Ga-68 Article Abstraction Form

Article ID: _____

N: _____ Country: _____ Age Range: _____
or Ave Age: _____

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Tumor type (s)

☐ Gastroenteropancreatic NET ☐ Paraganglioma
☐ Carcinoid ☐ Liver metastases / unknown primary
☐ NET not otherwise defined

- -

Reference Standard

☐ Histology ☐ Other Imaging (CT, MRI) ☐ Not well defined
☐ Consensus (biased, i.e. includes DOTATOC) ☐ Consensus (unbiased)

- -

Interpretation Criteria

☐ Blinded (No information) ☐ Blinded (Clinical info only)
☐ Unblinded (Aware of clinical and Imaging info)

- -

Type of Article

☐ Sensitivity, Specificity, etc
☐ Comparison with In-111 Octreoscan
☐ Change of Management
☐ Unknown primary
☐ Diagnostic test (biochemical and/or clinical indication, but no known tumor)
☐ Peptide Radionuclide RadioTherapy (PRRT)

- -

Sensitivity, Specificity, etc. & Comparison with In-111 Octreoscan
DOTATOC: TP: ____ FN: ____ TN: ____ FP: ____ Octreoscan: TP: ____ FN: ____ TN: ____ FP: ____

- -

Change of Management

Overall % Change of management: ___ % major change: ___ % minor change: ___ ☐ Not stated

- -

Unknown primary (UP)

Definition of UP: _____ or ☐ Not defined
% Yield in finding UP: _____ or ☐ Not analyzed separately

- -

Diagnostic test (biochemical and/or clinical indication, but no known tumor)

DOTATOC: TP: ____ FN: ____ TN: ____ FP: ____ Octreoscan: TP: ____ FN: ____ TN: ____ FP: ____

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QUADAS Article Abstraction Form

Article:						
Reviewer:						
		1	2	3	4	5
1. Blinded Read		Not clearly described	Unblinded	Blinded to clinical information only	Blinded to imaging information only	Blinded to both clinical and other information
		◎	◎	◎	◎	◎
2: Reference Standard		Not clearly described	Biased consensus (uses DOTATOC information)	Other Imaging (i.e, CT and/or MRI)	Unbiased consensus (no DOTATOC info used	Histology
		◎	◎	◎	◎	◎
3. Reference Standard (Comparison only)		No reference standard	Imaging-based Bias with DOTATOC	Imaging-based unbiased – no DOTATOC	Histology	
		◎	◎	◎	◎	◎
4. Patient Selection/Inclusion Criteria (Sensitivity/Specificity)		Not clearly described	Patients selected by somatostatin receptor imaging	Biased: Patients with only histologically proven NET disease	Consecutive patients referred for DOTATOC – particular NET disease	Consecutive patients referred for DOTATOC – all reasons or other unbiased methods
		◎	◎	◎	◎	◎
4. Patient Selection/Inclusion Criteria (Comparison with other radiotracers)		Not clearly described	Biased by lesion size, previous + study with other radiotracer, or other imaging bias	Biased by disease type or other limiting characteristic	Consecutive patients referred for DOTATOC or Octreoscan or other unbiased method	
		◎	◎	◎	◎	◎
5. Patient Selection/Inclusion Criteria (Change in Management)		Not clearly described	Patients with only histologically proven NET	Consecutive patients referred for DOTATOC – particular NET disease	Consecutive patients referred for DOTATOC – all reasons or other unbiased methods.	
		◎	◎	◎	◎	◎
6. General Study Design		Not clearly described	Retrospective	Prospective/Retrospective mixed	Prospective	
		◎	◎	◎	◎	◎
7. Image Interpretation Criteria		Not clearly described	Methodologies for interpreting only ancillary imaging (CT, MRI) well described	Methodologies for interpreting only DOTATOC well described	Methodologies for interpreting all imaging	
		◎	◎	◎	◎	◎
General Comments:						

Brief summaries of the references

• Hofmann et al, 2001 (*3*). Title: "Biokinetics and imaging with the somatostatin receptor PET radioligand ^{68}Ga-DOTATOC: preliminary data". Prospective. This was the first published paper on ^{68}Ga-DOTATOC imaging in patients. N = 8 patients with known metastatic carcinoid tumors. All patients had positive ^{111}In-octreotide scans prior to PET imaging. ^{68}Ga-DOTATOC PET imaging identified NET lesions in all patients. In every patient ^{68}Ga-DOTATOC showed more lesions than ^{111}In-octreotide.

• Gabriel et al. 2007 (*8*) . Title: "^{68}Ga-DOTA-Tyr^{3}-Octreotide PET in Neuroendocrine Tumors: Comparison with Somatostatin Receptor Scintigraphy and CT". Prospective. N = 84. Patients with known or suspected NET. The reference standard was based on all available histologic, imaging, and follow-up findings. Group 1. Suspected NET with symptoms and elevated biomarkers, but no evidence of disease by conventional imaging (N = 13); Group 2. Initial tumor staging (N = 36); Group 3. Follow-up after therapy (N = 35). Each patient was also imaged with ^{99m}Tc-HYNIC-TOC and ^{111}In-DOTATOC. Neither of these agents is widely used, and this comparison was not useful for the present analysis. In Group 1, there were 5 positives, including one false positive. In Group 2 sensitivity was 97% and specificity was 100%. In Group 3 sensitivity was also 97% and specificity was 100%.

• Versari et al, 2010 (*9*). Title: "Ga-68 DOTATOC PET, Endoscopic Ultrasonography, and Multi-detector CT in the diagnosis of duodenopancreatic neuroendocrine tumors". Retrospective. N = 19 patients suspected to have duodenopancreatic primitive NET. The reference standard was fine needle biopsy and/or surgery. On a per-patient basis, sensitivity for Ga-68 DOTATOC was 12/13 (92%) and specificity was 5/6 (83%).

• Ruf et al, 2011 (*10*). Title: "^{68}Ga-DOTATOC PET/CT of Neuroendocrine Tumors: Spotlight on the CT Phases of a Triple-Phase Protocol". Retrospective. N = 51 patients with known or suspected NET. The reference standard was clinical and imaging follow-up, histopathology (if available), and the decision of an interdisciplinary truth-panel. On a per-patient basis, sensitivity for Ga-68 DOTATOC was 32/39 (82%) and specificity was 8/12 (67%).

• Mayerhoefer et al, 2012 (*11*). Title: "Are contrast media required for (68)Ga-DOTATOC PET/CT in patients with neuroendocrine tumours of the abdomen?". Retrospective. N = 55. Patients with known or suspected NETs of the abdomen. The reference standard was a combination of histology reports, reports of other imaging examinations (MRI, ultrasound), or reports of follow-up PET/CT or CT performed 3–6 months after the original PET/CT. There were two 2-man teams of interpreters, junior and senior teams. Studies were done both with and without CT contrast. Image evaluation was completely blinded and was reported on a "per-region" basis. For un-enhanced PET/CT imaging sensitivity was 89.3% for the junior team and 92.0% for the senior team. Specificity was 99.1% for the junior team and 99.2% for the senior team. Performance improved slightly with contrast enhanced images. Results were also reported on a "per-patient" basis, and the results from the senior team were used in the combined summary in this paper.

• Beiderwellen et al, 2013 (*12*). Title: "Simultaneous ^{68}Ga-DOTATOC PET/MRI in Patients With Gastroenteropancreatic Neuroendocrine Tumors Initial Results". Prospective. N = 8. Patients all had histopathologically confirmed NET. The reference standard was clinical imaging, existing prior examinations, and histopathology (if available). Five of the eight patients had malignant NET lesions at the time of the examination. ^{68}Ga-DOTATOC PET alone identified 4 of the 5 patients as positive. ^{68}Ga-DOTATOC PET/MRI identified all 5.

• Schraml et al, 2013 (*13*). Title: "Staging of neuroendocrine tumours: comparison of [^{68}Ga]DOTATOC multiphase PET/CT and whole-body MRI". Prospective. N = 51. Patients had histologically proven NET and suspicion of metastases. All patients were imaged with [^{68}Ga]DOTATOC-PET/CT and separately with whole-body MRI. Reference standard was based on correlation of all imaging data, histologic and surgical findings, and clinical follow-up. The sensitivity for [^{68}Ga]DOTATOC-PET/CT was 98% (40/41) and the specificity was 100% (10/10).

• Venkitaraman et al, 2014 (*14*). Title: "Role of ^{68}Ga-DOTATOC PET/CT in initial evaluation of patients with suspected bronchopulmonary carcinoid". Prospective. N = 32. Patients had clinical suspicion of bronchopulmonary carcinoid studied using ^{68}Ga-DOTATOC and ^{18}F-FDG. The combined results from the two types of study were used as the reference standard. Based on the reference standard, 26 cases of carcinoid were found (21 typical and 5 atypical). The sensitivity of ^{68}Ga-DOTATOC was 100% for typical and 80% for atypical carcinoid.

• Frilling et al, 2010 (*15*). Title: "The Impact of ^{68}Ga-DOTATOC Positron Emission Tomography/Computed Tomography on the Multimodal Management of Patients With Neuroendocrine Tumors". Retrospective. N = 52. All patients had histologically proven NET. The reference standard was based on intraoperative findings, histopathologic reports, and follow-up data of at least 6 months. Sensitivity on a per-patient basis was 100%. They eliminated 7 of 15 patients being evaluated for liver transplantation, because of evidence of metastatic deposits not seen by conventional imaging. Overall, ^{68}Ga-DOTATOC PET/CT altered treatment management decisions, previously based on CT and/or MRI alone, in 31 (60%) of the 52 patients.

• Jindal et al, 2010 (*16*). Title: "Role of ^{68}Ga-DOTATOC PET/CT in the Evaluation of Primary Pulmonary Carcinoids". Retrospective. N = 20. Patients had typical (13) and atypical (7) carcinoids. DOTATOC PET/CT detected all the typical carcinoids and 6/7 of the atypical. Typical carcinoids showed significantly higher levels of DOTATOC uptake than atypical carcinoids.

• Kumar et al, 2011 (*17*). Title: "Role of ^{68}Ga-DOTATOC PET-CT in the diagnosis and staging of pancreatic neuroendocrine tumours". Prospective. N = 20. Patients had clinically suspected and/or histopathologically proven pancreatic NET. The reference standard was histopathology for primary tumor and clinical follow up with MRI and/or biopsy. Sensitivity on a per-patient basis was 100%.

• Nakamoto et al, 2015 (*18*). Title: "Additional information gained by positron emission tomography with ^{68}Ga-DOTATOC for suspected unknown primary or recurrent neuroendocrine tumors". Retrospective. N = 46: Group 1: Known NET metastatic disease with unknown primary (N = 14); Group 2: Looking for recurrent NET after curative treatment, with negative imaging, but with high biomarker levels (N = 7); Group 3: Suspected NET because of high biomarker levels (N = 25). The reference standard was histopathological confirmation or clinical follow-up for at least 6 months. In Group 1 they found 7 unknown primaries with one false positive. In Group 2 they found disease in 6. In Group 3 they found one site of disease.

• Poeppel et al, 2011 (*19*). Title: "^{68}Ga-DOTATOC Versus ^{68}Ga-DOTATATE PET/CT in Functional Imaging of Neuroendocrine Tumors". Prospective. N = 40. All patients had documented NETs as part of workup for possible peptide receptor radionuclide therapy. Reference standard was histology. Sensitivity on a per-patient basis was 100%. ^{68}Ga-DOTATOC found slightly more lesions than ^{68}Ga-DOTATATE (262 vs. 254). The average primary tumor standardized uptake Value (SUV) was somewhat higher with "^{68}Ga-DOTATOC than with ^{68}Ga-DOTATATE (33 $\pm$ 22 vs. 18 $\pm$ 12). The conclusion was "^{68}Ga-DOTATOC and ^{68}Ga-DOTATATE possess a comparable diagnostic value in the detection of lesions of NETs, with a potential advantage for ^{68}Ga-DOTATOC".

• Froeling et al, 2012 (*20*). Title: "Impact of Ga-68 DOTATOC PET/CT on the diagnosis and treatment of patients with multiple endocrine neoplasia (MEN)". Retrospective. N = 21. All patients had MEN. The reference standard was histopathologic proof or by clinical and radiologic follow-up. Ga-68 DOTATOC PET/CT findings led to a change in treatment in 10 of 21 (48%) patients. NET lesions were detected in all patients. On a lesion-by-lesion basis Ga-68 DOTATOC had a sensitivity of 92 % and specificity of 94 %.

• Ruf et al, 2010 (*21*). Title: "Impact of Multiphase ^{68}Ga-DOTATOC-PET/CT on Therapy Management in Patients with Neuroendocrine Tumors". Retrospective. N = 64. Patients had known or suspected NET. The reference standard was based on the results of combined PET and CT imaging, follow-up documentation by the department of gastroenterology, and the decision of the interdisciplinary tumor board. There were 50 true positives and 14 true negatives by ^{68}Ga-DOTATOC imaging. The major goal of the study was to determine the impact of ^{68}Ga-DOTATOC on patient management. ^{68}Ga-DOTATOC-PET/CT had a significant impact on therapeutic management in 24/64 (38%) of all NET patients.

• Schreiter et al, 2014 (*22*). Title: "Searching for primaries in patients with neuroendocrine tumors (NET) of unknown primary and clinically suspected NET: Evaluation of Ga-68 DOTATOC PET/CT and In-111 DTPA Octreotide SPECT/CT". Retrospective. N = 123: Group 1: metastatic NET with unknown primary (N = 83) Group 2: clinically suspected NET (N = 40). The reference standard was histopathology or clinical verification based on follow-up. Most patients only had Ga-68 DOTATOC or In-111 Octreotide scans but not both. 20 patients had both but were not analyzed separately. In Group 1 Ga-68 DOTATOC detected primaries in 15 patients (46%) and In-111 Octreotide in 4 patients (8%). In Group 2 only two primaries were detected, both with Ga-68 DOTATOC.

• Menda et al. 2017 (*23*). Title: "Localization of Unknown Primary Site with ^{68}Ga-DOTATOC PET/CT in Patients with Metastatic Neuroendocrine Tumor". Prospective. N=40. Patients with proven metastatic NET and unknown primary. Image evaluation: True positive (TP) was confirmation by biopsy or follow-up imaging. False positive (FP) if no primary lesion was found at site of uptake. Negative scans were classified as false negative (FN). Unconfirmed (UC) was a positive scan but no histology or follow-up imaging. Results: The TP, FP, FN and UC rates for unknown primary tumor were 38%, 7%, 50% and 5% respectively. Conclusion: ^{68}Ga-DOTATOC PET/CT is an effective modality in localization of unknown primary in patients with metastatic NET.

• Buchman et al, 2007(*24*). Title: "Comparison of 68Ga-DOTATOC PET and 111In-DTPAOC (Octreoscan) SPECT in patients with neuroendocrine tumours". Prospective. N = 27. All patients had histologically proven NETs. Results were compared with ^{111}In-octreotide. The reference standard was based on histopathology, MRI, or CT. Lesions were seen in all patients with both modalities. On a regional basis 52 regions were verified positive by ^{68}Ga-DOTATOC PET. 18 of these regions were missed by ^{111}In-octreotide. There were no regions identified by ^{111}In-octreotide that were missed with ^{68}Ga-DOTATOC PET.