

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

VOLKSWAGEN GROUP OF AMERICA, INC.,
Petitioner,

v.

LONGHORN AUTOMOTIVE GROUP LLC,
Patent Owner.

IPR2025-01064
U.S. Patent 8,265,353

Declaration of Shauna L. Wiest Regarding *Goerres*

I, Shauna L. Wiest, state and declare as follows:

I. Introduction

1. I have prepared this Declaration in connection with the Petition for *Inter Partes* Review of U.S. Patent No. 8,265,353, which I understand will be filed concurrently with this Declaration.

2. I am currently a Senior Research Analyst with the Research & Information Services team at Finnegan, Henderson, Farabow, Garrett & Dunner, LLP located at 3300 Hillview Avenue, Palo Alto, CA 94304.

3. I am over eighteen years of age, and I am competent to make this Declaration. I make this Declaration based upon my own personal knowledge, and my professional knowledge of library science practices.

4. I earned a Master of Science in Library Science degree from the University of North Carolina at Chapel Hill in 1999, and a Bachelor of Arts in Political Science degree from the University of California at San Diego in 1989. I have worked as a law librarian for twenty years. I have been employed at Finnegan, Henderson, Farabow, Garrett & Dunner, LLP since 2021. Before that, from 2000-2015, I was employed as a Law Librarian at Stoel Rives LLP, and from 2015-2016, I was employed as a Competitive Intelligence Specialist for Nossaman LLP. Additionally, as a graduate student at the University of North Carolina at Chapel Hill, I served as an intern at the Environmental

Protection Agency at Research Triangle Park (“EPA-RTP”) where one of my rotations included original cataloging for EPA technical documents, state agency reports and documents, international organization documents, dissertations, and, on occasion, monographs. In this role, I accessed OCLC, MARC records, and the EPA National Library Catalog daily.

II. Standard Library Practice for Receiving, Cataloging, and Making Materials, including Serial Publications, Publicly Available and Accessible

5. I have knowledge of and experience with standard library practices regarding the receipt, cataloging, shelving, and making materials, including serial publications, available and accessible to the public. I have knowledge of and experience with the Machine-Readable Cataloging (MARC) system, an industry-wide standard that libraries use to catalog materials.

6. Based on standard library practice, when a library receives an item, the cataloguer or cataloguer’s assistant will examine the item and stamp and/or affix a label to the item with the library name and/or barcode with the date it was received. Next, the library will catalog the item within a few days of receiving it. As a general practice, cataloguing is centralized and performed by a cataloguing department within a library or university setting.

7. Normally, after an item is cataloged, the public may access the item by searching a library catalog, browsing the library shelves, and/or

requesting the item from the library. Standard library practice is to make the item available to the public within several days of cataloging it. If an item requires original cataloging, the item will be made available to the public up to and including one week from the date of receipt.

III. Ownership and Date-Stamp

8. Libraries have different policies on whether or not to date stamp publications. It is becoming increasingly common for libraries to no longer date stamp the publications they receive. In the past, it was standard practice to affix an ownership stamp somewhere within the publication, usually on the cover page, verso of the cover page, or a designated page within the publication. The timing of when an ownership stamp is entered on the monograph or periodical can vary from one library to another. It could occur when the item is received in acquisitions after shipment to the library, or at the time of cataloging. Therefore, it is possible for there to be instances when the date of receipt precedes the cataloging date or vice versa.

IV. MARC Records

9. The MARC system was developed during the 1960s to standardize bibliographic catalog records so they could be read by computers and shared among libraries. By the mid-1970s, MARC had become the international standard for cataloging bibliographic materials and is still used today. Many libraries

provide public access to their MARC records via their electronic cataloging systems at the library. In a MARC record, each field provides specific information about the cataloged item, including how materials are held and when they were made available to the public.

10. The MARC record system uses a specific three-digit numeric code (“field tags”) (from 001-999) to identify each field in a catalog record. For example, field tag 008 provides the six-digit date an item was catalogued (*Date entered on file*). The first six characters of field tag 008 are always in the “**YYMMDD**” format. Descriptions and definitions of all of the character positions of field tag 008 are outlined here:

<https://www.loc.gov/marc/bibliographic/bd008a.html>.

11. As is relevant to this Declaration, MARC field tag 022 sets forth the International Standard Serial Number (“ISSN”), a unique identification assigned to every serial publication. MARC field tag 310 sets forth the current publication frequency of an item. MARC field Tag 362 sets forth the dates of publication and/or sequential date designation for a work.

V. Cataloguing Treatment of Serials

12. A serial publication, also known as a “journal,” “periodical,” “newspaper,” or “magazine,” is a resource that is issued in successive parts and has no predetermined conclusion. These successive parts are commonly

referred to as “issues,” and each issue is usually chronologically numbered, bears a unique date, and is received on an expected, ongoing basis. The presence of enumeration, years of coverage, regular receipt, and/or other chronological information, also indicates a serial publication.

13. There are differences between cataloging finite resources (books/monographs) and continuing resources (serials). For serials, the catalog record provides information about the serial as a whole, including the first or earliest available issue. It also provides information as to holdings – the breadth of volumes and issues received, checked in, and held by a library, including the public availability of those holdings. In serials cataloging, there are identifying characteristics unique to serials that are slightly different from monographs (books). The issue date for a serial publication, for example, generally appears on the cover (front or back), the masthead page, the title page (if any), the table of contents page(s), or on the pages of the individual articles contained within the issue. More information regarding the unique aspects of cataloging serials can be found at this link:

<https://www.loc.gov/aba/pcc/conser/scctppt/Basic-2014/Basic-Trainee-Mannual.pdf>.

VI. Public Availability and Accessibility of *Goerres*

14. Section VI of this Declaration relates to the date of receipt and public availability/accessibility for the following reference Goerres, G.W., Kamel, E., Heidelberg, TN.H. *et al.* PET-CT image co-registration in the thorax: influence of respiration. *European Journal of Nuclear Medicine and Molecular Imaging*, Volume 29, No. 3, pages 351–360 (March 2002) (“*Goerres*”). I understand that *Goerres* has been submitted as **Exhibit Ex-1021** in this proceeding. This reference is appended to my Declaration as **Appendix A**.

15. As detailed below, I have reviewed the print *Goerres* reference, which was supplied to me by Wisconsin Tech Search (a service of the University of Wisconsin Madison) on May 15, 2025, the University of Wisconsin public holdings information and MARC record for *Goerres* to determine the date of public availability for this reference.

16. **Appendix A** to this Declaration is a true and accurate copy of the cover, front matter, table of contents, and date stamp for the print issue of *European Journal of Nuclear Medicine and Molecular Imaging* containing *Goerres* held by the Health Sciences Library at the University of Wisconsin at Madison. **Appendix A** includes pages 351-360, which comprises the reference *Goerres*. **Appendix A** includes date-stamps on PDF pages 1 and 2 indicating that the issue

of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres* was received by the University of Wisconsin Health Sciences Library on May 8, 2002. **Appendix A** also sets forth the ISSN for the print journal as 0340-6997.

17. **Appendix B** to this Declaration is a true and accurate copy of the University of Wisconsin at Madison Library public catalog record for its copy of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres*, which was downloaded from <https://search.library.wisc.edu/catalog/999932262702121> on May 27, 2025.

18. The University of Wisconsin - Madison Library public catalog record (**Appendix B**) sets forth the publication and holding details for its copy of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres*. The public catalog record indicates that the Middleton Shelving Facility holds print Volume 29 No. 1 (2002) through Volume 33 Supplement 2 (2006) of the print serial publication European Journal of Nuclear Medicine and Molecular Imaging. **Appendix B** also sets forth the ISSN number as 0340-6997 (print).

19. **Appendix C** to this Declaration sets forth the individual holdings and onsite location information for members of the public seeking the print issue of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres*, which was downloaded from

<https://search.library.wisc.edu/catalog/999932262702121/holdings?from=locations> on May 27, 2025. **Appendix C** indicates that the print issue of the European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres* is held at the Middleton Shelving Facility and is available upon request at Call Number Q 7EU46461 (34-V-6).

20. **Appendix D** to this Declaration is a true and accurate copy of the University of Wisconsin Library MARC record for its holdings of the journal European Journal of Nuclear Medicine and Molecular Imaging, which was downloaded from <https://search.library.wisc.edu/catalog/999932262702121> (Click on “Library Staff Details” and then “Staff View”) on May 28, 2025.

21. **Appendix D** confirms the fixed data elements of MARC field tag 008 as 020320c20029999gw mr p 0 0eng c. As discussed above, the first six characters “020320” are in typical “YYMMDD” format and indicate that the print journal European Journal of Nuclear Medicine and Molecular Imaging was first catalogued by the University of Wisconsin - Madison Library on March 20, 2002. and that the journal began publication in 2002 and is a continuing resource currently published with no end date noted.

22. The University of Wisconsin - Madison Library MARC record (**Appendix D**) field tag 310 sets forth the publication frequency of European Journal of Nuclear Medicine and Molecular Imaging as monthly. MARC field tag

022 sets forth the print ISSN number as 0340-6997, which matches the ISSN in **Appendix A** and **Appendix B**. MARC field tag 362 denotes the dates of publication and/or sequential date designation for the European Journal of Nuclear Medicine and Molecular Imaging as \$aVol. 29, no. 1 (Jan. 2002)-.

23. Based on the information set forth in **Appendices A, B, C, and D** attached to this Declaration, standard library practices, and my experience as a librarian, the issue of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres* was received by the University of Wisconsin Health Sciences Library staff on May 8, 2002.

24. Accordingly, the issue of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres* would have been checked-in and catalogued by the University of Wisconsin Health Sciences Library within a few days of May 8, 2002, and would have subsequently been made available to the public within a few days of being checked-in and catalogued. The general public could have accessed the issue of European Journal of Nuclear Medicine and Molecular Imaging containing *Goerres* by (i) searching the University of Wisconsin - Madison Library catalog; (ii) visiting the library; or (iii) by asking a Library staff member and requesting the print issue available at the Middleton Shelving Facility at Call Number Q 7EU46461 (34-V-6) on or before May 20, 2002.

VII. Conclusion

25. In signing this Declaration, I understand it will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the United States Patent and Trademark Office. I understand I may be subject to cross-examination in this case and that cross-examination will take place within the United States. If cross-examination is required of me, I will appear for cross-examination within the United States during the time allotted for cross-examination.

26. I declare that all statements made herein of my knowledge are true, that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Executed on May 29, 2025.


Shauna L. Wiest

A 20612

Volume 29 • Number 3 • March 2002

HSL

European Journal of

Nuclear Medicine and Molecular Imaging

HEALTH SCIENCES LIBRARY
UNIVERSITY OF WISCONSIN

MAY 08 2002

1305 Linden Drive
Madison, WI 53706



Springer

European Journal of Nuclear Medicine and Molecular Imaging

Official Journal of the European Association of Nuclear Medicine (EANM)

Editor-in-Chief

P.J. Ell, London

Co-Editors

I. Carrió, Barcelona
W.H. Knapp, Hannover
G. Lucignani, Milano
V.R. McCready, Sutton
E.K.J. Pauwels, Leiden

Section Editors

S.S. Gambhir, Los Angeles
M. Schwaiger, München
H.W. Strauss, New York

Honorary Editor

W. Becker, Goettingen

Editor: Image of the month

D.C. Costa, London

Editorial Board

M. Aas, Oslo
H.M. Abdel Dayem, New York
P.D. Acton, Philadelphia
H. Amaral, Santiago
S. Askienazy, Paris
W.H. Bakker, Rotterdam
T.M. Behr, Marburg
H. Bergmann, Vienna
K.A. Bergstroem, Kuopio
H. Biersack, Bonn
A. Bischof Delaloye, Lausanne
J.A.K. Blokland, Leiden
B.D. Bok, Paris
E. Bombardieri, Milano
M.H. Bourguignon, Paris
F.J.H.N. Braga, Sao Paulo
A. Britten, London
U. Buell, Aachen
E.E. Camargo, Campinas

B.E. Caner, Ankara
J.M. Carril, Santander
J.F. Chatal, Nantes
J.-K. Chung, Seoul
A.J. Coakley, Canterbury
G. Cook, Sutton
F.H.M. Corstens, Nijmegen
R.A. Dierckx, Gent
A.A. Driedger, London/Ontario
H. Durak, Izmir
M. Eisenhut, Heidelberg
K. Endo, Gumna
M. Fischer, Kassel
A. Fischer Thom, Sao Paulo
J.S. Fleming, Southampton
L.M. Freeman, New York
I. Gordon, London
U. Haberkorn, Heidelberg
L.K. Harding, Birmingham
R. Hicks, Melbourne
D.J. Hnatowich, Worcester
C. Hoefnagel, Amsterdam
L. Højgaard, Copenhagen
B. Hutton, Sydney
R.B. Innis, Bethesda
M.P. Iturralde, Pretoria
P. Jarritt, Belfast
L. Johansson, Umea
A.G. Jones, Boston
M. Kelly, Victoria
E.E. Kim, Houston
J. Konishi, Kyoto
R.N. Krasikova, St. Petersburg
J.T. Kuikka, Kuopio
D.J. Kwekkeboom, Rotterdam
A.A. Lammertsma, Amsterdam
S.A. Larsson, Stockholm
C. Le Rest, Brest
V. Lele, Bombay
G.S. Limouris, Athens
J. Links, Baltimore
R.-S. Liu, Taipei
X.-J. Liu, Beijing
H.R. Maecke, Basle
M. Maisey, London

J. Malamitsi, Athens
G. Mariani, Pisa
P.Y. Marie, Nancy
J. Martin-Comin, Barcelona
J.S. Masjhur, Bandung
S.J. Mather, London
A.J.B. McEwan, Edmonton
J.A. Melin, Brussels
J.L. Moretti, Paris
P.J. Mountford, Staffordshire
D.L. Munz, Berlin
N. Nair, Bombay
A. Notghi, Birmingham
M.J. O'Doherty, London
A. Otte, Freiburg
A.C. Perkins, Nottingham
M. Peters, Cambridge
A. Piepsz, Brussels
V.W. Pike, Bethesda
L.S. Pilowsky, London
C. Reiners, Würzburg
M.D. Rutland, Auckland
M. Salvatore, Naples
M.P. Sandler, Nashville
Y. Sasaki, Chiba
K. Schmidt, Bethesda
O. Schober, Muenster
P.A. Schubiger, Villigen
J.P. Seibyl, New Haven
H. Sinzinger, Vienna
F.X. Sundram, Singapore
Y. Suzuki, Isehara
J. Szilvasi, Budapest
N. Tamaki, Sapporo
S. Tanada, Chiba
A. Tarkowska, Lublin
M.L. Thakur, Philadelphia
T. Treves, Boston
J. Turner, Christ Church
R. Underwood, London
H. van der Wall, Sidney
A. Verbruggen, Leuven
S.-C. Wang, Beijing
F. Wolf, Erlangen
R.E. Zimmerman, Boston

HEALTH SCIENCES LIBRARY
UNIVERSITY OF WISCONSIN

MAY 08 2007

1305 Linden Drive
Madison, WI 53706



Springer

European Journal of
Nuclear Medicine
and Molecular Imaging



Official Journal of the European Association of Nuclear Medicine (EANM)

Volume 29 Number 3 March 2002

Editorial

In Between Lakes 287

Original articles

Tatsumi M, Tsuruo T, Nishimura T:
Evaluation of MS-209, a novel multidrug-resistance-reversing agent, in tumour-bearing mice by technetium-99m-MIBI imaging 288

Doze P, Elsinga PH, van Waarde A, Pieterman RM, Pruim J, Vaalburg W, Willemsen ATM:
Quantification of β -adrenoceptor density in the human heart with (S)-[^{11}C]CGP 12388 and a tracer kinetic model 295

Tanis PJ, van Sandick JW, Nieweg OE, Valdés Olmos RA, Rutgers EJ, Hoefnagel CA, Kroon BBR:
The hidden sentinel node in breast cancer 305

Karanikas G, Becherer A, Wiesner K, Dudczak R, Kletter K:
ACE inhibition is superior to angiotensin receptor blockade for renography in renal artery stenosis 312

Weber B, Burger C, Biro P, Buck A:
A femoral arteriovenous shunt facilitates arterial whole blood sampling in animals 319

Henze M, Mohammed A, Mier W, Rudat V, Dietz A, Nollert J, Eisenhut M, Haberkorn U:
Pretreatment evaluation of carcinomas of the hypopharynx and larynx with ^{18}F -fluorodeoxyglucose, ^{123}I - α -methyl-L-tyrosine and $^{99\text{m}}\text{Tc}$ -hexakis-2-methoxyisobutylisocyanide 324

Takeuchi R, Yonekura Y, Matsuda H, Konishi J:
Usefulness of a three-dimensional stereotaxic ROI template on anatomically standardised $^{99\text{m}}\text{Tc}$ -ECD SPET 331

Shiga T, Kubo N, Takano A, Kobayashi J, Takeda Y, Nakamura F, Katoh C, Koyama T, Tsukamoto E, Tamaki N:

The effect of scatter correction on ^{123}I -IMP brain perfusion SPET with the triple energy window method in normal subjects using SPM analysis 342

Kamel E, Hany TF, Burger C, Treyer V, Lonn AHR, von Schulthess GK, Buck A:

CT vs ^{68}Ge attenuation correction in a combined PET/CT system: evaluation of the effect of lowering the CT tube current 346

Goerres GW, Kamel E, Heidelberg T-NH, Schwitter MR, Burger C, von Schulthess GK:
PET-CT image co-registration in the thorax: influence of respiration 351

Schirrmeister H, Bommer M, Buck AK, Müller S, Messer P, Bunjes D, Döhner H, Bergmann L, Reske SN:

Initial results in the assessment of multiple myeloma using ^{18}F -FDG PET 361

Short communications

Goerres GW, Hany TF, Kamel E, von Schulthess GK, Buck A:
Head and neck imaging with PET and PET/CT: artefacts from dental metallic implants 367

Lin W-Y, Chao T-H, Wang S-J:
Clinical features and gallium scan in the detection of post-surgical infection in the elderly 371

Puille M, Altland K, Linke RP, Steen-Müller MK, Klett R, Steiner D, Bauer R:
 $^{99\text{m}}\text{Tc}$ -DPD scintigraphy in transthyretin-related familial amyloidotic polyneuropathy 376

Occasional survey

Chajari M'H, Lacroix J, Peny A-M, Chesnay E, Batalla A, Henry-Amar M, Delcambre C, Génot J-Y, Fruchard C, Bardet S:

Gallium-67 scintigraphy in lymphoma: is there a benefit of image fusion with computed tomography? 380

Molecular imaging

Zinn KR, Chaudhuri TR:

The type 2 human somatostatin receptor as a platform for reporter gene imaging 388

Högemann D, Basilion JP:

"Seeing inside the body": MR imaging of gene expression 400

Controversies

Should SPET attenuation correction be more widely employed in routine clinical practice?

Ficaro EP:

For 409

Wockers FJT:

Against 412

Review article

Langer O, Halldin C:

PET and SPET tracers for mapping the cardiac nervous system 416

Letters to the editor

Schumacher T, Waldherr C, Mueller-Brand J, Maecke H:

Kidney failure after treatment with ^{90}Y -DOTATOC 435

Tanis PJ, Nieweg OE, Valdés Olmos RA, Hoefnagel CA:

An original approach in the diagnosis of early breast cancer: use of the same radiopharmaceutical for both non-palpable lesions and sentinel node localisation 436

With a reply by Feggi L, Prandini N, Basaglia E, Soliani G, Ascanelli S, Bergossi L, Pozza E, Carcoforo P, Corcione S, Querzoli P 437

News & Views 439

A Window on Japan 443

Image of the Month



Acton PD, Kung M-P, Hou C, Plössl K, Keeney C, Kung HF:
Ultra-high resolution single photon emission tomography imaging of the mouse striatum 446

Announcements 447

Abstracts

Radioactive Isotopes in Clinical Medicine and Research. 25th International Symposium
Bad Gastein, Austria, 8–11 January 2002 S1

Blue pages

European School of Nuclear Medicine

21st Seminar, 18–19 April 2002 BP1

22nd Seminar, 29–30 April 2002 BP2

23rd Seminar, 17–19 April 2002 BP3

Online edition in LINK – *Medicine Online Library* <http://link.springer.de>
Indexed in/abstracted by *Current Contents*, *Index Medicus* and *EMBASE*
Printed on acid free paper



Springer



0340-6997(200203)029:03;1-#

European Journal of Nuclear Medicine and Molecular Imaging

Official Journal of the European Association of Nuclear Medicine (EANM)

1 Aims and Scope

The aim of the *European Journal of Nuclear Medicine and Molecular Imaging* is to provide a forum for the exchange of clinical and scientific information for the nuclear medicine community and allied professions involved in the functional, metabolic and molecular investigation of disease. The *European Journal of Nuclear Medicine and Molecular Imaging* will remain of primary interest to those practising the field of nuclear medicine but will also report on original works relating to physics, dosimetry, radiation biology, computer science, radiochemistry and pharmacy. The Journal will welcome original material reflecting the growing field of molecular imaging probes, reporter gene assays, cell trafficking, targeting of endogenous gene expression and antisense methodologies.

The Journal will continue to publish in depth Reviews of topical interest, Occasional surveys, Short communications and Letters to the editor. A section on Controversies is also a new feature. Case reports are not published.

Manuscripts should be sent to:
Professor Peter J. Ell, Editor in Chief,
European Journal of Nuclear Medicine and
Molecular Imaging
Middlesex Hospital, Mortimer Street
London W1T 3AA, UK, Fax: +44-207-436 0603
e-mail: p.ell@nucmed.ucl.ac.uk

Manuscripts on Molecular Imaging should be sent to:

Sanjiv Sam Gambhir, MD, Section Editor,
European Journal of Nuclear Medicine
and Molecular Imaging,
Department Molecular & Medical Pharmacology,
Crump Institute for Molecular Imaging,
UCLA School of Medicine, Box 95 1770
Los Angeles, CA 90095-1770, USA
Fax: +1 310-206-9455,
e-mail: sgambhir@mednet.ucla.edu

2 Copyright

Submission of a manuscript implies: that the work described has not been published before (except in form of an abstract or as part of a published lecture, review or thesis); that it is not under consideration for publication elsewhere; that its publication has been approved by all co-authors, if any, as well as – tacitly or explicitly – by the responsible authorities at the institution where the work was carried out. Transfer of copyright to Springer-Verlag becomes effective if and when the article is accepted for publication. The copyright covers the exclusive right (for U.S. government employees: to the extent transferable) to reproduce and distribute the article, including reprints, translations, photographic reproductions, microform, electronic form (offline, online) or other reproductions of similar nature.

All articles published in this journal are protected by copyright, which covers the exclusive rights to reproduce and distribute the article (e.g., as off-prints), as well as all translation rights. No material published in this journal may be reproduced photographically or stored on microfilm, in electronic data bases, video disks, etc., without first obtaining written permission from the publisher. The use of general descriptive names, trade names, trademarks, etc., in this publication, even if not specifically identified, does not imply that these names are not protected by the relevant laws and regulations.

An author may make an article published by Springer-Verlag available on his/her personal home

page, provided the source of the published article is cited and Springer-Verlag is mentioned as the copyright holder. Authors are requested to create a link to the published article in LINK, Springer's internet service. The link must be accompanied by the following text: "The original publication is available on LINK at <http://link.springer.de>".

While the advice and information in this journal is believed to be true and accurate at the date of its publication, neither the authors, the editors, nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Special regulations for photocopies in the USA: Photocopies may be made for personal or in-house use beyond the limitations stipulated under Section 107 or 108 of U.S. Copyright Law, provided a fee is paid. All fees should be paid to the Copyright Clearance Center, Inc., 21 Congress Street, Salem, MA 01970, USA, stating the ISSN 0340-6997, the volume, and the first and last page numbers of each article copied. The copyright owner's consent does not include copying for general distribution, promotion, new works, or resale. In these cases, specific written permission must first be obtained from the publisher.

The Canada Institute for Scientific and Technical Information (CISTI) provides a comprehensive, world-wide document delivery service for all Springer-Verlag journals. For more information, or to place an order for a copyright-cleared Springer-Verlag document, please contact Client Assistant, Document Delivery, CISTI, Ottawa K1A 0S2, Canada
Tel. +1-613-9939251; Fax +1-613-9528243;
e-mail: cisti.docdel@nrc.ca

3 Subscription information

ISSN print edition 0340-6997
ISSN electronic edition 1432-105X

Volume 29 (12 issues) will appear in 2002.

European Journal of Nuclear Medicine and Molecular Imaging appears monthly. It is published by Springer-Verlag Berlin, Heidelberger Platz 3, 14197 Berlin, Germany. Periodicals Postage paid at New York, NY, and additional mailing offices. Springer-Verlag New York, Inc., 175 Fifth Avenue, New York, NY 10010, USA are our Mailing Agents.

Postmaster: Send all address changes to: European Journal of Nuclear Medicine and Molecular Imaging, Springer-Verlag New York Inc., Journal Fulfillment, P.O. Box 2485, Secaucus, NJ 07096-2485, USA.

■ North and South America

Please ask for the appropriate price list in US \$.

Please mail orders and inquiries to:

Springer-Verlag New York Inc. Journal Fulfillment,
P.O. Box 2485 Secaucus, NJ 07096-2485, USA
Tel.: +1-800-SPRINGER (77746437)
or +1-212-4601500
Fax: +1-201-3484505
e-mail: journals@springer-ny.com

■ All Countries except North and South America

Recommended annual subscription rate incl. basic LINK license: € 990 (Prices are net-prices subject to local VAT) plus carriage charges: (Germany: € 26,70 other countries: € 45,90). Single issue price available upon request. SAL delivery (surface airmail lifted) is mandatory to

Japan, North & South East Asia, India, Australia and New Zealand. Customers should ask for the appropriate price list. Airmail delivery to all other countries is available upon request.

Orders or claims can either be placed via a bookseller or sent directly to: Springer-Verlag, Customer Service Journals, Haberstrasse 7, 69126 Heidelberg, Germany; Tel.: +49-6221-345240, Fax: +49-6221-345229, e-mail: subscriptions@springer.de

Cancellations must be received by September 30 to take effect at the end of the same year.

Changes of address: Allow six weeks for all change to become effective. All communications should include both old and new addresses (with postal codes) and should be accompanied by a mailing label from a recent issue.

According to §4 Sect. 3 of the German Postal Service Data Protection Regulations if subscriber's address changes, the German Federal Post Office can inform the publisher of the new address even if the subscriber has not submitted a formal application for mail to be forwarded. Subscribers not in agreement with this procedure may send a written complaint to Customer Service Journals, Karin Tiks, within 14 days of publication of this issue.

Back volumes: Prices are available on request.

Microform editions are available from:

ProQuest. Further information available with: <http://www.proquest.com/umi>

4 Electronic edition

An electronic edition of this journal is available via the LINK Internet Service at <http://link.springer.de> or at <http://link.springer-ny.com>.

LINK Alert: Would you like to automatically receive via e-mail news of newly published articles listed in the journal's table of contents with direct links to the respective abstracts? Then take advantage of our free LINK Alert service. To register and obtain further information, go to <http://link.springer.de/alert/> or <http://link.springer-ny.com/alert/>.

This journal is included in the ADONIS service. In the ADONIS service copies of individual articles can be printed out from compact discs (CD-ROM) on demand. An explanatory leaflet giving further details of the scheme is available from the publisher on request.

Online First articles are published in electronic form weeks before distribution of the printed journal. An Online Publication date is published in each Online First article and its print version. Authors should be aware that after electronic publication they cannot withdraw an article or change its content. Any corrections have to be made in an Erratum which will be hyperlinked to the article. Online First articles can be cited using their Digital Object Identifier, a unique and consistent identification code included in both the print and the electronic versions.

5 Responsible for advertisements

Springer-Verlag, Edda Lückermann
and Noëla Krischer
Heidelberger Platz 3, 14197 Berlin, Germany
Tel. +49-30-827875739, Fax +49-30-827875300
e-mail: krischer@springer.de,
www.wikom.springer.de

6 Production

Springer-Verlag, Anneliese Sand
Journal Production Life Sciences & Medicine
Postfach 105280, 69042 Heidelberg, Germany
Tel.: +49-6221-4878901, Fax +49-6221-4878968
e-mail: sand@springer.de

Address for courier, express and registered mail:
Tiergartenstrasse 17, 69121 Heidelberg, Germany

Printers: Stürtz AG, Würzburg, Germany

Springer-Verlag Berlin Heidelberg New York
a member of BertelsmannSpringer
Science+Business Media GmbH
www.springer.de
Ownership and Copyright
© Springer-Verlag Berlin Heidelberg 2002
Printed in Germany

Instructions for authors

General

Submission of a manuscript implies: that the work described has not been published before (except in the form of an abstract or as part of a published lecture, review, or thesis); that it is not under consideration for publication elsewhere; that its publication has been approved by all coauthors, if any, as well as by the responsible authorities at the institute where the work has been carried out (including ethical committees and national licensing authorities); that, if and when the manuscript is accepted for publication, the authors agree to automatic transfer of the copyright to the publisher; and that the manuscript will not be published elsewhere in any language without the consent of the copyright holders.

Manuscripts must contain a statement to the effect that all human studies have been reviewed by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in an appropriate version of the 1964 Declaration of Helsinki. It should also be stated clearly in the text that all persons gave their informed consent prior to their inclusion in the study. Details that might disclose the identity of the subjects under study should be omitted.

Reports of animal experiments must state that the "Principles of laboratory animal care" (NIH publication No. 86-23, revised 1985) were followed, as well as specific national laws (e.g. the current version of the German Law on the Protection of Animals) where applicable.

The editors reserve the right to reject manuscripts that do not comply with the abovementioned requirements. The author will be held responsible for false statements or for failure to fulfil the above-mentioned requirements.

Manuscripts should be submitted in triplicate (original and two copies); they should be double-spaced, with wide margins on one side of the paper only, and should be carefully prepared in the style of this journal and checked before submission. Typing errors should be corrected legibly.

Pages should be consecutively numbered, starting with the title page. The desired position of figures and tables should be marked in the margin.

In order to reduce mailing costs, manuscripts will not normally be returned.

Changes in the proofs should be kept to a minimum; a charge will be made for changes introduced after the manuscript has been set in type.

Authors wishing to submit diskettes are requested to wait until the review process has been completed. When preparing the final version, please follow the technical instructions printed in the journal.

Short communications

With this feature our intention is to present to our readers the latest information, as Short

communications will be published within 3 months of acceptance. The four Co-Editors of the EJNM will be responsible for vetting these, and proofs will be checked by the Editorial Office in order to speed up publication. The usual style and guidelines for the EJNM will apply.

Short communications represent a vehicle for rapidly disseminating novel ideas of great interest to the nuclear medicine community, ideas which have not yet been extensively explored in a large clinical trial. Innovative work on instruments, methods, tracers and applications is most welcome. Preliminary clinical and/or experimental feasibility-type studies (as long as they are well planned and executed) are very appropriate candidates for publication.

Short communications should contain a maximum of 1200–1500 words and no more than 6 tables and/or figures, in whatever combination. Tables and/or figures should be prepared with appropriate, clear labels in a format of 8.6 × 8 cm. References should be confined to 10.

Short communications should clearly state the aim of the study, materials, methods and patients, results, a brief discussion and a conclusion. Titles should be concise and to the point. Well-prepared poster-type presentations could be used as a guide as to what could be meant by a short communication. Individual case reports are not appropriate for EJNM.

Organization of the manuscript

The speed of publication depends greatly upon following these guidelines precisely.

1. The manuscript should be divided clearly into an Introduction, Materials and methods, Results, Discussion and References. The text should be concise and consistent as to spelling, abbreviations, etc.
2. The title page should include the title of the work, first and last name(s) of author(s), name of institution, any footnotes referring to the title (marked with an asterisk), and the address of the author to whom the proofs are to be sent.

To facilitate communication between the authors, editors and publisher, the author should furnish a fax number or an e-mail number on the title page of the manuscript.

3. The abstract should be a summary of the hypothesis or aims of the work, the basic material and methods and the conclusion of the study.
4. Immediately following the abstract, up to five relevant key words should be supplied for subject indexing.
5. Footnotes, other than those referring to the title heading, should be numbered consecutively.
6. The accuracy of the References is the responsibility of the authors.

The list of references should only include works that are cited in the text and that have been published or accepted for publication.

Personal communications should be mentioned in the text only. References should be styled as follows:

1. Mahmood S, Buscombe JR, Ell PJ. The use of thallium-201 lung/heart ratios. *Eur J Nucl Med* 1992; 19:807–814.
2. Treves ST. *Pediatric nuclear medicine*. Berlin Heidelberg New York: Springer, 1985.
3. Mullins DE, Rifkin DB. Induction of proteases and protease inhibitors by growth factors. In: Sporn MB, Roberts AB, eds. *Peptide growth factors and their receptors II*. Berlin Heidelberg New York: Springer; 1990:481–548.

Citations in the text should be by arabic numerals in square brackets, e.g. [2, 5, 12], referring to a list numbered consecutively in the order they are first mentioned in the text.

7. Tables should be submitted on separate sheets. Numerical data given in graphs and tables must not be duplicated.

8. All figures, whether photographs, graphs or diagrams, should be numbered consecutively throughout and submitted on separate sheets. Plate layouts or single figures may either match the width of the column (8.6 cm) or of the entire page (17.8 cm), or be 11.8 cm in width with the legend at the side. The maximum height for a figure or plate is 23 cm, including the legend printed at its foot. Photographs can be grouped into plates. They must be mounted on regular bond paper, not on cardboard.

All photographs and electron micrographs should be supplied as high-contrast glossy prints trimmed at right angles. Inscriptions on illustrations should allow for reduction if this is necessary; figures and letters should have a final height of 2 mm after reproduction.

Colour illustrations will be accepted; however, the authors will be expected to make a contribution (approximately DM 350.00 per page) to the additional costs involved.

9. Typewritten mathematical equations should be clear, so that there is no opportunity for misinterpretation by the printer.

All letters contained in formulae as well as single letters in the text are automatically set in italics and therefore require no underlining. Hence, abbreviations that appear in formulae and are to be set in roman type (the type normally used for the text) should be specially marked.

All equations must be numbered sequentially in arabic numerals in parentheses on the right-hand side of the page.

10. One (1) complimentary copy is supplied. Offprints are available at cost price, provided the order form is returned together with the corrected page proofs.



Springer

In Between Lakes

Lakes are often beautiful and set amongst wonderful scenery. The air is fresh, there may be a vanishing morning mist and soon the sun will arrive and reflect from the calm waters. The whole scene suggests peace and tranquility, and invites reflection. I wonder how many sonnets and lyrics have been written at the shores of lakes, and how many new enterprises visualised when in the presence of these monuments to beauty.

When we are a little older we are particularly drawn to lakes. And we start to think. We know we have achieved a lot, we know that there is a huge amount still to be done, we feel that time is short and we still wish to make an impact. Somehow our position is no longer seen as prevalent, despite having been prominent and visible in our field of expertise for many, many years. So, what to do?

Someone once reported from a diplomatic dinner that, in response to an enquiry as to the origin of the many medals which resplendently adorned the prominent chest of his neighbour, came the clear and precise answer: "When one attends many dinners, the medals will arrive." And his advice was never to reduce the opportunities for further dinners.

The calm waters of the lake were whispering the solution to the question of what to do. As the distinguished guest was intimating: in case of doubt, create something and ensure you determine the menu. To become a little more transparent: create a new society. Oh, what genius thought – *de novo* prominent, *de novo* in the driving seat, able to vent all my frustrations: none of this nonsense of „et pluribus unum“ but rather to take charge in shaping a new future. Ah, what pleasures lie ahead: to ring all my friends, to explain what dire consequences will ensue if a new society is not born immediately, to canvass for support and developments, to bypass established bureaucracies whilst creating a new one, lots of food for thought and momentum. But at what price? Sorry, must go, time is over and I must agitate.

During a recent stay in Canada, one of our joys was to attend the Royal Canadian Institute public science lectures on Sunday afternoons in the biting Toronto winter. The lectures could be on anything from neuroimaging of the dopamine system by a world leader in the field to how a certain type of Canadian frog can be frozen to -70°C then unfrozen without any side effects – by increasing the glucose level in its blood to very high levels, allowing unfreezing to occur in a controlled manner, in case you ask. How did they know there were no side-effects? By carrying out the freezing and unfreezing experiment with a pair of copulating frogs!

I often think that the nineteenth century must have been a glorious time to be involved in medical science. The establishment of institutions such as the Royal Institution, the Academie Francaise, the Royal Canadian Institute and others served not only to inform the general public on scientific advances but also to create environments where, if you were a physician, you could hear about the latest advances in biology, pharmacology, chemistry, engineering or physics. There was extensive cross-fertilisation of ideas, concepts and solutions that resulted in an explosion in science and medicine that laid the foundations of modern society.

However, early in the twenty-first century I think we have forgotten the lessons of our nineteenth century forebears; as the volume of information has expanded, we have become more and more specialised and less and less knowledgeable about anything outside our narrow area of expertise. All of us argue that it is difficult enough keeping up with the literature in our own specialty and that we cannot find the time to read outside our narrow interests. The advent of search engines and computerised journals has accelerated this trend. It is all too easy to sit at a keyboard and type a few keywords into a search engine. Increasingly, we go to meetings populated only by those directly involved in our area of research who share not only our knowledge base but also all our scientific prejudices and background. Compounding this is the plethora of new societies being formed that cater for smaller and smaller specialised groups. Where will this all end? We will rapidly end up with every small group on its own scientific desert island where eventually communication between islands stops and each develops in its own way. The nineteenth century scientists showed us the power of cross-fertilisation of ideas, but we risk falling into the anarchy that William Golding famously described in his novel *Lord of the Flies*. Are we so far away from that scenario in science?

The great scientists are those who are able to recognise synergies in seemingly different problems and so identify solutions that are not apparent to the person who approaches every problem from within. This is why we must discourage the formation of endless splinter groups, multiple micro-societies and mini-journals and encourage wide representation in larger bodies such as the EANM and EJNM. It is essential that institutions such as the EANM and EJNM continue with their efforts to embrace this broad church before we descend into factional rivalry and endless self-serving splinter groups.

ANON

Eur J Nucl Med (2002) 29:287

Vol. 29, No. 3, March 2002 – © Springer-Verlag 2002

PET-CT image co-registration in the thorax: influence of respiration

Gerhard W. Goerres, Ehab Kamel, Thai-Nia H. Heidelberg, Michael R. Schwitter, Cyrill Burger, Gustav K. von Schulthess

Division of Nuclear Medicine, Department of Radiology, University Hospital Zurich, Raemistrasse 100, 8091 Zurich, Switzerland

Received 1 September and in revised form 26 October 2001 / Published online: 9 January 2002
© Springer-Verlag 2002

Abstract. Because anatomical information on fluorine-18 fluorodeoxyglucose (FDG) whole-body positron emission tomography (PET) images is limited, combination with structural imaging is often important. In principle, software co-registration of PET and computed tomography (CT) data or dual-modality imaging using a combined PET-CT camera has an important role to play, since "hardware-co-registered" images are thereby made available. A major unanswered question is under which breathing protocol the respiration level in the CT images of a patient will best match the PET images, which represent summed images over many breathing cycles. To address this issue, 28 tumour patients undergoing routine FDG PET examinations were included in this study. In ten patients, PET and CT were performed using a new combined high-performance in-line PET-CT camera without the need for repositioning of the patient, while in 18 patients imaging was performed on separate scanners located close to each other. CT was performed at four respiration levels: free breathing (FB), maximal inspiration (MaxInsp), maximal expiration (MaxExp) and normal expiration (NormExp). The following distances were measured: (a) between a reference point taken to be the anterior superior edge of intervertebral disc space T10–11 and the apex of the lung, (b) from the apex of the lung to the top of the diaphragm, (c) from the apex of the lung to the costo-diaphragmatic recess and (d) from the reference point to the lateral thoracic wall. Differences between CT and corresponding PET images in respect of these distances were compared. In addition, for each of 15 lung tumours in 12 patients, changes in tumour position between PET and CT using the same protocol were measured. CT during NormExp showed the best fit with PET, followed by CT during FB. The mean

differences in movement of the diaphragmatic dome on CT during NormExp, FB, MaxInsp and MaxExp, as compared with its level on PET scan, were, respectively, 0.4 mm (SD 11.7), –11.6 mm (13.3), –44.4 mm (25.5) and –9.5 mm (25.6). CT acquired in MaxExp and MaxInsp is not suitable for image co-registration owing to the poor match of images in MaxInsp and because of difficulties with patient performance in MaxExp. With reference to lung lesions, NormExp showed the best results, with a higher probability of a good match and a smaller range of measured values in comparison with FB. Image misregistration in combined PET-CT imaging can be minimized to dimensions comparable to the spatial resolution of modern PET scanners. For PET-CT image co-registration, the use of a normal expiration breath-hold protocol for CT acquisition is recommended, independent of whether combined PET-CT systems or stand-alone systems are used.

Keywords: PET-CT – Image fusion – Physiology – Respiration – Artefact

Eur J Nucl Med (2002) 29:351–360
DOI 10.1007/s00259-001-0710-4

Introduction

In modern oncology, diagnosis and staging of disease processes are based mainly on morphological cross-sectional imaging with computed tomography (CT) or magnetic resonance imaging (MRI). However, these modalities are neither as sensitive nor as specific as fluorine-18 fluorodeoxyglucose positron emission tomography (FDG PET) in identifying manifestations of many tumours or in defining their biological behaviour and response to therapy. Therefore, FDG PET has become an important imaging method. FDG accumulates in many different malignant tumours [1] and allows them to be identified with exquisite sensitivity. However, it shows few ana-

Gerhard W. Goerres (✉)
Division of Nuclear Medicine, Department of Radiology,
University Hospital Zurich, Raemistrasse 100, 8091 Zurich,
Switzerland
e-mail: gerhard.goerres@dmr.usz.ch
Tel.: +41-1-2552850, Fax: +41-1-2554414

Table 1. Respiration frequencies in healthy human subjects (adapted from Mead 1959)

Author	Year	No. of individuals	Age of individuals	Mean breaths/min (range)
Quetelet	1884	300	Birth	44 (23–70)
			15–20	20 (10–24)
			20–25	18.7 (14–24)
			25–30	16.0 (15–21)
			30–50	18.1 (11–23)
Hutchinson	1850	1,714	Adults	20.2 (6–31)
Handbook of Respiration	1958	5	Adults	11.7
Mead	1959	27	Adults	27

Frequency of respiration depends on many factors, such as age, body weight, and work load. There is a wide physiological range and each individual has its own normal respiration frequency dur-

ing rest. During the PET emission scan of 4 min and the PET transmission scan of 2 min, between 66 and 186 breathing cycles can be considered normal in healthy adult persons

tomical structures, thereby making it difficult to achieve precise lesion localization and, consequently, lesion specification and accurate staging. Hence, there has been increasing interest in combined imaging.

Recent developments in software for image co-registration and, particularly, advances in dual-modality imaging that provide “hardware” co-registration have led to the development of in-line PET-CT systems [2] that acquire morphological and functional information in the same examination. Software image co-registration is an established way of enhancing the interpretation of pathological findings in the brain. Fusion of anatomical and functional images of the thorax and abdomen is more difficult because body positioning is variable and motion artefacts due to respiration are poorly controlled. While hardware fusion can overcome the former problem, the latter affects both hardware and software fusion approaches. It is well known that there is a wide range of respiration frequencies in healthy individuals (Table 1) and that respiratory-induced thoracic movements strongly influence the quality of CT images [3,4]. The physiological range of movements of the thoracic cage and inner thoracic organs has been described previously, showing a difference between the left and right diaphragm as well as changes in chest circumference and vertical movements of the thoracic cage [5]. A large inter-individual range of these movements can be expected. Tumours and organs move widely during the breathing cycle, and the relative relationship between the tumour and surrounding normal structures may change [3,6,7,8,9]. In addition, the ability to breathe freely may be limited in patients with oncological disease. This not only may influence a patient’s capability to successfully undergo a PET or CT examination in the supine position but also may affect the co-registration of images.

To optimize fusion of PET and CT images, the respiratory levels of both types of examination should be adapted to a best fit. Since the acquisition of a PET scan takes several minutes per field of view (FOV), it is impossible for a patient to keep a defined breathing position during the scan. Respiratory gating of PET scanning

is possible in principle, but the time required in this already lengthy examination makes this approach clinically impractical. In contrast, patients can be asked to hold their breath during CT scanning, although defining the position of breath holding is less than perfect for most respiratory arrest positions.

The purpose of this study was to evaluate the optimum breath-holding position of patients during CT imaging, in terms of providing the best match with PET imaging of the thorax, by acquiring CT scans during different respiratory phases. This information should help to define standardized imaging protocols that optimize image co-registration in PET-CT imaging, particularly in integrated systems.

Materials and methods

Patients. The study group consisted of 28 patients (15 male, 13 female; mean age 56.4 years, range 34–81 years). All patients underwent a PET examination for oncological staging or restaging in a routine clinical setup. Eleven patients had bronchogenic cancer, four cancer of the head and neck, three melanoma, two cancer of the cervix, two breast cancer, three lymphoma and three colorectal carcinoma. The study was conducted according the guidelines of the institutional review board of the hospital, and written informed consent was obtained from each patient.

Patients were instructed to breathe normally during the PET scan and to perform four breathing manoeuvres during four sequential CT scans. During the first CT scan, patients breathed normally and freely (free breathing = FB). For the second, third and fourth CT scans, patients held their breath at levels of maximum inspiration (MaxInsp), maximum expiration (MaxExp) and normal expiration (NormExp), respectively. NormExp was defined as the respiratory level that was reached when the patient first inhaled and then exhaled without forcing expiration, and then held the breath in this position. Before PET and CT examinations started, these four levels of respiration were explained to and rehearsed with the patient.

Data acquisition. A first series of 18 patients were scanned on stand-alone PET and CT cameras (GEMS Advance Nxi and GEMS High Speed CT/i scanner, Milwaukee, Wis., USA) located approximately 10 m from each other in adjacent rooms, and a sec-

ond series of ten patients were evaluated on a new combined in-line PET-CT camera (GEMS Discovery LS, Milwaukee, USA). The PET camera has a 14.6-cm axial FOV and a transaxial resolution of 4.8 mm full-width at half-maximum at the centre. PET scans were obtained using an acquisition time of 4 min for the emission and 2 min for the transmission scan per cradle position, with a one-slice overlap at the borders of the FOV to avoid artefacts. Thus, an examination with six to seven cradle positions from the top of the head to the pelvic floor resulted in an acquisition time of roughly 45 min. All PET scans were acquired before the CT scans. This is not a system requirement. Patients fasted for at least 4 h prior to scanning, which started approximately 45 min after the injection of 330–430 MBq of FDG (mean 386 MBq).

Data acquisition with spiral CT was performed covering the same axial FOV of the body as with the FDG PET scan, with a 512×512 matrix size and a FOV of 50 cm. On the CT/i scanner, data acquisition was as follows: First, a scout view was obtained in the antero-posterior view using 120 kV, 10 mA and a maximal scan time of 13 s. During FB a whole-body CT scan was acquired from the top of the head to the pelvic floor, using 140 kV, 40 mA, a pitch of 1.7 and a 5-mm reconstruction interval to match the slice thickness of the PET scan. Furthermore, in each patient of the first series, CT scans of the thorax were acquired in the three different breathing positions described above using a pitch of 2.5, without changing the other low-dose radiation parameters, and covering a FOV from the shoulders to the upper abdomen. Scanning time was 17 s for each examination, MaxInsp, MaxExp and NormExp.

For the examination, the patients of the first series were positioned on a mattress containing plastic beads, which upon evacuation formed a body mould around the posterior and lateral aspects of the patients, but allowed normal respiration. The position of the patient was marked within the camera using a laser system, tape and pen lines. Immediately after the end of the PET scan, patients were moved within the mattress to the CT scanner, which was located in a room approximately 10 m away. Repositioning was performed using the tape landmarks and the laser system installed in the CT camera. Transfer of the patient and repositioning took between 5 and 10 min.

In the second series, the combined in-line PET-CT system permitted acquisition of perfectly matched data by simply moving the table position by 60 cm from the CT to the PET gantry. During system installation, the two gantries had been mechanically aligned using phantoms to ensure a "hardware" co-registration of images to within 2 mm in the three spatial directions. Further optimization down to a "hardware" co-registration match in phantoms of <1 mm was achieved by electronically adjusting the three spatial offset parameters. No further patient-specific software image co-registration was required to obtain the final matched data. PET scans in the combined system were acquired from the head to the pelvic floor using the same protocol as above, but CT scans were obtained with the PET table now also operating as a CT table. In contrast to the first series, the more powerful MDCT scanner used in the combined system made it possible to acquire a FOV of 867 mm in 22.5 s – a view from the head to the pelvic floor. Using 40 mA again, data were acquired with 140 kV and a pitch of approximately 6. After the CT scans, patients were asked how they could perform the breathing tasks, and were asked to rank them with respect to comfort.

Image reconstruction and co-registration. PET images were reconstructed using segmentation and a standard iterative algorithm (OSEM, two iterative steps). Images were reformatted into axial, coronal and sagittal views. Before co-registration of all images, CT data were resampled to the resolution of the PET scan, i.e. a matrix of 128×128 in the transaxial plane, although the original

CT images were available for viewing at all times. In the first series, co-registration of PET and CT images was done using in-house software (PMOD) [10] which allows the registration of two sets of images with a simple rigid transformation based on anatomical landmarks. Transformation between the two studies was interactively determined by the users, who practiced image processing in eight preliminary patients not taking part in the study.

In the second series, the combined PET-CT system directly provided co-registration as a result of the hardware configuration as described above. The acquired images were viewed with software providing multiplanar reformatted images of PET, CT and fused data with linked cursors (eNtegra GE Medical Systems, Haifa, Israel). Distance measurements in PET and CT images were performed using the PMOD software, as in the first series.

Measurement of respiratory and tumour movements. In all of the acquired PET and CT scans, displacement of the diaphragm and of the thoracic cage was measured (Fig. 1). In addition, movement of the 15 pulmonary lesions identified in the 28 patients was measured (these lesions were identified in 11 patients with bronchogenic carcinoma and one patient with advanced cancer of the head and neck).

As point of reference, the midline point at the upper anterior border of the intervertebral disc space between thoracic vertebrae 10 and 11 (T10–11) was chosen, which was easily identifiable on the CT scans of all patients. This choice was based on the assumption that the position of this point of reference in the vertebral column would be stable during the different parts of the scanning protocol in a supine patient. The reference point was always defined by the same experienced nuclear physician/radiologist and listed in a protocol to allow for an exact reference in aligned images. Because the intervertebral disc space T10–11 is not visible on PET scans, the reference point was matched from the FB CT onto the PET emission scan after alignment. The point was tagged with a cross visible in all three dimensions, and served as the reference for all comparisons between PET and CT in an individual patient. As measurements were performed on the non-attenuation-corrected PET images, in which the lung appears substantially darker than the surrounding tissues, the measuring points could be readily identified at the edge between the lung and the thoracic wall or diaphragm. Furthermore, the contrast level of images was defined and standardized to guarantee that both collaborators who measured the distances had equal image qualities and to reduce difficulties in identification of the border between the lung and adjacent structures on PET. The following distances were measured:

1. Point of reference to the upper border of the lung on the coronal section on which the reference point was visible (Fig. 1a and c).
2. Lung apex to the top of the diaphragm (Fig. 1b and d).
3. Lung apex to the posterior costo-diaphragmatic recess, on the sagittal view, showing the largest cranio-caudal extension of the lung (Fig. 1b and d).
4. Transverse distance from the point of reference to the lateral thoracic wall (Fig. 1a and c).

All measurements were performed independently by two collaborators, who practiced these measurements in eight preliminary patients before the study started. Displacements in relation to landmarks defined by normal mediastinal and hilar structures such as the carina and the xyphoid process were not measured because such structures could not be reliably identified on the FDG PET scans. Absolute distances were measured in PET and CT scans, and the differences in the distances between the CT measurement and the corresponding PET measurement were calculated.

Fig. 1a–d. Measurements. **a** In the first 18 patients distances were measured from the point of reference, i.e. the upper anterior border of the intervertebral disc space between thoracic vertebrae 10 and 11 in the midline, to the upper border of the lung visible in the same coronal view. From the reference point, additional measurements were performed to the lateral thoracic wall. **b** In the sagittal plane the image with the largest distance between the apex and the diaphragm was identified, and distances between the apex and the diaphragmatic dome and between the apex and the posterior costo-diaphragmatic recess were measured on the same slice. **c** The same measurements as in **a** are shown in a PET scan of another patient. The non-attenuation-corrected and filtered back-projected images were chosen for the measurements since the lung appears darker than in the attenuation-corrected images, thus improving edge detection between lung and thoracic wall. **d** The same measurements as in **b**. Due to difficulties in edge detection of organs in PET images, inter-observer agreement with respect to measured distances is worse than with CT. Identification of the posterior recess is more difficult than identification of the diaphragmatic dome. *Artefact due to paravascular injection of FDG



Based on the experience gained in the first 18 patients, only the difference in diaphragmatic positions (i.e. difference in distance between the apex and the diaphragmatic dome) was measured in the ten patients scanned on the new integrated PET-CT scanner, since during respiration the diaphragm has the largest range of movements.

Finally, as already mentioned, we analysed respiratory movements of lung lesions in 12 patients taking part in this study. Fifteen lung lesions were analysed in 11 patients with bronchogenic carcinoma and one patient with lung metastases of cancer of the head and neck. Of these tumours, four were located in the upper lobes, four in the lower lobes and seven near the hila, with two of them in the middle lobe. For each lesion, the distance to the reference point T10–11 was measured in the four CT scans and in the PET scan. The distance measured represents the length of the distance vector and thus the geometric mean of the three-dimensional movement of a lesion. Like the reference point, the point of measurement – in larger lesions an identifiable point within or at the border of the lesion – was defined by the nuclear physician/radiologist in charge of the study, and all measurements were done independently by the two trained collaborators.

Data analysis and statistical evaluation. For each of the measurements listed above, the difference between measured distances in PET and CT was used for statistical analysis using a paired, two-tailed *t* test to check for differences between the respiration levels. Furthermore, the percentage of good or bad matches between CT and PET was counted for each respiration level. Inter-observer agreement between the two collaborators was estimated by means of Bland-Altman plots [11]. By using this graphical approach the difference of two measurements against the mean of the same measurements is shown. This approach allowed visualisation of the extent to which the measurements differed from each other. Inter-observer agreement was evaluated for all PET and CT measurements of anatomical distances done on the separate PET and CT cameras and for the measurements of diaphragmatic movements on the new combined PET-CT system. Intra-observer agreement for PET and CT measurements was not assessed by the

Bland-Altman method, but repeated measurements performed by a single person were evaluated.

Results

Patient interview

All patients found that MaxExp was the least comfortable breathing position, and most of the patients were not able to maintain this position during the CT scan. Therefore, values as measured during MaxExp were not reliable.

Fig. 2a–d. Inter-observer agreement. **a** Bland-Altman plot showing the differences between all the measurements performed by two different collaborators in the CT images acquired on a stand-alone scanner. Mean -0.002 cm; SD 0.13 cm; mean+2SD = $+0.26$ cm; mean-2SD = -0.26 cm. 95% of all measurements are within a 3-mm range above/below the mean. **b** Bland-Altman plot showing the differences between all the measurements performed by two different collaborators in the PET images acquired on a stand-alone scanner. Mean $+0.01$ cm; SD 0.26 cm; mean+2SD = $+0.53$ cm; mean-2SD = -0.51 cm. 95% of all measurements are within a 5-mm range above/below the mean. This corresponds to the resolution of the PET scanner. **c** Bland-Altman plot showing the differences between two different collaborators with respect to the measured distance between the apex and the diaphragmatic dome (four different respiration levels) in the CT images acquired on a combined PET-CT scanner. Mean -0.01 cm; SD 0.07 cm; mean+2SD = $+0.13$ cm; mean-2SD = -0.15 cm. 95% of all measurements are within a 2-mm range above/below the mean. **d** Bland-Altman plot showing the differences between 2 different collaborators with respect to the measured distance between the apex and the diaphragmatic dome in the PET images acquired on a combined PET-CT scanner. Mean -0.09 cm; SD 0.23 cm; mean+2SD = $+0.37$ cm; mean-2SD = -0.55 cm. 95% of all measurements are within a 5-mm range above/below the mean.

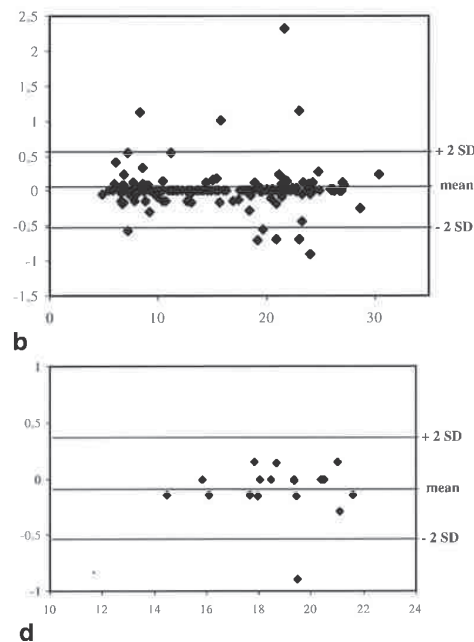
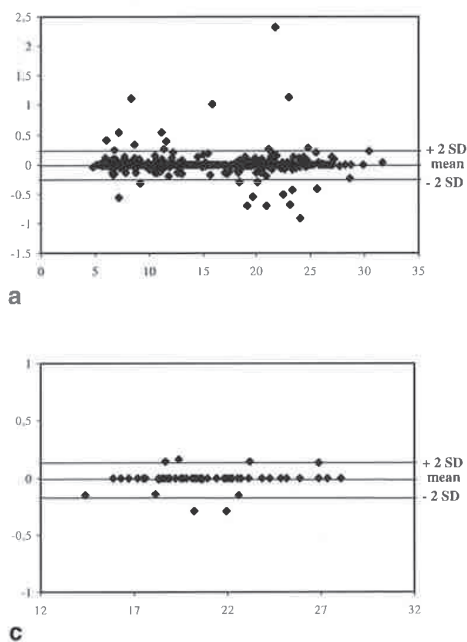
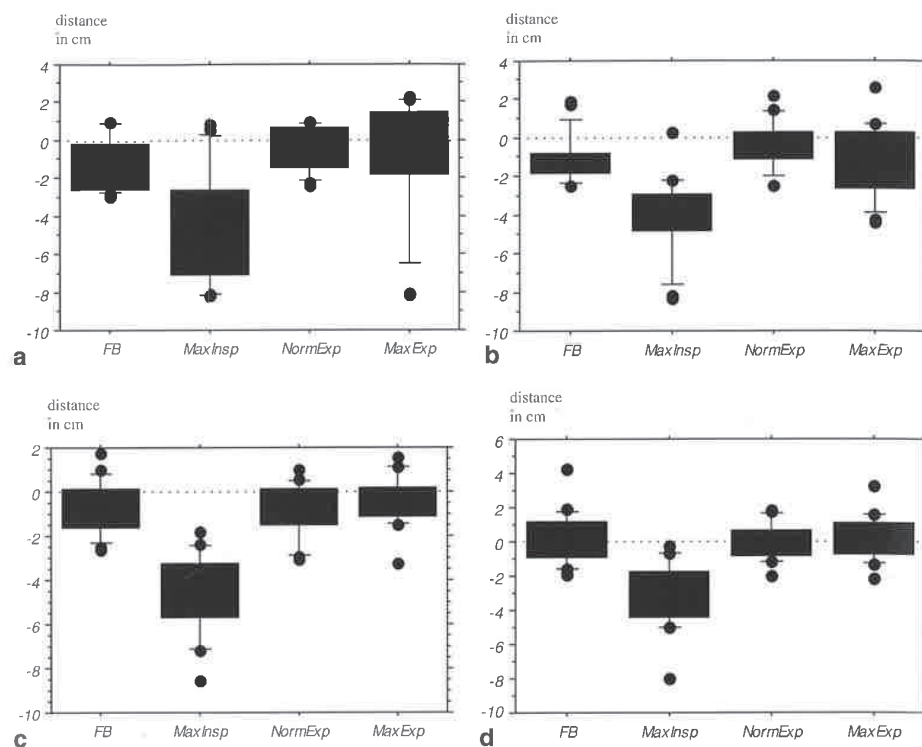


Fig. 3a–d. Movement of the diaphragm. **a, b** Distances between the apex of the lung and the right diaphragm (**a**) and the apex of the lung and the left diaphragm (**b**) measured on the combined PET-CT scanner (mean difference between CT and PET in cm). NormExp matches best for image co-registration. **c, d** Distances between the apex of the lung and the right diaphragm (**c**) and the apex of the lung and the left diaphragm (**d**) measured on the stand-alone PET and CT scanners (mean difference between CT and PET in cm). In these patients, NormExp seems to be slightly better than FB or MaxExp only on the left side, with a smaller range of values



MaxInsp was also felt to be difficult to perform. Most patients found that the NormExp level could be held without problems, but for some patients FB was more agreeable. One patient started to speak and one patient yawned during the FB CT scan. During NormExp, patients were more attentive and showed better compliance.

Reliability of measurements

Inter-observer agreement of the two collaborators in measuring distances in the four CT scans was better than the inter-observer variability of the measurements in the PET scan. In the first patient group scanned on the two separate PET and CT scanners, the measurements in PET by the two collaborators matched perfectly in 51.2% of cases. In CT, the agreement between the measurements was better: FB CT 74.6%, MaxInsp CT 74.9%, NormExp CT 70.5% and MaxExp CT 79.8%. In Fig. 2a and b, Bland-Altman plots of all PET and all CT measurements are shown. On the combined in-line PET-CT scanner, 20 measurements were done in ten patients. Two mismatches were found between the collaborators for each of FB CT, MaxInsp CT and MaxExp CT, while three mismatches were found for NormExp CT. Taking all the measurements together (80 distances), the mean difference between the collaborators was 1 mm (Fig. 2c). In contrast, an identical distance was measured in the PET images (20 distances) in only seven patients. The mean difference was 9 mm, with 95% of all measure-

ments lying within a 5-mm range above or below the mean (Fig. 2d).

Repeated measurements performed by a single person showed identical values in only 20% of measurements on PET, but in 80% of measurements on CT. If measurements within a 3-mm range in PET images were to be considered identical, then PET would have equalled the performance of CT.

Measurement of respiratory movements

In the first series of 18 patients, measurements between the reference point and the upper border of the lung visible in the same coronal section revealed small differences between the four respiration levels and between the left and right sides. Measured differences between PET and CT ranged between 6 and 20 mm. Differences between PET and CT were larger when measuring the distance between the diaphragmatic dome and the apex of the lung, reaching up to 57 mm on the left side and up to 41 mm on the right side for the four breathing tasks. The best or second best matches between PET and CT were found in 80.5% during NormExp and in 47.2% during FB for the left and right sides together. The worst matches were found during MaxInsp in 88.9% for the left and right sides together. Still larger differences between PET and CT were obtained when measuring the distance between the apex of the lung and the costo-diaphragmatic recess. Therefore, measurements of the dia-

Fig. 4a, b. Movement of the thoracic wall. Box plots illustrating the differences in measured distances between the reference point and the left (a) and right (b) thoracic wall (mean difference between CT and PET in cm). In the transverse plane the range of measured differences is in the order of several millimetres

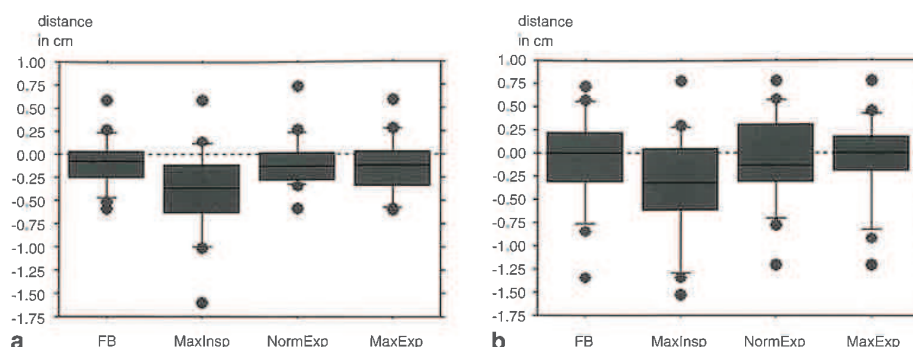


Table 2. Match of CT and PET for measurements between the apex and the diaphragmatic dome on the combined PET-CT camera^{a,b}

Respiration level	Best match (%)	2nd best match (%)	2nd worst match (%)	Worst match (%)
FB	27	13.5	59.5	0
NormExp	52.7	30.6	16.7	0
MaxInsp	5.3	7.9	5.3	81.5
MaxExp	16.2	35.1	24.3	24.4

^a If two measured distances were identical for two different respiration levels, they were both considered to be the second best or worst etc. If they were nearer to the worst match they were called the second worst; if they were nearer to the best match they were called the second best. For this reason, columns do not necessarily total 100%, though all columns together total 400%

^b Best match (given in % of measurements for the right and left thoracic sides together) was found with NormExp, i.e. the defined expiration level. Free shallow breathing (FB) had a higher range of measured values and showed worse fits with the PET scan than normal expiration. Maximal expiration was not performed correctly by most patients and, like maximal inspiration, is unsuitable for PET-CT image fusion

phragmatic dome provided more reliable information about diaphragmatic movements in this study. In patients scanned on the combined PET-CT scanner only this distance was evaluated.

In the second series of ten patients, best or second best matches between PET and CT were found with NormExp in 83.3% of all patients for the left and right sides together (Table 2), and with FB in 40.5% (Table 2). As in the first series, the worst match between PET and CT was found during MaxInsp (81.5% of all measurements) (Table 2, Fig. 3 and b). Mean differences in movement of the diaphragmatic dome on CT under the four registration levels, as compared with PET, are shown in Table 3, and statistical comparisons in Table 4. NormExp, MaxExp and FB CT images did sometimes fit the PET image, but the probability of a good fit increased when using NormExp for image co-registration and the range of measured values was smallest when us-

Table 3. Mean differences (and SD, range) in movement of the diaphragmatic dome on CT under the four different respiration levels, as compared with the level of the diaphragmatic dome on the PET scan

Respiration level	Mean	SD	Range
NormExp	0.4 mm	11.7 mm	-24.7 mm to 18.9 mm
FB	-11.6 mm	13.3 mm	-29.1 mm to 18.9 mm
MaxInsp	-44.4 mm	25.5 mm	-82.9 mm to 8.7 mm
MaxExp	-9.5 mm	25.6 mm	-81.4 mm to 26.2 mm

As values are in relation to the level of the diaphragmatic dome in the PET scan, they can be negative or positive

Table 4. Significance of the differences (paired two-tailed *t* test) in the movement of the diaphragmatic dome on CT under the four respiration levels

FB vs MaxInsp	S	<i>P</i> =0.0001 left and right
MaxInsp vs MaxExp	S	<i>P</i> =0.004 left, <i>P</i> =0.001 right
MaxInsp vs NormExp	S	<i>P</i> =0.001 left and right
FB vs MaxExp	NS	<i>P</i> =0.8 left, <i>P</i> =0.7 right
NormExp vs MaxExp	NS	<i>P</i> =0.1 left, <i>P</i> =0.6 right
FB vs NormExp	S/NS	<i>P</i> =0.009 left, <i>P</i> =0.1 right

No significant differences were revealed between NormExp or FB and MaxExp. This was mainly due to the bad performance of MaxExp caused by most patients inhaling during the CT scan. Box plots illustrating the mean values and the ranges measured for patients examined on the combined PET-CT scanner are shown in Fig. 3

ing NormExp (Fig. 3a and b, Table 3). This was less evident in the first series performed on two separate PET and CT scanners (Fig. 3c and d).

Measurements between the reference point and the left and right thoracic wall showed only small differences between the four respiration levels and a slight difference between the left and right side (Fig. 4, Tables 5 and 6). The range of measured values was within 1 cm for most respiration levels.

In 12 patients, 15 lesions within the lung were evaluated. The movements of lesions depended on their loca-

Table 5. Mean differences (and SD, range) between the distances from the reference point to the left and right thoracic wall measured on CT under the four different respiration levels, in relation to the distance measured in the PET scan

Respiration level	Mean	SD	Range
NormExp	-0.5 mm	3.1 mm	-5.9 mm to 7.4 mm
FB	-0.4 mm	2.9 mm	-5.9 mm to 5.9 mm
MaxInsp	-3.3 mm	4.5 mm	-16.1 mm to 5.9 mm
MaxExp	-0.7 mm	3.0 mm	-6.0 mm to 5.9 mm

Table 6. Significance of differences (two-tailed *t* test) in the measured distances from the reference point to the left and right thoracic wall on CT under the four respiration levels

FB vs MaxInsp	S	$P=0.0004$ left, $P=0.0001$ right
MaxInsp vs MaxExp	S	$P=0.0004$ left, $P=0.0004$ right
MaxInsp vs NormExp	S	$P=0.0007$ left, $P=0.0004$ right
FB vs MaxExp	NS	$P=0.8$ left, $P=0.2$ right
NormExp vs MaxExp	NS	$P=0.6$ left, $P=0.4$ right
FB vs NormExp	NS	$P=0.7$ left, $P=0.6$ right

Only MaxInsp showed significant differences compared with the other respiration levels. Box plots illustrating the mean values and the range measured for patients examined on the combined PET-CT scanner are shown in Fig. 4

Table 7. Match of PET-CT co-registered images in 15 lung lesions, for the four different respiration levels

Respiration level	Best and second best match (%)	Worst and second worst match (%)
NormExp	67	33
FB	47	53
MaxInsp	27	73
MaxExp	59	41

The best and second best match and the worst and second worst match are taken together and listed for the four different respiration levels. Measured distances in the MaxExp CT were not reliable since some patients could not perform this breathing task. Because the best and second best match and, respectively, the worst and second worst match are taken together, the added sum is 200% in each column

tion within the lung. Compared with lesions in the lower parts of the lung, lesions in the upper parts and near the hila tended to show a smaller range of movements. As in diaphragmatic movements, the worst matches between PET and CT measurements were found during MaxInsp (range between 5 mm and 33 mm; Table 7; Fig. 6). In contrast, best and second best matches were obtained during NormExp (range between 0 mm and 14 mm; Table 7). FB was not as good as NormExp, with a larger range of values, from 0 mm to 31 mm (Table 7).

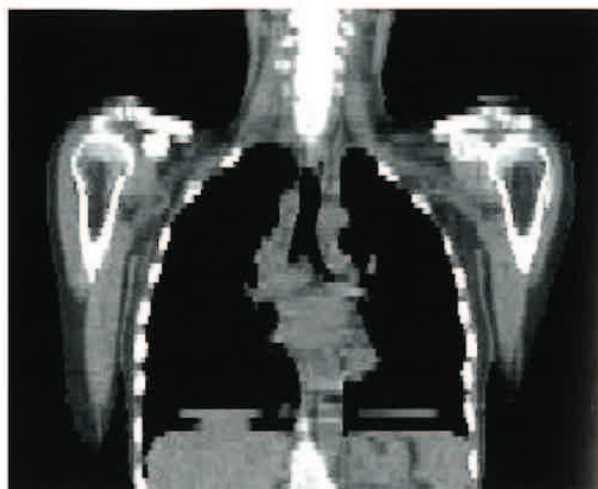


Fig. 5. A typical mushroom-shaped respiration-induced CT artefact. Such artefacts occur when CT of the thorax and abdomen catches the diaphragm at two different levels. Spiral CT scan should therefore be taken in one run over the whole examined body area

Discussion

With the introduction of combined PET-CT systems, co-registration of functional and morphological imaging studies is intrinsically available due to the hardware arrangement of the PET and CT systems. The only remaining potential co-registration errors in such systems are due to physiological motion, which in the chest is predominantly caused by breathing, except in the vicinity of the heart or with insufficient patient cooperation. Because a PET scan takes several minutes per FOV and a PET scan is an average image over many breathing cycles, the co-registration of PET images with CT images would require respiratory gating of the PET. This is not a promising approach owing to the substantial resulting increase in imaging time. In contrast, CT is fast and allows for more flexible imaging protocols; thus, optimization of co-registration has to focus on optimizing the CT data acquisition protocol.

The first important step in CT scanning is to acquire it in one continuous sweep over the whole area examined. This avoids imaging of the diaphragm at different positions, which can lead to blurred images and mushroom-shaped artefacts (Fig. 5) [12]. Continuous efforts have been made to compensate for motion artefacts on CT scans, e.g. by the use of ultra-short scanning times in electron beam CT, modified filtered back-projection algorithms and respiratory gating [13, 14]. Respiratory movements may cause artefacts in CT that can mimic disease and even lead to misdiagnoses [15]. With the advent of MDCT systems, the entire lung can be readily scanned while a patient holds his breath. In fact, the use of an MDCT in a combined PET-CT scanner permits scanning of the lungs with a slice thickness of 5 mm,

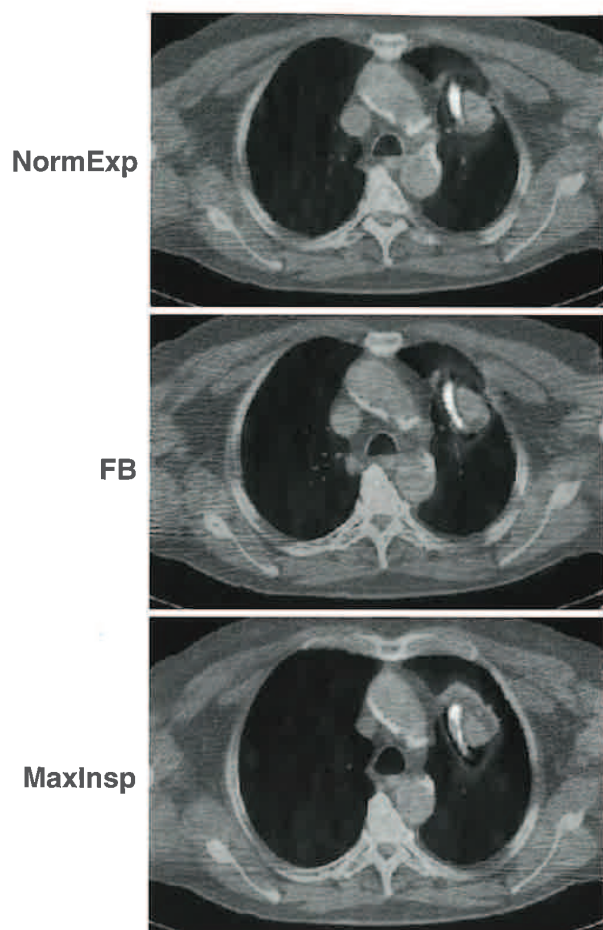


Fig. 6. PET-CT co-registration in a lung lesion. PET-CT co-registered images of a patient with bronchogenic cancer. The co-registration of the increased FDG uptake in PET to the anatomical lesion in CT differs only slightly in normal expiration (NormExp) and free breathing (FB). In maximal inspiration (MaxInsp), the tumour changes its position with a rotational component, and FDG activity appears to shift posteriorly.

which matches current PET scanner slice thickness, in less than 10 s. The only co-registration problem not addressed by a combined in-line PET-MDCT system is which respiratory level or manoeuvre during CT data acquisition will offer the best match between CT data and the “free breathing” PET data. Compensation for CT motion artefacts per se is not enough for successful co-registration of the data deriving from the two imaging systems. Movements of the thoracic wall and diaphragm, as well as within the thoracic cage, are quite different in magnitude in all three directions, thus leading to distortions and asymmetrical position changes. This is illustrated in Fig. 6, showing a PET-CT examination of a patient with non-small cell lung cancer. The co-registration of the increased FDG uptake in PET to the anatomical lesion in CT differs only slightly in NormExp and FB. In

MaxInsp, however, the PET lesion appears more posterior than the CT lesion, because the anterior parts of the lung move forward and upward during the CT image acquisition of MaxInsp. Also the shape of the tumour changes in the corresponding slice, because of the through-plane motion. Fifteen lesions were measured in 12 patients and a tendency towards larger relative movements in the lower parts of the lung was found. This is a preliminary finding and further studies in larger patient populations with pulmonary nodules will be needed to evaluate how the size of a lesion, its location within the lung and the complex three-dimensional movements during respiration influence the quality of co-registered PET and CT images and how the respiration protocol of the CT acquisition can be optimized.

With the spatial resolution of the best PET scanners in the range of 5 mm, the match between PET and CT imaging data has to be of that order to be qualitatively acceptable. Our data on the match of PET and CT imaging show that in all imaging protocols the differences are small enough to satisfy this condition. However, our data also show that it is rather difficult to adequately measure distances in PET scans, since it is not easy to identify edges of organs, even when using non-attenuation-corrected PET images and standardized contrast levelling. The relative difficulties in correctly measuring distances in PET images are reflected in the evaluation of inter-observer agreement, as shown in the Bland-Altman plots (Fig. 2). In the CT scans 95% of all measured differences between the two collaborators, corresponding to 2 standard deviations, were within 0.26 cm above and below the mean. In contrast, 95% of the PET measurements were within a range of 0.52 cm. Although the values measured in PET are much worse than the measurable differences on CT scans, they correspond to the spatial resolution of a PET image and, therefore, are considered to be qualitatively acceptable.

The movements near the diaphragm are clearly the largest, possibly reaching several centimetres, and are relatively unidirectional. Hence, the cranio-caudal mismatch of the diaphragmatic positions in PET and CT has to be minimized. CT acquisition using a NormExp protocol allows co-registration of such lesions with a mean fit of about 4 mm (SD 12 mm). Therefore, the use of normal expiration provides co-registration to dimensions comparable to the spatial resolution afforded by PET. The relatively large standard deviation suggests that there is substantial variability in patient behaviour. Frequently, a suboptimal image match of small lesions in the lung will not affect the diagnostic value of PET-CT, because the image interpreter will readily identify the lack of superposition as a misregistration artefact due to respiration. Small lesions in general, and particularly those located close to the pleura or the diaphragm, pose a potential problem. Small misregistrations may lead to placement of the lesion noted on PET onto a wrong anatomical structure on CT. In clinical practice, this poses a problem only if the lesion is located at the border of anatomical structures like the pleura. If a

lesion is located in the lung parenchyma on CT, even a misplacement of the PET lesion to the thoracic wall will not suggest pleural invasion. On the other hand, if a pleural lesion noted on CT abuts the chest wall, even a lesion on PET appearing separated from the pleural wall will not permit one to rule out chest wall invasion.

The data of this study further suggest that maximal inspiration and maximal expiration are unsuitable for the acquisition of high-quality fused PET-CT images in the chest. This is because, first, there is a large difference in the diaphragmatic positions on CT and PET images during maximal inspiration and, second, maximum inspiration and particularly maximal expiration are poorly tolerated by patients. Furthermore, a large mismatch of PET and CT images will not only cause anatomical misregistration but also prevent the use of the CT scan as an adequate attenuation map. It has been shown that the CT scan can be used to correct for the attenuation of photons within the patient [16]. Taking a mismatching CT scan for attenuation correction may lead to incorrect calculation of FDG activity in the PET image and eventually to misinterpretation of lesions adjacent to the diaphragm. This will have to be addressed in further studies.

While free breathing can be performed by all patients, we found that the defined expiration protocol in normal expiration provides a higher proportion of best-match imaging studies. This may be due to the higher variability of FB CT studies, leading to a respiration snapshot during the respiratory cycle. The reason why most patients were able to hold their breath at normal expiration without difficulties is the MDCT, which allows scanning of the entire patient from head to pelvic floor in slightly more than 20 s.

Whatever respiration protocol is used for CT acquisition, the patient should be informed about the beginning of the CT acquisition. However, during free breathing, we had two uncooperative patients (sighing/yawning and speaking) despite the fact that they had been told when the CT scan was starting. Because factors like deglutition, sniffing, sneezing, coughing, phonation or speech will decrease the quality of CT scans, it is important to keep the patient attentive during scanning. Using the normal expiration protocol, the patient inhales and then normally exhales before the CT scan is started, which may enhance attentiveness and cooperation.

Conclusion

Optimal co-registration is obtained with a normal expiration protocol independent of whether a stand-alone PET and CT system with patient motion restriction or an inline PET-CT system is used. The free breathing protocol is a second-best alternative. A perfect match between PET and CT is not possible, but the attainable quality of image co-registration is in the range of the resolution of the PET camera. Therefore, we recommend the Norm-Exp respiration level for clinical imaging.

Acknowledgements. The authors gratefully acknowledge the assistance of Dr. Thomas Hany, who helped with patient recruitment and guidance in image analysis, and Merrill Griff for his help in preparing this manuscript.

References

1. Smith TAD. FDG uptake, tumor characteristics and response to therapy: a review. *Nucl Med Commun* 1998; 19:97-105.
2. Beyer T, Townsend DW, Brun T, Kinahan PE, Charron M, Roddy R, Jerin J, Young J, Byars L, Nutt R. A combined PET/CT scanner for clinical oncology. *J Nucl Med* 2000; 41:1369-1379.
3. Ross CS, Hussey DH, Pennington EC, Stanford W, Doornbos JF. Analysis of movement of intrathoracic neoplasms using ultrafast computerized tomography. *Int J Radiat Oncol Biol Phys* 1990; 18:671-677.
4. Shimizu S, Shirato H, Kagei K, Nishioka T, Bo X, Dosaka-Akita H, Hashimoto S, Aoyama H, Tsuchiya K, Miyasaka K. Impact of respiratory movement on the computed tomographic images of small lung tumors in three dimensional (3D) radiotherapy. *Int J Radiat Oncol Biol Phys* 2000; 46:1127-1133.
5. Wade OL. Movements of the thoracic cage and diaphragm in respiration. *J Physiol* 1954; 124:193-212.
6. Ekberg L, Holmberg O, Wittgren L, Bjelkengren G, Landberg T. What margins should be added to the clinical target volume in radiotherapy treatment planning for lung cancer? *Radiother Oncol* 1998; 48:71-77.
7. Balter JM, Lam KL, McGinn CJ, Lawrence TS, Ten Haken RK. Improvement of CT-based treatment planning models of abdominal targets using static exhale imaging. *Int J Radiat Oncol Biol Phys* 1998; 41:939-943.
8. Davies SC, Hill AL, Holmes RB, Halliwell M, Jackson PC. Ultrasound quantitation of respiratory organ motion in the upper abdomen. *Br J Radiol* 1994; 67:1096-1102.
9. Kubo HD, Hill BC. Respiration gated radiotherapy treatment: a technical study. *Phys Med Biol* 1996; 41:83-91.
10. Mikolajczyk K, Szabatin M, Rudnicki P, Grodzki M, Burger C. A JAVA environment for medical image data analysis: initial application for brain PET quantitation. *Med Inform (Lond)* 1998; 23:207-214.
11. Martin JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 8:307-310.
12. Balter JM, Ten Haken RK, Lawrence TS, Lam KL, Robertson JM. Uncertainties in CT based radiation therapy treatment planning associated with patient breathing. *Int J Radiat Oncol Biol Phys* 1996; 36:167-174.
13. Ritchie CJ, Kim Y, Crawford CR, Godwin JD. CT motion artifact correction using pixel specific back-projection. *Proc IEEE Eng Med Biol Soc* 1992; 14:1782-1783.
14. Ritchie CJ, Hsieh J, Gard MF, Godwin JD. Predictive respiratory gating: a new method to reduce motion artifacts on CT scan. *Radiology* 1994; 190:847-852.
15. Traver RD, Conces DJ, Godwin JD. Motion artifacts on CT simulate bronchiectasis. *Am J Roentgenol* 1988; 151:1117-1119.
16. Kinahan PE, Townsend DW, Beyer T, Sashin D. Attenuation correction for a combined 3D PET/CT scanner. *Med Phys* 1998; 25:2046-2053.



Journals, Magazines, Newspapers

European journal of nuclear medicine and molecular imaging

AVAILABLE AS

Online

Physical



[View Online](#)



[Available Issues / Request a Copy](#)

[Citation](#)

Details

Physical Locations



Multiple items exist. Use [Available Issues / Request a Copy](#) to see what's on the shelf.

Middleton Shelving Facility

by request only

Q 7EU46461 (34-V-6)

This Location Has

v.29(2002)-v.31(2004)

v.32:no.1(2005)-v.32:no.3(2005)

v.32:no.5(2005)

v.32:no.7(2005)-v.32:no.12(2005)

v.33(2006)

Supplements

v.29:suppl.1(2002)-v.29:suppl.2(2002)

v.30:suppl.1(2003)-v.30:suppl.2(2003)

v.31:suppl.1(2004)-v.31:suppl.2(2004)

v.32:suppl.2(2005)

v.33:suppl.1(2006)-v.33:suppl.2(2006)

Publication Details**OTHER TITLE**

European journal of nuclear medicine

FORMAT

Journals, Magazines, Newspapers

LANGUAGE

English

CONTRIBUTORS[European Association of Nuclear Medicine](#)

PUBLICATION

Heidelberg, Germany : Springer-Verlag, c2001-

PUBLICATION DATES

Vol. 29, no. 1 (Jan. 2002)-

PHYSICAL DETAILS

volumes : illustrations ; 28 cm

ISSNS

1619-7089, 1619-7070

OCLC

ocm49348061, ocm51876601

PRECEDING TITLES

[European journal of nuclear medicine](#)

Notes

Title from cover.
Chemical abstracts
Index medicus v29n1, Jan. 2002-
MEDLINE v29n1, Jan. 2002-
PubMed v29n1, Jan. 2002-
Available also online.

Subjects

[Nuclear Medicine -- periodicals.](#)

Medical Subject Heading

[Radioisotopes -- therapeutic use -- periodicals.](#)

Medical Subject Heading

[Diagnostic Imaging -- periodicals.](#)

Medical Subject Heading

[Diagnostic Techniques, Radioisotope -- periodicals.](#)

Medical Subject Heading

Content Types

[periodicals](#)

Additional Information

Library Staff Details



The Library has...

Viewing the library holdings for: [European journal of nuclear medicine and molecular imaging](#)

Middleton Shelving Facility

NUMBER OF ITEMS
30 items

Details

LOCATION
by request only

CALL NUMBER
Q 7EU46461 (34-V-6)

COUNT
30 items

This Location Has

v.29(2002)-v.31(2004)

v.32:no.1(2005)-v.32:no.3(2005)

v.32:no.5(2005)

v.32:no.7(2005)-v.32:no.12(2005)

v.33(2006)

Supplements

v.29:suppl.1(2002)-v.29:suppl.2(2002)

v.30:suppl.1(2003)-v.30:suppl.2(2003)

<https://search.library.wisc.edu/catalog/999932262702121/holdings?from=locations>

1/3

Volkswagen Exhibit 1027, Page 33 of 41

v.31:suppl.1(2004)-v.31:suppl.2(2004)

v.32:suppl.2(2005)

v.33:suppl.1(2006)-v.33:suppl.2(2006)

Materials

✓ v. 33, suppl. 1-2 2006

Issue

✓ v. 33, no. 10-12 2006

Issue

✓ v. 33, no. 7-9 2006

Issue

✓ v. 33, no. 4-6 2006

Issue

✓ v. 33, no. 1-3 2006

Issue

✓ v. 32, suppl. 2 2005

Issue

✓ v. 32, no. 11-12 2005

Issue

✓ v. 32, no. 9-10 2005

Issue

✓ v. 32, no. 7-8 2005

Issue

✓ v. 32, no. 5 2005

Issue

✓ v. 32, no. 1-3 2005

Issue

✓ v. 31, suppl. 2 2004

Issue

✓ v. 31, no. 12 & suppl. 1 2004

Issue

✓ v. 31, no. 9-11 2004

Issue

 v. 31, no. 7-8 2004

Issue

 v. 31, no. 5-6 2004

Issue

 v. 31, no. 3-4 2004

Issue

 v. 31, no. 1-2 2004

Issue

 v. 30, suppl. 1-2 2003

Issue

 v. 30, no. 11-12 2003

Issue

 v. 30, no. 9-10 2003

Issue

 v. 30, no. 7-8 2003

Issue

 v. 30, no. 5-6 2003

Issue

 v. 30, no. 3-4 2003

Issue

 v. 30, no. 1-2 2003

Issue

 v. 29, suppl. 1-2 2002

Issue

 v. 29, no. 10-12 2002

Issue

 v. 29, no. 7-9 2002

Issue

 v. 29, no. 4-6 2002

Issue

 v. 29, no. 1-3 2002

Issue

Diagnostic Techniques, Radioisotope -- periodicals.
Medical Subject Heading

Content Types

periodicals

Additional Information

Library Staff Details

^

MARC Bibliographic Record

LEADER	01783cas a2200493 a 4500		
001	9957280323602122		
005	20150313114213.0		
008	020320c20029999gw mr p 0 0eng c		
010		\$a 2002252212	
016	7_	\$a101140988\$2DNLM	
022		\$a1619-7070\$y0340-6997	
030		\$aEJNMA6	
032		\$a10949\$bUSPS	
035		\$a(0CoLC)ocm49348061	
035		\$a5728032	

035		\$a(WU)5728032-uwmadisondb
035		\$a(EXLNZ-01UWI_NETWORK)999932262702121
040		\$aWAU\$beng\$cWAU\$dNLM\$dNSD\$dCAS
042		\$alcd
060	00	\$aW1\$bEU72DJ
210	10	\$aEur J Nucl Med Mol Imaging\$2dnlm
245	00	\$aEuropean journal of nuclear medicine and molecular imaging.
246	17	\$aEuropean journal of nuclear medicine
246	3_	\$aEuropean journal of nuclear medicine & molecular imaging
260		\$aHeidelberg, Germany :\$bSpringer-Verlag,\$cc2001-
300		\$avolumes :\$billustrations ;\$c28 cm
310		\$aMonthly
336		\$atext\$btxt\$2rdacontent
337		\$aunmediated\$bn\$2rdamedia
338		\$avolume\$bnc\$2rdacarrier
362	0_	\$aVol. 29, no. 1 (Jan. 2002)-
500		\$aTitle from cover.
510	0_	\$aChemical abstracts\$x0009-2258
510	1_	\$aIndex medicus\$x0019-3879\$bv29n1, Jan. 2002-
510	1_	\$aMEDLINE\$bv29n1, Jan. 2002-
510	1_	\$aPubMed\$bv29n1, Jan. 2002-

530		\$aAvailable also online.
550		\$aOfficial journal of the European Association of Nuclear Medicine (EANM).
650	12	\$aNuclear Medicine\$vperiodicals.
650	22	\$aRadioisotopes\$xtherapeutic use\$vperiodicals.
650	22	\$aDiagnostic Imaging\$vperiodicals.
650	22	\$aDiagnostic Techniques, Radioisotope\$vperiodicals.
710	2_	\$aEuropean Association of Nuclear Medicine.
780	00	\$tEuropean journal of nuclear medicine\$x0340-6997\$w(DLC)sn 82004503\$w(OCOLC)02502280
997		\$aMARCIVE
LEADER	02432nas--2200661-a-4500	
001	991021972777702122	
005	20250121180436.0	
006	m-----o--d-----	
007	cr-unu	
008	030318c20029999gw-mr-pso-----0---a0eng-c	
010		\$a 2008233049
016	7_	\$a013089518\$2Uk
022		\$a1619-7089
035		\$a(DE-599)ZDB1459062-1
035		\$a(OCOLC)51876601
035		\$a(CKB)111025029846004

035		\$a (CONSER)--2008233049
035		\$a (EXLCZ)99111025029846004
042		\$a pcc
050	00	\$a R895.A1
060	00	\$a W1 \$b EU72DJ
082	04	\$a 616.07575
130	0_	\$a European journal of nuclear medicine and molecular imaging (Online)
210		\$a EUR J NUCL MED MOL IMAGING
210		\$a EUROPEAN JOURNAL OF NUCLEAR MEDICINE & MOLECULAR IMAGING
210		\$a EUR. J. NUCL. MED. MOL. IMAGING
210		\$a EUR J NUCL MED MOL I
245	10	\$a European journal of nuclear medicine and molecular imaging.
246	13	\$a European journal of nuclear medicine
260		\$a Berlin : \$b Springer-Verlag
310		\$a Monthly
336		\$a text \$b txt \$2 rdaccontent
337		\$a computer \$b c \$2 rdamedia
338		\$a online resource \$b cr \$2 rdacarrier
362	1_	\$a Vol. 29, issue 1 (Jan. 2002)-
500		\$a Refereed/Peer-reviewed

525		\$aSupplements accompany some issues.
538		\$aMode of access: World Wide Web.
550		\$aOfficial journal of the European Association of Nuclear Medicine (EANM).
588	0_	\$aFirst issue; title from journal home page (SpringerLink, viewed Jan. 14, 2008).
588	1_	\$aVol. 46, issue 1 (Jan. 2018) (viewed Dec. 13, 2018).
650	_0	\$aNuclear medicine\$vPeriodicals.
650	_0	\$aDiagnostic imaging\$vPeriodicals.
650	12	\$aNuclear Medicine.
650	22	\$aDiagnostic Imaging.
650	22	\$aDiagnostic Techniques, Radioisotope.
650	22	\$aRadioisotopes\$xtherapeutic use.
650	_7	\$aNuclear Medicine.\$2ebps
650	_7	\$aMolecular Imaging.\$2ebps
650	_7	\$aDiagnostic imaging.\$2fast\$0(OCOLC)fst00892354
650	_7	\$aNuclear medicine.\$2fast\$0(OCOLC)fst01040348
655	_7	\$aPeriodicals.\$2fast\$0(OCOLC)fst01411641
655	_7	\$aPeriodicals.\$2lcgft
650	_7	\$aMedicina nuclear\$2thub
655	_7	\$aRevistes electròniques\$2thub
780	00	\$tEuropean Journal of Nuclear Medicine\$w(CKB)954925519624\$w(DLC)sn82004503\$x1432-

		105X
776	08	\$x1619-7070
710	2_	\$aEuropean Association of Nuclear Medicine,\$eissuing body.
906		\$aJOURNAL

MMS IDs**Document ID:** 999932262702121**Network Electronic IDs:** 9911030212602121**Network Physical IDs:** 999932262702121**mms_mad_ids:** 9957280323602122, 991021972777702122**mms_ec_ids:** 99925243318802134**mms_gb_ids:** 991006761691102123**mms_lc_ids:** 991016450659402125**mms_ml_ids:** 991012378487302124**mms_osh_ids:** 991004567788402126**mms_pl_ids:** 99901303943802127**mms_plt_ids:** 991013466417902128**mms_rf_ids:** 991013780026202129**mms_sf_ids:** 991014911017002130**mms_st_ids:** 991013503869602131**mms_sup_ids:** 99916320805902132**mms_ww_ids:** 991015504155402133