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New radiopharmaceuticals for in vivo diagnosis.

Summary:

The present invention refers to the use of Red blood cells (RBCs) intracellularly labelled with a specific radiopharmaceutical for *in vivo* diagnosis.

The images of the distribution of blood in the body with non-invasive techniques have many applications in research and at the clinical level. Currently its use is limited to SPECT and PET techniques. The use of SPECT imaging and single gamma-ray emitter Tc-99m labeled RBC as a blood pool imaging agent in nuclear cardiology is well established.

However, this technique has a poor image quality as well as a poor quantitative accuracy. In addition, shortage in Tc-99m production may limit its use in the future as it relies on old nuclear reactors that are about to be closed for its production.

In the other hand, PET imaging allows for accurate quantitative results and improved spatial resolution compared to SPECT. The most established PET tracer for blood pool imaging is carbon monoxide (CO), which has been labeled with positron emitting radionuclei such as ^{11}C or ^{15}O and has been used as an inhaled radiotracer over the last three decades. Carbon monoxide binds reversibly and with high affinity to the hemo group of hemoglobin, producing carboxyhemoglobin. Thus, the inhalation of radiolabeled CO leads to the in vivo radiolabeling of hemoglobin in the erythrocytes. However, this measurement is restricted to those facilities equipped with a cyclotron capable of producing 11C (half-life ~20 min.) or 15O (half-life ~2 min.). Additionally, as CO is a gas, its use as inhaled radiotracer presents radiation protection issues. In summary, these severe limitations make blood pool measurements rarely accessible to patients or researchers.

The present invention provides a solution to facilitate blood pool measurements accessible to patients or researchers.

Innovative aspects:

In the present invention, we solve the problem of facilitating blood pool measurements accessible to patients or researchers by using the said radiopharmaceutical for the in vitro intracellular labeling of RBCs (Red blood cells).

The radiopharmaceutical used in the invention is a tracer available worldwide and because of its chemical structure it may be incorporated by the erythrocytes and trapped intracellularly. In this sense, a blood sample (such as whole peripheral blood) can be extracted or isolated from a subject or from another subject with blood compatibility. The extracted or isolated blood can be then incubated in contact with the radiopharmaceutical for a period of time and later be reinjected into the patient. Labeling of RBCs with the tracer will expand the use of the PET technique to blood pool imaging with the consequent improvement in the field of clinical diagnosis.

The invention describes for the first time to in vitro use of the radiopharmaceutical for intracellular labeling red blood cells (RBCs). In addition, to improve the efficiency of the product obtained, researchers have found an optimal labeling method that produced a 3-5 fold increased labeling efficiency compared to direct incubation of whole blood with the tracer. By using the aforesaid optimum methodology we are able to provide a very stable and reproducible distribution of activity in blood across time and animal species.

Competitive advantages:

The proposed method provides widespread access to blood pool imaging with PET technique which is much more accurate than other currently used techniques such as SPECT imaging in term of image quality, spatial resolution, temporal resolution and quantitative accuracy, and does not require an in-house cyclotron as required for PET imaging with CO. Radiolabeled red blood cells (RBCs) have played an important role as diagnostic radiopharmaceuticals for many decades:

- Quantify in vivo the blood volume of other organs and tissues
- In neoplastic lesions, to evaluate tumor angiogenesis.
- Evaluation of cerebrovascular diseases.
- Visualize the cardiac cavities in order to precisely evaluate the myocardial oxygen consumption.
- Identification of sites of red blood cell destruction
- To investigate angiofibroma and gastrointestinal hemorrhage and for localizing intramuscular hemangioma
- Selective spleen imaging with damaged RBCs.

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Key words: radiotracer**,** radiopharmaceutical, erythrocytes, RBC, Diagnostic imaging, Nuclear medicine, in vivo imaging.

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