)
- Fast deterioration of the qualitative blood picture without any sign of improvement prior to isotope therapy
- Isotope therapy may not be or may only be carried out on the basis of individual assessment if the patient received extensive irradiation or chemotherapy within four weeks prior to treatment.
- Lack of appropriate cooperation

Radiopharmaceuticals that can be used for alleviating pain caused by bone metastases:

Radiopharmaceutical	Single administration activity
<sup>89</sup> Sr chloride	1.5-2.2 MBq/kg i.v.
<sup>90</sup> Y-EDTMP	400 MBq i.v.
<sup>117m</sup> Sn (IV)-DTPA	2.6-10.6 MBq/kg i.v.
<sup>153</sup> Sm-EDTMP	37-74 MBq/kg i.v.
<sup>177</sup> Lu-EDTMP/DTPMP/TTHMP	≤3700 MBq i.v.
<sup>186</sup> Re-HEDP	1295 MBq i.v.
<sup>188</sup> Re-HEDP	1900-3100 MBq i.v.

Subsequent to treatment of bone metastases with open radioactive isotopes, the patient does not necessarily have to be hospitalized and establishment of isotope therapeutic ward for this purpose is not verified. For radiation health protection reasons, within four hours after treatment, the patient is required to urinate at the nuclear medicine ward. Patients from other wards may go back to their ward after four hours waiting time spent in the active waiting room at the nuclear medicine ward and having used the WC at least once. For these patients there is no need for establishment of a separate isotope therapeutic ward but instead it is necessary for them to get to know and observe some general caution rules with respect to behavior and WC usage during the first three days subsequent to administration of radiopharmaceuticals.

Taking into account that the activity of the radioisotopes also emitting accompanying gamma radiation is beyond 1 GBq, an activity amounting to 1 to 10 μSv/h will be detected at 1 meter from the patient immediately after administration. Intensity of the radiation space at the time of administration is much lower than the 25 μSv/h level, considered as the limit value for discharging from hospital, and it rapidly decreases in time, therefore the patient cannot be considered as a considerable source of radiation. However, during the first few days, physical contact of the patient with children, pregnant or breast-feeding women should be prevented. In the case of hard beta emitters (<sup>90</sup>Y, <sup>89</sup>Sr, <sup>188</sup>Re), similar caution measures are verified due to the deceleration X-ray radiation produced.

Treatment of patients with bone metastases with open radioisotopes is initiated by the oncology team and carried out by the nuclear medicine physician at a coordinated time. The nuclear medicine physician participates in patient follow-up after therapy and patient's control examinations and he/she is also notified of the effect of treatment as well as the health status of the patient.

A medical physicist has to be involved in the dosimetric calculations and measurements.

Prior to isotope therapy, the nuclear medicine physician has to inform the patient both orally and in writing about the behavioral, life conduct and hygienic regulations that must be observed as regulations providing for the safety of fellow humans and the environment. Treatment may be implemented only if the nuclear medicine physician is convinced that the patient is capable of observing the radiation protection regulations. The patient acknowledges with his/her signature that he/she has understood the information about the treatment and the regulations to be observed, and being aware of all these he/she undertakes to observe such regulations.

Administration of the isotope may be carried out in the treatment room licensed for this purpose by the competent radiological health care authority.

If patient is transported by the vehicle of the National Ambulance Service or an alternative patient transporting enterprise, the head of the Service (transport organizer) has to be notified at least 24 hours before the planned discharge from hospital, so as to provide for adequately linked transport of the patient.

For patient registered in hospital wards, the nuclear medicine physician should enter the name, activity and date of administration (year, day, hour, minute) of the radiopharmaceutical applied as well as signing and stamping this entry with his/her physician's stamp. The final report has to include the name of address of the institute carrying out the isotope treatment, the name and contact data (phone number) of the physician carrying out the treatment, the name and activity of the radiopharmaceutical applied, the date of administration (year, day, hour, minute), and the dose value measured at the time of discharging from hospital.

One copy of the final report has to be sent directly to the family doctor of the patient and the oncology or radiotherapy physician recommending the treatment (or the member of the oncology team recommending the therapy), respectively.

For ambulant patients, the nuclear medicine physician shall be obliged to hand over a treatment sheet containing all data as specified above.

## **Patient Information sheet about analgesic isotope treatment**

Dear Patient,

Your treating physician recommended isotope treatment for you because metastatic tumor alterations were found in your bones, which cause heavy pain and such pain is difficult to alleviate with the administration of drugs. The recommended isotope treatment is simply: it is only one injection administered intravenously. The effective substance in this injection is a special radioactive compound that is bound to bones and it delivers radiation treatment to pathological parts of the bone.

This therapy does not cure the tumor but it alleviates pain as a form of symptom treatment. After treatment, pain is alleviated in 60-80 percent of patients, whereas full-scale pain-free status is achieved in 20 percent of them. It is a rare event that treatment has no effect. Favorable effect of the intravenous injection will be observed after 1 to 3 weeks only and it remains present for months. If pain returns after provisional improvement, the treatment may be repeated after a few months.

### **Preparation**

It is not necessary that you stay hungry for the treatment, however you have to take much liquid before the treatment and for a few days afterwards.

For safe implementation of the treatment, your treating physician has to know your renal function and the qualitative blood picture, therefore final establishment of the recommendation requires laboratory tests to be carried out with blood samples collected through taking blood from the your veins.

### **Radiological protection regulations**

Subsequent to the injection, an observation period of four hours is required, which you have to spend in the so-called "active waiting room" established in the premises of the isotope laboratory. You are called on to drink much during the waiting period. Radioactivity being not bound to the bone metastases is quickly excreted; therefore the first urine after the injection will contain the most radiating substance (isotopes). You have to use the WC of the Department of Nuclear Medicine during the first four hours.

After the end of the four hours observation period, if you are an inpatient in a hospital, you can get back to your inpatient ward, whereas if you are an outpatient, you can return home. The most recommended way of returning to your home is primarily by car. If required, vehicles of the ambulance and other patient transportation services are also available. The least recommended but allowable way of returning home is using the public transportation service. On public transportation vehicles try to avert the proximity of children, juvenile persons and pregnant ladies if possible.

In view of the fact that the unbound radioactive substance leaves the body with the urine during the first 24 to 48 hours following the treatment, great emphasis should be placed on personal hygiene, especially the usage of WC. During the first three days following the treatment gentlemen are also required to use the WC while sitting. The WC has to be thoroughly flushed at least twice after WC usage. You will have to thoroughly wash your hands afterwards.

On the first three days following administration of the isotopes, you have to separately wash, in excessive amount of water, your towel, underwear, your pajamas or anything else, which could be contaminated with urine.

On the first three days following administration of the isotopes, you are recommended to minimize to the smallest possible duration your physical contact with family members, especially with children or other persons.

Patients who cannot withhold their urine may receive isotope therapy only if a permanent catheter is inserted that is connected with collection bag. The catheter will stay inserted for three days. In order to prevent the skin of the hand from contamination, rubber gloves will have to be used for the replacement of the urine collection bag. Pour the collected urine into the WC by emptying the urine collection bag, then thoroughly flush the WC at least twice.

**Other regulations pertaining to way of life**

After the treatment carry on taking your usual analgesics and other drugs. If your pain is considerably alleviated or terminated, the modification of the established doses of analgesics or stopping their administration have to be done in line with recommendations of your family doctor.

Try to avert situations that may easily lead to falling down, injuries or bone fracture (e.g. dangerous sports, cycling).

Isotope treatment of bone metastases has no impact on driving.

**Side effects**

Pain may increase during the first two days following treatment, which is often the sign of favorable effect later on. In about one week, the pain caused by the treatment is over.

As a result of treatment, the number of white blood cells and platelets will start to decrease in about 2 weeks, and this decrease will continue for 4 to 6 weeks, therefore the qualitative blood picture will have to be checked every 2 weeks (or at a frequency recommended by the treating physician) for a period of about 6 to 12 weeks after the isotope treatment.

**Other advises**

For ladies capable of conception, the substance containing radioactive isotopes may be administered only after the exclusion of pregnancy. If you intend to have a baby after the treatment, consult with your family doctor, by all means.

**I have understood the above regulations and the answers to the questions I asked. I acknowledge these regulations as obligatory for me and I verify this with my signature.**

..... (year)                      (.....month)                      (.....day)

.....  
Physician providing for information

.....  
patient

**Treatment form**

**for patients having received ambulant palliative isotope treatment**

**Name of patient:** .....

Social security identification (TAJ):.....Date of birth:.....

Address: .....

**Name of physician recommending the isotope therapy:**.....

**Name of nuclear medicine physician carrying out the therapy:** .....

**Date of isotope treatment:** ..... year ..... month.....day .....hour ....min: .....

**Name of the radiopharmaceutical applied:** .....

**Amount of activity:** .....

**Special instructions:**

As a side effect of the therapy applied, a decrease in the cellular components of the qualitative blood picture is expected; the change is not considerable and it is spontaneously reversible. Because of this side effect, regular qualitative blood testing is required: 1, 3, 5, 7, 9, 12 and 15 weeks after therapy.

Control bone scintigraphy will have to be carried out three months after therapy.

.....  
Signature of the nuclear medicine physician  
carrying out the therapy