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The Significance of the Cobalt-55 Tracer in Positron Emission Tomography of the Brain

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Abstract:

Cobalt-55 (55Co) is a positron emission tomography (PET) tracer used to demonstrate brain damage, possibly associated to calcium-mediated processes. Different diseases such as multiple sclerosis, brain trauma and primary brain tumours have been examined with this technique. However most studies have focussed on ischemic strokes. 55-Co PET can be used, according to its uptake rate, to determine the age of cerebral infarcts, including the silent ones. An increasing 55-Co uptake is observed for infarcts up to 2 months with a gradual decrease afterwards, leading its absence after 6 months. 55-Co PET also demonstrates that in remote regions, after large cerebral middle cerebral infarcts, the associated metabolic depression can lead to irreversible brain damage. In vascular dementia brains increase of 55-Co is only observed in the cerebral white matter and not in the cerebral cortex and in the deep brainstem nuclei.

55-Co PET is useful as addition to other used blood flow and metabolic tracers. Both can be combined in a same session. 55-Co PET can now more easily be replaced by single photon emission tomography using the 57-Co as tracer. However, it cannot be combined with other tracers.

Key Words: cobalt-55 positron emission tomography; brain infarcts; vascular dementia; multiple sclerosis; traumatic brain disease; primary brain tumours; cobalt-57 single photon emission tomography

Introduction

^{18} F-2-fluoro-2-desoxy-D-glucose is the most used tracer in positron emission tomography (PET) for examination of the brain metabolism [1]. PET imaging with [^{15}O]-oxygen tracers, either through continuous or bolus inhalation, provides non-invasive assessment of blood flow, oxygen extraction fraction and cerebral metabolic rate of oxygen in cerebrovascular diseases [2].

Cobalt 55 (Co-55) is a positron emission tracer that is used as a radiolabel of the angiogenesis [3]. Co-55 is a marker for calcium chloride [4]. It is mainly used to study cerebral ischemic lesions [5].

The present review will cover the methodology applied to humans and the available clinical studies.

Methodology

For most of the presented studies we used an ECA 951/31 PET scanner (Siemens AG, Munchen, Germany).

The subjects receive 24 hours before the PET examination an intravenous administration of 20 MBq sterile ^{55}cobalt chlorides. Contiguous scans are made parallel to the orbitomeatal line with image reconstruction of 31 planes of 3.375 mm thickness. After that a transmission scan is achieved with an external ^{66}Ge/ ^{68} Ga ring-source for 10 minutes a 55-Co scan is performed in a dynamic mode (8 frames of 5 minutes). In the cases of ischemic strokes, during the same session, regional cerebral blood flow is measured according to the steady state technique by inhalation of C$^{15}O_2$ at a rate of 0.7 GBq and an equilibration for 10 minutes by scanning for 300 seconds. Arterial blood samples are obtained at the beginning and the end of the procedure. For measuring regional cerebral metabolic rate of oxygen, $^{15}O_2$ is inhaled at a rate of 1.5 GBq/min and after an equilibration period of 10 minutes the scan time is extended to 400 seconds and arterial samples are obtained at the same time as described previously. For cerebral

blood volume measurements, $C^{15}O$ is inhaled at a rate of 0.7 GBq/min and scanning for 300 seconds is performed after the same procedure.

Of the 30 upper planes, 6 are reconstructed by summation of 5 consecutive planes for ^{55}Co, as well as for the $C^{15}O2$,$^{15}O2$ and $C^{15}O$ scans. Fixed ellipsoid regions of interest with axial axis of 30 mm and lateral axis of 15 mm are drawn over the cortical rim of each reconstructed plane. For striatum, thalamus and cerebellum circular regions of interest are adapted to the sizes of the structures [6].

In stroke patients the total counts of 55-Co activity in the affected region is compared to the areas with a normal rate of cerebral blood flow, cerebral metabolic rate of oxygen and cerebral blood volume. The latter have already been validated previously by comparing with magnetic resonance imaging (MRI) [7].

Results

In relapsing-progressive multiple sclerosis (MS) 55-Co PET demonstrates significantly more lesions in the diseased brains than in the healthy control, both in the periventricular and subcortical white matter. Every single MRI lesion can be retrieved as a 55-Co PET lesion [8].

In traumatic brain injury 55-Co PET shows focal uptake that extends beyond the morphological abnormalities shown by MRI in brain regions that but detected by electroencephalography [9].
Within primary malign tumours of the brain 55-Co PET provides mainly additional details concerning the site and size of the necrotic core and the surrounding rim [10].

Inside cerebral infarcts 55-Co accumulates in the areas with diminished oxygen metabolism but with preserved blood flow independently of the blood-brain barrier breakdown [11]. The 55-Co-uptake is only found in a part of the gadolinium (Ga) enhanced brain tissue with a tendency to be located peripherally or outside the Ga demarcated brain tissue [12]. The 55-Co accumulation tends to increase during the weeks after stroke onset and decreases down to normal levels after 6 months [6].

The age of recurrent ischemic strokes can be documented by the difference in Co-55 uptake. Recent infarcts, less than 2 months have a high 55-Co uptake level, whereas ischemic lesions of 6 months to 1 year have a ratio comparable to normal brain tissue. In infarcts older than 2 years the Co-55 uptake ratio is even decreased compared to the normal surrounding tissue [13].

No differences are found in 55-Co uptake between territorial and border zone infarcts due to symptomatic atherosclerotic carotid artery disease, indicating a similar ischemic origin [14].

It is still a matter of debate whether the ipsilateral thalamic and the crossed cerebellar hypo-metabolism, observed on PET examination in brains with large middle cerebral artery infarcts, represent only a metabolic depression of these areas or can lead to structural damage. A significant increase of 55-Co influx in these remote regions is observed in half of the patients, indicating some degree of structural damage [15].

In vascular dementia the 55-Co uptake is similar in the cerebral and the deep gray nuclei, compared to normal controls. However, 55-Co is significantly increased in the cerebral white matter of the demented patients compared to stroke patients without significant cognitive decline [16].

Discussion

PET using 55-Co as a calcium tracer may visualize Co-transport across neuronal membranes. This imaging technique shows calcium mediated inflammatory processes and passive leakage through a breach in the blood-brain barrier [17].

Whole-body CO-PET reveals that the highest incidence of the tracer is observed in the liver and in the bladder of as well humans as animals [18].

Post-mortem examination has confirmed the increase of cobalt in traumatic brain injury, similar to a rise in iron content. On the other hand, the level of other elements such as copper, magnesium, manganese, phosphorus, potassium, rubidium, selenium and zinc remains unchanged [19].

The use of 55-Co is mainly indicated as additional PET tracer in patients at risk of stroke. It is mainly useful to detect silent and recurrent infarcts, which is of importance for therapeutic decisions [20]. Although on PET examination the 55-Co uptake is similar, impaired cerebral perfusion is a more frequent cause of border zone than of territorial infarcts [21].

A cheaper alternative to the 55-Co PET scan is the use of Cobalt-57 for single-photon emission computerized tomography (SPECT) [22]. This has been validated in patients with ischemic brain damage [23] and in relapsing-progressive multiple sclerosis [24]. However, it cannot be combined with the use of other tracers.

Conclusion

Cobalt PET and SPECT are useful additional techniques to magnetic resonance imaging, mainly in cerebrovascular and inflammatory demyelinising diseases.

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