1. Introduction
Osteoporosis is characterised by low bone mass, disruption of the micro-architecture of bone and increased skeletal fragility. It is a common disease which leads to increased fracture risk. Besides advanced age, previous fracture(s), long term glucocorticoid therapy, low body weight, family history, cigarette smoking and alcohol abuse, bone mineral density (BMD) is an independent predictor of fracture risk.
The measurement of BMD with Dual Energy X-Ray Absorptiometry (DEXA) is based on the principal of difference in absorption of photons between soft tissue and bone. Denser and thicker tissue allows fewer photons to pass through to the detector than soft tissue. During acquisition there is transmission through the body of photon beams of two different energy levels. The difference in absorption of these beams distinguishes bone from soft tissue and allows quantification of BMD. The calculated BMD is compared to the reference population, which leads to a diagnosis and estimated fracture risk.

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
a. Patients 50 years or older with a recent non-spinal fracture or with a high risk score for fractures (≥ 4 points, see fracture risk table from CBO guidelines on Osteoporosis and fracture prevention 2011).
b. Patients 50 years or older with a proven spine fracture, may benefit from a DEXA.
c. Patients older than 60 years and without a recent fracture but at high risk of fractures (≥ 4 points).
d. Patients with underlying condition or medication associated with possible bone loss.
e. Follow-up after 5 years of treatment with Bisphosphonates, strontiumranelaat or Raloxifen.
f. Follow-up after 2 years of therapy with teripatide/PTH(1-84).
g. Follow-up can be useful 2-3 years after cessation of medication.
h. Additional vertebral fracture analysis (VFA) or, when VFA is not available, conventional X-ray, is recommended in all of the above mentioned indications (a-f) when either T-scores are between -1,0 and -2,5 or when there is a suspicion of a new vertebral fracture.
i. Total body composition with regional analysis can be used in patients with:
HIV: to assess fat distribution in patients using antiretroviral agents which are associated with a risk of lipo-atrophy

Obesity undergoing bariatric surgery or interventions with anticipated large weight loss. (Uncertain impact on clinical outcome.)

Muscle weakness or poor physical function. (Uncertain impact on clinical outcome.)

Fracture risk score: DEXA is advised at 4 or more points. CBO guidelines Osteoporosis and fracture prevention 2011.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Risk score</th>
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<tbody>
<tr>
<td>Weight &lt;60 kg and/or BMI &lt;20 kg/m²</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt;60 years</td>
<td>1</td>
</tr>
<tr>
<td>Age &gt;70 years (do not add score for &gt;60 years)</td>
<td>2</td>
</tr>
<tr>
<td>Previous fracture after the age of 50</td>
<td>1</td>
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<tr>
<td>Hip fracture at older age</td>
<td>1</td>
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<tr>
<td>Reduced mobility</td>
<td>1</td>
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<tr>
<td>Rheumatoid arthritis</td>
<td>1</td>
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<tr>
<td>More than one fall in the previous year</td>
<td>1</td>
</tr>
<tr>
<td>Underlying condition associated with secondary osteoporosis*</td>
<td>1</td>
</tr>
<tr>
<td>Glucocorticoid use (&gt;3 months; ≥7,5 mg/day)</td>
<td>4</td>
</tr>
</tbody>
</table>

*Untreated hypogonadism, inflammatory bowel disease, malabsorption, organ transplantation, Diabetes mellitus (type 1 and type 2), untreated hyperthyroidism or over treated hypothyroidism, primary hyperparathyroidism, COPD, pernicious anaemia.

4. Relation to other diagnostic procedures

- Quantitative computerised tomography (QCT) and peripheral QCT (pQCT) measure volumetric bone density and can analyse cortical and trabecular bone separately. In postmenopausal women measurement of spinal trabecular BMD with QCT has at least the same ability to predict vertebral fractures as AP measurement of spinal BMD. There is insufficient evidence to support this in men and there is also a lack of evidence to recommend spine measurements with QCT for hip fracture prediction in both men and women. pQCT of the forearm (ultra-distal radius) predicts hip, but not spine, fracture risk in postmenopausal women only. Furthermore the costs and radiation dose are higher in (p)QCT compared to DEXA.

- Quantitative ultrasonography (QUS) does not measure BMD, but the transmission of ultrasound through the limbs or reflectance of ultrasound waves of the bone surface. The only validated site for the clinical use in osteoporosis is the heel. QUS can predict fracture risk in postmenopausal women (hip, spine and global) and men over 65 years (all non-vertebral fractures), independently of DEXA measurements. Compared to DEXA, QUS has lower costs and no radiation exposure, however it is not useful in follow-up and cannot be used for diagnostics classification since the WHO criteria are based upon BMD measurements with DEXA.

- Peripheral DEXA devices are portable dedicated instruments that use the same technique as DEXA to measure BMD at peripheral sites (forearm, heel or finger).
Low T-scores are associated with increased fracture risk, but can only be used for classification with measurements at the distal one-third radius site (WHO criteria). It is not useful in response monitoring.

5. Medical information necessary for planning
- Age, sex, height and weight.
- Pregnancy (contra-indication)
- History of fracture including site
- Prosthetics in the areas of interest
- Menopausal status and age of menopausal onset
- Hormonal therapy
- Underlying condition or medication associated with possible bone loss
- Family history

6. Radiopharmaceutical
DEXA measures BMD by using X-rays. No radioactive sources are used.

7. Radiation safety
Because of the ionizing radiation, DEXA is contra-indicated in pregnancy. However the amount of radiation is very low with an effective dose less than 0,01 mSv. Shielding for personnel is not necessary.

8. Patient preparation/essentials for procedure
- Daily quality control should be performed according to the manufacturers prescriptions for the specific type of bone densitometer.
- Prior to the investigation, patients should remove metal objects which are in the area of interest.
- Patients’ height and weight should be measured.
- If the patient is undergoing investigations with radiopharmaceuticals on the same day, the DEXA should be done first. Both ⁹⁹mTc and ¹⁸F-FDG can influence the DEXA results.
- Recent use of (radio opaque) oral contrast can also render the DEXA unreliable.

9. Acquisition and processing
a. Positioning of the patient and acquisition parameters according to the manufacturer’s descriptions.
b. Postero-anterior imaging of the lumbar spine should be performed with flexion of the hips to minimise lumbar lordosis. Vertebrae L1 to L4 are analysed, unless there is severe deformity e.g. due to severe osteoarthritis or after radical surgery either with or without prosthetic material. All evaluable vertebrae should be used. Only exclude vertebrae that are affected by structural change or artefact. Also consider exclusion when a vertebra has > 1,0 T-score difference compared to its adjacent vertebrae. The BMD cannot be based on the analysis of a single vertebra. If only one intact vertebra remains, diagnosis should be based on a different valid skeletal site.
c. Measurement of the hip should occur in a standardized position. The BMD may be measured on either hip. Use femoral neck and total proximal femur for ROI.
d. If indicated, use 33% (1/3 radius) of the non-dominant forearm ROI for diagnosis.

e. If previous DEXA has been performed, it is of great importance that the ROI is the same as for previous measurements.

f. After defining the ROI, the bone mineral content (BMC) is calculated by the computer, and will be related to the measured area.

g. An image print should be made of each site measured (containing at least 1 ROI), the BMD, T-scores, Z-scores and curves.

h. Preferably use the NHANES III data as a standard reference for femoral neck and total hip T-scores. Use the manufacturer's own database for the lumbar spine.

i. The methodology for VFA (lateral image of the thoracic and lumbar spine) should be similar to standard radiological approaches. Specific software is available for the determination of the vertebral height, in which six reference points are placed on the contour of each vertebra. The anterior, medial and posterior heights are measured. Vertebral deformities are determined and classified as wedge, biconcave or crush. These deformities are subdivided into mild (20-25%), moderate (25-40%) or severe (>40%).

10. Interpretation

a. BMD is compared to reference values expressed in the amount of standard deviations (SD) difference with the average of age and sex matched controls (Z-score) and young adults (T-score). The diagnosis is based on the T-score following the WHO criteria. T-score ≥1 correlates with normal bone mineral content, T-score of <1 but ≥-2.5 signifies osteopenia and a T-score < -2.5 is defined as osteoporosis.

b. The above mentioned WHO-criteria and fracture risk assessment are based on uniform Caucasian (non-race adjusted) female normative database. Most systems, however, use sex based databases and therefore sex based T-scores, which are higher in men than in women. A T-score of -2.5 of the femoral neck and total hip in females is comparable with a T-score of -2.74 and -2.81 in men. Therefore if sex based databases are used for the diagnosis of osteoporosis in men a cut-off T-score < -2.8 should be used.

c. With children, the diagnosis is based on Z-score.

d. Degenerative, sclerotic changes of the lumbar spine/ hip and sclerotic changes of blood vessels can lead to overestimation of BMD. The images should be carefully examined for such changes. If present, this should be mentioned in the report.

e. If lateral measurements of spine are obtained, the results can be influenced by over projection of the ilium onto L4 or a rib onto L2. Lateral measurements of the lumbar spine are less reliable/ useful when scoliosis is present.

f. Follow-up BMD testing should only be done when the expected change in BMD equals or exceeds the least significant change (LSC) or when several measurements are performed over a longer time period. The LSC depends on the precision of the technique. With a precision of respectively 1,2 and 3%, the LSC's are 2,8%, 5,5% and 8,3% (two-tailed test with 95% confidence interval).

g. In patients with osteoporosis the precision is lower due to decreased BMC.

h. Quantitative comparison of BMD between different systems or facilities is not possible without cross-calibration.
11. Report
a. The report should contain the indication for the test, the measured sites and their calculated T- and Z-scores.
b. If lumbar spine and/or hip are measured T-and Z-scores of the total lumbar spine, femoral neck and total hip should be mentioned in the report.
c. If one or both of the sites are not suitable for measurement or if the patient has primary hyperparathyroidism, T-and Z-score of the distal 33% (1/3) radius should be reported.
d. If the WHO Fracture Risk Assessment Tool (FRAX) is used for determination of the absolute 10-year fracture risk, the BMD of the femoral neck should be used.
e. When VFA is performed, the absence or presence of vertebral fractures should be mentioned, preferably defined as more than 25-40% or more than 40%. If other abnormalities are seen, recommend further investigation. VFA is only suitable for detection of vertebral fractures.
f. The conclusion should contain the diagnosis in terms of normal, osteopenia or osteoporosis and if present, the amount, degree and location of vertebral fractures.

12. Literature
• Richtlijn Osteoporose en fractuurpreventie derde herziening (2011), CBO.
• NHG-standaard fractuurpreventie 2012.
• Official positions of the International Society for Clinical Densitometry 2013.