Warning
The tracer 131I 6ß-iodomethylnorcholesterol, used in this protocol, is unregistered.

1. Introduction
Functioning adrenal cortex tissue can be visualised by ‘trapping’ a radiolabelled cholesterol precursor. Once taken up in the adrenal cortex, the radiopharmaceutical is not further metabolised. Since the tracer is taken up by the normal cortisol-producing adrenal tissue, this investigation must be performed under dexamethasone suppression when aldosterone or androgen-producing lesions are suspected.

2. Methodology
This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indications
Usually, the adrenal cortex scintigraphy is a complementary procedure for localising abnormal adrenal cortex tissue after the (biochemical) diagnosis of adrenal dysfunction. The main indication is the differentiation between bilateral hyperplasia and a tumour in patients with hypercortisonism (Cushing’s syndrome), hyperaldosteronism or hyperandrogenism.

4. Relation to other diagnostic procedures
a. Ultrasound can locate most large adrenal tumours, but is notoriously operator-dependent. Overlying intestinal organs or bone may complicate the interpretation.

b. Computer tomography (with thin, contiguous slices) is considered the best initial screening test for visualisation of morphological abnormalities of the adrenal cortex. The main limitation is the difficulty in detecting tumours with a diameter less than 5 mm. Furthermore, CT offers little information on the type and functionality of tumour.

c. Quantitative ‘uptake’ measurements to assess adrenal function, are usually not required. There are simpler and clearer ways to determine this, such as cortisol secretion, excretion of steroid metabolites, etc.

d. MRI has roughly the same sensitivity as CT for the localisation of adrenal masses. Given the lack of ionising radiation, MRI is considered in paediatric, obstetric and x-ray contrast sensitive patients.

5. Medical information necessary for planning
Clinical, biochemical and relevant radiological data is required in order to assess whether or not the adrenal cortex scintigraphy should be carried out and if it is to be with or without dexamethasone suppression.
6. Radiopharmaceutical
Tracer: $^{131}$I $\beta$-iodomethylnorcholesterol
Nuclide: Iodine-131
Activity: 20 MBq
Administration: Slow intravenous injection over a period of approximately 30 sec

7. Radiation safety
a. Pregnancy
The external radiation dose to the foetus after intravenous administration of the radiopharmacon to the mother is approximately 1.0-1.35 mGy (early stage) and 5.5 mGy (9 months). Foetal risks are thus low. Foetal thyroid doses are much higher than whole body dose 0.5-1.1 Gy/MBq

b. Lactation
Breast feeding should be interrupted for at least 3 weeks according to ICRP 106

c. The absorbed dose to the adrenals is 0.068-0.15 mGy/MBq for adult patients.

8. Patient preparation/essentials for procedure
a. Block unintentional radioactive iodine uptake in the thyroid with sodium or potassium iodide (100-150 mg per day) or sodium or potassium perchlorate (200-400 mg per day) for 5-10 days, starting the day before administration of the radiopharmaceutical.

b. Stop all interacting drugs, such as oral contraceptives, dexamethasone, diuretics, propranolol, ketoconazole, cholestyramine and corticosteroids at least 48 h prior to the investigation. If the clinical question is whether there is an aldosteronoma, spironolactone must be stopped at least 6 weeks in advance, as it can lead to increased radiopharmaceutical uptake in the adrenal glands.

c. If dexamethasone suppression required prescribe 4 mg/day starting one week prior to the administration of the radiopharmaceutical and continue this for as long as the investigation lasts.

d. Laxatives are not routinely necessary but can be considered if there appears to be stasis of the radiopharmaceutical in the bowel. In that case, give laxatives for several days between scintigraphies.

e. The patient should be aware of the length of time required for the investigation. Scintigraphy should occur on a least two separate occasions following the administration of the radiopharmaceutical.

9. Acquisition and processing
a. The patient is positioned sitting or supine for posterior acquisition, with the gamma camera centred at the level of the twelfth thoracic vertebra.

b. For a standard adrenal cortex scintigraphy, two recordings are made. These take place on the fifth and eighth day post radiopharmaceutical administration (the day of administration is day 0).

c. If the examination is performed under dexamethasone suppression, daily recordings should be made from day 2 until the adrenal glands become clearly visible. Sometimes recordings are made only on the 3rd and 5th days after injection.

d. A SPECT(CT) may be added to improve accuracy and localisation.

e. If only static images are made, imaging of the kidneys (e.g. with $^{99m}$Tc-DTPA or $^{99m}$Tc-
DMSA) may lead to better localisation of abnormalities.

f. Lateral images are not routinely required. They should be made when radiopharmaceutical uptake is quantified or when determining the depth of residual adrenal tissue. The depth can be measured by placing a marker on the skin.

g. Consuming a high fat content meal may be helpful for differentiating between adrenal and gall bladder activity.

10. Interpretation
The interpretation of adrenal cortex scintigraphy must be done in correlation with clinical, biochemical and radiographic data.

Standard Scintigraphy
a. Symmetrical distribution of activity:
   • Normal pattern.
   • In Cushing’s syndrome or hyperaldosteronism, one sees symmetrically increased uptake as a result of bilateral hyperplasia and ectopic production of adrenocorticotropic hormone.
   • Rarely: adenogenital syndrome secondary to 17- or 11ß-hydroxylase deficiency.

b. Asymmetrical distribution of activity:
   • Normal pattern: the right adrenal gland can be somewhat larger than the left (the normal size of the right adrenal gland is between 0,9 en 1,2 times that of the left adrenal gland). Also, there may appear to be more activity in the right adrenal due to overprojection of the liver (especially in the first days).
   • Macronodular hyperplasia (hyperaldosteronism).
   • Small aldosteronoma.
   • An aldosterone or androgen-producing carcinoma.
   • Micronodular hyperplasia (hyperaldosteronism).
   • Residue after unilateral adrenalectomy.

c. Unilateral uptake:
   • Adrenal cortex adenoma (Cushing’s syndrome).
   • Post adrenalectomy.
   • Aldosterone or androgen-producing carcinoma.
   • Adrenal infarction.
   • Gallbladder visualisation.

d. Bilateral absence of uptake:
   • Adrenal cortex carcinoma (Cushing’s syndrome).
   • Hormonal therapy.
   • Hyperlipidaemia, hypercholesterolaemia.
   • Poor labelling.

Scintigraphy under dexamethasone suppression
a. Bilateral absence of uptake:
   • Normal.
   • Essential (low renin) hypertension.

b. Unilateral uptake:
   • Aldosteronoma.
• Adrenal cortex adenoma (hyperandrogenism).

c. Symmetrical distribution of activity:
• Normal from the 5th day onwards.
• Macro- or micronodular hyperplasia (hyperaldosteronism).
• Secondary aldosteronism, e.g. due to stenosis of the renal artery.
• Medication (oral contraceptives, diuretics).
• Dexamethasone administration stopped too early.

11. Report
Describe whether one or both adrenal glands are visible and the intensity of activity relative to the liver. If under dexamethasone suppression, indicate on which day the adrenal glands become visible.

12. Literature