**Table 2: Characteristics of the 18 studies eligible for meta-analysis.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author, Year | Index Test(s) | Study Design | Population | HU Excl  (HU) | Size Excl  (mm) | Other Exclusions | Patients/  lesions  (N) | Incidental/ Known Malignancy/ Symptom-atic (%) | Hormone excess (confirm-ed) (%) | Reference Standard: Histol/ FU/Other  (%) | Diseased  N; % | No. ACC | No. Mets | Threshold for malignancy |
| Studies investigating incidentally detected tumors (n=7) | | | | | | | | | | | | | | |
| Angelelli; 2013 | CT | BPC  P | Imaging series, ≥50% incidental | No | <10, >120 | Cysts, myelolipoma | 50/50 | 74/0/26 | NR | 42/58/0 | 28; 56% | 7 | 13 | 1. >10HU 2. APW <60% OR RPW <40% at 10'  3. APW <60% OR RPW <40% at 15' |
| Marin; 2012 | MRI | NC  R | Imaging series, ≥90% incidental | No | <10 | No | 59/66 | 100/0/0 | NR | 35/55/11 | 17; 26% | 5 | 11 | 1. SII ≤ 23% (OP/IP dataset) **ǁ** |
| Maurea; 2004 | MRI | NC  P | Imaging series, ≥50% incidental | NR | NR | Functioning masses; Pheos (n=4) excluded by Bham team | 30/30 | 66/33/0 | 0 | 63/37/0 | 8; 31% | 4 | 3 | 1. ALR – qualitative**\*** 2. SI - qualitative **‡** |
| Nunes; 2010 | PET | WPC  R | Imaging series, ≥50% incidental | <10 | NR | Pheos; prior cancer; ACC on CT; eventual washout of contrast >50% on CT | 23/23 | 65/0/35 | 43 | 100/0/0 | 3; 13% | 2 | 0 | 1. ALR maxSUV > 1.6 **§** 2. maxSUV > 3.4 |
| Sandra-segaran; 2011 | MRI | NC  R | Imaging series, ≥50% incidental | No | <10 | Myelolipoma; cysts; artefacts on diffusion weighted imaging; lack of adequate reference | 48/49 | 69/31/0 | 2 | 38/63/0 | 12; 24% | 1 | 9 | 1. ASR ≥ 62 (ADC) **¶** 2. SII ≤ 23% (ADC) **ǁ** |
| Tessonier; 2008 | PET | WPC  P | Imaging series, ≥90% incidental | <10 | No | Functioning masses; washout on delayed enhanced CT, decrease of signal intensity on CS MRI | 37/41 | 100/0/0 | 0 | 71/29/0 | 12; 29% | 3 | 4 | 1. ALR maxSUV > 1.8 **§** 2. maxSUV > 3.28 |
| Vilar; 2008 | CT | NC  R | Imaging series, ≥90% incidental | NR | NR | None reported | 52/52 | 100/0/0 | 25% | 38/40/17 | 13; 25% | 2 | 5 | 1. >10HU |
| |  | | --- | | Studies investigating tumors in participants with current or prior non-adrenal malignancy (n=11) | | | | | | | | | | | | | | | |
| Burt; 1994 | MRI | NC  P | Operable NSCLC, ≥90% known malignancy | NR | No | None reported | 27/27 | 0/100/0 | NR | 100/4/0 | 4; 16% | 0 | 5 | 1. ALR qualitative\* |
| Choi; 2013 | CT | WPC  R | Imaging series, ≥90% known malignancy | No | No | All diagnoses other than adenoma and metastasis | 36/40 | 0/100/0 | NR | 100/30/0 | 19; 48% | 0 | 19 | 1. >10HU 2. APW at 15’ <60% 3. RPW at 15’ <40% |
| Del Moral; 2010 | PET–CT | NC  R | Imaging series, ≥50% known malignancy | NR | NR | Symptomatic tumors; Contraindications to PET; | 15/15 | 0/53/47 | NR | 87/13/0 | 11; 73% | 3 | 5 | 1. ALR maxSUV>1.8 **§** 2. maxSUV>6 |
| Frilling; 2004 | CT | WPC  P | Adrenalect-omy series, ≥90% known malignancy | No | ≤ 60 | Evidence of extra-adrenal tumor spread | 42/44 | 0/100/0 | 0 | 100/0/0 | 31; 70% | 0 | 31 | >10HU |
| Kunik-owska; 2014 | PET-CT | WPC  R | Imaging series, ≥90% known malignancy | No | No | Functioning masses | 85/104 | 0/100/0 | NR | 100/0/0 | 32; 31% | 1 | 30 | 1. ALR maxSUV>1.53 **§** 2. maxSUV>5.2 |
| Lang; 2015 | PET-CT | NC  R | Adrenalect-omy series,  ≥90% known malignancy | No | No | Functioning masses; no clinical suspicion of metastasis (based on CT findings) | 39/39 | 0/100/0 | 0 | 100/0/0 | 29; 74% | 0 | 28 | 1. ALR maxSUV>1.29 **§** 2. maxSUV > 3.7 |
| Mc-Nicholas; 1995 | CT  MRI | WPC  P | Imaging series, ≥90% known malignancy | NR | <10 | Pheos | 33/37 | 0/100/0 | NR | 51/46/0 | 19; 51% | 0 | 18 | CT: >10HU MRI: ASR ≥ 75 **¶** |
| Porte; 1999 | CT MRI | WPC  P | Operable NSCLC, ≥90% known malignancy | NR | <10 | Pheos | 32/32 | 0/100/0 | NR | 100/44/0 | 18; 56% | 0 | 18 | CT: >10HU MRI: ALR qualitative**†** |
| Ream; 2014 | MRI | NC  R | Imaging series, ≥50% known malignancy | No | <8 | Myelolipoma; cysts; nonstandardised imaging protocol; Lack of adequate reference | 36/37 | NR/78/NR | NR | 19/76/5 | 10; 28% | 0 | 8 | 1. ALR > 0.674 **††** 2. ASR > 64.1 **‡‡** 3. AMR > 70.7 **§§** |
| Schwartz; 1995 | MRI | NC  P | Biopsy referrals, ≥90% known malignancy | NR | NR | None reported | 68/68 | 0/100/0 | NR | 71/29/0 | 23; 34% | NR | NR | 1. ALR ≥ 1.5 \*\* 2. ASR ≥ 55 **¶** |
| Uemura; 2012 | CT | WPC  R | Imaging series, ≥90% known malignancy | NR | NR | Grades 4 or 5 disease; bleeding tendency & coagulopathy | 12/16 | 0/100/0 | NR | 93/0/7 | 6; 40% | 0 | 6 | 1. >10HU |

ACC – adrenocortical carcinoma; BPC – between–person comparison (multiple index tests evaluated in partial study population) APW – absolute percentage washout; ADC – apparent diffusion coefficient; ALR – adrenal to liver ratio; ASR – adrenal to spleen ratio; AMR – adrenal to muscle ratio; ASR – adrenal to spleen ratio; CT – computed tomography; CS – chemical shift; Excl – exclusion; HU – Hounsfield units; IP – in-phase; METS – metastases; MRI – magnetic resonance imaging; NC – non–comparative study; NR – not reported; OP – opposed phase; P – prospective data collection; PET – positron emission tomography; R – retrospective data collection; RPW – relative percentage washout; SI – signal intensity; SII – signal intensity index; SUVmax - maximum standardized uptake value; WPC – within–person comparison (multiple index tests evaluated in all study participants).

\* masses considered to be malignant if their signal was more intense than liver signal

† masses considered to be metastases if their signal was more intense than liver signal and inferior to kidney signal.

‡ masses considered to be malignant if no loss of signal intensity observed on chemical shift

§ALR maxSUV - ratio of SUVmax in the adrenal gland compared to the liver

**Formulae for calculating quantitative thresholds:**

ǁ Signal intensity index = (SI adrenal IP) – (SI adrenal OP)] / (SI adrenal IP)

¶ MRI adrenal to spleen ratio = (SI adrenal OP/SI Spleen OP)/(SI adrenal IP/SI spleen IP)

\*\* MRI adrenal to liver ratio = SI adrenal/SI liver

†† MRI adrenal to liver ratio = [(SI adrenal OP/SI liver OP)/(SI adrenal IP/SI liver IP)]–1) x 100%

‡‡ MRI adrenal to spleen ratio = [(SI adrenal OP/SI Spleen OP)/(SI adrenal IP/SI Spleen IP)]–1) x 100%

§§ MRI adrenal to muscle ratio = [(SI adrenal OP/SI Muscle OP)/(SI adrenal IP/SI Muscle IP)]–1) x 100%]