PART III - 543

# <sup>99m</sup>Tc erythrocytes (in-vivo)

Technescan PYP®, Angiocis®

# 1. Indications

<sup>99m</sup>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 vivo labeling requires pre-tinning of red blood cells. In vivo labeling is the simplest and safest technique as it does not require handling of blood, however the labeling efficiency is generally lower and more variable. The best labeling yield of the red blood cells is with a Sn(II) concentration of at least 10  $\mu$ g/kg. A lower amount of Sn(II) will result in suboptimal binding efficiencies.

In vivo labelling

- The stannous pyrophosphate lyophilisate is first reconstituted with isotonic sodiumchloride 0,9%.
- Injection of the reconstituted solution of the stannous pyrophosphate complex and consecutive injection of <sup>99m</sup>Tc 30 min later.

# 3. Quality control

When red blood cells are labeled in vivo, the labelling efficiency can only be determined after administering the radionuclide, and thus no preventive steps to improve labelling efficiency can be taken.

A 5 ml blood sample can be obtained 5-10 min after administering <sup>99m</sup>Tc. The labeling efficiency of radiolabelled red blood cells can be determined by gamma counting radioactivity in aliquots of the blood before and after centrifugation of the samples at 2000 g for 20 min. The pre-centrifugation count then represents the total activity, whereas the remaining pellet after centrifugation and subsequent removal of the supernatant is a measure of cell bound activity.

The total percentage of bound radioactivity can be calculated as:

% bound activity=	activity in the pellet	x100
	activity before centrifugation of the sample	;

Also, images of the thyroid can be obtained to exclude free pertechnetate owing to poor labeling efficiency.

## 4. Interactions, contraindications & adverse reactions

## Interactions

Drug interference with <sup>99m</sup>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.
  B-blockers, calcium channel blockers, nitrates.
- 2. Agents that inhibit or diminish the radiolabeling or red blood cells by <sup>99m</sup>Tc.

Drug	Possible mechanism
Heparin	Formation of 99mTc-heparin
lodinated contrast agents	Competition between iodide and free <sup>99m</sup> Tc for transport
Methyldopa	Oxidation of Sn <sup>2+</sup>
Hydralazine	Oxidation of Sn <sup>2+</sup>
Teflon <sup>®</sup> catheter	Binding of Sn <sup>2+</sup> to tubing
Stannous overload	Direct reduction free 99mTc
Antracyclines (for example doxorubicin)	Disrupts erythrocyte cell membrane
Quinidine	Blocks transmembrane transport
Digoxin	Interfering Sn <sup>2+</sup> upake
Prazosin	Unknown

It is recommended that in vivo [<sup>99m</sup>Tc] RBC labelling be performed prior to administration of iodinated contrast media. Otherwise, labeling efficiency will be adversely affected.

### 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 (<sup>99m</sup>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 (<sup>99m</sup>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.
- International Atomic Energy Agency (IAEA). Radiolabelled Autologous Cells: Methods and Standardization for Clinical Use. IAEA Human Health Series no. 5. Vienna 2015.
- 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 99mTc: a new approach to blood pool visualization. J Nucl Med, 1977;18:305-8.
- SmPC Angiocis®, 2010
- SmPC Technescan PYP, downloaded www.cbg-meb.nl feb 2016.
- Lee HB et al. Pharmacologic alterations in Tc-99m binding by red blood cells: concise communication. J Nucl Med, 1983;24:397-401.