^{99m}Tc erythrocytes (modified in-vivo)

Technescan PYP®, Angiocis®

1. Indications

^{99m}Tc erythrocytes are used for blood pool imaging, including cardiac first pass and multiple gated equilibrium imaging and for detection of sites of gastrointestinal bleeding and hepatic lesions.
See chapters *'Scintigraphy of gastrointestinal tract haemorrhage', 'Hepatic haemangioma scintigraphy'* and *'Equilibrium radionuclide angiography MGA'.*

2. Preparation

Approved product, see summary of product characteristics (SmPC).
In order to optimize the biological behavior of ^{99m}Tc in erythrocytes, modifications of the in vivo labeling techniques have been developed. One of these methods is the modified in vivo labeling method. This method isolates pretinned erythrocytes.

Modified in vivo labeling

- The stannous pyrophosphate lyophilisate is first reconstituted with isotonic sodium-chloride 0,9%.
- Administration of stannous pyrophosphate to the patient.
- Thirty minutes after injection withdraw approximately 5-10 ml blood into a syringe containing ACD.
- Centrifuge the syringe in inverted position for 10 min at 1000 g.
- Take the syringe out of the centrifuge and transfer the erythrocytes in sterile vial containing 1000-1500 MBq ^{99m}Tc pertechnetate in 5 ml NaCl 0,9%.
- Incubate during 5 min.
- Centrifuge during 5 min at 1000 g and discard the supernatant.
- Determine the radiochemical purity.
- If the radiochemical purity <90%, repeat washing step.
- Reinject ^{99m}Tc erythrocytes to the patient.

There is also a method described without centrifugation and washing *(in "vivtro" method)*. This has a lower labeling efficiency.

Special considerations:
Working with blood can introduce risks to both the operator and the patient. The department labeling the cells should comply with all regulations. Adequate facilities, equipment, procedures and training for operators should be present. Additional the risks for blood contamination should be recognizes and precautionary measures should be implemented to minimize those risks.

3. Quality control

The labeling efficiency of radiolabelled red blood cells can be determined by gamma

counting radioactivity in aliquots of the blood before reinjection to the patient.

Radiochemical purity
The total percentage of bound radioactivity can be calculated as:

$$\% \text{ binding} = \frac{\text{activity of RBC}}{\text{activity of (RBC + supernatant)}} \times 100$$

4. Interactions, contraindications & adverse reactions

Interactions

Drug interference with ^{99m}Tc red blood cells for equilibrium blood pool imaging can be classified into two general categories:
Agents that alter, by a direct pharmacological effect, cardiac function and have the potential to interfere with the interpretation of equilibrium blood pool images i.e. ß-blockers, calcium channel blockers, nitrates.
Agents that inhibit or diminish the radiolabeling or red blood cells by ^{99m}Tc.

Drug	Possible mechanism
Heparin	Formation of ^{99m}Tc-heparin
Iodinated contrast agents	Competition between iodide and free ^{99m}Tc for transport
Methyldopa	Oxidation of Sn^{2+}
Hydralazine	Oxidation of Sn^{2+}
Teflon® catheter	Binding of Sn^{2+} to tubing
Antracyclines (for example doxorubicin)	Disrupts erythrocyte cell membrane
Quinidine	Blocks transmembrane transport
Digoxin	Interfering Sn^{2+} upake
Prazosin	Unknown

When a washing step is used in the modified in vivo labeling of erythrocytes, there is no interaction with stannous overload.

Adverse reactions

Adverse reactions have been reported in isolated cases (1-5 per 100.000 uses). Usually, these adverse events are mild to moderate and of short duration, although some have been described as serious. Side effects reported after the use of stannous pyrophosphate lyophilisate were mostly intolerance reactions of the allergy type including e.g. dizziness and headache, nausea and vomiting, flushing, skin rashes, face oedema, or hypotension. Also vasovagal reactions, cardiac arrythmias, and local reactions at the injection site have been reported.

5. Biodistribution & pharmacokinetics

Under normal circumstances intravenously injected pertechnetate freely diffuses into and out from the erythrocytes. However, when the erythrocytes have been preloaded with stannous ion, the sodium (^{99m}Tc) pertechnetate is reduced within the cells and becomes bound to the chains of globin. However, 20% of injected pertechnetate enters the red cell and binds to a beta chain of globin.

While the remaining 70-80% of pertechnetate is believed to be located in the cytoplasm or on the red cell membrane. On the other hand reducing the surface charge of the erythrocytes decreases the efficiency of labelling down to 20%. Up to eight days after the examination, labelling of erythrocytes with (^{99m}Tc) pertechnetate may still be observed.

6. Stability

The expiry date is 12 months from the day of manufacture.

The reconstituted product should be used within 4 or 6 h, see SmPC of the product concerned.

7. Literature

- Callahan RJ et al. Radiolabeled red blood cells: method and mechanisms. Continuing education for nuclear pharmacists and nuclear medicine professionals. University of New Mexico 2009; volume 12, lesson 1.
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- Adalet I, Cantez S. Poor quality red blood cell labeling of Technetium-^{99m}: case report and review of literature. Eur J Nucl Medi, 1994;21:173-5.
- Pavel DG et al. In vivo labeling of red blood cells with ^{99m}Tc: a new approach to blood pool visualization. J Nucl Med, 1977;18:305-8.
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