實證醫學
診斷肺癌病人骨轉移的方法

Evidence-Based Medicine
Diagnosis of bone metastases in patients with lung cancer

核子醫學科
R1 張意苓
Supervisor: VS莊雅雯

實證醫學六大步驟-六個A

- 臨床場景分析(Analysis)
- 提出臨床問題(Asking)： background及foreground question
- 搜尋最有用的資料(Acquire)： 5S model
- 嚴格評讀文獻(Appraisal)
- 應用到病人身上(Apply)
- 自我評估(Audit)

臨床場景(clinical scenario)

- 71 y/o, female
- Lung cancer, cT3NoMB
- s/p operation
- Adenocarcinoma, pT3(m)No
- OPD F/U: Order bone scan
- Back pain(-)
- Suspicion for bone metastases

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Asking

1.提出Background question
2.提出Foreground question

Background question

- What are the sites of lung cancer metastasis?
- What is the method used to diagnose lung cancer metastasis in our nuclear medicine department?

Overview of the risk factors, pathology, and clinical manifestations of lung cancer

- Extrathoracic metastases
  - The most frequent sites of distant metastasis are the liver, adrenal glands, bones, and brain.
- Bone
  - Metastasis from lung cancer to bone is frequently symptomatic. Pain in the back, chest, or extremity, and elevated levels of serum alkaline phosphatase are usually present in patients who have bone metastasis. The serum calcium may be elevated due to extensive bone disease. Approximately 20 percent of patients with NSCLC have bone metastases on presentation.
  - An osteolytic radiographic appearance is more frequent than an osteoblastic one, and the most common sites of involvement are the vertebral bodies.
  - Bone metastases are even more frequent in SCLC and can be found in 30 to 40 percent of patients.
  - PET and PET-CT have improved the ability to identify metastases to many organs, including bone, with greater sensitivity than CT or bone scan.

PICO

P Patient and/ problem	Patients with lung cancer
I Intervention	Bone scintigraphy
C Comparison	18FDG-PET–CT, 18FDG-PET, MRI
O Outcomes	Sensitivity, specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV)

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Searching strategy

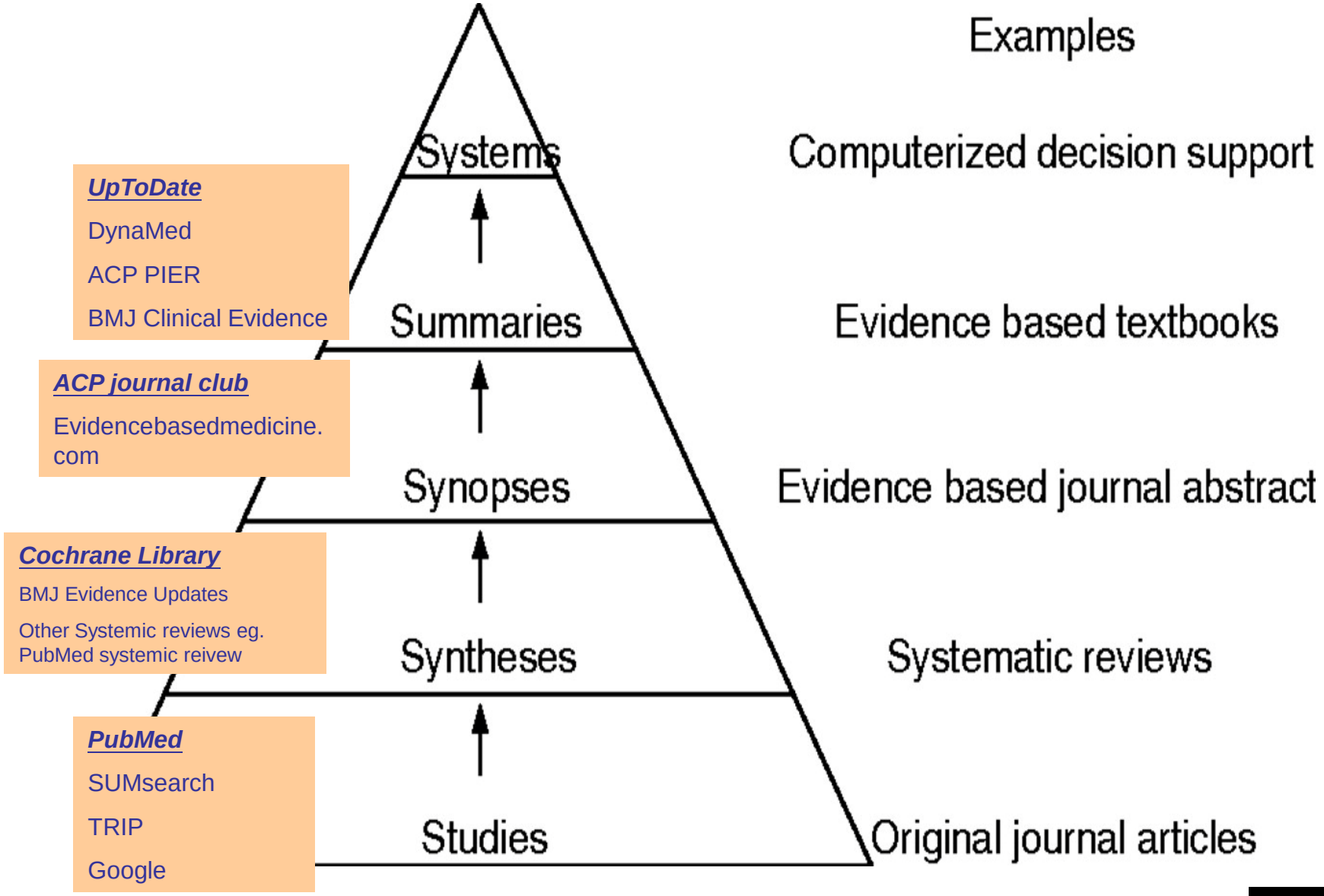
- Use MeSH to help identify terms

MeSH terms：

- Lung cancer
- Bone scintigraphy

The "5S" levels of organisation of evidence from healthcare research

Brian Haynes, R Evid Based Med 2006;11:162-164



Searching Evidence

- 實証醫學資料庫來源：
  - Uptodate
  - ACP journal club
  - Cochrane library
  - PubMed

Summaries

- Key words:
  - bone scintigraphy and lung cancer

UpToDate.

Bone scintigraphy | All Topics | Search

New Search | Patient Info | What's New | Calculators

Search Results for **"Bone scintigraphy"**

- **All Topics**
- **Adult**
- **Pediatric**
- **Patient**
- **Graphics**

- Approach to imaging modalities in the setting of suspected osteomyelitis
- Diagnostic imaging of joint pain
- Initial staging and evaluation of men with newly diagnosed prostate cancer
- Diagnostic testing for low back pain
- Overview of stress fractures
- Radiologic evaluation of the painful hip in adults
- Clinical manifestations and diagnosis of Paget disease of bone
- Bone metastases in advanced prostate cancer: Clinical manifestations and diagnosis
- Rising serum PSA following local therapy for prostate cancer: Diagnostic evaluation
- Role of imaging in the staging of non-small cell lung cancer
- Evaluation and diagnosis of hematogenous osteomyelitis in children
- Overview of hip pain in childhood
- Etiology, clinical manifestations, and diagnosis of complex regional pain syndrome in adults
- Management of bone metastases in advanced prostate cancer
- Thymic neuroendocrine (carcinoid) tumors

Role of imaging in the staging of non-small cell lung cancer

IMAGING MODALITIES

- Chest radiography
- Computed tomography
  - Technique
  - Tumor
  - Lymph nodes
  - Metastases
- Positron emission tomography
  - Technique
  - Tumor
  - Lymph nodes
  - Metastases
- Integrated PET/CT
  - Tumor
  - Lymph nodes
  - Metastases
  - Overall impact
- Magnetic resonance imaging
- Bone scan

- Bone scan — Imaging of the skeleton is indicated in patients who have symptoms (eg, focal bone pain), signs (eg, difficulty weight bearing), or laboratory abnormalities (eg, elevated alkaline phosphatase with normal gammaglutamyl transpeptidase) that raise the suspicion for bone metastases
- Bone metastases can be identified with a technetium 99m MDP nuclear medicine scan.
  - Such bone scans were once common, but they have been largely displaced by PET for two major reasons.
    - First, PET detects bone metastases with similar sensitivity and better specificity than bone scans.
    - Second, PET has the added advantage of being able to identify metastases in visceral organs.

- Advantages of bone scans include that they are less time-consuming and less likely to have false negative results from osteoblastic lesions, compared to PET.
- According to a meta-analysis of eight studies (723 patients), bone scans identified bone metastases with a sensitivity, specificity, positive predictive value, and negative predictive value of 82, 62, 32, and 90 percent, respectively, in a population with a prevalence of 20 percent.

Syntheses

ACP Journal Club℠
The Best New Evidence for Patient Care

- Key words:
  - bone scintigraphy and lung cancer

Search ACP Journal Club

bone scan and lung cancer Search

Search Help

Results **1** - **1** of about **1** for **bone scan and lung cancer**.

2009 - PET plus CT was better than conventional methods for ...

Therapeutics

PET plus CT was better than conventional methods for correctly upstaging early NSCLC

337 patients > 18 years of age (mean age 67 y, 51% women) with histologically or cytologically confirmed clinical stage I to IIIA NSCLC and technically resectable primary lesions based on chest radiography and thoracic CT done within 8 weeks of randomization.

Intervention

PET-CT using 18F-fluorodeoxyglucose (FDG), 5 MBq/kg of body weight (maximum 500 MBq), plus cranial imaging (n = 170), or conventional staging (abdominal CT that included the liver and adrenals and a whole-body bone scan) plus cranial imaging (n = 167).

Outcomes

Correct upstaging of cancer to stage IIIB or IV (confirmed by biopsy or other diagnostic imaging procedures) with avoidance of stage-inappropriate surgery. Other outcomes included incorrect upstaging of disease, incorrect understaging (pathologic stage IIIA or B disease on mediastinoscopy or thoracotomy, or local recurrence or distant metastases within 1 y of thoracotomy), and survival.

Conclusion

In early non-small-cell lung cancer, positron emission tomography plus computed tomography was better than conventional methods for correctly upstaging disease and avoiding stage-inappropriate surgery.

Synopses

- Key words:
  - bone scintigraphy and lung cancer

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Search | Search Manager | Medical Terms (MeSH)

Title, Abstract, Keywords

bone scintigraphy and lung cancer

Search Limits View search tips (Word variations have been searched)

There are 3 results from 18986 records for your search on '**bone scintigraphy and lung cancer in title abstract keywords** in **Other Reviews**'

Sort by Relevance

Select all | Export all | Export selected

A meta-analysis of 18FDG-PET-CT, 18FDG-PET, MRI and **bone scintigraphy** for diagnosis of **bone** metastases in patients with **lung cancer** (Provisional abstract)

Centre for Reviews and Dissemination

Original Author(s): Qu X , Huang X , Yan W , Wu L and Dai K

2012, 1007-1015

New

Meta-analysis: comparison of F-18 fluorodeoxyglucose-positron emission tomography and **bone scintigraphy** in the detection of **bone** metastasis in patients with **lung cancer** (Provisional abstract)

Centre for Reviews and Dissemination

Original Author(s): Chang MC , Chen JH , Liang JA , Lin CC , Yang KT , Cheng KY , Yeh JJ and Kao CH

2012, 349-357

Fluorine-18 deoxyglucose Positron Emission Tomography, Magnetic Resonance Imaging and **Bone Scintigraphy** for the Diagnosis of **Bone** Metastases in Patients with **Lung Cancer** : Which One is the Best? - a Meta-analysis (Structured abstract)

Centre for Reviews and Dissemination

Original Author(s): Liu T , Xu JY , Xu W , Bai YR , Yan WL and Yang HL

Clinical Oncology, 2011, 23(5), 350-358

Studies

- Key words:
  - bone scintigraphy and lung cancer

PubMed

搜尋關鍵字：bone scintigraphy and lung cancer

Clear all

Text availability clear

Abstract available

Free full text available

✓ **Full text available**

Publication dates clear

✓ **5 years**

10 years

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Article types clear

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1. **Meta-analysis**: comparison of F-18 fluorodeoxyglucose-positron emission tomography and **bone scintigraphy** in the detection of **bone** metastasis in patients with **lung cancer**.

Chang MC, Chen JH, Liang JA, Lin CC, Yang KT, Cheng KY, Yeh JJ, Kao CH.
Acad Radiol. 2012 Mar;19(3):349-57. Epub 2011 Dec 14. Review.
PMID: 22173321 [PubMed - indexed for MEDLINE]
Related citations

2. A **meta-analysis** of ^{18}FDG-PET-CT, ^{18}FDG-PET, MRI and **bone scintigraphy** for diagnosis of **bone** metastases in patients with **lung cancer**.

Qu X, Huang X, Yan W, Wu L, Dai K.
Eur J Radiol. 2012 May;81(5):1007-15. Epub 2011 Feb 26. Review.
PMID: 21354739 [PubMed - indexed for MEDLINE]
Related citations

3. Fluorine-18 deoxyglucose positron emission tomography, magnetic resonance **imaging** and **bone scintigraphy** for the diagnosis of **bone** metastases in patients with **lung cancer**: which one is the best?--a **meta-analysis**.

Liu T, Xu JY, Xu W, Bai YR, Yan WL, Yang HL.
Clin Oncol (R Coll Radiol). 2011 Jun;23(5):350-8. Epub 2010 Nov 20.
PMID: 21094027 [PubMed - indexed for MEDLINE]
Related citations

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Level of evidence

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

Diagnostic Study Appraisal Worksheet-1

European Journal of Radiology 81 (2012) 1007–1015

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

A meta-analysis of ^{18}FDG-PET–CT, ^{18}FDG-PET, MRI and bone scintigraphy for diagnosis of bone metastases in patients with lung cancer

Xinhua Qu[a,b], Xiaolu Huang[c], Weili Yan[d], Lianming Wu[e], Kerong Dai[a,b,*]

[a] *Shanghai Key Laboratory of Orthopaedic Implant, Department of Orthopaedics, Shanghai Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, 639 Zhizaoju Road, Shanghai 200011, PR China*

[b] *Engineering Research Center of Digital Medicine, Ministry of Education, PRC, 1954 Huashan Road, Shanghai 200030, PR China*

[c] *Department of Plastic and Reconstructive Surgery, Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine, 639 Zhizaoju Road, Shanghai 200011, PR China*

[d] *Department of Nuclear Medicine, Renji Hospital, Shanghai Jiao Tong University School of Medicine, 1630 Dongfang Road, Shanghai 200127, PR China*

[e] *Department of Radiology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, 1630 Dongfang Road, Shanghai 200127, PR China*

Step 1: Are the results of the study valid?

Was the diagnostic test evaluated in a Representative spectrum of patients (like those in whom it would be used in practice)?	
What is best?	Where do I find the information?
It is ideal if the diagnostic test is applied to the **full spectrum of patients** - those with mild, severe, early and late cases of the target disorder. It is also best if the patients are randomly selected or consecutive admissions so that selection bias is minimized.	The ***Methods*** section should tell you how patients were enrolled and whether they were randomly selected or consecutive admissions. It should also tell you where patients came from and whether they are likely to be representative of the patients in whom the test is to be used.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

•evaluate patients with suspected or previously diagnosed bone metastasis form lung cancer
•Patients enrollment: Consecutive or ND

Was the reference standard applied regardless of the index test result?	
What is best?	Where do I find the information?
Ideally both the **index test and the reference standard should be carried out on all patients** in the study. In some situations where the reference standard is invasive or expensive there may be reservations about subjecting patients with a negative index test result (and thus a low probability of disease) to the reference standard. An alternative reference standard is to follow-up people for an appropriate period of time (dependent on disease in question) to see if they are truly negative.	The ***Methods*** section should indicate whether or not the reference standard was applied to all patients or if an alternative reference standard (e.g., follow-up) was applied to those who tested negative on the index test.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

In order to be included in our analysis, articles had to meet the following qualifications: (a) use 18FDG-PET–CT, 18FDG-PET, MRI and BS to evaluate patients with suspected or previously diagnosed bone metastasis form lung cancer

(b) have used histopathological analysis and/or close clinical follow-up for at least 3 months as the reference standard

(c) have presented sufficient data to allow us to calculate the true positive (TP), false negative (FN), false positive (FP) and true negative (TN) values for per-patient or per-lesion statistics using each imaging modality

(d) include 10 or more patients.

The reasons for study exclusion after reviewing the full article were as follows: The authors of the study did not use histopathology analysis and/or close clinical and imaging follow-up for at least 3 months as the reference standard

Table 1
Main characteristics of the included studies.

Author	Year of publication	Country	Patients (Lesions) number	Male percentage(%)	Mean age (range)	Noninvasive modalities	Study design	Patients enrollment	Histopathology	Reference standard	Readers blinded to results of reference tests?	Prevalence[a] (%)
Bury T [13]	1998	Belgium	110	66.4	66.5	BS/PET	ND	Consecutive	NSCLC	Histopathological analysis, CT, MRI, close clinical and imaging follow-up for at least 9 months	Yes	19.1
Earnest F 4th [14]	1999	USA	29(112)	75.9	67.2 (48–80)	BS/MRI	Prospective	ND	NSCLC	Histopathological analysis, and/or follow-up CT or MRI data for at least 12 months	Yes	17.2
Hsia TC [15]	2002	Chinese Taipei	48(138)	58.3	ND(37–47)	BS/PET	ND	ND	NSCLC	Operative,histopathological findings or clinical follow-up longer than 1 year by additional imaging	No	ND
Gayed I [16]	2003	USA	82(100)	44.7	58.6±11	BS/PET	Retrospective	ND	NSCLC,SCLC and BAC	CT, MRI, close clinical and imaging follow-up	ND	13.4
Cheran SK [17]	2004	USA	257	58.8	64.1(38–89)	BS/PET	Retrospective	Consecutive	NSCLC,SCLC, PC,ASC and BAC	Bone biopsy,close clinical and imaging follow-up	ND	22.2
Ebert W [18]	2004	Germany	138	100	63.6(40–80)	BS	ND	ND	NSCLC and SCLC	Histopathological examination and plain radiography and/or CT	ND	35.5
Schirrmeister H [3]	2004	Germany	100	71	64.5(40–83)	BS	Prospective	Consecutive	NSCLC	MRI, PET/CT, clinical and imaging follow-up for at least 18 months	Yes	31
Erturan S [19]	2005	Turkey	125	88.8	61(34–79)	BS	Retrospective	ND	NSCLC	Clinical factors, MRI, pathologic confirmation	ND	21.6
Fischer BM [20]	2007	Denmark	29	61.9	63(44–77)	PET/PET–CT	Prospective	Consecutive	SCLC	Histopathological analysis, CT, MRI, close clinical and imaging follow-up	Yes	34.5
Ohno Y [21]	2007	Japan	90(153)	53.3	68(35–83)	PET/MRI	Prospective	Consecutive	NSCLC and SCLC	Results of standard imaging, pathological examinations, CT-guided or surgical biopsies, and follow-up examinations for more than 20 months	ND	ND
Ursavas A [22]	2007	Turkey	106	84.9	ND	BS	Retrospective	ND	NSCLC	MRI and/or biopsy, close clinical and imaging follow-up	ND	31.1
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Krüger S [24]	2009	Germany	58	ND	>18	BS/PET–CT	Retrospective	ND	NSCLC	Radiological and clinical follow-up	Yes	27.6

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Takenaka D [27]	2009	Japan	115(1025)	60.6	72	BS/MRI/PET–CT	Prospective	Consecutive	NSCLC	Pathological examinations, clinical and imaging follow-up for at least 12 months	Yes	21.7
Liu N [28]	2010	China	362(820)	64.6	56.9(17–85)	PET/PET–CT	Retrospective	Consecutive	NSCLC	Histopathological analysis, CT,MRI,BS,close clinical and imaging follow-up for at least 9 months	Yes	ND

Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?	
What is best?	Where do I find the information?
There are two issues here. First the **reference standard should be appropriate** - as close to the 'truth' as possible. Sometimes there may not be a single reference test that is suitable and a combination of tests may be used to indicate the presence of disease. Second, the reference standard and the index test being assessed should be applied to each patient **independently and blindly**. Those who interpreted the results of one test should not be aware of the results of the other test.	The ***Methods*** section should have a description of the reference standard used and if you are unsure of whether or not this is an appropriate reference standard you may need to do some background searching in the area. The ***Methods*** section should also describe who conducted the two tests and whether each was conducted independently and blinded to the results of the other.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

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Step 2: What were the results?

Are test characteristics presented?

There are two types of results commonly reported in diagnostic test studies. One concerns the **accuracy** of the test and is reflected in the sensitivity and specificity. The other concerns how the test performs in the population being tested and is reflected in **predictive values** (also called post-test probabilities).

Results:

•A total of 17 articles (9 18FDG-PET–CT studies, 9 18FDG-PET studies, 6 MRI studies and 16 BS studies) that included 2940 patients who fulfilled all of the inclusion criteria were considered for inclusion in the analysis.

•The pooled sensitivity for the detection of bone metastasis in lung cancer using 18FDGPET–CT, 18FDG-PET, MRI and BS were 0.92 (95% CI, 0.88–0.95), 0.87 (95% CI, 0.81–0.92), 0.77 (95% CI, 0.65–0.87) and 0.86 (95% CI, 0.82–0.89), respectively.

•The pooled specificity for the detection of bone metastasis from lung cancer using 18FDG-PET–CT, 18FDG-PET, MRI and BS were 0.98 (95% CI, 0.97–0.98),

•0.94 (95% CI, 0.92–0.96), 0.92 (95% CI, 0.88–0.95), 0.88 (95% CI, 0.86–0.89), respectively.

•The pooled DORs estimates for 18FDG-PET–CT 449.17 were significantly higher than for 18FDG-PET (118.25, $P < 0.001$), MRI (38.27, $P < 0.001$) and BS (63.37, $P < 0.001$).

•The pooled sensitivity of BS was not correlated with the prevalence of bone metastasis.

Step 3: Applicability of the results

Were the methods for performing the test described in sufficient detail to permit replication?	
What is best?	Where do I find the information?
The article should have sufficient description of the test to allow its **replication** and also interpretation of the results.	The ***Methods*** section should describe the test in detail.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

Conclusion:

The results showed that both 18FDG-PET–CT and 18FDG-PET were better imaging methods for diagnosing bone metastasis from lung cancer than MRI and BS.

18FDG-PET–CT has higher diagnostic value (sensitivity, specificity and DORs) for diagnosing bone metastasis from lung cancer than any other imaging methods.

Diagnostic Study Appraisal Worksheet-2

Clinical Oncology 23 (2011) 350–358

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.elsevier.com/locate/clon

Original Article

Fluorine-18 deoxyglucose Positron Emission Tomography, Magnetic Resonance Imaging and Bone Scintigraphy for the Diagnosis of Bone Metastases in Patients with Lung Cancer: Which One is the Best? — a Meta-analysis

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Received 12 March 2010; received in revised form 14 September 2010; accepted 12 October 2010

Step 1: Are the results of the study valid?

Was the diagnostic test evaluated in a Representative spectrum of patients (like those in whom it would be used in practice)?	
What is best?	Where do I find the information?
It is ideal if the diagnostic test is applied to the **full spectrum of patients** - those with mild, severe, early and late cases of the target disorder. It is also best if the patients are randomly selected or consecutive admissions so that selection bias is minimized.	The ***Methods*** section should tell you how patients were enrolled and whether they were randomly selected or consecutive admissions. It should also tell you where patients came from and whether they are likely to be representative of the patients in whom the test is to be used.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

The inclusion criteria were as follows:

18FDG PET, MRI or 99mTc-MDP bone scintigraphy imaging was used to identify and characterise bone metastases in patients with lung cancer

Table 1
Results of the distribution of study design characteristics in 34 studies

	Question	Response	
		Yes	No
1	Was the spectrum of patients representative of the patients who received the test in practice?	33	1
2	Were selection criteria clearly described?	29	5
3	Is the reference standard likely to help correctly classify the target condition?	29	5
4	Is the time between performance of reference standard and index test short enough?	34	0
5	Did the whole sample or a random selection of the sample receive verification by using a reference standard?	34	0
6	Did patients undergo examination with the same reference standard regardless of the index test result?	6	28
7	Was the reference standard performed independently of the index test?	34	0
8	Was the execution of the index test described in sufficient detail to permit replication of the test?	33	1
9	Was the execution of the reference standard described in sufficient detail to permit replication of the test?	32	2
10	Were the index test results interpreted without knowledge of the results of the reference standard?	34	0
11	Were the reference standard results interpreted without knowledge of the results of the index test?	1	33
12	Were the same clinical data available when test results were interpreted as would be available in practice?	34	0
13	Were uninterpretable and/or intermediate test results reported?	34	0
14	Were withdrawals from the study explained?	33	1

Data were the numbers of responses from the QUADAS tool. The numbers indicate how many articles were assigned a score of 'yes' or 'no'. The responses of 'no' and 'unclear' were summarised together as 'no'.

Was the reference standard applied regardless of the index test result?	
What is best?	Where do I find the information?
Ideally both the **index test and the reference standard should be carried out on all patients** in the study. In some situations where the reference standard is invasive or expensive there may be reservations about subjecting patients with a negative index test result (and thus a low probability of disease) to the reference standard. An alternative reference standard is to follow-up people for an appropriate period of time (dependent on disease in question) to see if they are truly negative.	The ***Methods*** section should indicate whether or not the reference standard was applied to all patients or if an alternative reference standard (e.g., follow-up) was applied to those who tested negative on the index test.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

The inclusion criteria were as follows:

(a) 18FDG PET, MRI or 99mTc-MDP bone scintigraphy imaging was used to identify and characterise bone metastases in patients with lung cancer

(b) histopathological analysis and/or close clinical and imaging follow-up and/or radiographic confirmation by multiple imaging modalities were used as the reference standard

Table 1
Results of the distribution of study design characteristics in 34 studies

	Question	Response	
		Yes	No
1	Was the spectrum of patients representative of the patients who received the test in practice?	33	1
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14	Were withdrawals from the study explained?	33	1

Data were the numbers of responses from the QUADAS tool. The numbers indicate how many articles were assigned a score of 'yes' or 'no'. The responses of 'no' and 'unclear' were summarised together as 'no'.

Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?	
What is best?	Where do I find the information?
There are two issues here. First the **reference standard should be appropriate** - as close to the 'truth' as possible. Sometimes there may not be a single reference test that is suitable and a combination of tests may be used to indicate the presence of disease. Second, the reference standard and the index test being assessed should be applied to each patient **independently and blindly**. Those who interpreted the results of one test should not be aware of the results of the other test.	The ***Methods*** section should have a description of the reference standard used and if you are unsure of whether or not this is an appropriate reference standard you may need to do some background searching in the area. The ***Methods*** section should also describe who conducted the two tests and whether each was conducted independently and blinded to the results of the other.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

Table 1
Results of the distribution of study design characteristics in 34 studies

	Question	Response	
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The interpretation of reference standard results without knowledge of the index test results was also hard to carry out in practice, because not only did many cases or lesions use 'clinical and imaging follow-up and/or radiographic confirmation by multiple imaging modalities' as the reference standard, but also because the choice for a treatment strategy strongly depends on the outcome of the diagnosis.

Step 2: What were the results?

Are test characteristics presented?

There are two types of results commonly reported in diagnostic test studies. One concerns the **accuracy** of the test and is reflected in the sensitivity and specificity. The other concerns how the test performs in the population being tested and is reflected in **predictive values** (also called post-test probabilities)

Table 3
Summary estimates of sensitivity, specificity and diagnostic odds ratio (DOR) for positron emission tomography (PET), magnetic resonance imaging (MRI) and bone scintigraphy and the results of the subgroup analysis of technique difference for non-small cell lung cancer

Modality and group	Number of datasets	Sensitivity (%)	Specificity (%)	DOR	*Q index
Per-patient					
PET					
Overall	8	91.9(88.8–94.3)†	96.8(96.0–97.6)†	365.5(137.99–968.1)†	0.933†
PET	3	87.5(81.4–92.2)	95.1(92.9–96.7)	149.0(60.4–367.6)	0.902
PET/computed tomography	5	94.6(91.1–97.0)§	97.5(96.6–98.3)	663.1(233.8–1880.8)§	0.948
^{68}Ge for attenuation correction	3	93.6(89.1–96.6)	97.2(96.1–98.1)	397.0(91.1–1729.2)	0.942
Computed tomography for attenuation correction	4	90.5(85.7–94.1)	96.1(94.5–97.4)	362.1(68.4–1915.6)	0.921
MRI	3	80.0(67.0–89.6)‡	90.6(85.8–94.3)	53.8(8.3–347.5)‡	0.903†
Bone scintigraphy	11	91.8(89.1–94.1)†	68.8(65.8–71.6)‡	34.4(17.5–67.3)‡	0.857‡
Per-lesion					
PET	5	95.0(93.5–96.2)†	94.6(93.5–95.5)	431.9(99.2–1898.8)†	0.953†
MRI	3	83.8(77.0–89.2)	96.3(95.3–97.1)†	158.1(41.0–609.8)	0.962†
Bone scintigraphy	4	71.5(66.9–75.8)‡	91.0(89.2–92.7)‡	9.0(0.5–169.3)‡	0.778‡

† The highest sensitivity, specificity, DOR or *Q index among PET, MRI and bone scintigraphy.
‡ The lowest sensitivity, specificity, DOR or *Q index among PET, MRI and bone scintigraphy.
§ Significantly higher compared with PET.

- Conclusion:
  - 18FDG PET: the best modality to detect bone metastasis in patients with lung cancer, both on a per-patient basis and a per-lesion basis;
  - MRI: the highest specificity on a per-lesion basis.
  - For the subgroup analysis of 18FDG PET, PET/computed tomography was shown to be better than PET
  - no significant differences between using 68Ge and computed tomography for attenuation correction on a per-patient basis.

Step 3: Applicability of the results

Were the methods for performing the test described in sufficient detail to permit replication?	
What is best?	Where do I find the information?
The article should have sufficient description of the test to allow its **replication** and also interpretation of the results.	The ***Methods*** section should describe the test in detail.
This paper: Yes ☐ No ☐ Unclear ☐ Comment:	

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實證醫學六大步驟-六個A

- 臨床場景分析(Analysis)
- 提出臨床問題(Asking)： background及foreground question
- 搜尋最有用的資料(Acquire)： 5S model
- 嚴格評讀文獻(Appraisal)
- 應用到病人身上(Apply)
- 自我評估(Audit)

醫療現況（臨床專業+最佳研究實證）

1.Lung cancer and suspicious bone metastasis
2.健保給付規範
全民健保險支付「正子造影」之適應症如下：
一）腫瘤部分之適應症：
1.乳癌、淋巴癌之分期、治療及懷疑復發或再分期。
2.大腸癌、直腸癌、食道癌、頭頸部癌(不包含腦瘤)、原發性肺癌、黑色素癌、甲狀腺癌及子宮頸癌之分期及懷疑復發或再分期

- 分期：評估腫瘤之期別。
- 治療：評估腫瘤對治療之反應，擬改變治療方式時。
- 懷疑復發或再分期：使用於患者已接受一階段之正統治療後，偵測疑似有復發或轉移及評估復發之程度(不得用於例行之追蹤檢查)。
- 以上各階段須符合：經電腦斷層、核磁共振、核子醫學掃瞄等檢查仍無法分期者，或認定電腦斷層、核磁共振等檢查不足以提供足夠資訊以供治療所需者，且須於病歷中說明施行正子造影之必要性理由。
- 配合腫瘤治療計畫者方得以正子造影作為療效評估項目，未有後續積極處置之計畫者，不得施行。

是否符合經濟效益(花費不會太高) ?PET-CT:NT $ 36500(自費), 36500點(健保); BS:2542點

病人意願

Radiation dose

Procedure	Average effective dose (mSv)	Number of chest x-rays (PA/lateral) with equivalent radiation dose*
Bone scan	6.3	63
Whole body PET	14. 1	141

PA and lateral chest radiograph = .1 mSv. From uptodate: Radiation-related risks of imaging studies

生活品質

1.早期偵測骨轉移對治療之好處
Physical: 減少癌症進展的發生
Psychological: 減少疾病恐慌, 正面生活動力

社會經濟脈絡

1. 當病人骨骼掃描或核磁共振與電腦斷層為陰性時，當臨床症狀強烈懷疑有骨骼轉疑時，可開予正子造影檢查，給與肺癌病人評估是否有骨轉移，使臨床醫師對癌症治療治療計畫評估可以有所幫助。
2.早期偵測骨轉移對治療之壞處
Economical: 增加治療骨轉移的醫療支出

實證醫學六大步驟-六個A

- 臨床場景分析(Analysis)
- 提出臨床問題(Asking)： background及foreground question
- 搜尋最有用的資料(Acquire)： 5S model
- 嚴格評讀文獻(Appraisal)
- 應用到病人身上(Apply)
- 自我評估(Audit)

- 在「提出臨床問題」方面的自我評估
  - 提出的問題有臨床重要性問題，清楚的知道自己問題的定位。
- 在「搜尋最佳證據」方面的自我評估
  - 已盡全力搜尋，知道我的問題的最佳證據來源，在搜尋上愈來愈熟練了。
- 關於「嚴格評讀文獻」方面的自我評估
  - 盡全力做評讀了，盡量了解 worksheet 每一項的意義，做出了結論。
- 關於「應用到病人身上」的自我評估
  - 將搜尋到的最佳證據應用到我的臨床工作中，以實證醫學的結果來做解釋做為最佳證據用於實際臨床。
- 效率評估
  - 花了一週完成這篇報告，進行實證醫學的過程是值得的。

Thank you for attention!