

CLINICAL PERSPECTIVES ON

Philips Astonish TF





Professor Norbert Avril (Guest Editor)
*Professor of Nuclear Medicine, Barts Cancer Institute,
Queen Mary University of London, West Smithfield
(QE II), London, UK*

INTRODUCTION

The Philips Astonish TF technology offers the advantages of time-of-flight (TOF) imaging, rapid list-mode TOF reconstruction, point-spread function correction, and 4D respiratory-gated PET images.

PET AND PET/CT

Positron emission tomography (PET) has become well established as an essential tool in molecular imaging, allowing the visualization of metabolically active cells and biological processes.^{1,2}

The wide use of PET in oncology has been a driver of technological improvements in detector design and architecture as well as in software applications, which have combined to substantially improve image quality.³ The first PET scanners operated in 2D, limiting potential system sensitivity by up to 80%. 3D PET imaging allows the detection of photon pairs along lines of response between planes, resulting in a significant increase in system sensitivity and image quality.⁴

The combination of PET with computed tomography (CT) was a major advance allowing the integration of high-quality anatomical imaging and functional molecular imaging. In oncology, PET/CT has become an established imaging technique for staging and restaging, and for monitoring responses, offering significant improvements over PET or CT alone in a wide range of malignancies.⁵ It has also proven valuable in radiation therapy planning for target-volume delineation and the planning of treatment strategies.⁶

Philips Astonish TF operates in 3D data acquisition mode and utilizes the recent innovations of TOF technology and 4D PET to further improve image resolution and to reduce potential image degradation resulting from patient or organ movement. The clinical evidence supporting these innovations is discussed below.

TOF TECHNOLOGY

TOF technology has addressed one of the important limitations of conventional PET imaging. The image reconstruction algorithm of conventional imaging assumes a uniform probability of an annihilation event being somewhere along the line of response. By measuring the difference between the arrival times of the individual photons of a generated photon pair, TOF technology allows the position of the annihilation event to be accurately located along the line of response.⁴

The advantage of 3D TOF PET over conventional 3D PET in lesion detection during whole-body oncological scans

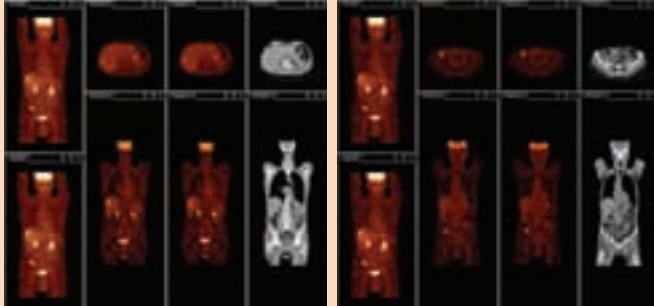
POSITRON EMISSION TOMOGRAPHY (PET)

PET makes use of the annihilation event that is a consequence of the collision of a positron released from a tracer molecule with a nearby electron. In oncology, the tracer is usually ¹⁸F-labeled 2-fluoro-D-glucose (FDG), which is taken up at a higher rate by cancer cells than normal cells, but which is subsequently only partly metabolized, leading to intracellular accumulation.³ As the tracer decays, releasing a positron, the pair of photons resulting from the subsequent annihilation event travel in approximately 180° opposite paths (the line of response) and are detected by the scanning device. Conventional PET was unable to localize the annihilation event along the line of response. Time-of-flight (TOF) PET does not have this limitation, and so has improved image quality, leading to increased diagnostic confidence.

CASE STUDY I

Enhanced identification of metastases using Astonish TF

A 75-year-old male patient had been diagnosed 3 months earlier with colorectal cancer, staged via contrast-enhanced CT as T3, N1. The primary tumor had been surgically removed approximately 1 month after diagnosis, but the patient had undergone no chemotherapy or radiotherapy. The patient was referred for further evaluation prior to continuing treatment. PET/CT was performed using PET/CT imaging with Astonish TF. The acquired images were analyzed using the standard TF-OSEM algorithm at 4 mm voxel size, and at higher resolution using 2 mm voxel reconstruction of the same whole-body raw-data set. The 2 mm and 4 mm voxel reconstructions are shown side by side in the figure.



Identification of colorectal cancer metastases using PET/CT imaging with Astonish TF. 2 mm (left) and 4 mm (right) voxel reconstructions are shown, identifying approximately 15 metastatic lesions present in the liver and an area of high ^{18}F -FDG uptake within the cecum.

The 2 mm voxel images represent an improvement in image resolution, quality, and contrast that was achieved with the enhanced performance of the Astonish TF technology.

Findings: Approximately 15 metastatic lesions were identified, which were present in all liver segments (shown in the left of the figure), and a focal area of highly increased FDG uptake within the cecum (on the right of the figure), corresponding to a soft-tissue abnormality not identified during the previous CT scans. There was no evidence of metastatic disease in other locations.

has been demonstrated in the clinical setting using a Philips GEMINI TF PET/CT scanner. A study was conducted that included 100 patients with body mass indices (BMIs) in the range of 16–45.⁷ In order for the presence and exact location of each lesion to be known, healthy subjects were included, to provide realistic patient anatomical backgrounds. Data were acquired for artificial lesions (10 mm plastic spheres containing 5–50 MBq/mL ^{18}F -FDG) in air at positions corresponding to the subjects' lungs or liver; representing low and high tracer-uptake backgrounds, respectively. These data were fused with whole-body scans taken 1 hour after injection of 555 MBq of ^{18}F -FDG, allowing for the production of a set of lesion-present or lesion-absent data. Reconstruction of images was achieved with and without TOF data using a basis-function list-mode iterative algorithm. A 3-minute scan time allowed for both 1-minute and 3-minute scan time reconstructions. The performance of TOF PET and non-TOF PET was evaluated using a numeric observer as a function of BMI, acquisition time, location of lesion, contrast, and reconstruction iteration number.

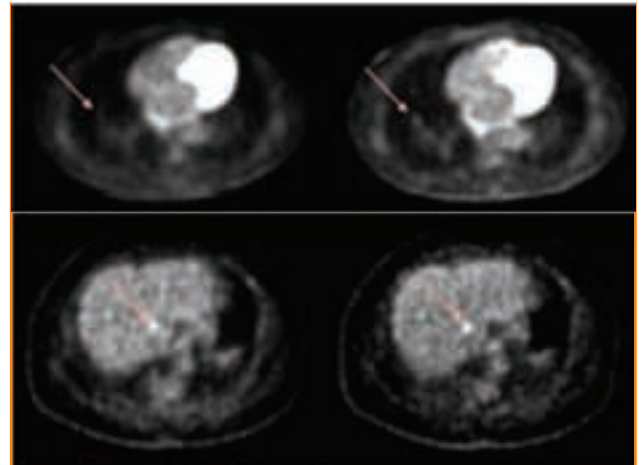


Figure 1. Comparison of non-TOF PET (left) and TOF PET (right) images in patients with normal and high BMI. Top: transverse section in patient with BMI = 19 at 3.5:1 contrast showing lung lesion (arrows). Bottom: transverse section in patient with BMI = 42 at 2:1 contrast showing liver lesion (arrows). (Reproduced from El Fakhri G, et al.⁷ © 2011 by the Society of Nuclear Medicine, Inc., with permission)

Compared with non-TOF imaging, TOF PET yielded a significant improvement in lesion detection with the highest gain in performance (20.3%) at the lowest lesion contrast (2.0:1), and the lowest gain in performance (7.5%) at the highest lesion contrast (5.7:1). From pooled lesion contrasts, TOF PET produced an improvement in lesion detection of 8.3% ($p < 0.01$) in the liver and 15.1% ($p < 0.01$) in the lungs. The advantage of TOF PET at low lesion contrast could be crucial in the identification of marginally detectable lung tumors (Figure 1).

Compared with non-TOF imaging, TOF PET gave a greater improvement in tumor detection in individuals with BMI > 30 (11.1%) than in those with BMI < 30 (9.8%). Furthermore, a greater improvement was seen for 1-minute scans than for 3-minute scans. The detection gains achieved by TOF PET offer the potential to reduce scanning time, thereby improving patient comfort and reducing movement artifacts, and to reduce the dose of injected tracer, decreasing radiation exposure for both patients and healthcare professionals.

A similar study evaluated the impact of TOF imaging on artificial lesion detection by human observers.⁸ The study demonstrated that although short scan times (1 minute) may be adequate in smaller patients, observer performance improves in more difficult clinical situations – such as the identification of low-uptake lesions – in both larger and smaller patients at longer scan times (3 minutes).

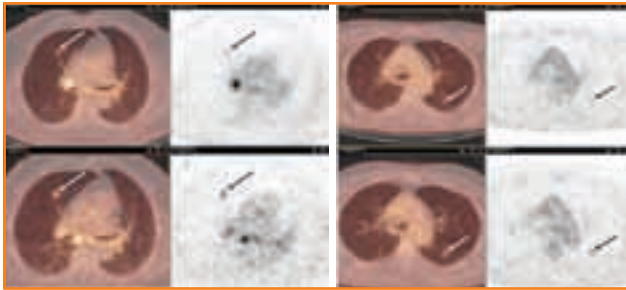


Figure 2. Comparison of ungated (top) and respiratory-gated (bottom) PET/CT images of small pulmonary lesions. (Source: Moinuddin A, et al.¹⁰)

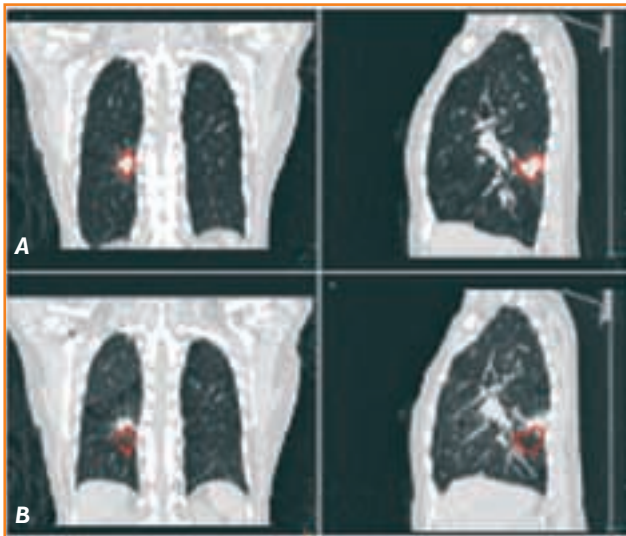


Figure 3. Respiratory-gated multiphasic CT images showing tumor movement during breathing. **A:** coronal (left) and sagittal (right) views at maximum inhalation. **B:** the same contours mapped to the maximum expiration phase reveal tumor movement. (Source: Klahr P, et al.¹¹)

A statistically significant difference in the area under the localized receiver operating characteristic (ALROC) curve for non-TOF PET and TOF PET was evident for many readers. In every case, the accuracy of reading TOF images was higher than that of reading non-TOF images. For imaging of larger individuals (BMI ≥ 26) and for both larger and smaller individuals with low-uptake lesions, a longer scan time combined with TOF PET was found to give the best results. For a given lesion type and organ site, TOF PET was able to demonstrate a similarly high performance, irrespective of the size of the scanned individuals.

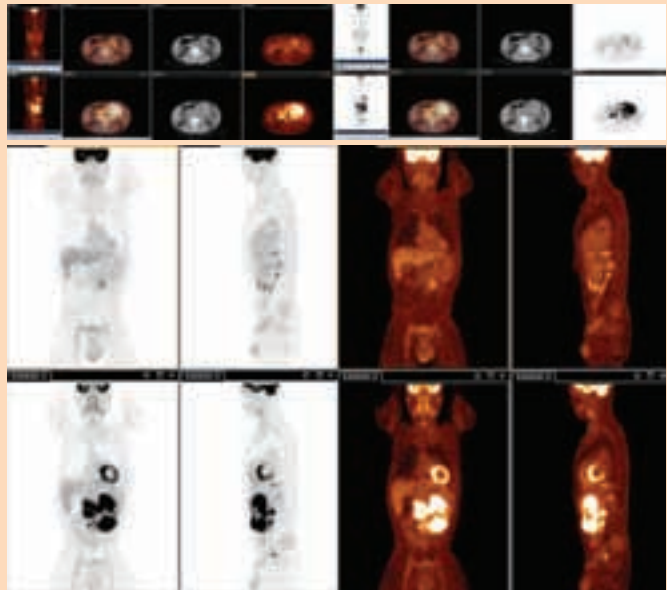
4D TOF PET

Cardiac and respiratory motion during data acquisition are an important source of image degradation during both PET and CT. This potential problem can have a negative impact not only on quantitative accuracy during diagnostic imaging, but also on the precision of target-volume delineation during oncological radiation therapy. Imaging of small or low-uptake lesions is particularly vulnerable to blurring into the background due to respiratory motion.⁹ By including

CASE STUDY 2

TOF PET/CT with a low-activity protocol to evaluate treatment response

A 50-year-old male patient had previously been diagnosed with follicular lymphoma. For staging and baseline measurements, PET/CT had been carried out using 320 MBq ¹⁸F-FDG with imaging 60 minutes after injection. The patient was prescribed 6 cycles of chemotherapy. After the second therapy cycle, an abdominal mass was still present, and the decision was made to perform an interim scan in order to assess treatment response using a low-activity protocol. The interim scan was performed with 185 MBq ¹⁸F-FDG using a 64-channel GEMINI PET/CT system and TOF reconstruction.¹⁸



Interim PET/CT scan of patient with follicular lymphoma acquired using a half-dose protocol demonstrating positive response to ongoing chemotherapy.

Findings: While there was residual metabolically active disease in mesenteric nodes, tracer uptake elsewhere had resolved. The overall response to chemotherapy was seen to be positive, justifying continuation of treatment.

the factor of timing, 4D PET is able to reduce motion artifacts and achieve further gains in image quality. Philips Astonish TF makes use of 4D TOF PET/CT technology to reduce motion artifacts, producing well-matched PET and CT images that correspond to a specific point in the respiratory cycle of a patient.⁹ There are two approaches to achieving this:

- **Prospective gating:** images are collected at a specific segment of the respiratory cycle of the patient
 - *benefits* include exposure to a low CT radiation dose, due to the single-phase acquisition, and fast clinical interpretation, due to the smaller data volume
 - *limitations* include the acquisition and interpretation of data in only one phase, and the inability to evaluate tumor motion.

IMAGING 2.0 AND PET/CT IMAGING WITH PHILIPS ASTONISH TF

The world of radiology is rapidly evolving. Radiologists and nuclear medicine physicians are under constant pressure to streamline workflows in order to increase productivity and minimize costs while at the same time improving patient satisfaction. Imaging 2.0 is a concept that integrates Philips equipment and software, producing a seamless imaging environment allowing specialists easy access to a multitude of imaging modalities and software applications, aiming to maximize both effectiveness and efficiency. Imaging 2.0 aims to:

- Enhance clinical collaboration and integration by creating hybrid modalities and medical networking tools that position radiology and nuclear medicine at the center of diagnosis and care
- Increase patient focus by developing patient-adaptive systems to provide excellent patient comfort during scanning procedures
- Improve economic value by providing reliable tools and flexible applications that increase uptime.

PET/CT imaging is an essential element of Imaging 2.0, combining high-quality anatomical imaging with functional molecular imaging. The Philips Astonish TF technology offers the advantages of time-of-flight (TOF) imaging, full-fidelity list-mode TOF reconstruction in seconds, point-spread function correction, and 4D respiratory-gated PET images. Astonish TF gives up to 30% better contrast resolution, compared with non-TOF technology, and with up to 5 times higher sensitivity than non-TOF scanners, radiologists and nuclear medicine physicians may be able to reduce radiopharmaceutical dosing in some or all of their studies.

- **Retrospective gating:** images are collected for the whole breathing cycle and are retrospectively assigned to a phase of the cycle
 - *benefits* include the acquisition of data for the whole breathing cycle, which increases flexibility to choose different phases, and the possibility to review breathing in cine mode
 - *limitations* include exposure to an increased radiation dose during CT, increased complexity of data interpretation, and long reconstruction times.

The flexibility of Astonish TF to use either approach has the potential to maximize the benefits of both to match specific clinical applications. There is a growing body of clinical evidence supporting the use of respiratory gating techniques in specific settings.

Increasing the accuracy of the standardized uptake value (SUV)¹⁰

In a study of 24 patients with pulmonary lesions (≥ 1 cm), whole-body PET/CT scans were compared with and without respiratory gating (Figure 2). The mean SUVmax was 2.9 before respiratory gating and 3.5 after – a 22.5% increase. Lesion size was not found to be significantly different (1.3 cm before and after gating).

Improving radiation therapy planning¹¹

Respiratory-gated multiphase CT data sets have been shown to enable visualization of tumor movement during breathing (Figure 3). This allows the identification of patients

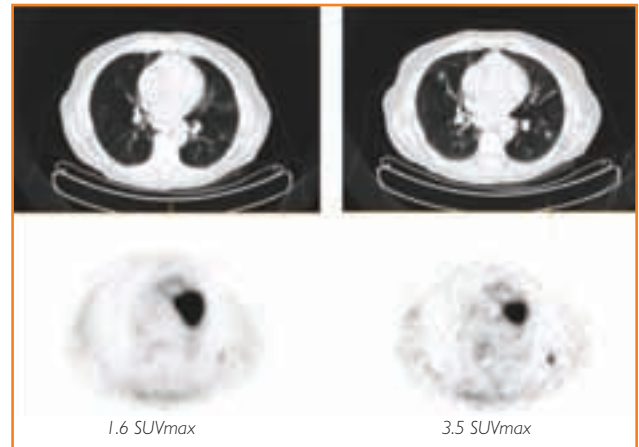


Figure 4. Comparison of TOF PET/CT images of small pulmonary nodule acquired without (left) and with (right) respiratory gating. (Source: Benard F, et al.¹²)

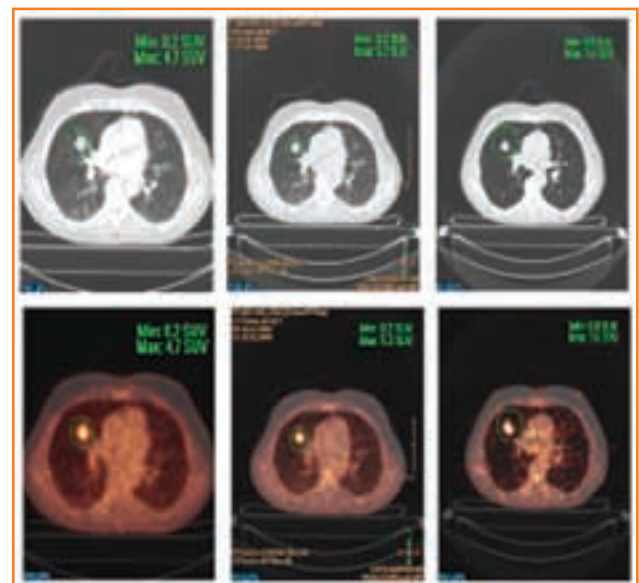


Figure 5. Reduction of motion artifacts using ultrafast PET acquisition and breath-hold techniques to image non-small-cell lung cancer lesion. **Left:** whole-body CT (top) and whole-body PET/CT (bottom). **Center:** 4D CT (top) and 4D PET/CT (bottom). **Right:** breath-hold CT (top) and breath-hold PET/CT (bottom). (Source: Czyborra-Brinkman J.¹³)

with minimal tumor movement, and facilitates planning to maximize the proportion of the target tumor receiving the prescribed radiation dose most of the time, while reducing radiation to surrounding healthy tissues.

Enhancing small-lesion detection¹²

In a series of 15 patients with small pulmonary nodules, TOF PET/CT images were acquired for the lesion of interest with and without retrospective respiratory gating (Figure 4). For small lesions located within the lung parenchyma, respiratory gating resulted in significantly reduced blurring, and increases in SUVmax of 23–123%.

Facilitating patient motion management¹³

A group of 17 patients with non-small-cell lung cancer underwent a PET/CT scan while breathing freely, followed by an ultrafast PET/CT scan holding their breath with deep

'The combination of advanced TOF technology with a newer PET/CT system has contributed to significant improvements in image quality, which helps us see small lesions in lymph nodes of overweight patients that may have been overlooked on non-TOF systems. We believe Astonish TF is the next evolution in TOF PET/CT imaging and we are excited to see how it can help us in our daily practice.'

Professor Wolfgang Weber, Nuclear Medicine Department, University Clinic Freiburg, Freiburg, Germany

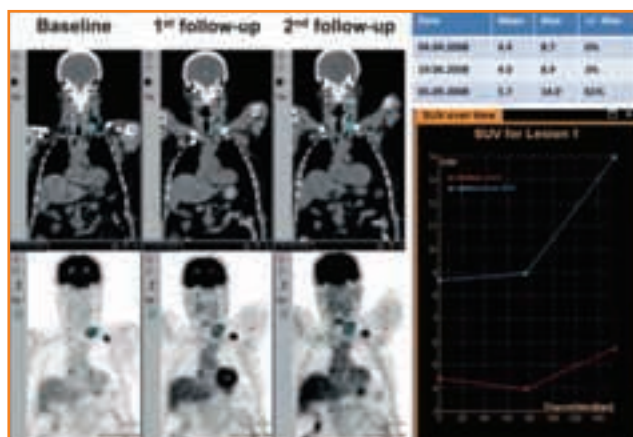


Figure 6. Computer-assisted semiquantitative analysis of 18F-FDG PET/CT showing automatic lesion tracking during a baseline scan and two follow-up scans. (Reproduced from Apostolova I, et al.¹⁷ © Schattauer 2011, with permission).

inspiration. A comparison was made between the free-breathing and breath-hold results. (Figure 5). All 43 tumors (1–4 cm size) were identified by both techniques. Compared with free-breathing measurements, the mean SUVmax was higher for breath-hold ultrafast PET/CT (11.5 vs 7.0 for pulmonary lesions; 8.8 vs 5.6 for mediastinal metastases).

SOFTWARE TOOLS FOR PATIENT MANAGEMENT

In the assessment of tumor response to therapy in cancer patients, the RECIST criteria (Response Evaluation Criteria In Solid Tumors) are widely used.^{14–16} Since RECIST involves the evaluation of the largest tumor diameter, the new imaging modalities are having a considerable impact in this setting. Although uniform criteria have yet to be developed, 18F-FDG PET/CT data are increasingly becoming accepted as a surrogate measure in the evaluation of treatment response, time to progression, and progression-free survival.¹⁷ A software tool has recently been developed and tested for the computer-assisted 3D semiquantitative analysis of 18F-FDG PET/CT, combining automatic lesion tracking and lesion segmentation in a baseline scan and up to two follow-up scans (Figure 6).¹⁷

When tested in 10 patients with a total of 18 tumors, the reliability of automatic analysis was demonstrated. Compared with manual analysis, computer-assisted SUV analysis was significantly less time-consuming (median 1.6 minutes vs 2.3 minutes per tumor; $p = 0.01$). Additionally, unlike manual analysis, in which the calculation of SUVmean is restricted to a single 2D region of interest, computer-assisted analysis allows for calculation of the total 3D glycolytic volume.

REFERENCES

- Plathow C, Weber WA. Tumor cell metabolism imaging. *J Nucl Med.* 2008;49 Suppl 2:43S-63S.
- Martinez A, Maniawski P, Suhy J, Kaus M. PET imaging in radiation oncology: clinical drivers, workflow and future applications. *Medicamundi.* 2010;54:67-75.
- Basu S, Kwee TC, Surti S, et al. Fundamentals of PET and PET/CT imaging. *Ann NY Acad Sci.* 2011;1228:1-18.
- Perkins AE. Astonish TF. A technical overview of Philips time-of-flight PET design and its clinical benefits. Available from: http://clinical.netforum.healthcare.philips.com/us_en/Explore/White-Papers/PetCT/Astonish-TF.
- Czernin J, Allen-Auerbach M, Schelbert HR. Improvements in cancer staging with PET/CT: literature-based evidence as of September 2006. *J Nucl Med.* 2007;48:78S-88S.
- Weber WA, Mix M. Target volume delineation with PET: two case studies. *Medicamundi.* 2010;54:76-7.
- El Fakhri G, Surti S, Trott CM, et al. Improvement in lesion detection with whole-body oncologic time-of-flight PET. *J Nucl Med.* 2011;52:347-53.
- Surti S, Scheuermann J, El Fakhri G, et al. Impact of time-of-flight PET on whole-body oncologic studies: a human observer lesion detection and localization study. *J Nucl Med.* 2011;52:712-9.
- Suhy J, Maniawski PJ. Routine clinical application of 4D time-of-flight PET/CT. Available from: http://clinical.netforum.healthcare.philips.com/us_en/Explore/White-Papers/PetCT/Routine-clinical-application-of-4D-Time-of-Flight-PET-CT.
- Moinuddin A, Tran I, Osman M. Impact of respiratory gating on the metabolic activity of pulmonary lesions in FDG PET/CT: initial experience. *J Nucl Med.* 2009;50 Suppl 2:1785.
- Klahr P, Subramanian P, Yanof JH. Respiratory-correlated multislice CT for radiation therapy planning: imaging and visualization methods. *Medicamundi.* 2005;49:34-7.
- Benard F, Turcotte E, Scheuermann J, et al. Respiratory synchronization to improve the detection of small pulmonary nodules on PET/CT. *J Nucl Med.* 2007;48 Suppl 2:123P.
- Czyborra-Brinkman J. Feasibility of a single breath hold PET/CT to avoid motion artefacts. *J Nucl Med.* 2009;50 Suppl 2:108.
- Therasse P, Arbuuck SG, Eisenhauer EA, et al. New guidelines to evaluate the response to treatment in solid tumors. European Organization for Research and Treatment of Cancer; National Cancer Institute of the United States; National Cancer Institute of Canada. *J Natl Cancer Inst.* 2000;92:205-16.
- Therasse P, Eisenhauer EA, Verweij J. RECIST revisited: a review of validation studies on tumour assessment. *Eur J Cancer.* 2006;42:1031-9.
- Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer.* 2009;45:228-47.
- Apostolova I, Renisch S, Opfer R, et al. FDG PET/CT in cancer therapy monitoring. Computer-assisted analysis of baseline together with up to two follow-ups. *Nuklearmedizin.* 2011;50:83-92.
- Wenzel F, Young S, Wilke F, et al. B-spline-based stereotactical normalization of brain FDG PET scans in suspected neurodegenerative disease: impact on voxel-based statistical single-subject analysis. *Neuroimage.* 2010;50:994-1003.

© 2011 Koninklijke Philips Electronics N.V.
All rights are reserved.

Philips Healthcare reserves the right to make changes in specifications and/or to discontinue any product at any time without notice or obligation and will not be liable for any consequences resulting from the use of this publication.

Printed in The Netherlands
4522 962 79661 * NOV 2011

