Computed tomography versus magnetic resonance imaging for diagnosing cervical lymph node metastasis of head and neck cancer: a systematic review and meta-analysis

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Abstract: Computed tomography (CT) and magnetic resonance imaging (MRI) are common imaging methods to detect cervical lymph node metastasis of head and neck cancer. We aimed to assess the diagnostic efficacy of CT and MRI in detecting cervical lymph node metastasis, and to establish unified diagnostic criteria via systematic review and meta-analysis. A systematic literature search in five databases until January 2014 was carried out. All retrieved studies were reviewed and eligible studies were qualitatively summarized. Besides pooling the sensitivity (SEN) and specificity (SPE) data of CT and MRI, summary receiver operating characteristic curves were generated. A total of 63 studies including 3,029 participants were involved. The pooled results of meta-analysis showed that CT had a higher SEN (0.77 [95% confidence interval {CI} 0.73–0.87]) than MRI (0.72 [95% CI 0.70–0.74]) when node was considered as unit of analysis (P<0.05); MRI had a higher SPE (0.81 [95% CI 0.80–0.82]) than CT (0.72 [95% CI 0.69–0.74]) when neck level was considered as unit of analysis (P<0.05) and MRI had a higher area under concentration-time curve than CT when the patient was considered as unit of analysis (P<0.05). With regards to diagnostic criteria, for MRI, the results showed that the minimal axial diameter of 10 mm could be considered as the best size criterion, compared to 12 mm for CT. Overall, MRI conferred significantly higher SPE while CT demonstrated higher SEN. The diagnostic criteria for MRI and CT on size of metastatic lymph nodes were suggested as 10 and 12 mm, respectively.

Keywords: computed tomography, magnetic resonance imaging, metastasis, head and neck cancer, meta-analysis

Introduction
The occurrence of cervical lymph node metastasis in patients with head and neck cancers is very common.¹ The presence of cervical lymph node metastasis may affect the optimal treatment choice as well as prognosis in patients.² Management of patients presenting with cervical lymph node metastasis includes selective or radical neck dissection, followed by radiotherapy and/or chemotherapy depending on the pathological findings of the nodes.³–⁵ Besides, the detection of cervical lymph node metastasis is very important for predicting prognosis in patients with head and neck cancers.⁶–⁸

Many imaging techniques exist for identifying cervical lymph node metastasis in patients with head and neck cancers.⁹–¹² Among them, computed tomography (CT) and magnetic resonance imaging (MRI) are the most widely used tools.¹³ Both of them have improved accuracy of nodal staging over clinical palpation and the nodes which are clinically occulted can be visualized through these techniques.¹⁴ Usually the
cervical lymph nodes demonstrate similar density as muscle on pre-contrast images of CT examination, and they can be separated from adjacent vessels by their differential enhancement after contrast administration. On the other hand, MRI is considered to have similar accuracy for identifying the cervical lymph node metastasis of head and neck cancer. Because of the intrinsic high soft-tissue discrimination, MRI has become the preferred method for evaluating the soft tissues of the head and neck recently. Under current health care settings, the routine practice for evaluating patients with head and neck cancer is to perform either CT or MRI, but not both. Thus, to determine whether one of the two techniques is superior to the other is critical for providing guidance for clinical practice. Besides, since relevant studies utilized very different diagnostic criteria, it is warranted to determine the unified criteria that are most appropriate. A systematic review to assess all available evidence is thus needed for providing a comprehensive evaluation for these aims.

The aim of this study was thus to compare CT and MRI for detecting cervical lymph node metastasis in patients with head and neck cancer and to establish the unified diagnostic criteria by performing a systematic review and meta-analysis.

Methods
Inclusion criteria
The inclusion criteria were as follows: a) types of study: diagnostic accuracy test studies designed as cohort studies; b) participants: patients with biopsy proven head and neck cancers who would undergo neck dissection; c) index tests: CT and/or MRI; d) target condition: cervical lymph node metastasis; e) reference standard: histopathology examination; f) outcome: rates of true positive, false positive, false negative, and true negative or related data that could be used to calculate them.

Literature search
With no language restriction, the following databases were searched for retrieving studies: MEDLINE (1948 to 25 January 2014), EMBASE (1980 to 25 January 2014), China National Knowledge Infrastructure (1994 to 25 January 2014), VIP Chinese Journal Database (1989 to 25 January 2014), and Chinainfo (1998 to 25 January 2014).

The search strategy was optimized for all consulted databases, taking into account the differences in the various controlled vocabularies as well as the differences of database-specific technical variations. Once relevant articles were identified, their reference lists were searched for additional articles. Both Medical Subject Headings (MeSH) and free text words were used in the search strategy with the following MeSH terms: “head and neck neoplasm”, “neoplasm metastases”, “SEN and SPE”, “Tomography, Spiral Computed” and “Magnetic Resonance Imaging”.

Study selection
Two reviewers independently examined the titles and abstracts of each search record to remove obviously irrelevant ones, and then retrieved the full text articles for potentially eligible articles. The full-texts were further examined according to the inclusion criteria. Discrepancies were resolved by consensus.

Data extraction
A standardized data extraction form was used by two authors independently for data extraction from included studies. Discrepancies were resolved by discussion, with input from a third author. The contents of the form included: name of first author, publication year, country, participants’ age, sex, number of included patients, tumor location, unit, details of CT and/or MRI, study design (prospective or retrospective).

Quality assessment
The methodological quality of included studies was assessed by The Quality Assessment Diagnostic Accuracy Studies statement-2 (QUADAS-2), which included four domains: patient selection, index test, reference standard, and flow and timing. Each domain was assessed in terms of risk of bias and the first three were assessed in terms of concerns regarding applicability. Signaling questions were included to assist judgments on risk of bias. The signaling questions in the QUADAS-2 were presented as shown in Table 1. The result for each item was categorized as yes (Y), unclear (U), or no (N). The summary risk of bias for each study was categorized as low (A), unclear (B), or high (C).

Meta-analysis
Measures of diagnostic efficacy of CT and/or MRI included sensitivity (SEN), specificity (SPE), positive likelihood ratio (+LR), negative likelihood ratio (−LR), accuracy (ACC), and diagnostic odds ratios (DOR) with 95% confidence intervals (CIs). Summary receiver operating characteristic (SROC) curves were then drawn. The area under the curve (AUC) and Q* (the point where SEN is equal to SPE on the SROC curve) were calculated.

To detect any differences for SEN, SPE, AUC, and Q* between CT and MRI, a Z-test was conducted
(Z = (VAL1–VAL2)/\sqrt{SE1^2+SE2^2}). The test standard was set at \(\alpha=0.05\). VAL indicates the mean of SEN, SPE, AUC or \(Q^*\) of the CT or MRI and SE indicates the standard error of the corresponding variable.

### Heterogeneity analysis

Heterogeneity between studies was evaluated by \(I^2\) statistic.\(^{22,23}\) If \(I^2\leq50\%\) and \(P\geq0.10\), the heterogeneity was considered not significant and in such case the fixed-effects model would be used in meta-analysis. Otherwise, the random-effects model would be used.\(^{24,25}\)

### Meta-regression

Meta-regression was used to determine any potential source of heterogeneity that might influence the overall assessment. The test standard for meta-regression was set at \(\alpha=0.10\). Relevant variables which might cause heterogeneities were tested, and any suggested sources of heterogeneity were considered as proof for a subgroup analysis. Variables detected by meta-regression included publication year (0= published before 2000; 1= published in or after 2000), race (0= Mongolian; 1= Caucasian), study type (0= retrospective; 1= prospective), risk of bias (0= high; 1= unclear; 2= low), blinding of the radiologists (0= no or unclear; 1= yes) and blinding of the pathologists (0= no or unclear; 1= yes). Meta-disc 1.4 and STATA 11.0 (StataCorp LP, College Station, TX, USA) were used to perform the statistical analyses.\(^{26,27}\)

### Results

#### Selection of literature

The computerized and manual search retrieved a total of 306 articles. After assessing the titles and abstracts, 144 articles were found to be potentially relevant. After the full text assessment, 63 studies met the inclusion criteria and were included in this meta-analysis (Figure 1).\(^{28-90}\)

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### Table 1 Signaling questions in the QUADAS-2

| Domain                        | Patient selection | Index test                                                                 | Reference standard                                                                 | Flow and timing                                                                 |
|-------------------------------|-------------------|---------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Signaling questions           | 1 Was a consecutive or random sample of patients enrolled? | 4 Were the index test results interpreted without knowledge of the results of the reference standard? | 5 Is the reference standard likely to correctly classify the target condition? | 7 Was there an appropriate interval between index test(s) and reference standard? |
| (yes/no/unclear)              | 2 Was a case-control design avoided?               |                                                                            | 6 Were the reference standard results interpreted without knowledge of the results of the index test? | 8 Did all patients receive a reference standard? |
|                               | 3 Did the study avoid inappropriate exclusions?    |                                                                            |                                                                                   | 9 Were all patients included in the analysis? |

**Abbreviation:** QUADAS-2, The Quality Assessment Diagnostic Accuracy Studies statement-2.

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**Figure 1** Flow chart of the literature search and selection.

**Abbreviations:** CT, computed tomography; MRI, magnetic resonance imaging.
Study characteristics
Of the 63 included studies, 24 were retrospective and 39 were prospective. A total of 3,029 participants were involved in these studies. Among those patients, 1,044 underwent both CT and MRI examination, 2,395 underwent MRI examination, and 1,678 underwent CT examination. Three kinds of unit of analysis were used, including node, neck level (the neck was classified as five levels according to anatomical landmarks), and patients. When node was considered as the unit of analysis, available studies involved 22 with CT and 30 with MRI. When neck level was considered as the unit of analysis, eight studies with CT and 16 with MRI were available. When patient was considered as the unit of analysis, available studies included eight with CT and eleven with MRI. The tumor locations included floor of mouth, nasopharynx, retro-molar trigonum, mandible, maxilla, supra-glottic larynx, oropharynx, laryngopharynx, hypopharynx, parotid gland, submandibular gland, tonsil, thyroid gland, cervical esophageal, paranasal sinuses et al. The characteristics of included studies are listed in Table 2.

Quality of included studies
All included studies had fairly good applicability. For the risk of bias assessment, only two studies had a low risk of bias, five had a high risk, and 56 had an unclear risk (Table 3).

Comparison of CT and MRI in detecting cervical lymph node metastasis with node as unit of analysis
For CT, meta-regression analysis showed that the diagnostic efficacy was not affected by any of the tested variables. These variables thus did not account for heterogeneity between studies. After pooling 22 studies, we detected that CT had a mean (CI) SEN of 0.77 (95% CI 0.73–0.80), SPE of 0.85 (0.84–0.87), +LR of 3.84 (2.51–5.87), −LR of 0.34 (0.24–0.27), ACC of 0.8357, and DOR of 13.57 (6.99–26.33). The SROC was demonstrated in Figure 2 and the AUC was 0.8429 and Q* was 0.7745. For MRI, meta-regression analysis also showed that the diagnostic efficacy was not affected by any of the tested variables. After pooling 30 studies, we identified that MRI had a mean (CI) SEN of 0.80 (0.77–0.82), SPE of 0.81 (0.80–0.82), +LR of 5.34 (3.24–8.82), −LR of 0.27 (0.20–0.37), ACC of 0.7745, DOR of 24.61 (12.21–49.61) and the AUC was 0.8860 and Q* was 0.8165 (Figure 3). For CT, similarly none of the tested variables accounted for heterogeneity. The pooling of available studies identified that CT had a mean (CI) SEN of 0.79 (0.73–0.84); SPE, 0.56 (0.51–0.62); +LR, 2.42 (0.99–5.91); −LR, 0.70 (0.32–1.52); DOR, 5.24 (2.13–14.73) (Figure S3). Pooling of the overall nine studies indicated that MRI had a mean (CI) SEN of 0.80 (0.77–0.82), SPE of 0.81 (0.80–0.82), +LR of 5.06 (2.13–14.73), −LR of 0.26 (0.19–0.36), ACC of 0.8860, DOR of 23.76 (7.87–71.79) and the AUC was 0.8787 and Q* was 0.8091 (Figure 3).

Comparison of CT and MRI in detecting cervical lymph node metastasis with neck level as unit of analysis
For MRI, meta-regression analysis detected that none of the tested variables accounted for heterogeneity between studies. After pooling 16 studies, it was detected that MRI had a mean (CI) SEN of 0.80 (0.77–0.82), SPE of 0.81 (0.80–0.82), +LR of 5.34 (3.24–8.82), −LR of 0.27 (0.20–0.37), ACC of 0.5257, DOR of 24.61 (12.21–49.61) and the AUC was 0.8860 and Q* was 0.8165 (Figure 3). For CT, similarly none of the tested variables accounted for heterogeneity. The pooling of available studies identified that CT had a mean (CI) SEN of 0.79 (0.73–0.84); SPE, 0.56 (0.51–0.62); +LR, 2.42 (0.99–5.91); −LR, 0.70 (0.32–1.52); DOR, 5.24 (2.13–14.73) (Figure S3). Pooling of the overall nine studies indicated that MRI had a mean (CI) SEN of 0.80 (0.77–0.82), SPE of 0.81 (0.80–0.82), +LR of 5.06 (2.13–14.73), −LR of 0.26 (0.19–0.36), ACC of 0.8860, DOR of 23.76 (7.87–71.79) and the AUC was 0.8787 and Q* was 0.8091 (Figure 3).

Comparison of CT and MRI in detecting cervical lymph node metastasis with patient as unit of analysis
For the two studies, the pooled results showed that CT had a mean (CI): SEN, 0.81 (0.65–0.92); SPE, 0.35 (0.24–0.42); +LR, 1.14 (0.87–1.50); −LR, 0.70 (0.32–1.52); DOR, 1.66 (0.57–4.82) (Figure S1). For MRI, which included ten studies, meta-regression analysis showed that study type significantly affected the assessment of diagnostic efficacy (P=0.04) (Table 5). Based on the subgroup analysis according to study types, for the four retrospective studies, the pooled results indicated that MRI had a mean (CI) SEN, 0.77 (0.69–0.85); SPE, 0.48 (0.42–0.55); +CR, 2.42 (0.99–5.91); −CR, 0.54 (0.27–1.06); DOR, 5.24 (0.96–28.55) (Figure S2). For the five prospective studies, the pooled results showed that MRI had a mean (CI) SEN, 0.80 (0.72–0.86); SPE, 0.35 (0.67–0.86); +LR, 2.79 (1.44–5.40); −LR, 0.25 (0.08–0.76); DOR, 14.63 (3.64–58.70) (Figure S3). Pooling of the overall nine studies indicated the mean (CI) values for the following parameters to be: SEN, 0.79 (0.73–0.84); SPE, 0.56 (0.51–0.62); +LR, 2.64 (1.30–5.34); −LR, 0.37(0.20–0.71); DOR, 8.87 (2.42–32.55); AUC (0.8158); Q* (0.7498) (Figure S4).
| Study ID | Country                | Patients (M/F) | Age (yr), mean (range) | Imaging modality | Unit       |
|----------|------------------------|----------------|------------------------|-------------------|------------|
| Adams et al 1998 | Germany | P | 60 (16/44) | 58.3 (38–76) | Tongue, FOM, Palate, MAN, MAX | MRI, CT node |
| Akoglu et al 2005 | Turkey | P | 23 (19/4) | 58.3 (40–78) | Head and neck | MRI, CT node |
| Anzai et al 1994 | USA | P | 12 (7/5) | 39–78 | EAC, MAN, BCC, RMT, Lip, Oral cavity, Larynx | MRI node |
| Ao et al 1998 | Japan | R | 42 (9/33) | 60 (39–78) | Larynx | MRI, CT node |
| Bondt et al 2009 | The Netherlands | P | 16 (9/7) | 40–77 | Tongue, NP, RMT, SMG, Cheek, RMT, SP, Nose | MRI, CT neck level |
| Braams et al 1996 | The Netherlands | P | 11 (7/4) | 62.3 (46–73) | FOM, RMT, Cheek, Gingiva | MRI node |
| Braams et al 1995 | The Netherlands | P | 12 (8/4) | 65.3 (48–85) | Tongue, Lip, Gingiva, RMT, FOM | MRI node |
| Bruschiini et al 2003 | Italy | P | 22 (19/3) | 62.3 (46–79) | Larynx, OP, Oral cavity, Skin | CT node |
| Curtin et al 1997 | Canada | R | 213 (150/63) | 59.6 (18–84) | Oral cavity, OP, HP, Larynx | MRI, CT neck level |
| Damann et al 2005 | Germany | R | 64 (43/21) | 56 (26–83) | Oral cavity, OP | MRI, CT neck level |
| Ding et al 2005 | People's Republic of China | P | 92 (58/34) | 53 (24–81) | Tongue | MRI neck level |
| Dijkstra et al 2010 | Sweden | P | 22 (13/9) | 60 (41–83) | MRI node |
| Eida et al 2005 | Japan | P | 11 (7/4) | 53.6 (45–70) | Tongue, Gingiva, Buccal, MAN, FOM | CT node |
| Fuku et al 2010 | Japan | R | 20 | 58 (23–81) | MRI node |
| Gross et al 2001 | USA | P | 26 (8/18) | 40 (10–80) | Thyroid | MRI node |
| Gu et al 2000 | People's Republic of China | P | 62 | 58 (44–77) | Head and neck | MRI node |
| Guzen et al 2013 | Germany | P | 120 (95/25) | 41–85 | MRI node |
| Guo et al 2006 | People's Republic of China | R | 48 (28/20) | 56 (21–66) | Tongue, Buccal, Gingiva, FOM, Palate | MRI node |
| Hannah et al 2002 | Australia | P | 48 (34/14) | 61 (26–92) | Oral cavity, OP, SGL, HP | CT neck level |
| Hao et al 2000 | People's Republic of China | P | 60 | 56 (32–80) | MRI node |
| Hafidh et al 2006 | Ireland | R | 48 (42/6) | 56 (32–80) | OP, Larynx | MRI node |
| Hlawitschka et al 2002 | Germany | P | 38 (28/10) | 59 (41–89) | MRI, CT node |
| Hoffmann et al 2000 | USA | P | 9 (6/3) | 43–76 | MRI, OP, Lip | MRI, CT neck level |
| Jeon et al 2007 | Greece | R | 47 (11/6) | 56.3 | MRI, Australia | MRI node, neck level |
| Kawai et al 1999 | Germany | P | 111 (95/16) | 29–78 | MRI, CT neck level |
| Kawai et al 2005 | Japan | P | 29 (23/6) | 60 (28–81) | Tongue, OP, NP, Larynx, Buccal, Palate, PG, Gingiva | MRI node |
| Ke et al 2006 | People's Republic of China | R | 20 (15/5) | 54.5 (31–69) | MRI, CT, Thyroid gland | CT, MRI node |
| Krabbe et al 2008 | The Netherlands | R | 38 (21/17) | 59 (53–680) | MRI, CT node |
| Laubenbacher et al 1994 | Germany | P | 22 (20/2) | 54.4 (38–70) | MRI, CT node, neck level |
| Lee et al 2013 | People's Republic of China | P | 22 (21/1) | 49.8 (26–66) | MRI, CT node, neck level |
| Lu et al 2007 | People's Republic of China | P | 13 (11/2) | 58 (47–71) | Tongue, Buccal, OP, FOM, HP, Palate, RMT, epiglottis, Pyriform sinus | MRI, CT node |
| Lwin et al 2012 | UK | R | 102 (68/34) | 39 (23–89) | MRI, CT node |
| McQuirt et al 1995 | UK | P | 49 | 61.8 (44–73) | MRI, CT node |
| Nakamoto et al 2009 | Japan | R | 65 (50/15) | 62 (27–81) | MRI, CT node |
| Nishimura et al 2006 | Japan | P | 16 (13/3) | 65.8 (37–76) | MRI, CT node |
| Olimos et al 1999 | The Netherlands | P | 12 (6/6) | MRI, CT node, neck level |

(Continued)
| Study ID     | Country                      | Study type | Patients (M/F) | Age (yr)     | Tumor location                                         | Imaging modality | Unit          |
|-------------|------------------------------|------------|----------------|--------------|--------------------------------------------------------|------------------|---------------|
| Ou et al    | People’s Republic of China   | R          | 24 (19/5)      | 50 (23–80)   | Tongue, OP, Palate, Cheek, Maxillary sinus, Branchial cleft | MRI              | node          |
| Paulus et al 1998 | Belgium                     | R          | 25 (21/4)      | 48–74        | SGL, Tongue, Glottis, Palate, RMT, FOM, HP, Vocal cord, Vestibule, Pyriform sinus | CT               | node          |
| Perrone et al 2011 | Italy                       | R          | 17 (10/7)      | 63 (15–85)   | Head and neck                                          | MRI              | patient       |
| Peters et al 2013 | The Netherlands              | R          | 149 (120/29)   | 62 (40–78)   | SGL, Glottis, N, Cervical Esophageal                   | MRI, CT         | patient       |
| Pohar et al 2006 | USA                         | R          | 25 (17/8)      | 63.4         | Oral cavity, OP, HP, Larynx, Nasal cavity             | CT               | node, neck level |
| Ren et al 2000 | People’s Republic of China   | P          | 20 (18/2)      | 45–68        | SGL                                                   | MRI              | node          |
| Schwartz et al 2004 | USA                         | P          | 20 (20/0)      | 61 (42–78)   | Oral cavity, OP                                       | MRI              | node          |
| Semedo et al 2006 | Portugal                    | P          | 20 (20/0)      | 57.3 (36–78) | HP, Larynx, OP                                         | MRI              | node          |
| Seitz et al 2009 | Germany                    | R          | 66 (39/27)     | 63 (25–89)   | Oral cavity, OP                                       | MRI              | node, patient |
| Stokkel et al 2000 | The Netherlands            | P          | 54 (31/23)     | 60 (34–81)   | Tongue, FOM, Gingiva, RMT, OP                          | CT               | node          |
| Stuckensen et al 2000 | Germany                   | P          | 106 (89/17)    | 59.6 (33–87) | FOM, Tongue, RMT, MAN, MAX, Buccal                   | MRI, CT         | neck level    |
| Sumi et al 2007 | Japan                      | R          | 38 (32/6)      | 65           | HP, Gingiva, OP, Tongue, Larynx, FOM                  | MRI, CT         | node          |
| Sumi et al 2007 | Japan                      | P          | 26            | 24–80        | OP, Gingiva, Tongue                                     | MRI              | node          |
| Sumi et al 2003 | Japan                      | P          | 32            | 45–68        | OP, Gingiva, FOM, Tongue, Buccal, EAC                  | MRI              | node          |
| Sun et al 2013 | People’s Republic of China | R          | 114 (60/54)    | 51.2 (34–70) | Thyroid gland, Larynx, NP, HP, Tongue, PG, Cervical Esophageal, Maxillary sinus, Ear | CT               | node          |
| Sun et al 2013 | People’s Republic of China | R          | 86 (45/41)     | 52.7 (35–75) | Thyroid gland, Larynx, NP, HP, Tongue, PG, Cervical Esophageal, Maxillary sinus, Ear | MRI              | node          |
| Tai et al 2002 | People’s Republic of China | P          | 40 (24/16)     | 25–65        | NP                                                    | MRI              | patient       |
| Takashima et al 1997 | Japan                  | R          | 50 (13/37)     | 57 (24–81)   | Thyroid                                               | MRI              | node          |
| Tuli et al 2008 | India                     | P          | 20 (12/8)     | 54.75 (30–65) | Tongue                                                | MRI, CT         | patient       |
| Van den Brekel et al 1991 | The Netherlands | P          | 100           | 63±1.28      | Tongue, FOM, SP, Lip, Tonsil, Pharyngeal wall, Ear, Tonsil, PS, SGL, Gingiva | MRI              | patient       |
| Vandecaveye et al 2008 | Belgium               | P          | 36            | 41–81        | Nasal cavity, SGL, FOM, Glottis, Tongue, HP           | MRI              | node, neck level, patient |
| Wang et al 1999 | Japan                    | P          | 14 (10/4)     | 46 (26–71)   | Thyroid                                               | MRI              | node          |
| WIDE et al 1999 | UK                        | R          | 58            | 58.1 (32–82) | Tongue, FOM, Buccal, RMT, OP, Gingiva                 | MRI              | neck level    |
| Wilson et al 1994 | UK                        | P          | 12            | 53.6 (45–85) | FOM, Tongue, Tonsillar, Skin, Pinna, PG, Thyroid         | MRI              | neck level    |
| Wu et al 2010 | People’s Republic of China | R          | 24 (23/1)     | 53.6 (45–85) | Larynx, HP                                            | CT               | node          |
| Yoon et al 2008 | Korea                     | R          | 67 (58/9)     | 60 (24–85)   | Larynx, Pharynx, Tonsil, Tongue, Oral cavity, Skin, MAX | MRI, CT         | neck level    |
| Yuan et al 2000 | People’s Republic of China | R          | 19 (12/7)     | 42–66        | Larynx                                               | MRI              | neck level    |

Abbreviations: M, male; F, female; R, Retrospective; P, Prospective; EAC, external auditory canal; BCC, branchial cleft cyst; PS, piriform sinus; SGL, supra-glottic larynx; TGL, trans-glottic larynx; CT, computed tomography; MRI, magnetic resonance imaging; FOM, floor of mouth; MAN, mandible; MAX, maxilla; RMT, retro-molar trigonum; NP, nasopharynx; SMG, submandibular gland; OP, oropharynx; HP, hypopharynx; LP, laryngopharynx; PG, parotid gland; SP, supropharynx; yr, years.
| Study ID          | Patient selection 1 | Patient selection 2 | Patient selection 3 | Index test | Reference standard 4 | Reference standard 5 | Reference standard 6 | Flow and timing 7 | Summary risk of bias 8 | Applicability |
|------------------|---------------------|---------------------|---------------------|------------|----------------------|----------------------|----------------------|-------------------|-----------------------|---------------|
| Adams et al³⁷ 1998 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | Y                     | B             |
| Akoglu et al³² 2005 | Y                   | Y                   | Y                   | U          | Y                    | U                    | U                    | Y                 | Y                     | B             |
| Anzai et al³³ 1994 | U                   | Y                   | Y                   | U          | Y                    | U                    | Y                    | Y                 | Y                     | B             |
| Ao et al³¹ 1998   | U                   | Y                   | Y                   | U          | Y                    | U                    | U                    | Y                 | Y                     | B             |
| Bondt et al³¹ 2009 | Y                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Braams et al³³ 1996 | U                   | Y                   | Y                   | Y          | U                    | Y                    | U                    | Y                 | Y                     | B             |
| Braams et al³³ 1995 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | Y                     | B             |
| Bruschini et al³³ 2003 | U               | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | Y                     | B             |
| Curtin et al³³ 1997 | Y                   | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Dammann et al³⁷ 2005 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | Y                     | B             |
| Ding et al³³ 2005 | U                   | Y                   | Y                   | Y          | Y                    | U                    | U                    | Y                 | Y                     | B             |
| Dirix et al³³ 2010 | U                   | Y                   | Y                   | U          | Y                    | Y                    | U                    | Y                 | Y                     | B             |
| Eida et al³³ 2003 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | Y                     | B             |
| Fan et al³³ 2006 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | N                     | A             |
| Fukunari et al³³ 2010 | U               | Y                   | Y                   | U          | U                    | U                    | Y                    | Y                 | B                     | H             |
| Gross et al³³ 2001 | U                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Gu et al³³ 2000 | U                   | Y                   | Y                   | Y          | U                    | Y                    | U                    | Y                 | Y                     | B             |
| Guenzel et al³³ 2013 | U               | Y                   | Y                   | U          | U                    | Y                    | U                    | Y                 | Y                     | B             |
| Guo et al³³ 2006 | U                   | Y                   | Y                   | U          | U                    | Y                    | U                    | Y                 | N                     | A             |
| Hannah et al³³ 2002 | U                   | Y                   | Y                   | U          | U                    | Y                    | U                    | Y                 | Y                     | B             |
| Hao et al³³ 2000 | U                   | Y                   | Y                   | Y          | U                    | Y                    | U                    | Y                 | Y                     | B             |
| Hafidi et al³³ 2006 | U                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Hlawitscha et al³³ 2002 | Y               | Y                   | Y                   | U          | Y                    | U                    | U                    | Y                 | N                     | A             |
| Hoffman et al³³ 2000 | U                   | Y                   | Y                   | U          | U                    | U                    | Y                    | Y                 | B                     | H             |
| Jeong et al³³ 2007 | U                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | B                     | H             |
| Kau et al³³ 1999 | Y                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Kawai et al³³ 2005 | Y                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Ke et al³³ 2006 | Y                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Krabbe et al³³ 2008 | U                   | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Laubenbacher et al³³ 1994 | U              | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Lee et al³³ 2013 | Y                   | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Lu et al³³ 2007 | Y                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Lwin et al³³ 2012 | U                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Mguirt et al³³ 1995 | Y                   | Y                   | Y                   | U          | Y                    | U                    | Y                    | Y                 | B                     | H             |
| Nakamoto et al³³ 2009 | U               | Y                   | Y                   | U          | U                    | U                    | Y                    | Y                 | B                     | H             |
| Nishimura et al³³ 2006 | Y               | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | B                     | H             |
| Olmos et al³³ 1999 | U                   | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | N                     | A             |
| Ou et al³³ 2007 | U                   | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Paulus et al³³ 1998 | U                   | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Perrone et al³³ 2011 | U                   | Y                   | Y                   | U          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Peters et al³³ 2013 | U                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Pohar et al³³ 2006 | Y                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Ren et al³³ 2000 | U                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Schwartz et al³³ 2004 | U               | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Semedo et al³³ 2006 | Y                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Seitz et al³³ 2009 | Y                   | Y                   | Y                   | Y          | Y                    | Y                    | Y                    | Y                 | Y                     | C             |
| Stokkel et al³³ 2000 | U                   | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | Y                     | B             |
| Stuckensen et al³³ 2000 | Y               | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | Y                     | B             |
| Suni et al³³ 2007 | U                   | Y                   | Y                   | U          | U                    | Y                    | Y                    | Y                 | Y                     | B             |
| Suni et al³³ 2006 | Y                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | Y                     | B             |
| Suni et al³³ 2003 | Y                   | Y                   | Y                   | Y          | U                    | U                    | Y                    | Y                 | Y                     | B             |
| Sun et al³³ 2013 | Y                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | Y                     | B             |
| Tai et al³³ 2002 | U                   | Y                   | Y                   | Y          | U                    | U                    | U                    | Y                 | N                     | A             |
| Takashima et al³³ 1997 | U                   | Y                   | Y                   | Y          | U                    | Y                    | Y                    | Y                 | Y                     | B             |

(Continued)
### Table 3 (Continued)

| Study ID | Patient selection | Index test | Reference standard | Flow and timing | Summary risk of bias | Applicability |
|----------|-------------------|------------|--------------------|-----------------|----------------------|----------------|
| Tuli et al\(^{89}\) 2008 | Y | Y | Y | Y | Y | Y | Y | B | H |
| Van den Brekel et al\(^{91}\) 1991 | U | Y | Y | Y | U | U | Y | Y | B | H |
| Vandecaveye et al\(^{94}\) 2008 | Y | Y | Y | Y | Y | U | Y | Y | B | H |
| Wang et al\(^{96}\) 1999 | U | Y | Y | Y | Y | Y | Y | C | H |
| WIDE et al\(^{96}\) 1999 | U | Y | Y | Y | U | U | Y | Y | B | H |
| Wilson et al\(^{94}\) 1994 | Y | Y | Y | Y | U | U | Y | Y | B | H |
| Wu et al\(^{99}\) 2010 | U | Y | Y | U | Y | U | Y | Y | B | H |
| Yoon et al\(^{89}\) 2008 | U | Y | Y | U | Y | U | Y | Y | B | H |
| Yuan et al\(^{90}\) 2000 | U | Y | Y | U | Y | U | Y | Y | B | H |

Abbreviations: Y, yes; U, unclear; N, no; A, high risk of bias; B, unclear risk of bias; C, low risk of bias; H, high applicability.

The comparison between CT and MRI showed that MRI had significantly higher AUC than CT while the other variables demonstrated no statistical significance between them. The details are listed in Table 4.

### Lymph node size criteria

The size of metastatic lymph nodes used as diagnostic criteria of MRI and CT varied considerably among studies and among different neck levels (Table S1). To determine the best diagnostic criteria, a meta-analysis was conducted for different neck levels with lymph node unit data. For each neck level, the SROC curve was drawn to show the diagnostic efficacy of MRI for different node sizes (Figure 4). The results revealed that the minimal axial diameter of 10 mm in lymph node-bearing regions could be considered as the best size criterion for assessing cervical lymph node metastasis in patients with head and neck cancer (Table S2). For CT, the suggested criterion was 12 mm (Table S3). Considering the limited number of studies for CT, SROC curves were not drawn.

### Discussion

Head and neck cancer is a common malignant neoplasm worldwide.\(^1\) One of the most important factors that influences treatment approaches and therapeutic outcomes for patients with head and neck cancer is the presence of metastatic cervical lymph node. The accurate detection of the cervical lymph node metastasis is thus very important.\(^{91,92}\) Clinical palpation used to be the method to detect cervical nodal metastasis before the development of imaging technologies. However, studies have shown that both the SEN and the SPE of this technique were unsatisfactory, with a high false positive rate of 25%–51%. The improvements in imaging technologies may make it possible for cervical lymph nodes metastasis in head and neck cancer patients can be effectively diagnosed, especially with CT and MRI.\(^{1,12,93-96}\) However, under current health care settings usually only one imaging technique will be performed. Thus a systematic evaluation regarding whether one of the two imaging techniques (CT and MRI) can have a better efficacy than the other will be critical to better guide the clinical practice.

In our systematic review and meta-analysis, we comprehensively evaluated all available evidence from 63 studies for evaluating this question whether one of the two imaging techniques (CT and MRI) can have a better efficacy.
Besides pooling results from available studies, we assessed potential sources of heterogeneities via meta-regression and conducted sub-group analyses for significant heterogeneity sources detected. Our meta-analyses suggested that CT had a higher SEN than MRI when node was used as unit of analysis; MRI had a higher SPE when neck level was used as unit of analysis; and MRI had a higher AUC when patient was used as unit of analysis. Our findings showed that CT and MRI are effective tools for detecting the cervical lymph node metastasis in patients with head and neck cancer. Since the diagnostic criteria presented in relevant studies varied significantly, we also summarized available evidence to reveal the most appropriate ones for these two techniques, respectively. Usually, the diagnosis of metastatic cervical lymph nodes consisted of two parts, namely, structural and size changes. The structural changes included central necrosis or cystic degeneration, spherical (rather than flat or bean) shape, or abnormal grouping of nodes (a cluster of three or more lymph nodes of borderline size). In different studies, the description of the structural changes differed only mildly. However, the criteria for sizes differed considerably. Most authors recommended using the minimal axial diameter to assess metastasis. The criterion for minimal axial diameter varied between 5 to 15 mm. Our meta-analysis showed that the minimal axial diameter of 10 mm in lymph node-bearing regions could be considered as the best criterion for assessing cervical lymph node metastasis in patients with head and neck cancer for MRI, compared to 12 mm for CT. Several limitations should be acknowledged for the interpretation of our findings. Firstly, although we conducted meta-regression analyses and showed that the assessed variables largely did not account for heterogeneities between studies, additional undetected variables may account for heterogeneities which warrants further research. Secondly, in some of our analyses, only a very limited number of studies were available. For example, when focusing on the 12 mm size criterion, there was only one study available for evaluating CT with node unit, and future studies for evaluating relevant topics are warranted. In conclusion, through this comprehensive systematic review and meta-analysis, we identified that CT and MRI had acceptable diagnostic efficacy in detecting cervical lymph node metastasis in patients with head and neck cancer. When node was used as unit of analysis, CT had a higher SEN. When neck level was used as unit of analysis, MRI had a higher SPE. Our findings suggest that MRI is superior to CT in the diagnosis of cervical lymph node metastasis, especially in diagnosis confirmation. While CT had a better efficacy in diagnosis exclusion. The diagnostic criteria for MRI and CT for size of metastatic lymph nodes were established. Further high-quality studies are warranted to confirm our findings.

Table 4 Comparison of meta-analysis results on diagnostic efficacy between CT and MRI

| Unit        | Variable | Number detected | SEN (95% CI) | SPE (95% CI) | AUC (SE) | Q* (SE) |
|-------------|----------|-----------------|-------------|-------------|----------|---------|
| Node        | CT       | 2,483           | 0.77 (0.73–0.87) | 0.85 (0.84–0.87) | 0.8429 (0.0341) | 0.7745 (0.0318) |
|             | MRI      | 7,100           | 0.72 (0.70–0.74) | 0.84 (0.83–0.85) | 0.9054 (0.0198) | 0.8371 (0.0215) |
|             | P        |                 | 0.0176       | 0.2739       | 0.1098    | 0.1262  |
| Neck level  | CT       | 1,665           | 0.84 (0.75–0.84) | 0.72 (0.69–0.74) | 0.8787 (0.0268) | 0.8091 (0.0270) |
|             | MRI      | 4,022           | 0.80 (0.77–0.82) | 0.81 (0.80–0.82) | 0.8860 (0.0262) | 0.8165 (0.0269) |
|             | P        |                 | 1.0000       | 0.0000       | 0.8689    | 0.8702  |
| Patient     | CT       | 230             | 0.67 (0.52–0.80) | 0.74 (0.68–0.81) | 0.8680 (0.0815) | 0.6418 (0.0643) |
|             | MRI      | 716             | 0.78 (0.70–0.81) | 0.76 (0.72–0.80) | 0.8631 (0.0437) | 0.7937 (0.0424) |
|             | P        |                 | 0.1992       | 0.6161       | 0.0491    | 0.0683  |

Abbreviations: AUC, area under the curve; CI, confidence interval; SE, standard error; CT, computed tomography; MRI, magnetic resonance imaging; SEN, sensitivity; SPE, specificity.
Table 5 Results of meta-regression (MRI patient)

| Variable               | Coefficient | SE      | P-value  | RDOR       | 95% CI     |
|------------------------|-------------|---------|----------|------------|------------|
| Cte                    | –0.511      | 2.5493  | 0.8539   | –          | –          |
| S                      | –0.330      | 0.1896  | 0.1798   | –          | –          |
| Publication year       | 0.881       | 1.5156  | 0.6020   | 2.41       | (0.02–300.01) |
| Race                   | 1.786       | 1.1884  | 0.2298   | 5.97       | (0.14–262.04) |
| Study type             | 3.288       | 0.9742  | 0.0432   | 26.80      | (1.21–595.04) |
| Blinding of radiologists | –0.774     | 1.1952  | 0.5636   | 0.46       | (0.01–20.70) |
| Blinding of pathologists | –0.290    | 1.5278  | 0.8615   | 0.75       | (0.01–96.74) |
| Risk of bias           | –0.227      | 0.9225  | 0.5636   | 0.46       | (0.01–15.02) |

Abbreviations: MRI, magnetic resonance imaging; CI, confidence interval; SE, standard error; RDOR, relative diagnostic odds ratio.

Figure 4 Summary receiver operator characteristic curves of CT and MRI (lymph node size criteria).
Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; SROC, summary receiver operating characteristic.
Disclosure
The first and corresponding authors had full access to all of the data in the study and had final responsibility for the decision to submit for publication. The authors have no conflicts of interest in this work.

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Supplementary materials

Figure S1 Meta-analysis of CT for detecting cervical lymph node metastasis in head and neck cancer patients (patient as unit of analysis).

Abbreviations: CT, computed tomography; CI, confidence interval; LR, likelihood ratio; df, degrees of freedom; SROC, summary receiver operating characteristic; AUC, area under the curve; SE, standard error.

Figure S2 Meta-analysis of MRI for detecting cervical lymph node metastasis in head and neck cancer patients (patient as unit of analysis) (retrospective studies).

Abbreviations: MRI, magnetic resonance imaging; CI, confidence interval; LR, likelihood ratio; OR, odds ratio.
Figure S3 Meta-analysis of MRI for detecting cervical lymph node metastasis in head and neck cancer patients (patient as unit of analysis) (prospective studies).

Abbreviations: MRI, magnetic resonance imaging; CI, confidence interval; df, degrees of freedom; LR, likelihood ratio; OR, odds ratio.
Figure S4 Meta-analysis of MRI for detecting cervical lymph node metastasis in head and neck cancer patients (patient as unit of analysis).

Abbreviations: MRI, magnetic resonance imaging; CI, confidence interval; df, degrees of freedom; LR, likelihood ratio; OR, odds ratio; SROC, summary receiver operating characteristic; AUC, area under the curve; SE, standard error.
### Table S1 Study characteristics of lymph node size per neck level

| Study ID                  | Method     | Unit        | I  | II  | III | IV  | Retro | Others | TP   | FP   | FN   | TN   |
|---------------------------|------------|-------------|----|-----|-----|-----|-------|--------|------|------|------|------|
| Adams et al11 1998        | CT         | node        | 12 | 12  | 12  | 12  | 12    | 12     | 96   | 21   | 175  | 992  |
| Adams et al11 1998        | MRI        | node        | 12 | 12  | 12  | 12  | 12    | 12     | 94   | 23   | 250  | 917  |
| Akoglu et al12 2005       | CT         | node        | 15 | 15  | 15  | 15  | 15    | 15     | 21   | 6    | 2    | 12   |
| Akoglu et al12 2005       | MRI        | node        | 15 | 15  | 15  | 15  | 15    | 15     | 16   | 11   | 11   | 13   |
| Anzai et al11 1994        | MRI        | node        | 10 | 10  | 10  | 10  | 10    | 10     | 38   | 2    | 34   |      |
| Braams et al12 1995       | CT         | node        | 11 | 10  | 10  | 10  | 10    | 10     | 5    | 4    | 10   | 13   |
| Braams et al12 1995       | MRI        | node        | 10 | 11  | 10  | 10  | 10    | 10     | 5    | 6    | 10   | 134  |
| Braams et al12 1995       | MRI        | node        | 11 | 10  | 10  | 10  | 10    | 10     | 8    | 10   | 14   | 167  |
| Curtin et al11 1997       | CT         | neck level  | 5  | 5   | 5   | 5   | 5     | 5      | 57   | 1    | 415  | 62   |
| Curtin et al11 1997       | CT         | neck level  | 7  | 7   | 7   | 7   | 7     | 7      | 56   | 2    | 396  | 81   |
| Curtin et al11 1997       | CT         | neck level  | 8  | 8   | 8   | 8   | 8     | 8      | 55   | 3    | 372  | 105  |
| Curtin et al11 1997       | CT         | neck level  | 9  | 9   | 9   | 9   | 9     | 9      | 53   | 5    | 329  | 148  |
| Curtin et al11 1997       | CT         | neck level  | 10 | 10  | 10  | 10  | 10    | 10     | 51   | 7    | 291  | 186  |
| Curtin et al11 1997       | CT         | neck level  | 11 | 11  | 11  | 11  | 11    | 11     | 46   | 12   | 210  | 267  |
| Curtin et al11 1997       | CT         | neck level  | 12 | 12  | 12  | 12  | 12    | 12     | 43   | 15   | 157  | 320  |
| Curtin et al11 1997       | CT         | neck level  | 15 | 15  | 15  | 15  | 15    | 15     | 32   | 26   | 76   | 401  |
| Curtin et al11 1997       | MRI        | neck level  | 5  | 5   | 5   | 5   | 5     | 5      | 53   | 5    | 382  | 95   |
| Curtin et al11 1997       | MRI        | neck level  | 7  | 7   | 7   | 7   | 7     | 7      | 52   | 6    | 367  | 110  |
| Curtin et al11 1997       | MRI        | neck level  | 8  | 8   | 8   | 8   | 8     | 8      | 50   | 8    | 329  | 148  |
| Curtin et al11 1997       | MRI        | neck level  | 9  | 9   | 9   | 9   | 9     | 9      | 48   | 10   | 281  | 196  |
| Curtin et al11 1997       | MRI        | neck level  | 10 | 10  | 10  | 10  | 10    | 10     | 47   | 11   | 248  | 229  |
| Curtin et al11 1997       | MRI        | neck level  | 11 | 11  | 11  | 11  | 11    | 11     | 41   | 17   | 167  | 310  |
| Curtin et al11 1997       | MRI        | neck level  | 12 | 12  | 12  | 12  | 12    | 12     | 38   | 20   | 134  | 343  |
| Curtin et al11 1997       | MRI        | neck level  | 15 | 15  | 15  | 15  | 15    | 15     | 30   | 28   | 67   | 410  |
| Dammann et al13 2005      | CT         | neck level  | 10 | 10  | 10  | 10  | 10    | 10     | 32   | 8    | 17   | 236  |
| Dammann et al13 2005      | MRI        | neck level  | 10 | 10  | 10  | 10  | 10    | 10     | 37   | 3    | 14   | 239  |
| Ding et al14 2005         | MRI        | neck level  | 8  | 8   | 8   | 8   | 8     | 8      | 132  | 34   | 27   | 255  |
| Dirix et al11 2010        | MR-DW      | neck level  | 10 | 10  | 10  | 10  | 10    | 10     | 30   | 2    | 93   |      |
| Dirix et al11 2010        | MR-DW      | node        | 10 | 10  | 10  | 10  | 10    | 10     | 40   | 5    | 4    | 149  |
| Dirix et al11 2010        | MR-DW      | patient     | 10 | 10  | 10  | 10  | 10    | 10     | 13   | 0    | 2    | 6    |
| Eida et al12 2003         | CT         | neck level  | 8  | 9   | 6   | 7   | 6     | 7      | 3    | 3    | 5    | 162  |
| Fan et al12 2006          | CT         | patient     | 10 | 11  | 10  | 10  | 10    | 10     | 23   | 4    | 11   | 4    |
| Fukunari et al12 2010     | MR         | node        | 10 | 10  | 10  | 10  | 10    | 10     | 19   | 66   | 13   | 0    |
| Gross et al12 2001        | MR         | node        | 11 | 10  | 10  | 10  | 10    | 10     | 143  | 6    | 22   | 39   |
| Gu et al13 2000           | MRI        | node        | 10 | 11  | 10  | 10  | 10    | 10     | 8    | 1    | 3    | 50   |
| Guenzel et al14 2013      | MR         | node        | 10 | 10  | 10  | 10  | 10    | 10     | 23   | 2    | 26   | 8    |
| Guenzel et al14 2013      | MR         | node        | 15 | 15  | 15  | 15  | 15    | 15     | 20   | 2    | 6    | 28   |
| Guo et al14 2006          | MRI        | node        | 10 | 10  | 10  | 10  | 10    | 10     | 8    | 1    | 3    | 36   |
| Hafidh et al15 2006       | CT         | node        | 10 | 10  | 10  | 10  | 10    | 10     | 8    | 12   | 10   | 2    |
| Hafidh et al15 2006       | MRI        | node        | 10 | 10  | 10  | 10  | 10    | 10     | 11   | 9    | 10   | 2    |
| Hao et al15 2000          | MRI        | node        | 15 | 15  | 15  | 15  | 15    | 15     | 10   | 11   | 175  | 38   |

(Continued)
### Table S1 (Continued)

| Study ID       | Method | Unit       | I  | II | III | IV | Retro | Others | TP | FP | FN | TN |
|----------------|--------|------------|----|----|-----|----|-------|--------|----|----|----|----|
| Kau et al 2009 | CT     | neck level | 15 | 15 | 15  | 15 | 15    | 15     | 6  | 17 | 1  | 17 |
| Kau et al 2009 | MRI    | neck level | 15 | 15 | 15  | 15 | 15    | 15     | 2  | 17 | 1  | 15 |
| Kau et al 2009 | CT     | node       | 15 | 15 | 15  | 15 | 15    | 15     | 13 | 20 | 7  | 18 |
| Kau et al 2009 | MRI    | node       | 15 | 15 | 15  | 15 | 15    | 15     | 23 | 22 | 3  | 15 |
| Kawai et al 2005 | MRSPiR | neck level I | 5  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 6  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 7  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 8  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 9  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 10 |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 5  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 6  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 7  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 8  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 9  |     |     |     |       |        |     |     |     |     |
| Kawai et al 2005 | MRSPiR | neck level I | 10 |     |     |     |       |        |     |     |     |     |
| Kawai et al 2006 | CT     | node       | 15 | 10 | 10  | 10 | 10    | 10     | 10 | 3  | 3  | 4  |

*Note: TP = True Positive, FP = False Positive, FN = False Negative, TN = True Negative.*
| Study                  | Imaging Modality | Tumor | Sensitivity | Specificity | Accuracy | PPV | NPV | TPR | TNR | FPR | FNR |
|-----------------------|------------------|-------|-------------|-------------|----------|-----|-----|-----|-----|-----|-----|
| Laubenbacher et al. 1994 | MRI              | neck level | 15 | 15 | 15 | 15 | 15 | 13 | 7 | 5 | 9 |
| Lee et al. 2013       | MR-DW            | patient | 2 | 2 | 2 | 2 | 2 | 7 | 3 | 1 | 11 |
| Lee et al. 2013       | MR-TSE           | patient | 2 | 2 | 2 | 2 | 2 | 7 | 6 | 1 | 8 |
| Lu et al. 2007        | CT               | node   | 15 | 10 | 10 | 19 | 10 | 10 | 11 | 1 | 3 |
| Lwin et al. 2012      | MR               | patient | 10 | 15 | 10 | 10 | 5 | 10 | 63 | 82 | 15 |
| McGuint et al. 1995   | CT               | patient | 10 | 15 | 10 | 10 | 10 | 10 | 18 | 3 | 1 |
| Nakamoto et al. 2009  | MRI              | patient | 10 | 10 | 10 | 10 | 10 | 10 | 16 | 2 | 4 |
| Olmos et al. 1999     | MRI              | neck level | 10 | 10 | 10 | 10 | 10 | 10 | 22 | 11 | 2 |
| Paulus et al. 1998    | CT               | node   | 15 | 15 | 10 | 10 | 10 | 10 | 8 | 1 | 0 |
| Peters et al. 2013    | CT               | patient | 3 | 3 | 3 | 3 | 3 | 3 | 10 | 56 | 0 | 1 |
| Peters et al. 2013    | CT               | patient | 4 | 4 | 4 | 4 | 4 | 4 | 8 | 48 | 2 | 9 |
| Peters et al. 2013    | CT               | patient | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 29 | 4 | 28 |
| Peters et al. 2013    | CT               | patient | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 18 | 5 | 39 |
| Peters et al. 2013    | CT               | patient | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 5 | 6 | 51 |
| Peters et al. 2013    | CT               | patient | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 4 | 5 | 6 |
| Peters et al. 2013    | CT               | patient | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 3 | 1 | 7 |
| Peters et al. 2013    | CT               | patient | 10 | 10 | 10 | 10 | 10 | 10 | 3 | 1 | 7 |
| Ren et al. 2000       | CT               | node   | 5 | 5 | 5 | 5 | 5 | 5 | 36 | 9 | 2 | 11 |
| Schwartz et al. 2004  | CT               | node   | 10 | 15 | 10 | 10 | 10 | 10 | 21 | 1 | 6 | 68 |
| Semedo et al. 2006    | MR               | node   | 10 | 10 | 10 | 10 | 10 | 10 | 24 | 8 | 1 | 30 |
| Seitz et al. 2009     | MR               | node   | 10 | 10 | 10 | 10 | 5 | 10 | 92 | 6 | 12 | 18 |
| Tai et al. 2002       | MRI              | patient | 11 | 10 | 10 | 10 | 10 | 10 | 3 | 1 | 10 | 2 |
| Van den Brekel et al. 1991 | MRI     | neck level | 10 | 10 | 10 | 10 | 10 | 10 | 87 | 13 | 42 | 415 |
| Van den Brekel et al. 1991 | MRI     | patient | 10 | 10 | 10 | 10 | 10 | 10 | 63 | 6 | 15 | 46 |
| Vandecaveye et al. 2008 | MR-TSE  | neck level | 10 | 10 | 10 | 10 | 10 | 10 | 27 | 10 | 20 | 208 |
| Vandecaveye et al. 2008 | MR-TSE  | neck level | 10 | 10 | 10 | 10 | 10 | 10 | 34 | 10 | 40 | 217 |
| Vandecaveye et al. 2008 | MR-TSE  | patient | 10 | 10 | 10 | 10 | 10 | 10 | 20 | 5 | 1 | 7 |
| Wang et al. 1999      | MRI              | node   | 10 | 10 | 10 | 10 | 10 | 10 | 23 | 0 | 15 | 130 |
| WiDE et al. 1999      | MRI              | neck level | 10 | 15 | 10 | 10 | 10 | 10 | 18 | 11 | 9 | 34 |
| Wilson et al. 1994    | MRI              | node   | 5 | 5 | 5 | 5 | 5 | 5 | 17 | 16 | 0 | 18 |
| Wu et al. 2010        | CT               | node   | 8 | 8 | 8 | 8 | 8 | 8 | 10 | 1 | 2 | 11 |
| Yoon et al. 2008      | CT               | node   | 15 | 15 | 10 | 10 | 10 | 10 | 57 | 2 | 17 | 326 |
| Yoon et al. 2008      | MRI              | neck level | 15 | 15 | 10 | 10 | 10 | 10 | 57 | 2 | 17 | 326 |
| Yuan et al. 2000      | MRI              | neck level | 12 | 12 | 10 | 10 | 10 | 10 | 12 | 1 | 2 | 9 |

**Abbreviations:** MRI, magnetic resonance imaging; CT, computed tomography; MR-TSE, MR-DW, MR-STIR, MR-SPIR, TP, true positive; FP, false positive; TN, true negative.
Table S2  Meta-analysis results on diagnostic efficacy of MRI on size of metastatic lymph nodes

| Unit | Node size (mm) | SEN (95% CI)         | SPE (95% CI)         | AUC (SE)         | Q* (SE)         |
|------|----------------|----------------------|----------------------|------------------|-----------------|
|      |                | 0.768 (0.725–0.808) | 0.901 (0.880–0.919) | 0.9159 (0.0348) | 0.8487 (0.0394) |
| Level I | 10            | 0.883                | 0.866                |                  |                 |
|       | 11            | 0.803                | 0.786                |                  |                 |
|       | 12            | 0.774 (0.709–0.830) | 0.721 (0.682–0.758) | 0.8653 (0.0295) | 0.7959 (0.0287) |
|       | 15            | 0.812 (0.778–0.844) | 0.883 (0.861–0.902) | 0.9151 (0.0341) | 0.8477 (0.0385) |
| Level II | 10            | 0.542                | 0.953                |                  |                 |
|       | 11            | 0.803                | 0.786                |                  |                 |
|       | 15            | 0.774 (0.709–0.830) | 0.721 (0.682–0.758) | 0.8653 (0.0295) | 0.7959 (0.0287) |
| Level III | 10           | 0.801 (0.767–0.833) | 0.894 (0.875–0.911) | 0.9121 (0.0314) | 0.8444 (0.0350) |
|       | 12            | 0.803                | 0.786                |                  |                 |
|       | 15            | 0.785 (0.712–0.846) | 0.704 (0.662–0.742) | 0.8385 (0.0274) | 0.7705 (0.0253) |
| Level IV | 10           | 0.801 (0.767–0.833) | 0.894 (0.875–0.911) | 0.9121 (0.0314) | 0.8444 (0.0350) |
|       | 12            | 0.803                | 0.786                |                  |                 |
|       | 15            | 0.785 (0.712–0.846) | 0.704 (0.662–0.742) | 0.8385 (0.0274) | 0.7705 (0.0253) |
| Retro | 5             | 0.885                | 0.750                |                  |                 |
|       | 10            | 0.780 (0.742–0.814) | 0.899 (0.880–0.915) | 0.9138 (0.0315) | 0.8464 (0.0354) |
|       | 12            | 0.803                | 0.786                |                  |                 |
|       | 15            | 0.785 (0.712–0.846) | 0.704 (0.662–0.742) | 0.8385 (0.0274) | 0.7705 (0.0253) |
| Others | 10            | 0.801 (0.767–0.833) | 0.894 (0.875–0.911) | 0.9121 (0.0314) | 0.8444 (0.0350) |
|       | 12            | 0.803                | 0.786                |                  |                 |
|       | 15            | 0.785 (0.712–0.846) | 0.704 (0.662–0.742) | 0.8385 (0.0274) | 0.7705 (0.0253) |

Abbreviations: MRI, magnetic resonance imaging; SEN, sensitivity; CI, confidence interval; SPE, specificity; AUC, area under the curve; SE, standard error.
### Table S3 Meta-analysis results on diagnostic efficacy of CT on size of metastatic lymph nodes

| Unit   | Node size (mm) | SEN (95% CI) | SPE (95% CI) | AUC (SE) | Q* (SE)  |
|--------|----------------|--------------|--------------|----------|----------|
| **Level I** |                |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 8      | 0.722 (0.465–0.903) | 0.966 (0.928–0.988) |           |          |          |
| 10     | 0.617 (0.464–0.755) | 0.864 (0.770–0.930) |           |          |          |
| 11     | 0.556          |              |              |          |          |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.802 (0.711–0.875) | 0.677 (0.573–0.771) | 0.8519 (0.0818) | 0.7830 (0.0776) |
| **Level II** |       |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 8      | 0.769          |              |              |          |          |
| 9      | 0.500          |              |              |          |          |
| 10     | 0.607 (0.468–0.735) | 0.510 (0.363–0.656) | 0.7272 (0.1426) | 0.6747 (0.1157) |
| 11     | 0.556          |              |              |          |          |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.802 (0.711–0.875) | 0.818 (0.746–0.876) | 0.9083 (0.0599) | 0.8402 (0.0658) |
| **Level III** |     |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 6      | 0.500          |              |              |          |          |
| 8      | 0.500          |              |              |          |          |
| 10     | 0.746 (0.659–0.820) | 0.809 (0.739–0.867) | 0.8499 (0.0783) | 0.7811 (0.0740) |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.723 (0.574–0.844) | 0.577 (0.432–0.713) |           |          |          |
| **Level IV** |      |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 7      | 0.500          |              |              |          |          |
| 8      | 0.500          |              |              |          |          |
| 10     | 0.746 (0.659–0.820) | 0.809 (0.739–0.867) | 0.8499 (0.0783) | 0.7811 (0.0740) |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.723 (0.574–0.844) | 0.577 (0.432–0.713) |           |          |          |
| **Retro** |       |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 8      | 0.500          |              |              |          |          |
| 10     | 0.746 (0.659–0.820) | 0.809 (0.739–0.867) | 0.8499 (0.0783) | 0.7811 (0.0740) |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.723 (0.574–0.844) | 0.577 (0.432–0.713) |           |          |          |
| **Others** |      |              |              |          |          |
| 5      | 0.947          |              |              |          |          |
| 8      | 0.500          |              |              |          |          |
| 10     | 0.746 (0.659–0.820) | 0.809 (0.739–0.867) | 0.8499 (0.0783) | 0.7811 (0.0740) |
| 12     | 0.821          |              |              |          |          |
| 15     | 0.723 (0.574–0.844) | 0.577 (0.432–0.713) |           |          |          |

**Abbreviations:** CT, computed tomography; SEN, sensitivity; CI, confidence interval; SPE, specificity; AUC, area under the curve; SE, standard error.

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