

REVIEW ARTICLE

Attenuation-Corrected vs. Nonattenuation-Corrected 2-Deoxy-2-[F-18]fluoro-D-glucose-Positron Emission Tomography in Oncology, A Systematic Review

Urvi Joshi,¹ Pieter G. H. M. Raijmakers,^{1,4} Ingrid I. Riphagen,² Gerrit J. J. Teule,³ Arthur van Lingen,¹ Otto S. Hoekstra¹

¹Department of Nuclear Medicine and PET Research, VU University Medical Centre, 1117 De Boelelaan, 1081 HV, Amsterdam, The Netherlands

²Medical Library, Vrije Universiteit, Amsterdam, The Netherlands

³Department of Nuclear Medicine, Academic Hospital Maastricht, Maastricht, The Netherlands

⁴Department of Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, The Netherlands

Abstract

Purpose: To perform a systematic review and meta-analysis to determine the diagnostic accuracy of attenuation-corrected (AC) vs. nonattenuation-corrected (NAC) 2-deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography (FDG-PET) in oncological patients.

Procedures: Following a comprehensive search of the literature, two reviewers independently assessed the methodological quality of eligible studies. The diagnostic value of AC was studied through its sensitivity/specificity compared to histology, and by comparing the relative lesion detection rate reported with NAC-PET vs. AC, for full-ring and dual-head coincidence PET (FR- and DH-PET, respectively).

Results: Twelve studies were included. For FR-PET, the pooled sensitivity/specificity on a patient basis was 64/97% for AC and 62/99% for NAC, respectively. Pooled lesion detection with NAC vs. AC was 98% [95% confidence interval (95% CI): 96–99%, $n=1,012$ lesions] for FR-PET, and 88% (95% CI: 81–94%, $n=288$ lesions) for DH-PET.

Conclusions: Findings suggest similar sensitivity/specificity and lesion detection for NAC vs. AC FR-PET and significantly higher lesion detection for NAC vs. AC DH-PET.

Key words: Deoxyglucose (MeSH), Tomography, X-ray computed (MeSH), Tomography, emission-computed (MeSH), Neoplasms (MeSH), Human (MeSH), Systematic review (MeSH), Attenuation correction, Positron emission tomography

Introduction

The attenuation of photons originating from the subject before they are detected by the camera is a generic limitation of nuclear medicine imaging. This attenuation

can lead to image distortion and impairs adequate quantification. Attenuation correction has been commonly employed in 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) imaging in an attempt to correct for these effects. With positron emission tomography (PET) scanners, this is accomplished by transmission scanning using a radionuclide source, such as germanium-68 or cesium-137, and with PET/computed tomography (CT) using CT. With respect to

Correspondence to: Pieter G. H. M. Raijmakers; e-mail: p.raijmakers@vumc.nl

visual interpretation of the images, the added value of attenuation correction has been controversial. Whereas attenuation correction provides a more realistic image of FDG distribution, its application significantly increases acquisition times on standard full-ring (FR) PET scanners. In addition, the performance of attenuation correction can introduce noise and even artifact. Paradoxically, even if the nuclear medicine community sees attenuation correction, or the lack of it, as a potential effect-modifier of test accuracy, its impact is rarely accounted for in systematic reviews on the diagnostic accuracy of PET. As a result, the impact of attenuation correction on lesion detectability and interpretation of PET for oncological purposes is not well established. With PET/CT scanning, it is customary to evaluate either modality (primarily to account for artifacts), but one needs to know how to deal with discrepancies.

The objective of this systematic review and meta-analysis was to determine the diagnostic accuracy of nonattenuation-corrected (NAC) and attenuation-corrected (AC) FDG-PET in oncological patients. We studied the effects of attenuation correction for both FR-PET and dual-head coincidence PET (DH-PET), and as a function of different body locations (head/neck, chest, abdomen/pelvis).

Materials and Methods

Literature Search

A computer-aided literature search was performed in both Medline and Embase databases without time range or language restrictions, applying controlled vocabulary (MeSH and Emtree keywords, respectively) as well as free text words. The search date was February 10, 2006. The search strategy (Appendix) included terms for PET with FDG, modified from Mijnhout et al. [1] as well as search terms identifying both radionuclide and X-ray transmission, emission, attenuation correction, and oncological studies in humans. In addition, the reference lists of the eligible articles were reviewed to ensure that relevant articles had not been missed.

Study Selection

From the list of retrieved articles, articles were initially evaluated for eligibility on the basis of title and abstract by two independent reviewers (UJ, PR). If there was uncertainty as to whether an article was eligible for inclusion, the entire article was reviewed. Inclusion criteria were (1) clinical studies evaluating FDG imaging with and without attenuation correction in oncology patients; (2) study population of at least ten patients; (3) sufficient detail to reconstruct a 2x2 contingency table expressing FDG imaging results by disease status, or sufficient detail to reconstruct relative lesion detection measurement of AC vs. NAC imaging; and (4) studies utilizing FR-PET and/or DH-PET. We excluded abstracts, editorials, and reviews, although the latter two categories were used for cross-referencing.

Methodological Quality Assessment

The methodological quality of each article was independently assessed by each reviewer in terms of internal and external validity (Table 1), based on the Cochrane Methods Group in Screening and Diagnostic Tests, modified for our area of interest [2]. Internal validity items focus on whether a valid reference test was used and whether this reference test was uniformly and independently applied and interpreted as well the type of study design. The external validity items evaluate the applicability of the results in terms of the type of patient population and spectrum, demographics, the inclusion/exclusion criteria, the knowledge of previous test/clinical information that could influence interpretation, and the index test characteristics. Items were scored as positive, negative, or unclear.

Data Extraction and Quantitative Analysis

In addition to methodological quality assessment, data related to the type of camera, the FDG dose, the time interval between injection and imaging, the transmission and emission acquisition protocols, the reconstruction protocol, and the interpretation protocol were independently

Table 1. Methodological assessment of individual diagnostic studies: criteria

Test	Criteria
A. Internal study validity	
A1. Valid reference test	Histology, AC FR or DH coincidence PET
A2. Blind measurement of reference test(s) without knowledge of index test	Assessment of reference test independent of index test(s) results
A3. Avoidance of verification bias	Choice of patients assessed by reference test independent of index test result
A4. Index test(s) interpreted independently of all clinical information	Mentioned in publication
A5. Prospective study	Mentioned in publication
B. External study validity	
B1. Spectrum of diseases	Localization of disease described (selected or general)
B2. Demographic information	Age and sex given
B3. Inclusion criteria described	Mentioned in publication
B4. Exclusion criteria described	Mentioned in publication
B5. Avoidance of selection bias	Consecutive series of patients
B6. Standardized execution of index test(s)	Described technical aspects of index test(s)
C. Reproducibility described	Mentioned in publication

extracted from each study by each reviewer. For studies where it was possible, a contingency 2×2 table was constructed. Disagreements were solved by consensus.

For studies using an independent gold standard (histopathology), we determined the sensitivity and specificity of the index tests using the number of true positive, false positive, true negative, and false negative results from the 2×2 contingency table. Furthermore, we calculated the “relative lesion detection,” defined as the percentage of lesions scoring equally positive or negative with NAC vs. AC images. We performed a subgroup analysis for different locations of lesions and analyzed sensitivity, specificity, or relative lesion detection of NAC vs. AC for lesion location in the head and neck region, the chest, and the abdominopelvic region. In cases of discrepancy of relative lesion detection between NAC and AC, we extracted data to analyze whether this was related to lesion size and/or intensity.

The statistical diagnostic heterogeneity of the sensitivity and specificity per index test across studies was tested by the chi-square test. In case of statistical heterogeneity of DH- or FR-FDG-PET imaging, a random effect model for pooling was used, whereas in case of statistical homogeneity, a fixed-effect model was used. Sensitivity, specificity, and relative lesion detection were pooled independently, all pooled estimates are presented with 95% confidence intervals (95% CI). The logit transformed sensitivity, specificity, relative lesion detection, and corresponding 95% CI of the index tests were compared using z-test statistics. A *p* value of less than 0.05 was considered significant.

All statistical analyses were performed with the SPSS 11.0.01 program for Windows (version 11.0.1., SPSS, Chicago, IL, USA).

Results

The search strategy yielded 2,202 references, 1,477 in Medline and 725 in Embase on February 10, 2006. Of the Embase references, 370 were also included in Medline, leaving a total of 1,832 unduplicated references. On the basis of title and abstract alone, 1,806 references were

excluded. After review of the full text of the remaining 26 articles, an additional 11 studies [3–12] proved to be ineligible because they did not perform a direct comparison of the yield of NAC vs. AC images in oncological patients. One study [13] was excluded because it was published in abstract form only. Another study [14] was excluded because it was published in Japanese and was not readily translatable. Finally, the study of Hustinx et al. [15], who evaluated the effect of attenuation correction in abdominal tumors for a sodium iodide crystal (NaI) PET scanner, was excluded because no 2×2 contingency tables could be constructed. Eventually, we included 12 studies for review [16–27].

A summary of the methodological quality assessment results can be found in Table 2. Methodological quality was scored as negative when quality items were unclear or absent in the original article. In a minority (4/12=33%) of studies, histology served as the reference test. However, nine of the 12 studies provided a direct comparison of AC and NAC PET. In three studies, blind measurement of reference test was performed without knowledge of index test. All but one study avoided verification bias. In four studies, the index test(s) was evaluated independently of all clinical information. All studies provided information about the spectrum of diseases being evaluated and standardized the execution of the index test(s). Almost all studies (11/12=92%) described the demographics of the study population and inclusion criteria. However, only one study mentioned specific exclusion criteria. Six studies were prospective. Only two of the 12 studies specifically mentioned including consecutive patients, and only three studies specifically described the reproducibility of their results.

Meta-Analysis

Three FR-PET studies were eligible for pooling of sensitivity on a patient basis [22, 24, 25]. The pooled sensitivities for AC and NAC FR-PET were 64% (95% CI 52–74%) and 62% (95% CI 51–73%), respectively (*n*=182 patients). Two FR-PET studies provided data that allowed pooled analysis of specificity [22, 24]. Weber et al. [25] could not be

Table 2. Quality assessment of included studies

Study	Year	A1	A2	A3	A4	A5	B1	B2	B3	B4	B5	B6	C
Bleckmann	1999	+	+	+	+	–	+	–	+	–	–	+	–
Chan	2001	+	–	+	–	–	+	+	+	–	–	+	–
Delbeke	2001	+	–	+	–	+	+	+	+	–	–	+	–
Even-Sapir	2004	+	–	+	–	+	+	+	+	–	+	+	–
Kotzerke	1999	+	–	+	–	–	+	+	+	–	+	+	+
Lonneux	1999	+	–	+	–	+	+	+	–	–	+	+	+
Nakamoto	2002	+	+	+	+	+	+	+	+	–	–	+	+
Reinhardt	2005	+	–	+	–	–	+	+	+	+	–	+	–
Schauwecker	2003	+	–	–	–	–	+	+	+	–	–	+	+
Weber	1999	+	–	+	–	+	+	+	+	–	–	+	–
Zimny	1999	+	+	+	+	–	+	+	+	–	–	+	–
Zimny	2003	+	–	+	+	+	+	+	+	–	–	+	–

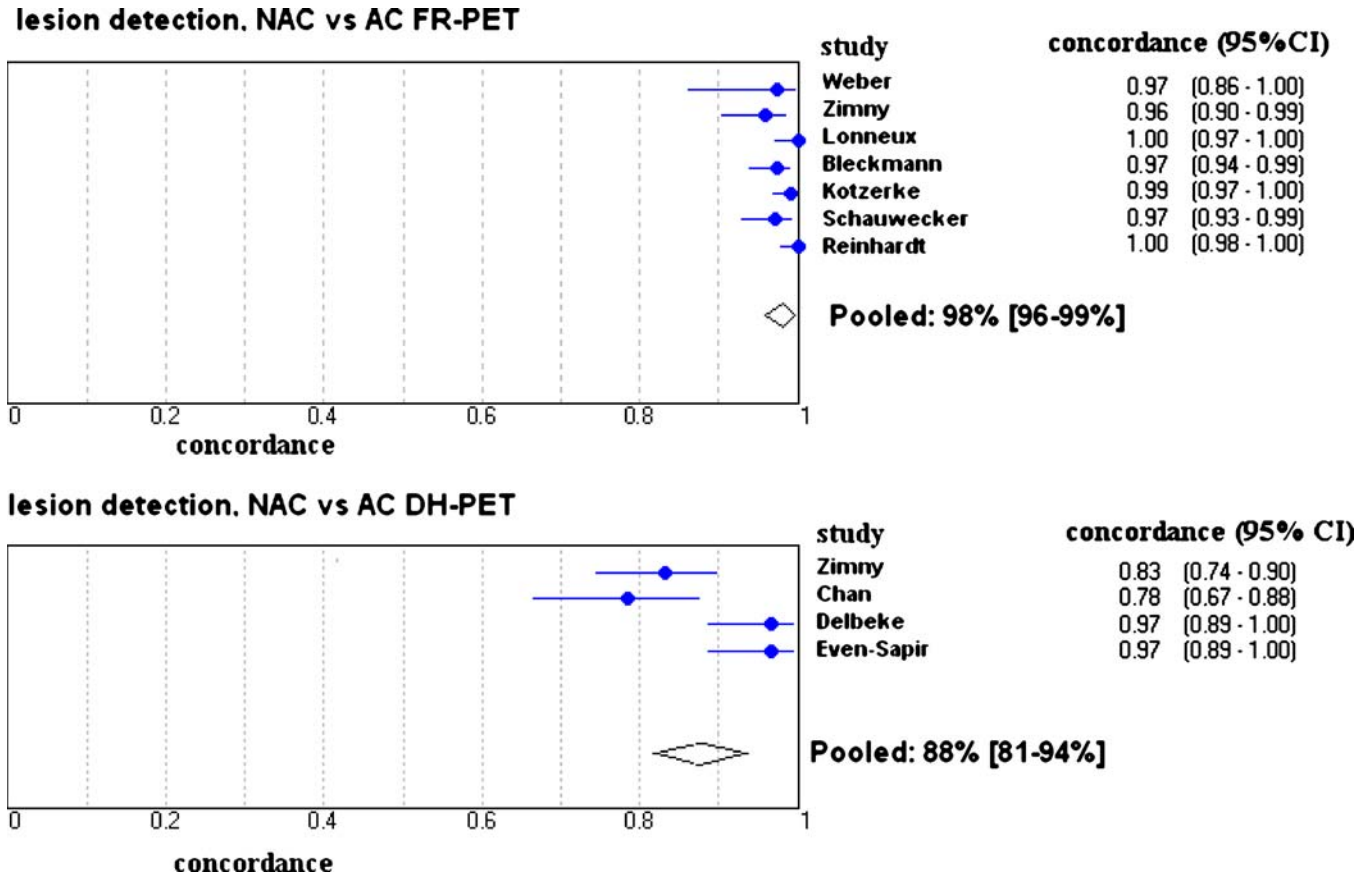


Fig. 1. Pooled lesion detection of NAC vs. AC images for FR-PET and DH-PET.

included as there were no patients without disease. The pooled specificities for AC and NAC FR-PET were 97% (95% CI 92–99%) and 99% (95% CI 95–100%), respectively ($n=155$ patients). For DH-PET, only one study provided data on sensitivity and specificity [27].

Relative lesion detection for NAC vs. AC PET was pooled for 11 studies, which are demonstrated in Fig. 1. Lesion detection of NAC FR-PET vs. AC FR-PET was 98% (95% CI: 96–99%) for $n=1,012$ lesions (pooling of $n=7$ studies); 79% of which were classified FDG positive at AC FR-PET. Lesion detection of NAC DH-PET vs. AC DH-PET was 88% (95% CI: 81–94%) for $n=288$ lesions (pooling of $n=4$ studies); 74% of which were classified as FDG-positive at AC DH-PET.

In addition, we evaluated the relative lesion detection depending on body location (head/neck, chest, abdomen/pelvis) in the four FR-PET [20, 21, 23, 26] and in the three DH-PET studies that provided sufficiently detailed information [17, 18, 26]. The relative sensitivity and specificity based on body location could not be calculated due to an insufficient number of studies. For FR-PET, we found similar relative lesion detection for the three body locations: 95% for head/neck (95% CI 84–98%, $n=61$ lesions), 97% for the chest (95% CI 94–99%, $n=396$ lesions), and 97% for the abdomen/pelvis (95% CI 93–0.99%, $n=205$ lesions). For

DH-PET, relative detection rates for NAC were not significantly different for the various body sites: 78% in the abdomen/pelvis (95% CI 65–88%; 53 lesions), 84% in the chest (95% CI 74–91%; 136 lesions), and 90% in the head/neck area (95% CI 73–97%; 38 lesions). However, in chest ($p=0.000089$) and abdomen/pelvis ($p=0.0037$), the relative detection rates with NAC (vs. AC) for DH-PET were significantly lower than those obtained with FR-PET.

A comprehensive analysis of the potential association of relative detection and lesion size and/or intensity, for lesions with discrepant AC and NAC results, was not possible due to a lack of detailed information. We summarized the results in Table 3: findings of Bleckmann et al. and Reinhardt et al. [16, 23] suggest that AC and NAC discrepancies may relate to (intrapulmonary) lesion size with more discrepancies occurring with smaller lesions at the subcentimeter level (an average of 3% of lesions were correctly detected with NAC and not with AC). The single discrepant lesion in the study of Weber et al. concerned a <1-cm lesion in the mediastinum [25]. However, the discrepant lesions in the studies of Nakamoto et al., Schauwecker et al., and Delbeke et al. included both small- and moderate-sized lesions (in relation to lesions included each study) [18, 22, 24]. In the study of Schauwecker et al., the discrepant lesions demonstrated SUVmax values rang-

Table 3. Evaluation of discrepant lesions between AC and NAC images with respect to lesion size and intensity

Study	Camera type	Number of discrepant lesions	Size range	Intensity (semiquantitative or qualitative)
Bleckmann et al.	FR-PET	5	<1 cm	Not given
Nakamoto et al. ^a	FR-PET	1	1.8 cm	Not given
Reinhardt et al.	FR-PET	6	0.5–1.1 cm	79/174 lesions demonstrated discrepancy in qualitative lesion intensity: 72/174 lesions demonstrating higher intensity (i.e., better visibility) on NAC images
Schauwecker et al. ^a	FR-PET	4	0.8–3.9 cm ³	1.8–2.6 (SUVmax)
Weber et al.	FR-PET	1	0.8 cm	Not given
Delbeke et al.	DH-PET	2	1.0–3.0 cm	“Mild uptake” at AC, “equivocal uptake” at NAC

^aHistology used as gold standard and detailed information given only for true positive lesions

ing from 1.8 to 2.6, whereas, in the study of Delbeke et al., the two discrepant lesions demonstrated only mildly enhanced uptake on AC images and equivocal uptake on NAC images.

Discussion

The cumulated evidence summarized in this systematic review of oncological FDG imaging studies suggests that the accuracy of attenuation and nonattenuation corrected FR-PET are similar. However, with DH coincidence imaging NAC images detect 12% less lesions than AC images, without prominent differences between body areas.

Although in the nuclear medicine field attenuation correction is generally seen as an important issue, it is surprising to find that several large systematic reviews did not thoroughly consider this as a potential effect-modifier. Gould et al. performed systematic reviews on FDG PET in pulmonary lesions [28] and mediastinal lymph node staging in non-small cell lung cancer [29]: in the former review, the item was not mentioned, and in the latter, attenuation correction was an item of study quality, but no analysis of potential impact was performed.

The choice of the reference test is obviously relevant in studies on test accuracy. In oncology, histopathology is the typical endpoint. Of the 12 eligible studies, four used histology as an independent gold standard. Meta-analysis of sensitivity and specificity was only possible for FR-PET, and we found no significant difference for either measure. We chose to use the AC detection rate as an alternative reference test, which defines the relative lesion detection of NAC vs. AC images. This choice theoretically biases in favor of AC: Bleckmann et al. and Reinhardt et al. [16, 23] reported an average of 3% more true positive lesions with NAC FR-PET. However, we expect that the resulting error is small because, in the comparison with histopathology, false positive rates were quite low for either modality. Despite this theoretical negative bias towards NAC, similar lesion detection rates were observed with both AC and NAC for FR-PET. Hence, attenuation correction may not contribute to the detection of malignancy using FR-PET. Conversely, with DH-PET, AC images demonstrated a significantly higher detection rate as opposed to NAC images, which is surprising given that AC images are

usually significantly noisier than NAC images. We postulate that this may be secondary to differences in reconstruction/filtering algorithms.

In addition, there are limitations associated with performing a meta-analysis and data pooling, such as the homogeneity of the data and the quality of the published studies. Homogeneous data have higher statistical strength than heterogeneous data. The data in our study were heterogeneous so that we used a random effect model for pooling. In addition, the statistical strength of the meta-analysis is limited by the quality of the published studies included in it. As mentioned earlier and summarized in Table 2, the studies had several quality limitations. Finally, meta-analyses are limited by publication bias, which biases towards the publication of favorable results or popular subjects.

We were surprised by the limited number of good comparative studies evaluating the value of attenuation correction. It appears that attenuation correction has been accepted as the standard of practice without sound scientific evidence to support it.

The introduction of PET/CT machines has made the time constraints associated with transmission scanning less of an issue. However, PET/CT is not a panacea; X-ray transmission scanning has its own problems and numerous PET/CT publications have demonstrated artifact that can be introduced with X-ray transmission scanning [5, 30–45]. Furthermore, in the study of Reinhardt et al. [23], a significantly improved visibility was demonstrated for 41% of lung metastases with NAC images as opposed to CT-AC images. This higher visibility for NAC images was even more pronounced for lesions smaller than 1 cm. These findings underline that even as PET/CT use becomes more widespread, evaluation of both NAC and AC images should remain an integral part of image interpretation, and not just to recognize image artifacts. At the same time, NAC vs. AC discrepancies at PET/CT offer an obvious opportunity for further investigation.

Conclusions

In this meta-analysis, we found no significant difference in sensitivity, specificity, or relative lesion detectability between AC and NAC FR FDG PET. However, attenuation

correction improved lesion detection for DH coincidence imaging.

Appendix

Detailed search strategy

("x ray" OR x-ray OR cine-ct OR "Tomography, X-Ray Computed" [mesh] OR transmission OR attenuat* OR nonattenuat* OR ac[tw] OR nac [tw] OR nonac OR germanium OR ge[tw] OR gallium OR ga[tw] OR cesium OR cs[tw]) AND (oncolog* OR cancer* OR neoplas* OR neoplasms[mesh] OR tumor* OR tumor OR tumors OR carcinom* OR melanom* OR lymphom* OR malignan*) AND (Deoxyglucose[mesh] OR Deoxyglucose[tw] OR Desoxyglucose[tw] OR Desoxy-glucose[tw] OR deoxy-glucose [tw] OR Deoxy-d-glucose[tw] OR Desoxy-d-glucose[tw] OR fluorodeoxyglucose[tw] OR Fluorodesoxyglucose[tw] OR fluorodeoxy-glucose[tw] OR Fluorodeoxy-d-glucose[tw] OR Fluoro-d-glucose[tw] OR Fludeoxyglucose[tw] OR Fluorodeoxyglucose[tw] OR Fluordesoxyglucose[tw] OR 18fluorodeoxyglucose[tw] OR 18fluorodeoxy-glucose OR 18fluordesoxyglucose[tw] OR 18Fluorodeoxyglucose[tw] OR fdg*[tw] OR 18fdg*[tw] OR 18f-dg*[tw] OR 2deoxyglucose[tw] OR 2deoxy-d-glucose[tw] OR ((fluor[tw] OR fluoro[tw] OR 18fluor[tw] OR 18fluoro[tw]) AND glucose[tw])) AND (pet[tw] OR pet/* OR petscan* OR "Tomography, emission-computed" [mesh] OR (positron[tw] AND emission[tw] AND tomograph*[tw]) OR (emission[tw] AND computed[tw] AND tomograph*[tw])) NOT (animal [mesh] NOT human[mesh])

References

- Mijnhout GS, Riphagen II, Hoekstra OS (2004) Update of the FDG PET search strategy. *Nucl Med Commun* 25:1187–1189
- The Cochrane Collaboration. The Cochrane Manual. <http://www.cochrane.org/admin/manual.htm>
- Bengel FM, Ziegler SI, Avril N, Weber W, Laubenbacher C, Schwaiger M (1997) Whole-body positron emission tomography in clinical oncology: comparison between attenuation-corrected and uncorrected images. *Eur J Nucl Med* 24:1091–1098
- Etchebhere EC, Macapinlac HA, Gonen M, et al. (2002) Qualitative and quantitative comparison between images obtained with filtered back projection and iterative reconstruction in prostate cancer lesions of (18)F-FDG PET. *Q J Nucl Med* 46:122–130
- Goerres GW, Hany TF, Kamel E, von Schulthess GK, Buck A (2002) Head and neck imaging with PET and PET/CT: artefacts from dental metallic implants. *Eur J Nucl Med Mol Imaging* 29:367–370
- Imran MB, Kubota K, Yamada S, et al. (1998) Lesion-to-background ratio in nonattenuation-corrected whole-body FDG PET images. *J Nucl Med* 39:1219–1223
- Kamel E, Hany TF, Burger C, et al. (2002) CT vs 68Ge attenuation correction in a combined PET/CT System: evaluation of the effect of lowering the CT tube current. *Eur J Nucl Med Mol Imaging* 29:346–350
- Laubenbacher C, Saumweber D, Wagner-Manslau C, et al. (1995) Comparison of fluorine-18-fluorodeoxyglucose PET, MRI and endoscopy for staging head and neck squamous-cell carcinomas. *J Nucl Med* 36:1747–1757
- Pitman AG, Hicks RJ, Binns DS, et al. (2002) Performance of sodium iodide based (18)F-fluorodeoxyglucose positron emission tomography in the characterization of indeterminate pulmonary nodules or masses. *Br J Radiol* 75:114–121
- Stevens H, Bakker PF, Schlosser NJ, van Rijk PP, de Klerk JM (2003) Use of a dual-head coincidence camera and 18F-FDG for detection and nodal staging of non-small cell lung cancer: accuracy as determined by 2 independent observers. *J Nucl Med* 44:336–340
- Turlakow A, Larson SM, Coakley F, et al. (2001) Local detection of prostate cancer by positron emission tomography with 2-fluorodeoxyglucose: comparison of filtered back projection and iterative reconstruction with segmented attenuation correction. *Q J Nucl Med* 45:235–244
- Zasadny KR, Kison PV, Quint LE, Wahl RL (1996) Untreated lung cancer: quantification of systematic distortion of tumor size and shape on non-attenuation-corrected 2-[fluorine-18]fluoro-2-deoxy-D-glucose PET scans. *Radiology* 201:873–876
- Wong T, Coleman R, Hagge R, Borges-Neto S, Hanson M (2000) PET image interpretation: attenuation-corrected (ATN) vs non-attenuation corrected (NATN) images. *Clin Positron Imaging* 3:181 (Abstract)
- Yasuda S, Ide M, Takagi S, et al. (1996) Cancer detection with whole-body FDG PET images without attenuation correction. *Kaku Igaku* 33:367–373
- Hustinx R, Dolin RJ, Benard F, et al. (2000) Impact of attenuation correction on the accuracy of FDG-PET in patients with abdominal tumors: a free-response ROC analysis. *Eur J Nucl Med* 27:1365–1371
- Bleckmann C, Dose J, Bohuslavizki KH, et al. (1999) Effect of attenuation correction on lesion detectability in FDG PET of breast cancer. *J Nucl Med* 40:2021–2024
- Chan WL, Freund J, Pocock NA, et al. (2001) Coincidence detection FDG PET in the management of oncological patients: attenuation correction versus non-attenuation correction. *Nucl Med Commun* 22:1185–1192
- Delbeke D, Martin WH, Patton JA, Sandler MP (2001) Value of iterative reconstruction, attenuation correction, and image fusion in the interpretation of FDG PET images with an integrated dual head coincidence camera and X-ray-based attenuation maps. *Radiology* 218:163–171
- Even-Sapir E, Yuzefovich B, Miller E, et al. (2004) Coincidence imaging using 2 dual-head gamma-camera systems, with and without attenuation correction. *J Nucl Med Technol* 32:190–197
- Kotzerke J, Guhlmann A, Moog F, Frickhofen N, Reske SN (1999) Role of attenuation correction for fluorine-18 fluorodeoxyglucose positron emission tomography in the primary staging of malignant lymphoma. *Eur J Nucl Med* 26:31–38
- Lonneux M, Borbath I, Bol A, et al. (1999) Attenuation correction in whole-body FDG oncological studies: the role of statistical reconstruction. *Eur J Nucl Med* 26:591–598
- Nakamoto Y, Chang AE, Zasadny KR, Wahl RL (2002) Comparison of attenuation-corrected and non-corrected FDG-PET images for axillary nodal staging in newly diagnosed breast cancer. *Mol Imaging Biol* 4:161–169
- Reinhardt MJ, Wiethoelter N, Matthies A, et al. (2006) PET recognition of pulmonary metastases on PET/CT imaging: impact of attenuation-corrected and non-attenuation-corrected PET images. *Eur J Nucl Med Mol Imaging* 33:134–139
- Schauwecker DS, Siddiqui AR, Wagner JD, et al. (2003) Melanoma patients evaluated by four different positron emission tomography reconstruction techniques. *Nucl Med Commun* 24:281–289
- Weber WA, Neverve J, Sklarek J, et al. (1999) Imaging of lung cancer with fluorine-18 fluorodeoxyglucose: comparison of a dual-head gamma camera in coincidence mode with a full-ring positron emission tomography system. *Eur J Nucl Med* 26:388–395
- Zimny M, Kaiser HJ, Cremerius U, et al. (1999) Dual-head gamma camera 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography in oncological patients: effects of non-uniform attenuation correction on lesion detection. *Eur J Nucl Med* 26:818–823
- Zimny M, Hochstenbag M, Lamers R, et al. (2003) Mediastinal staging of lung cancer with 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography and a dual-head coincidence gamma camera. *Eur Radiol* 13:740–747
- Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK (2001) Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis. *JAMA* 285:914–924
- Gould MK, Kuschner WG, Rydzak CE, et al. (2003) Test performance of positron emission tomography and computed tomography for mediastinal staging in patients with non-small-cell lung cancer: a meta-analysis. *Ann Intern Med* 139:879–892
- Antoch G, Freudenberg LS, Egelhof T, et al. (2002) Focal tracer uptake: a potential artifact in contrast-enhanced dual-modality PET/CT scans. *J Nucl Med* 43:1339–1342
- Beyer T, Antoch G, Blodgett T, Freudenberg LF, Akhurst T, Mueller S (2003) Dual-modality PET/CT imaging: the effect of respiratory

- motion on combined image quality in clinical oncology. *Eur J Nucl Med Mol Imaging* 30:588–596
32. Bujenovic S, Mannting F, Chakrabarti R, Ladnier D (2003) Artfactual 2-deoxy-2-[(18)F]fluoro-D-glucose localization surrounding metallic objects in a PET/CT scanner using CT-based attenuation correction. *Mol Imaging Biol* 5:20–22
 33. Cohade C, Wahl RL (2003) Applications of positron emission tomography/computed tomography image fusion in clinical positron emission tomography—clinical use, interpretation methods, diagnostic improvements. *Semin Nucl Med* 33:228–237
 34. DiFilippo FP, Brunken RC (2005) Do implanted pacemaker leads and ICD leads cause metal-related artifact in cardiac PET/CT? *J Nucl Med* 46:436–443
 35. Goerres GW, Ziegler SI, Burger C, Berthold T, von Schulthess GK, Buck A (2003) Artifacts at PET and PET/CT caused by metallic hip prosthetic material. *Radiology* 226:577–584
 36. Goerres GW, Burger C, Kamel E, et al. (2003) Respiration-induced attenuation artifact at PET/CT: technical considerations. *Radiology* 226:906–910
 37. Goerres GW, Schmid DT, Eyrich GK (2003) Do hardware artefacts influence the performance of head and neck PET scans in patients with oral cavity squamous cell cancer? *Dento-maxillo-facial Radiol* 32:365–371
 38. Gorospe L, Raman S, Echeveste J, et al. (2005) Whole-body PET/CT: spectrum of physiological variants, artifacts and interpretative pitfalls in cancer patients. *Nucl Med Commun* 26:671–687
 39. Kamel EM, Burger C, Buck A, von Schulthess GK, Goerres GW (2003) Impact of metallic dental implants on CT-based attenuation correction in a combined PET/CT scanner. *Eur Radiol* 13:724–728
 40. Nehmeh SA, Erdi YE, Kalaigian H, et al. (2003) Correction for oral contrast artifacts in CT attenuation-corrected PET images obtained by combined PET/CT. *J Nucl Med* 44:1940–1944
 41. Osman MM, Cohade C, Nakamoto Y, Wahl RL (2003) Respiratory motion artifacts on PET emission images obtained using CT attenuation correction on PET-CT. *Eur J Nucl Med Mol Imaging* 30:603–606
 42. Otsuka H, Graham MM, Kubo A, Nishitani H (2005) The effect of oral contrast on large bowel activity in FDG-PET/CT. *Ann Nucl Med* 19:101–108
 43. Papatthanassiou D, Liehn JC, Bourgeot B, Amir R, Marcus C (2005) Cesium attenuation correction of the liver dome revealing hepatic lesion missed with computed tomography attenuation correction because of the respiratory motion artifact. *Clin Nucl Med* 30:120–121
 44. Sarikaya I, Yeung HW, Erdi Y, Larson SM (2003) Respiratory artefact causing malpositioning of liver dome lesion in right lower lung. *Clin Nucl Med* 28:943–944
 45. Sureshabu W, Mawlawi O (2005) PET/CT imaging artifacts. *J Nucl Med Technol* 33:156–161