## VRAAG 3: KARAKTERISTIEKEN BEELDVORMING INCIDENTALOMA

### Diagnostische studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Method</th>
<th>Patient characteristics</th>
<th>Intervention(s)</th>
<th>Results primary outcome</th>
<th>Critical appraisal of study quality</th>
</tr>
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</table>
| Kang HW 2004 | Diagnostic study, retrospective | • Eligibility criteria: patients referred for evaluation of impalpable thyroid nodules < 1.5 cm, incidentally detected by routine US check-up of the thyroid gland, carotid artery, or other regions of the neck, and via other diagnostic modalities such as CT or PET scan  
  • Patient characteristics:  
    o Mean age: benign 49y vs. malignant 46y  
    o Females: 66% vs. 84%  
  • Prevalence of disease: 28.8% | Index test: US (only performed on 184 cases, and reported for 179 cases)  
Reference standard:  
(1) FNAB  
(2) Follow-up thyroid US: benign if no change in size after 2 consecutive exams | • Individual US criteria:  
  o Ill-defined margin: Se 30%, Sp 96%, PPV 68%, NPV 81%  
  o Irregular shape: Se 0%, Sp 100%, NPV 76%  
  o Solid echostructure: Se 98%, Sp 27%, PPV 30%, NPV 97%  
  o Hypo(iso)echoic: Se 98%, Sp 18%, PPV 27%, NPV 96%  
  o Calcification: Se 53%, Sp 92%, PPV 68%, NPV 86% | Level of evidence: B  
• Differential verification  
• Blinding not reported  
• Incorporation bias: US used as reference standard in some patients |
| Kim BH 2010 | Diagnostic study, retrospective | • Eligibility criteria: patients with focal thyroid incidentaloma on PET/CT for staging of cancer, treatment response evaluation, detection of recurrent and metastatic disease or evaluation for cancer of unknown primary origin  
  • Patient characteristics:  
    o Mean age: malignant 55.0y vs. benign 54.3y  
    o Females: 95% vs. 84%  
  • Prevalence of disease: 23.2% | Index test: FDG-PET/CT  
Reference standard:  
(1) FNAB (140/159)  
(2) High resolution thyroid US (19/159) | • Visual grade 3:  
  o Se: 70%  
  o Sp: 80%  
  o PPV: 52%  
  o NPV: 90%  
  o AUC: 0.782  
• SUVmax cut-off = 4.46:  
  o Se: 51%  
  o Sp: 80%  
  o PPV: 43%  
  o NPV: 84%  
  o AUC: 0.641  
• SUVmean cut-off = 2.03:  
  o Se: 84%  
  o Sp: 48%  
  o PPV: 33%  
  o NPV: 91%  
  o AUC: 0.605  
• CT attenuation ≤ 3:  
  o Se: 84%  
  o Sp: 36%  
  o PPV: 28% (wrongly reported in article)  
  o NPV: 88% (wrongly reported in article)  
  o AUC: 0.531 | Level of evidence: B  
• Differential verification  
• Blinded image evaluation, blinded |
| Kim SJ 2011 | Diagnostic study, retrospective | • Eligibility criteria: patients with incidentally detected thyroid nodule during cancer evaluation with PET/CT | Index test: FDG-PET/CT  
Reference standard:  
(1) Visual grade > 3  
(2) SUVmax cut-off = 1.86:  
  o Se: 71%  
  o Sp: 82%  
  o PPV: 46%  
  o NPV: 93%  
  o AUC: 0.610  
• CT attenuation ≤ 3:  
  o Se: 84%  
  o Sp: 36%  
  o PPV: 28% (wrongly reported in article)  
  o NPV: 88% (wrongly reported in article)  
  o AUC: 0.531 | Level of evidence: B  
• Differential verification  
• Blinded image evaluation, blinded |
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<tr>
<td></td>
<td></td>
<td>Patient characteristics:</td>
<td>Reference standard: Cytological findings on FNA</td>
<td>o Ill-defined margin: Se 48%, Sp 73%, PPV 51%, NPV 84%</td>
<td>Selection bias: only inclusion of patients that underwent FNA, possibly exclusion of some patients with simple cysts</td>
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<td></td>
<td></td>
<td>o Mean age: 51y</td>
<td></td>
<td>o Solid architecture: Se 91%, Sp 33%, PPV 26%, NPV 93%</td>
<td>Blinding not reported</td>
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<td></td>
<td></td>
<td>o Females: 78%</td>
<td></td>
<td>o Hypoechoic: Se 68%, Sp 53%, PPV 27%, NPV 87%</td>
<td>Only per-lesion analysis available; 101 inadequate samples were excluded from analysis</td>
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<td>o None of the patients had any radiation therapy to the head and neck area</td>
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<td>o Punctuate calcification: Se 36%, Sp 85%, PPV 39%, NPV 84%</td>
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<td></td>
<td></td>
<td>o Mean size nodules: 0.9 cm (range 0.2-1.5 cm)</td>
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<td></td>
<td></td>
<td>Prevalence of disease: 16.4% (including inadequate samples)</td>
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<td>Combination of criteria</td>
<td></td>
</tr>
<tr>
<td>Pagano L 2011</td>
<td>Diagnostic study, retrospective</td>
<td>Eligibility criteria: patients with incidental thyroid PET/CT uptake in a study performed for the following: (i) metastasis</td>
<td>Index test: FDG-PET/CT</td>
<td>SUVmax cut-off = 5.0:</td>
<td>Level of evidence: B</td>
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<td></td>
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<td>Reference standard:</td>
<td>o Se: 87%</td>
<td>Potential selection bias: selection based on receiving of thyroid</td>
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<td>o Sp: 65%</td>
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<td>o PPV: 50%</td>
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</tbody>
</table>

- **Setting:** single university centre, Korea
- **Sample size:** N=50
- **Duration:** not reported

- **Setting:** single university centre, Korea
- **Sample size:** N=267 with 317 nodules
- **Duration:** inclusion 1/2000-12/2001
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<tr>
<td>Sanitaria e Finalizzata” (protocol no. 2997 of 2008 to G.A.) from Regione Piemonte; no CoI declared</td>
<td>Setting: single university centre, Italy</td>
<td>Evaluation in the follow-up of patients with nonthyroid cancer; (ii) localization of a primitive cancer, in presence of metastases of unknown origin; (iii) localization of an infective or inflammatory process in patients with fever of unknown origin; thyroid function evaluation, US and US-FNAB, thyroid Tc99 scintigraphy when indicated, performed for the diagnostic work-up of the incidental thyroid uptake</td>
<td>US-FNAB</td>
<td>o NPV: 92%</td>
<td>Function evaluation, US and US-FNAB</td>
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<td></td>
<td>Duration: 2005-2009</td>
<td>Patient characteristics:</td>
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<td></td>
<td>From 191 cases with incidental thyroid uptake, 139 were excluded because they didn’t satisfy all inclusion criteria</td>
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<td></td>
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<td>o Mean age: 64.1y</td>
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<td>Focal uptake:</td>
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<td></td>
<td></td>
<td>o Females: 73%</td>
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<td>o Sp: 93%</td>
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<td>o Diffuse uptake: 31%; focal uptake: 69%</td>
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<td>o PPV: 39%</td>
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<td></td>
<td></td>
<td>Prevalence of disease: 28.8%</td>
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<td>o NPV: 94%</td>
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<tr>
<td>Bartolotta TV 2006</td>
<td>Diagnostic study</td>
<td>Eligibility criteria: patients with incidentally detected thyroid nodules through Doppler US of the epiaortic trunks; no history, symptoms or signs of thyroid disease</td>
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<td>Level of evidence: B</td>
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<td></td>
<td>Funding/CoI: not reported</td>
<td>Patient characteristics:</td>
<td></td>
<td>Hypoechoic:</td>
<td>• Differential verification</td>
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<td></td>
<td>Setting: single university centre, Italy</td>
<td>o Mean age: 59.4y</td>
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<td>o Sp: 35%</td>
<td>Incorporation bias: for patients without suspicious US criteria, US was used as reference standard</td>
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<td></td>
<td>Sample size: N=233 with 711 nodules</td>
<td>o Females: 61%</td>
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<td>o Intranodular flow:</td>
<td>• Blinded image review, unclear if pathology review was blinded</td>
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<td></td>
<td>Duration: 1/2003-10/2003</td>
<td>Prevalence of disease: 0%</td>
<td>Index test:</td>
<td>o Sp: 76%</td>
<td>• Only per-lesion analysis available</td>
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<td></td>
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<td>High-resolution US</td>
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<td>Real-time spatial compound sonography</td>
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<td>Reference standard:</td>
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<td>(1) FNAC</td>
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<td>(2) Yearly follow-up with US</td>
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Abbreviations: AUC: area under the curve; CoI: conflict of interest; CT: computed tomography; FDG: fluoro-deoxy glucose; FNAB: fine-needle aspiration biopsy; FNAC: fine-needle aspiration cytology; NPV: negative predictive value; PET: positron-emission tomography; PPV: positive predictive value; ROC: receiver operating curve; Se: sensitivity; Sp: specificity; SR: systematic review; TT: total thyroidectomy; US: ultrasonography.
References


