cancer care ontario | action cancer ontario
program in evidence-based care | programme de soins fondé sur des preuves

PET Recommendation Report 11

Clinical Utility of Positron Emission Tomography in the Diagnosis, Staging, and Management of Sarcoidosis

J. You, B. Hyland, and S. Henderson

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: August 24, 2011

PET Recommendation Report 11 consists of 2 sections and is available on the CCO Web site (http://www.cancercare.on.ca)
PEBC PET Recommendation Reports page at:
https://www.cancercareontario.ca/en/search?nav_field_type_of_contents=All&nav-search=PET+Recommendation

Section 1: Guideline Recommendations

Section 2: Evidentiary Base

For further information about this report, please contact:

Dr. John You, Assistant Professor, McMaster University
1280 Main Street West, Room HSC-2C8
Hamilton, Ontario, Canada L8S 4K1
Phone: 905-525-9140 ext. 21858 Fax: 905-521-4971 Email: jyou@mcmaster.ca

For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775

Citation (Vancouver Style): You J, Hyland B, Henderson S. Clinical utility of positron emission tomography in the diagnosis, staging, and management of sarcoidosis. Toronto (ON): Cancer Care Ontario; 2011 Aug 24. Program in Evidence-based Care PET Recommendation Report No.: 11.

PET Recommendation Report 11: Section 1

Clinical Utility of Positron Emission Tomography in the Diagnosis, Staging, and Management of Sarcoidosis: Guideline Recommendations

J. You, B. Hyland, and S. Henderson

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: August 24, 2011

QUESTION

Is positron emission tomography/computed tomography (PET/CT) beneficial in the diagnosis, staging, or clinical management of patients with suspected or proven sarcoidosis?

TARGET POPULATION

These recommendations apply to patients with suspected or proven non-cardiac sarcoidosis. The decision to narrow the scope to non-cardiac sarcoidosis was based on the rationale that the cardiac sub-committee of the Ontario PET Steering Committee is currently conducting a review of the role of PET in cardiac sarcoidosis. As such, it would not be practical to include these studies in this review.

INTENDED PURPOSE

- This recommendation report is primarily intended to guide the Ontario PET Steering Committee in their decision making concerning indications for the use of PET imaging.
- This recommendation report may also be useful to inform clinical decision making regarding the appropriate role of PET imaging and to guide priorities for future PET imaging research.

RECOMMENDATIONS AND KEY EVIDENCE

No recommendation for or against the use of PET in the diagnosis, staging, or clinical management of sarcoidosis can be made at this time due to insufficient evidence.
Seven retrospective studies (1-7) evaluated ^{18}F-FDG PET in the diagnosis, staging, or clinical management of sarcoidosis. The included studies are small and of low quality and did not present any quantitative data with respect to patient-important outcomes. They did, however, present very preliminary evidence suggesting that ^{18}F-FDG PET may have greater sensitivity than other imaging modalities for the diagnosis of sarcoidosis and that changes to ^{18}F-FDG PET may correlate with treatment response.

Qualifying Statements

None

FUTURE RESEARCH

Based on the findings of the systematic review of the evidence, prospective studies of PET in sarcoidosis are warranted. As the disease is relatively uncommon, multicentre studies would be optimal. Additionally, the quantitative assessment of patient-important outcomes (e.g., using validated quality-of-life or disease-activity instruments) should be included in the data collection.

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Contact Information

For further information about this report, please contact:

Dr. John You, Assistant Professor, McMaster University
1280 Main Street West, Room HSC-2C8
Hamilton, Ontario, Canada L8S 4K1
Phone: 905-525-9140 ext. 21858 Fax: 905-521-4971 Email: jyou@mcmaster.ca

For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775

REFERENCES

1. Braun JJ, Kessler R, Constantinesco A, Imperiale A. 18F-FDG PET/CT in sarcoidosis management: review and report of 20 cases. Eur J Nucl Med Mol Imaging. 2008;35(8):1537-43.
2. Keijsers RG, Grutters JC, Van Velzen-Blad H, Van Den Bosch JM, Oyen WJ, Verzijlbergen FJ. 18F-FDG PET patterns and BAL cell profiles in pulmonary sarcoidosis. Eur J Nucl Med Mol Imaging. 2010;37(6):1181-8.
3. Keijsers RGM, Verzijlbergen JF, van Diepen DM, van den Bosch JMM, Grutters JC. 18F-FDG PET in sarcoidosis: An observational study in 12 patients treated with infliximab. Sarcoidosis Vasc Diffuse Lung Dis. 2008;25(2):143-50.
4. Nishiyama Y, Yamamoto Y, Fukunaga K, Takinami H, Iwado Y, Satoh K, et al. Comparative evaluation of 18F-FDG PET and 67Ga scintigraphy in patients with sarcoidosis. J Nuclear Med. 2006;47(10):1571-6.
5. Prager E, Wehrschuetz M, Bisail B, Woltsche M, Schwarz T, Lanz H, et al. Comparison of 18F-FDG and 67Ga-citrate in sarcoidosis imaging. Nuklearmedizin. 2008; 47(1):18-23.
6. Seve P, Billotey C, Janier M, Grange JD, Broussolle C, Kodjikian L. Fluorodeoxyglucose positron emission tomography for the diagnosis of sarcoidosis in patients with unexplained chronic uveitis. Ocul Immunol Inflamm. 2009;17(3):179-84.
7. Teirstein AS, Machac J, Almeida O, Lu P, Padilla ML, Iannuzzi MC. Results of 188 whole-body fluorodeoxyglucose positron emission tomography scans in 137 patients with sarcoidosis. Chest. 2007;132(6):1949-53.

PET Recommendation Report #11: Section 2

Clinical Utility of Positron Emission Tomography in the Diagnosis, Staging, and Management of Sarcoidosis: Evidentiary Base

J. You, B. Hyland, and S. Henderson

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Report Date: August 24, 2011

QUESTION

Is positron emission tomography-computed tomography (PET/CT) beneficial in the diagnosis, staging, or clinical management of patients with suspected or proven sarcoidosis?

INTRODUCTION

Sarcoidosis is a chronic disease of unknown etiology characterized by the formation of noncaseating epithelioid granulomas in the affected systems (1,3-9). While sarcoidosis is multisystemic, it primarily affects the respiratory system (1,3). Common extrathoracic sites of involvement include the heart, skin, eyes, liver, spleen, lymph nodes, parotid glands, central nervous system, genitourinary system, muscles, and bones (4). In the majority of cases, sarcoidosis is a relatively benign disorder, and there is a high likelihood of remission with no therapy required; however, some manifestations of the disease can present complications that are potentially life threatening. Sarcoidosis is estimated to affect approximately 15 to 40 per 100,000 individuals annually (1). In Ontario, that statistic translates to approximately 1900 to 5200 people a year.

No single confirmatory test to diagnose sarcoidosis currently exists: Common diagnostic modalities include chest x-ray, ^{67}Gallium (Ga) scintigraphy, CT scanning of the chest, magnetic resonant imaging (MRI), and bronchoalveolar lavage (BAL) with C4/C8 cell ratio. In recent years, clinical professionals have seen the utility in PET for the diagnosis and clinical management of sarcoidosis. Sarcoid tissues generally exhibit more rapid glycolysis than normal tissues, and the ^{18}fluorodeoxyglucose (^{18}FDG) tracer allows for the metabolic imaging of this tissue. In response to this, the Ontario PET Steering Committee made a special request to the Clinical Council of Cancer Care Ontario (CCO) to co-lead the development of recommendations regarding the role of PET imaging in sarcoidosis. The following systematic review of the evidence attempts to summarize the current state of the science and provide

potential recommendations for the use of PET in the diagnosis, staging, and clinical management of PET in sarcoidosis patients.

METHODS

The evidence-based series (EBS) guidelines developed by PEBC, CCO, use the methods of the Practice Guidelines Development Cycle (2). For this project, the core methodology used to develop the evidentiary base was the systematic review. Evidence was selected and reviewed by two members of the PEBC and one methodologist.

The systematic review is a convenient and up-to-date source of the best available evidence on PET/CT in sarcoidosis. The body of evidence in this review is primarily comprised of retrospective studies with limited study populations. That evidence forms the basis of the recommendations developed by the lead authors. The systematic review and companion recommendations are intended to promote evidence-based practice in Ontario, Canada. The PEBC is supported by the Ontario Ministry of Health and Long-Term Care through CCO. All work produced by the PEBC is editorially independent from its funding source.

Literature Search Strategy

The literature was searched using the MEDLINE (1948 to April Week 1 2011) and EMBASE (1980 to 2011 Week 14) databases in OVID. OVID was used to remove any duplicate citations from the results please see Appendix 1). The Canadian Medical Association Infobase (http://www.cma.ca/index.cfm/ci_id/54316/la_id/1.htm), the National Guidelines Clearinghouse (http://www.guideline.gov/), and other Web sites were searched for existing evidence-based practice guidelines. Relevant articles and abstracts were selected and reviewed by two reviewers, and the reference lists from these sources were searched for additional studies, as were the reference lists from relevant review articles.

The literature search combined disease specific terms (sarcoidosis/ or sarcoid$.ti,ab. or sarcoid$.mp) with treatment specific terms (Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or flourine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluordeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET$CT.ti,ab.)

Study Selection Criteria

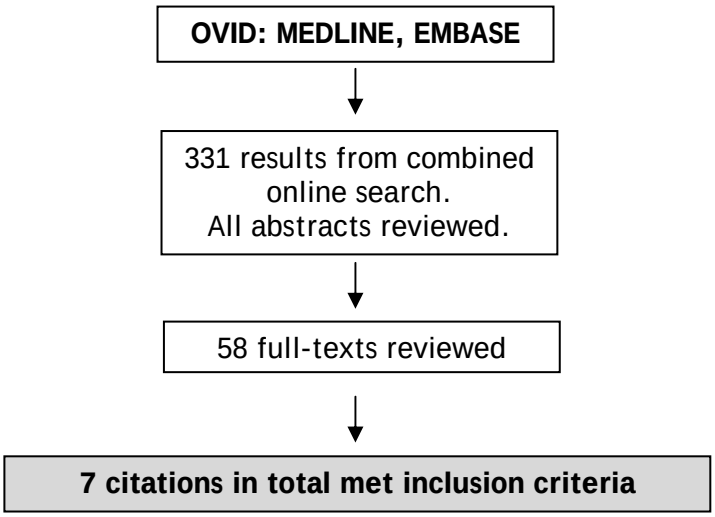
Articles (either full papers or abstracts) were selected for inclusion in this recommendation report if they were:

- Prospective or retrospective clinical studies evaluating the use of ^{18}F-FDG PET or ^{18}F-FDG PET/CT in sarcoidosis;
- Trials that included 12 or more patients with sarcoidosis;
- Comparison tests that included ^{67}Ga scanning, CT, BAL, MRI, chest x-ray, CD4/CD8 ratio and others;
- Studies that used a suitable reference standard (pathological confirmation and clinical follow-up) when appropriate.
- Studies that reported numeric data on at least one objective outcome of interest for the key questions of the technology assessment (diagnostic performance, treatment decisions and management strategy, changes in therapy, or patient-centred outcomes);
- Studies that did not exclusively report on PET in cardiac sarcoidosis.

- Studies in the English language with a human patient population and published after the year 2002.

The decision to exclude studies specifically related to cardiac sarcoidosis was based on the rationale that the cardiac subcommittee of the Ontario PET Steering Committee is currently conducting a review of the role of PET in cardiac sarcoidosis. The opinion was that it would not be practical to include these studies in this review.

Figure 1. Flow diagram of literature results from search strategy up to April 2011.



Synthesizing the Evidence

The current evidence base is of low quality. Pooling the results of the studies included in the systematic literature review was considered but was not feasible due to heterogeneity in study design and the populations studied.

RESULTS

Literature Search Results

No existing evidence-based clinical practice guidelines were found pertaining to the use of PET to diagnose and/or stage, assess treatment response, or evaluate the recurrence of sarcoidosis.

Literature search results are displayed in Figure 1. Abstracts for 331 studies were retrieved, and of these, seven studies were eligible for inclusion in the systematic review of the evidence. All were fully published reports and were retrospective (3-9). No high-quality randomised controlled trials (RCTs), evidence-based practice guidelines, or systematic reviews were identified in the literature.

Trial characteristics including the objective, patient population, study design, diagnostic test and comparator test(s) are outlined in Table 1. The patient population varied but was generally low. Common comparator tests included ^{67}Ga Scintigraphy, followed by CT, BAL, and MRI.

Table 1. Study characteristics.

Author, year	Objective	Patient Population	Study Design	Reference standard	Comparison Test
Braun et al, 2008 (3)	To compare diagnostic accuracy of ^{18}F-FDG PET/CT with ^{67}Ga scintigraphy in patients with biopsy proven sarcoidosis. To assess the ability of ^{18}F-FDG PET/CT to evaluate response to treatment with corticosteroids (in 5 patients).	20	Retrospective	Histopathology	^{67}Ga Scintigraphy
Keijsers et al, 2010 (4)	To assess whether metabolic activity imaged by ^{18}F-FDG PET represents signs of disease activity as reflected by BAL; ^{18}F-FDG PET patterns were compared with BAL cell profiles.	77	Retrospective	Histopathology	BAL
Keijsers et al, 2008 (5)	Correlation of ^{18}F-FDG-PET with standard sarcoidosis activity parameters during infliximab treatment.	12	Retrospective	Histopathology	Conventional parameters (i.e., Serum ACE, sIL-2R, VC, DLCO, Chest radiography
Nishiyama et al, 2006 (6)	To compare the uptake of ^{18}FDG PET and ^{67}Ga Scintigraphy in the evaluation of pulmonary and extrapulmonary involvement in patients with sarcoidosis.	18	Retrospective	Histopathology if available/imaging follow-up in majority (e.g., resolution of lesion on imaging after corticosteroid treatment)/"Guideline for diagnosis of cardiac sarcoidosis", Japanese Ministry of Health and Welfare	^{67}Ga Scintigraphy
Prager et al, 2008 (7)	Analyze possible advantages of F-FDG PET over ^{67}Ga citrate scintigraphy during the primary assessment of patients with sarcoidosis.	24	Retrospective	Histopathology	^{67}Ga Scintigraphy

Author, year	Objective	Patient Population	Study Design	Reference standard	Comparison Test
Seve et al, 2009 (8)	To assess the value of F-FDG PET in patients with unexplained chronic uveitis	19	Retrospective	Histopathology	Biopsy, BAL, ^{67}Ga Scintigraphy, ACE.
Teirstein et al, 2007 (9)	To study the role of whole-body ^{18}F-fluorodeoxyglucose positron emission tomography cans in the identification of occult biopsy sites and reversible granulomatous disease in patients with sarcoidosis.	137	Retrospective	Histopathology (not clear, actually?)	Radiographic Chest Scans

Abbreviations: ^{18}FDG, ^{18}fluorodeoxyglucose; ^{67}Ga, ^{67}gallum; ACE, angiotensin converting enzyme; BAL, bronchoalveolar lavage; DLCO, diffusion capacity of the lung for carbon monoxide; PET/CT, positron emission tomography/computed tomography; sIL-2R, soluble interleukin-2 receptor VC, vital capacity.

Description of Included Studies

Diagnosis/Staging

- Six studies have evaluated the diagnostic accuracy of PET or PET/CT for determining the involvement of sarcoidosis compared to CT, MRI, or ^{67}Ga scintigraphy (6-9). One study (3) evaluated the sensitivity of PET as compared to ^{67}Ga scintigraphy. The remaining four studies reported only SUV outcomes (6-9). While these results indicated that PET may be useful in the diagnosis and screening of sarcoidosis, in each case the authors state the necessity for long-term prospective studies to corroborate and validate the preliminary results.
- Two studies evaluated PET with respect to the staging of sarcoidosis (3, 9). Each study evaluated the stage of sarcoidosis by correlating the standardized uptake value (SUV) with the radiographic stage of the disease. As with the diagnostic evaluations, long-term prospective studies with a larger patient population are need to validate these results. At this time the role of PET in the clinical management of sarcoidosis remains to be determined.

Assessment of Treatment Response

- Studies have suggested that corticosteroids have been effective in the treatment of sarcoidosis. Three studies evaluated the efficacy of PET to evaluate treatment response (3,5,6). While the preliminary data suggests that the change in SUV values correlated with the patient response to treatment, the authors suggest the need for larger scale trials and quantitative data to validate these results.

Recurrence/Restaging

- No studies were identified in the literature that contained evidence of the role of PET in the recurrence and restaging of sarcoidosis.

Results of Included Studies

Diagnosis/Staging

The role of PET in the diagnosis of sarcoidosis was evaluated in five studies (3,6-9). The Braun et al retrospective study (3) assessed PET/CT in 20 patients with biopsy-proven thoracic or extra-thoracic sarcoidosis and reported a sensitivity of 78%, which improved to 87% after excluding sites of skin involvement, and a sensitivity of 100% for thoracic involvement. In a subset of 12 patients who received both PET/CT and ^{67}Ga scintigraphy, PET/CT was found to have greater sensitivity than ^{67}Ga scintigraphy (86% versus [vs.] 67%, respectively, although no formal testing for statistical significance was performed). Because their analyses were restricted only to sites with biopsy-proven disease, data regarding false positives or specificity with PET/CT (or gallium scintigraphy) were not reported (3). Furthermore, because these studies did not include patients with suspected sarcoidosis, the data do not reflect how PET/CT would perform in the more relevant clinical scenarios where sarcoidosis is suspected but is not yet confirmed on biopsy (3). Four studies (6-9) suggested that PET may have greater sensitivity than other diagnostic modalities to detect sarcoidosis. Additionally, some researchers found that whole-body PET scans may be able to detect extrathoracic areas of concern; however, this could not be histologically confirmed (6).

Two studies evaluated the role of PET in the staging of sarcoidosis. Keijser et al (4) found that SUV_{max} of the lung parenchyma or of the mediastinum/hila on ^{18}F-FDG-PET was correlated to cell profiles on BAL (BAL cell profiles have been proposed as measures of disease activity in patients with sarcoidosis (1)). Teirstein et al (9) observed that positive pulmonary PET scan findings occurred in 66% of patients with stages II and III sarcoidosis. Negative PET scans occurred in patients 88% of patients with stages 0, I, and IV sarcoidosis.

Assessment of Treatment Response

In addition to diagnosis, Braun et al (3) also evaluated the role of PET in observing treatment response and suggested that changes in F-FDG uptake may reflect the efficacy of the treatment. Keijser et al (5) evaluated the correlation of PET with disease activity during the treatment of 12 sarcoidosis patients with infliximab. A decrease in SUV was correlated with an improvement in vital capacity but not with other parameters (serum angiotensin-converting enzyme levels, soluble interleukin-2 receptor, and diffusion capacity of the lung for carbon monoxide). A decrease in SUV also appeared to correlate with an improvement in symptoms, but the symptom burden was not reported using any validated instruments and was only described in a qualitative fashion.

Ongoing Trials

No ongoing trials regarding the use of PET in sarcoidosis were identified in the systematic review of the evidence.

DISCUSSION

The evidence base for the role of PET in sarcoidosis includes small, low-quality studies. Limitations such as small population size and retrospective study design were common across all these studies. Many studies included only patients with biopsy-confirmed sarcoidosis, and, therefore, did not provide insight into the diagnostic performance of PET in the more relevant clinical scenario of assessing patients with signs or symptoms suggestive of sarcoidosis for whom a diagnosis is being sought. Data regarding false positives or specificity are not reported by any of the included studies but would be relevant, given that ^{18}F-FDG uptake indicates increased tissue glucose metabolism, and would be expected to be increased in a number of disease states besides sarcoidosis (e.g., malignancy, infection). Some studies provided a qualitative description of the association between changes on ^{18}F-FDG PET imaging and the symptomatic improvement with treatment; however, no quantitative data using validated measures of patient-important outcomes (e.g., quality of life or disease-activity instruments or questionnaires) were reported. Additionally, some studies introduced population bias by selecting only patients with a severe phenotype of sarcoidosis, thus limiting the applicability of the results across all patients with sarcoidosis.

A higher quality evidence is needed to guide clinical and policy decision making regarding the use of PET in the diagnosis and clinical management of sarcoidosis. This evidence should be generated by well-designed, prospective studies. Given that sarcoidosis is an uncommon disease, multicentre studies would be optimal. The collection of quantitative data regarding patient important outcomes using validated instruments is also warranted.

CONCLUSIONS

These data, taken as a whole, cannot exclude a potential benefit with PET in the diagnosis and clinical management of sarcoidosis. Since current evidence is sparse and of low quality, no recommendation can be made to the Ontario PET Steering Committee for or against the use of PET in sarcoidosis. Further evaluation of PET in the diagnosis and clinical management of sarcoidosis is warranted, ideally in prospective, multicentre studies.

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

Disclaimer

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

Contact Information

For further information about this report, please contact:

Dr. John You, Assistant Professor, McMaster University
1280 Main Street West, Room HSC-2C8
Hamilton, Ontario, Canada L8S 4K1
Phone: 905-525-9140 ext. 21858 Fax: 905-521-4971 Email: jyou@mcmaster.ca

For information about the PEBC and the most current version of all reports,
please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775

REFERENCES

1. Hoang DQ, Nguyen ET. Sarcoidosis. Semin Roentgenol. 2010;45(1):36-42.
2. Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol. 1995;13:502-12. Comment in: Ann Oncol. 2002 Sep;13(9):1507-9; author reply: 1509.
3. Braun JJ, Kessler R, Constantinesco A, Imperiale A. 18F-FDG PET/CT in sarcoidosis management: review and report of 20 cases. Eur J Nucl Med Mol Imaging. 2008;35(8):1537-43.
4. Keijsers RG, Grutters JC, Van Velzen-Blad H, Van Den Bosch JM, Oyen WJ, Verzijlbergen FJ. 18F-FDG PET patterns and BAL cell profiles in pulmonary sarcoidosis. Eur J Nucl Med Mol Imaging. 2010;37(6):1181-8.
5. Keijsers RGM, Verzijlbergen JF, van Diepen DM, van den Bosch JMM, Grutters JC. 18F-FDG PET in sarcoidosis: An observational study in 12 patients treated with infliximab. Sarcoidosis Vasc Diffuse Lung Dis. 2008;25(2):143-50.
6. Nishiyama Y, Yamamoto Y, Fukunaga K, Takinami H, Iwado Y, Satoh K, et al. Comparative evaluation of 18F-FDG PET and 67Ga scintigraphy in patients with sarcoidosis. J Nucl Med. 2006;47(10):1571-6.
7. Prager E, Wehrschuetz M, Bisail B, Woltsche M, Schwarz T, Lanz H, et al. Comparison of 18F-FDG and 67Ga-citrate in sarcoidosis imaging. Nuklearmedizin. 2008; 47(1):18-23.
8. Seve P, Billotey C, Janier M, Grange JD, Broussolle C, Kodjikian L. Fluorodeoxyglucose positron emission tomography for the diagnosis of sarcoidosis in patients with unexplained chronic uveitis. Ocul Immunol Inflamm. 2009;17(3):179-84
9. Teirstein AS, Machac J, Almeida O, Lu P, Padilla ML, Iannuzzi MC. Results of 188 whole-body fluorodeoxyglucose positron emission tomography scans in 137 patients with sarcoidosis. Chest. 2007;132(6):1949-53.

Appendix 1. MEDLINE and EMBASE search strategy.

The search strategy was executed on April 5, 2011. The search was conducted simultaneously in MEDLINE and EMBASE in OVID, and OVID was used to remove any duplicates (see line 24). This search is based on the strategies used for the other PEBC PET Recommendation Reports and the PEBC PET Monitoring Reports.

#	Searches	Results
1	Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or flourine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluordeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET$CT.ti,ab.	147489
2	deoxyglucose/ or deoxyglucose.ti,ab. or desoxyglucose.ti,ab. or desoxy-glucose.ti,ab. or desoxy-d-glucose.ti,ab. or deoxy-d-glucose.ti,ab. or 2deoxyglucose.ti,ab. or 2deoxy-d-glucose.ti,ab. or fluorodeoxyglucose.ti,ab. or fluorodesoxyglucose.ti,ab. or fludeoxyglucose.ti,ab. or fluordeoxyglucose.ti,ab. or fluodeoxyglucose.ti,ab. or fluordesoxyglucose.ti,ab. or 18fluorodeoxyglucose.ti,ab. or 18fluorodesoxyglucose.ti,ab. or fdg$.ti,ab. or 18fdg$.ti,ab. or 18f-dg$.ti,ab.	60119
3	(fluor or 2fluor$ or fluoro or flouro or fluorodeoxy or fludeoxy or flourodeoxy or fluorine or 18f or 18flu$ or 18fluo$).ti,ab.	63295
4	glucose.ti,ab	566891
5	(pet or petscan$ or pet ct).ti,ab.	90421
6	Tomography, Emission-Computed/	34568
7	emission.ti,ab.	170139
8	(tomograph or tomographs or tomographic$ or tomogrpahy or tomographies).ti,ab.	63647
9	7 and 8	6404
10	5 or 6 or 9	110786
11	3 and 4	11104
12	2 or 11	61205
13	10 and 12	11104
14	exp sarcoidosis/ or sarcoid$.ti,ab. or sarcoid$.mp.	48719
15	1 and 14	858
16	13 and 14	70
17	15 or 16	858
18	limit 17 to english language	738
19	limit 18 to human	686
20	(comment or editorial or letter or case reports).pt	3541743
21	(conference or conference proceeding or conference proceeding$ or conference paper or conference paper$ or discussion or discussion$ or in brief or invited comment or invited comment$).ti,ab.	398701
22	19 not (20 or 21)	515
23	limit 22 to yr="2002 -Current"	468
24	remove duplicates from 23	331