THERANOSTIC: A NEW TECNIQUE AGAINTS CANCER

J. Sanchez Segovia[1], C. Salgado Gracia[2], I. Martel[1]

[1] CCTH Universidad de Huelva. Departamento de Ciencias Integradas. Huelva

[2]Hospital Universitario Juan Ramón Jiménez. Servicio de Medicina Nuclear y Radiofarmacia. Huelva.

**e-mail: (jose.sanchez@dci.uhu.es)*

Abstract:

Theranostic, has positioned itself as a promising technique to fight cancer, especially when using radioactive isotopes, where it has demonstrated good efficiency in human cancer treatment and in the animal phase study. The technique basically consists in using a chemical element with several radioactive isotopes. One diagnostic (gamma or β+ emitter) and another isotope of the same therapeutic element (alpha, β+, β- or Auger electrons). These isotopes must be linked to a vector molecule expressed by the tumor cells of the corresponding type of cancer. Radioisotopes can also be encapsulated in nanoparticles.

Keywords: Theranostic, radioisotopes, nanoparticles.

1. INTRODUCTION

The treatment of cancer with radiation therapy begins at the beginning of the XX century with the early works of Marie Curie [1] and the treatment of skin cancer. At present times, external radiation (external radiotherapy-RTE) and interstitial or intracavitary radiation (brachytherapy-BQT) of tumours is used in 60% of different types of cancer, with results around 60% of cure with acceptable quality of life [2]. However, both RTE and BQT have the disadvantage that dose delivered to healthy tissues is relatively high (larger in the first one), so that the maximum dose is conditioned by the damage caused to the healthy tissues surrounding the tumour. Techniques that radiate as little as possible to healthy tissues are being permanently sought, such as IMRT (intensity modulated radiotherapy), proton therapy, VMAT (volumetric arc-therapy), etc. All of them are RTE-type techniques [3].

At the end of last century new treatment methods were developed consisting of cell therapies, among which being the most notorious the theranostic technique using radioactive isotopes.

2. MATERIALS AND METHODS

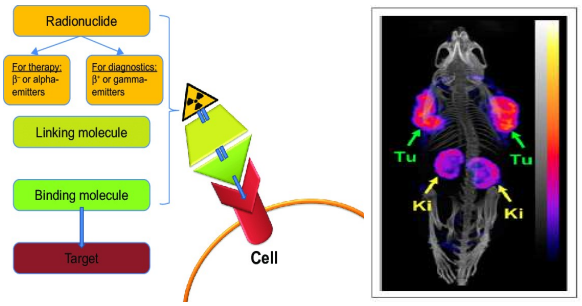

Figure 1. Left Simple outline of the theranostic. Right SPECT with radiosiotopes (Muller, C., et all . *Journal of Nuclear Medicine* 55(10):1658–64).

The theranostic with radioisotopes makes use of a chemical element that has at least two radioactive isotopes. One of them is a gamma or positron emitter used to obtain the image of the tumour. The other is an alpha, beta or Auger electron emitter, delivering the required dose for therapy.

The most important feature of the theranostic approach is that the technique produces minimum damage to the cells of healthy tissues located in the vicinity of the tumour: it is thus a targeted-cell therapy. In order to distinguish between cancer cells and healthy tissue, vectors (ligand molecules) must be made available, to which the radioisotope is attached (Figure 1, Left). For example, in ovarian cancer it is known that it primarily expresses folate [4]. If a radioactive isotope is attached to the folate molecule, by injecting this radiopharmaceutical into the bloodstream, the vast majority of this radiopharmaceutical will be absorbed by the ovarian cancer cells. With the diagnostic radioisotope we will verify, by means of the Nuclear Medicine imaging system (SPECT-CT or PET) and once assured of this, the therapeutic isotope that will cause the death or

apoptosis of the tumor cells is introduced (Figure 1, right) .

A recently emerging theranostic technology is based on the use of nanoparticles to encapsulate the radioisotope and dope the nanoparticles with ligand molecules expressed by the various types of tumors [5].

3. RESULTS AND DISCUSSION

Some radioisotopes such as ^{131}I have been widely used for some time in therapy, both for thyroid cancer and as a therapeutic measure for hyperthyroidism.

Other radioactive isotopes under development for targeting bone cancer are ^{89}Sr, ^{153}Sm, ^{177}Lu and $^{188/186}$Re. Somatostatin receptor peptides labeled with ^{90}Y or ^{177}Lu showed effectiveness for the treatment of neuroendocrine tumors in ongoing clinical trials, though they are not yet approved for clinical usage. Some clinical trials recall the use of 213Bi in acute myelogenous leukemia (AML), melanoma, and lymphoma; ^{225}Ac for AML; ^{223}Ra for bone cancer, and ^{211}At for glioblastoma and ovarian cancer [6].

Other new radioisotopes such as Terbium (^{149,152,155,161}Tb) are being positioned in the market as elements of great destruction capability of specific tumor cells. However, there are difficulties in obtaining these isotopes. Only some for some few cases such as Xofigo©, the radiopharmaceuticals are not yet produced commercially and only available in some research centers, which makes difficult to develop this technique in hospitals not included in the clinical trials. On the other hand, there is still an important question to clarify: what is the most adequate prescription dose for each type of tumor? It is necessary to develop clinical dosimetry techniques, similarly as it is done in the RTE or BQT. So far almost all treatments are carried out considering the injected activity, in mCi, but not the dose received by the tumor, in Gy.

4. CONCLUSIONS

The theranostic method presents many appealing advantages over RTE or BQT since it is a local treatment at the cellular level whereby, if the appropriate ligand molecule can be obtained to produce the corresponding radiopharmaceutical, the tumor cells can be destroyed or killed by apoptosis, and the damage of healthy tissues is minimal. If the cancer cells are treated with α radiation, the overall penetration in the tissues is only of a few hundred microns, and of a few millimiters when using β- radiation, therefore minimizing the damage over healthy tissues. On the other hand, the imaging technique allows to monitor and control the dose deposited over the tumour, its evolution and the area to be treated, thus offering an absolutely personalized treatment. The big challenge is to find the right molecule for each type of cancer and adequate dosimetry.

5. REFERENCES

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